

The trouble with nevirapine

ANTHONY BRINK

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The cover photograph of a European nurse syringing nevirapine syrup down a newborn African baby's throat was supplied as a promotional image under open licence by Boehringer Ingelheim GmbH.

The author

Anthony Brink is an advocate of the High Court of South Africa, and the convener and national chairman of the Treatment Information Group (www.tig.org.za). He is also the author of *Debating AZT: Mbeki and the AIDS drug controversy* (2001) and *Lying and Thieving: The fraudulent scholarship of Ronald Suresh Roberts in 'Fit to Govern: The Native Intelligence of Thabo Mbeki with reference to chapters 8 and 9 on AIDS: 'A clash of fundamentalisms 1: medical politics' and 'A clash of fundamentalisms 2: racial politics' (2007). RUDE LETTERS, Introducing AZT: 'A world of antiretroviral experience' and Poisoning our Children: AZT in pregnancy* are in press. *'Just say yes, Mr President': Mbeki and AIDS*, in preparation, will be a comprehensive history of the AIDS treatment and causation controversies in South Africa, and a multi-disciplinary interrogation and deconstruction of their medical and ideological foundations. His work has been translated into Spanish, French, Russian, Italian, German, and Dutch.

To the memory of Peter Mokaba

‘He was our voice. Who will replace him?’
President Thabo Mbeki

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Foreword

The world seems to have fallen prey to the cult of the writer as pleaser, confirmer and feel-good man, fashionably sailing the winds of consensus reality, validating concepts that are familiar and ideas that don't offend. You know him by the adoring crowds he draws and the clever books he writes in measured, self-protective tones about nothing much, his prose de-weeded of all words and sentiment that grow against prediction – a very precisely measured height of grass blade. All else makes us panic and reach for our 'crazy' metaphors.

When blood flows into language, when feelings get to be real feelings, sulphuric and ungovernable, the tendency is to rush in to close the wound, an instinctive tourniquet against blood flow. You won't find any such complex decorum in this book. I read the manuscript of *The trouble with nevirapine* while researching the drug for an article I was writing for the March 2006 issue of *Harper's Magazine*, 'Out of Control: AIDS and the Corruption of Medical Science'. It struck me then, as it does now, as a truly radical form of investigative literature – no one else seemed to be within miles of it: the swirling indictment, the cascading shards of evidence, the crescendo of controlled rage, the moral phosphorescence.

Anthony Brink is a writer with that rarest quality: nerve. The nerve to stand alone, write alone, feel alone, be alone. To be battered, bereft, called crazy, but never to double-back and try to seem less crazy by betraying what he has seen, heard, knows, or suspects. To go into the heart and bones of the story, and then tell it relentlessly, fearlessly, uncompromisingly – sparing nothing and no one. To taste the blood inside the cheek and to keep going, keep writing, telling this astonishing tale of the madness that was, so that you, the reader, through his despair might learn what happened.

Most popular writers of redress, that is to say writers of the Left, broadly speaking, only pick up material that keeps their hands soft. The literature of real dissent is invariably met with fear and loathing by the guardians and gardeners of faux dissent. Against what are they dissenting? Things that are bad? That's not particularly necessary. It is things that are ostensibly good we need help with.

The front cover of this book affords a glimpse of the ghastly reality Brink describes beneath the lulling patina of the ostensibly good, and to see it is to gasp. When I first saw that image of the white nurse dosing the black infant with nevirapine, I presumed it was a send-up. It was not until recently that I realized it was actually a promotional photograph provided by the drug's manufacturer Boehringer Ingelheim.

To borrow a phrase from Martin Amis's *Koba the Dread: Laughter and the Twenty Million*, about the Western Left's justification of the crimes of Stalin, the AIDS Drug Wars in South Africa have been 'a typhoon of unreason'. For exposing nevirapine, and the other drugs they tout, the country's professional 'treatment activists' would have you believe that Brink is a 'madman', a 'lunatic' baying at the moon, and that like President Mbeki and Health Minister Dr Tshabalala-Msimang he is happy to stand by and watch millions of Africans die. But Brink nails his case to the wall with a thousand facts per square inch, building it with a lawyerly accumulation of citations from all sides – medical and scientific research literature, court documents, media reports, activist propaganda, street talk, and more – all salted with his own Greek chorus-style commentary, soaked in satirical acid.

In the winter of 2004, as I was writing my article for *Harper's*, a senior whistleblower named Jonathan Fishbein surfaced on the landscape, just suspended from the US National Institutes of Health for bringing to light the elaborate rot surrounding the Ugandan HIVNET 012 trial – nevirapine's launch-pad into the Developing World. One day I got an email out of the blue from Dr. Fishbein, attached to one to him from Brink. Following Fishbein's initial disclosures to Associated Press, Brink had recommended to him that as far as the media was concerned, he should talk to me and only me. In American football, this might have gone down at the time as a Hail Mary Pass in need of a prayer. But it worked. Fishbein agreed to speak with me. I set off to Washington soon after, and conducted the first of many interviews that led to the final story. For making that connection, and for the generous way he made it, I owe Brink an enormous debt of thanks. Every time I needed something – a scientific paper, a reference, a fact, a check,

a triple check – Brink was there with it in minutes, on the phone or by email. He seemed to have the capacity to be everywhere and to have read everything, all the while writing a truckload of other books, articles and open letters.

As I write this – a year after the publication of my *Harper's* article – *The New Yorker* has just appeared on the newsstands featuring a belated journalistic morning-after pill by Michael Specter, titled 'The AIDS Denialists' ('you people', he calls us). Written to 'deal with' the effect of my 'lengthy and irresponsible' article in defending what he considers 'denialism', his piece focuses its rue on South Africa, a country forever forced to serve as a Kabuki theater through which Western liberals assert their violet-scented pieties. It is a pillar of their faith that the government's resistance to embracing Western antiretroviral drugs is a kind of murderous self-inflicted medical apartheid.

Specter claims that HIVNET 012 'found that just a few doses of Nevirapine, an antiretroviral given to the mother at the beginning of labor, and then to the infant within the first three days of life, dramatically reduced the risk of passing on the virus. The regimen is cheap and easy to use, and is now in place throughout the developing world. In just a few years, it has saved the lives of hundreds of thousands of infants. But not in South Africa.' In fact, the South African government does supply nevirapine to mothers and babies – forced to do so by the Constitutional Court.

My article in *Harper's* used the story of nevirapine as a lens to lay bare the hidden machinery of the global AIDS industry – how the parts intersect, and how it produces its billowing 'truths'. It is a machinery that Specter found to be humming along swimmingly, saving 'hundreds of thousands' of African babies' lives. *The trouble with nevirapine* leaves it a vast pile of broken bolts and tubes, from which one can still hear the mechanical repetitions of the propaganda ministers echoing out over the junkyard.

—Celia Farber
New York City
March 12, 2007

Celia Farber has written for *Esquire*, *Rolling Stone*, *Harper's Magazine*, *Spin*, *Gear*, *Mothering*, *Salon*, *Red Flags*, *Alive*, and the *New York Press*, and is the author of *Serious Adverse Events: An Uncensored History of AIDS* (New York: Melville House, 2006). On 13 May 2008 the Semmelweis Society honoured her journalism with its 'Clean Hands Award'.

Preface

I could not stop something I knew was wrong and unnecessary. It was terrible. I had an awful sense of powerlessness.

Andrei Sakharov

On 15 December 2001 I'm cruising down the Cape Garden Route in verdant summer splendour, on my way to Cape Town. I'm trying serious crime on the Regional Court bench for a while, having quit the Bar in Pietermaritzburg a few months earlier, and it's the start of my court's year-end recess. I've got the coolest jazz swinging loudly through my sound system, double bass pumping through my new Infinity sub-woofers, and I'm looking forward to the Christmas break, feeling totally carefree. The only dampener on things is the news that the Treatment Action Campaign had won an order in the High Court the day before, compelling the government to provide nevirapine to HIV-positive women giving birth in public hospitals and to their newborn babies.

My cell phone rings. It's my friend Sam Mhlongo, Professor and Head of the Department of Primary Health Care and Family Medicine at Medical University of Southern Africa, recently home after thirty-five years of political exile in England. 'The party' wants my help in reversing the nevirapine disaster, he tells me. And I think to myself, I need this like a hole in the head.

It wasn't as if I hadn't already tried. When the TAC launched its application earlier in the year, I'd promptly contacted the government's attorney Gadija Behardien in the Pretoria State Attorney's office and cautioned her that unless the TAC's core, foundational claim about the efficacy of perinatally administered nevirapine was addressed and refuted the case would surely be lost, given the climate of public opinion and moral fervour that the TAC had whipped up – with Supreme Court of Appeal Judge Edwin Cameron pitching in to fan it. Getting his judicial colleagues all excited too. With how the little babies were going to die. Without the special strong medicine from overseas.

I'd informed the attorney that an exhaustive 130 000-word critique of the use of AZT and nevirapine in pregnancy – indeed,

of modern medicine's entire 'mother-to-child HIV transmission' bogey – had just been completed by a group of scientists, mostly based in Perth, Australia, and that this monograph, *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence* by Papadopoulos-Eleopoulos et al., would be available in print in a couple of weeks. She thanked me for the information and for volunteering to assist the government's lawyers draw the answering papers on the technical aspects – being an honorary co-author of the big paper just mentioned – but after that I'd heard no more.

In the event, Health Director General Dr Ayanda Ntsaluba put up the main answering affidavit, in which he agreed with the TAC that nevirapine was wonderful, but contended that it's not for the courts to determine health policy. A supporting affidavit by the Medicines Control Council's Jonathan Levin asserted that 'NVP would save 10 out of every 100 babies born to HIV-positive mothers' and 'HIVNET 012 provides conclusive evidence of the efficacy of NVP'. At which point I threw up my hands. It's really no wonder the case was lost.

I told Mhlongo that I'd commenced writing a brief review of the drug, *The trouble with nevirapine*, including an exposition for lay readers of the fatal shortcomings of HIVNET 012, the study on which the TAC's case had been based, and that I thought the data set out in it would be useful if brought to the attention of the appeal court. I'd been collecting and filing materials on nevirapine for a while but had avoided looking too closely at it, because researching and writing *Debating AZT: Mbeki and the AIDS drug controversy* had been hugely disruptive, both professionally and personally, and I'd really had enough of drugs. But as the TAC case went on, I found myself returning to my files and decided to write a brief article about nevirapine to be included as an appendix to my next book that I'd begun, *Just say yes, Mr President: Mbeki and AIDS*, a history and multi-tack analysis of the South African AIDS causation controversy, which had followed hotly after the treatment one. That was the original idea, but *The trouble with nevirapine* just took off like Jack's beanstalk.

In late February 2002 Mhlongo phoned again with a specific request regarding legal strategy that kept me busy for the next few

weeks. His call was followed by another in the beginning of April, this time from a senior ANC politician. He reiterated that the leadership of the party was very unhappy about the nevirapine debacle in the High Court, and said Peter Mokaba MP wanted to meet me for advice as to what might be done about it. I agreed to consult with him, but asked for a few more days to finish my nevirapine review, particularly the ‘mother to child’ part, which explained for non-experts why the drug was both unsafe and useless for administration to mothers and their babies.

On completing it a week later I emailed it to Mhlongo. The following day, on 9 April, he requested me to fly up to Johannesburg immediately to confer with Mokaba and discuss my proposals for heading off the dangers that I foresaw in the looming appeal. ‘Was he keen to meet?’ I asked Mhlongo, struck by his urgency. ‘He’s not keen,’ he answered, ‘he’s desperate.’

I’d first met Mokaba around 1990 when he came to the University of KwaZulu-Natal’s Pietermaritzburg campus to address a political rally in the Students’ Union. The SRC had hired me to handle the sound with my PA rig. His stage presence was electric, and the political spirit of the students that he channelled I remember still. We spoke outside afterwards and I liked him immediately. When we met again at Mhlongo’s house he’d been appointed ANC Election Officer and was close to the top of the party ranks. He was also completely on top of AIDS science and its basic holes, sharp to its ideological underpinnings, and vocal about both, so it was no surprise to me that he’d been deputed to try to sort the whole mess out.

At our meeting on 13 April I told Mokaba that just three weeks earlier, on 22 March, Boehringer Ingelheim had withdrawn its application to the US Food and Drug Administration for a licence to market nevirapine in the US for preventing mother to child transmission of HIV. The reason, according to official public statements at the time, was that most of the original medical case files were missing in HIVNET 012 – the Ugandan clinical trial on which the company was relying – and consequently couldn’t be audited by the FDA for the licence application (the real, much graver reasons would emerge in mid-December 2004).

Since the MCC had thereupon written to Health Minister Dr Tshabalala-Msimang – ‘We are to review nevirapine in the light of these developments and will inform you of the decision as soon as information is available’ – I suggested that she be encouraged to press the MCC to report to her about what action it had taken, because it seemed to me that in the circumstances a licence granted here but not in the US implied an indefensible double standard, one for the First World and one for the Third. I proposed that if the MCC failed to suspend its provisional licence for the supply of nevirapine to African women in labour and their newborn babies, it could be compelled to do so by way of a mandatory interdict.

Despite an enquiry by Dr Tshabalala-Msimang along the lines I’d suggested, the MCC appeared to be doing nothing as the appeal drew nearer, so I made a second proposal to Mhlongo: apply to the Constitutional Court for a hearing as a ‘friend of the court’ in order to bring the American developments to its attention, as well as the radical flaws in HIVNET 012 that had been identified by the Perth Group in their comprehensive ‘mother to child’ monograph. Mhlongo conveyed this to Mokaba, and again I was asked to fly up to Johannesburg to discuss the proposal with him. As before, we met at Mhlongo’s house and my suggestion was taken up.

But the discussion went way beyond legal stratagems. The political implications of what was taking place dominated our conversation. Zackie Achmat and his TAC were marching like the Nazi *Sturmabteilung* through the Weimar Republic, advancing and imposing a pernicious corporate, political and ideological agenda under the guise of national interest, opening up new offices countrywide with masses of foreign cash, disparaging the democratically elected leadership of our country as ignorant, callous, even murderous, and rapidly consolidating and expanding its political gains, just like the aforementioned – and not a word again was being publicly spoken, not a question was being asked about what was really going down. Instead, everyone was clapping; everyone adored them.

At the end of my meeting with Mokaba and Mhlongo, I began settling the application papers (pro bono) from a skeleton draft that I’d brought with me. I completed them well into the early hours,

and then, too confused by fatigue to navigate my way through Mhlongo's house to my room, fell asleep on the floor of his study.

Mhlongo's application was moved before the commencement of argument in the main appeal on 2 May, but Chief Justice Arthur Chaskalson ruled that despite his 'compelling argument' the court declined to hear him.

Although judgment was reserved after argument, it was obvious from the way the judges and the TAC's lawyers had been waxing in unison that the government's appeal was lost. The day after the third and final session of the appeal hearing, Mhlongo called to convey another request for advice. To cut a very involved and confidential story short, we went on to file a 100-point submission with the MCC, setting out why its continued registration of nevirapine for perinatal use was insupportable – including the knockout new fact that on 17 May the US Centers for Disease Control and Prevention (CDC) had pointedly omitted nevirapine from its latest revised guidelines for 'preventing mother to child transmission of HIV' in the US.

On returning from a Sunday night jazz performance at a restaurant on 9 June, I checked my email and was stunned to discover that Peter Mokaba was dead, having been in vibrant good health a couple of days earlier – so journalist Patrick Laurence told me, having just interviewed him for the Helen Suzman Foundation magazine *Focus*. He'd died at the worst possible time, a critical one, leaving no one to step into his shoes. We'd lost an immensely able leader. I was shattered.

The Constitutional Court dismissed the government's appeal on 4 July, forcing it to accept Boehringer Ingelheim's unwanted charity – in the form of free nevirapine for a while (a marketing stratagem) – and to make the drug available for administration to all women in labour and to their newborn babies as their human right.

To date, notwithstanding the widely publicised revelations in December 2004 of a top-ranking whistleblower in the US National Institutes of Health (NIH) concerning the shocking full extent of the corruption of HIVNET 012, the NIH's suppression of damning drug safety data in the trial, a disgraceful sham of an enquiry about the former by the Institutes of Medicine, and a criminal

investigation on the go about it, the MCC has yet to deregister or even suspend its registration of nevirapine for administration to mostly African women and their newborn babies – an extremely toxic drug, not licensed for administration to white mothers and their babies in any country of the First World accordingly.

Understandably afraid of being sued by the TAC, seeing that the latter passed a resolution on 5 August 2002 to go to court if nevirapine for perinatal use is deregistered, the MCC has sought to evade its basic statutory responsibility to protect the South African public from the pharmaceutical industry's marketing of useless and harmful chemicals by recommending, on 12 July 2004, that nevirapine in future always be combined with AZT – to avoid the development of 'resistance', it said. This is a frying-pan-into-the-fire horror you can read about in a forthcoming book of mine (already online), *Poisoning our Children: AZT in pregnancy*, a review of the latest research findings on the harm that AZT has been found to cause unborn and newly born babies.

On 7 October 2006, while in Europe on a speaking tour, I received crushing news of another fallen comrade: Sam Mhlongo had been killed in a car accident the evening before.

In November Professors Jerry Coovadia and Daya Moodley of the Nelson R Mandela Medical School at the University of KwaZulu-Natal won a High Court order overruling the MCC's rejection of their proposal to give nevirapine every day for six months to about 500 HIV-negative babies breastfed by their HIV-positive mothers. The MCC, they complained, was infringing their 'right to academic freedom of research' (giving toxic drugs to African babies is progressive these days, and after generally supporting apartheid judges are eager to look progressive).

The MCC appealed, but on 4 April 2007 Coovadia won another order for interim compliance, directing the Registrar of the MCC to immediately sign 'all necessary certificates and documents' to approve the trial ('Protocol HPTN046') and permit it to go ahead irrespective of the MCC's pending appeal.

What the judgment portends hits you full blast when you consider that nevirapine is so dangerously poisonous that on the advice of the FDA it was banned by the CDC on 5 January 2001 for even a couple of weeks use by American doctors and nurses

accidentally pricked by syringe needles. This followed reports of death, total liver failure requiring transplant, and other serious ill effects – among adults – after an average of just two weeks prophylactic treatment. It's accordingly not recommended for the short-term treatment of rape victims either. But to Coovadia and Moodley's minds it's good for babies, African babies. 'What more appropriate project can we do for the children of Africa? This is a study for Africa and for the poor,' Coovadia whined in the *Mail&Guardian* on 10 November. Actually it was for the rich like him: according to a University press release, he'd landed a foreign grant of R50 million to do the trial (in fact R47m). That Coovadia would be seriously injuring and killing many of the African children in his experiment on them never entered his dull head. As he was choosing his new Mercedes (he likes them). Nor did it occur to the incompetents running the MCC, who'd blocked the study on spurious grounds having nothing to do with the real issue: nevirapine's demonstrated life-threatening toxicity for babies, even with a single dose (we'll read), never mind six months of it. Not mentioning which obviously lost them the case.

An application for leave to appeal against the interim compliance order was thrown out on 3 July. The MCC's totally misdirected objection that the trial would lead to the infection of innocent babies predictably didn't wash. It was just being 'obstructive' in holding up vital HIV research, ruled Judge Willie Hartzenberg (of Wouter Basson case fame). Nevirapine had been registered and was safe, he said, so there could be no objection to the proposed trial.

With the benediction of the courts, the next chapter in this atrocity begins.

AB
Cape Town
30 June 2008

Part One

The writer has a place in his age. Each word has an echo. So does each silence. I hold Flaubert and Goncourt responsible for the repression that followed the Commune because they did not write a single line to prevent it. You may say: it was none of their business. But then, was the Calas trial Voltaire's business? Was the condemnation of Dreyfus Zola's business?

Jean-Paul Sartre

11-cyclopropyl-5,11-dihydro-4-methyl-6H-dipyrido [3,2-b:2',3'-e] [1,4] diazepin-6-one – nevirapine for short – was synthesized in the early nineties as a potential anti-HIV agent by the German pharmaceutical manufacturer Boehringer Ingelheim. It was a new sort of hi-tech drug, the first in its chemical class, described as a ‘non-nucleoside analogue reverse transcriptase inhibitor’ – the idea being that it would prevent ‘viral replication’ by binding ‘directly to the HIV RT enzyme’, thereby disrupting its ability to foster the formation of pro-viral HIV DNA. In simple terms, stop HIV.

Let's close our eyes and pretend just for now that reverse transcriptase has unambiguously been shown to exist as a distinct enzyme; that reverse transcription is unique to retroviruses and not also healthy human cells; that retroviruses exist outside textbooks, such as John Coffin's, and children's imaginations, as in the Superman cartoon movie *Cold Vengeance*: ‘a Roscoe's retrovirus ... 100% fatal’; that retroviruses can be malevolent and have sufficient genetic complexity for the execution of their nefarious intentions; and that HIV is one of them.

Sociology professor Steven Epstein tells us in *Impure Science: AIDS, Activism and the Politics of Knowledge* (University of California Press, 1996) that

The second generation of antiviral AIDS drugs – the non-nucleoside reverse transcriptase inhibitors that had looked so promising in vitro – performed poorly in clinical trials.

This news was ‘nothing short of shattering’ to guys such as Theo Smart of ACT UP New York, sister to our own Treatment Action Campaign – big expectations for it having been pumped up by the

manufacturer and its salesmen in gay AIDS activist organisations across the country.

Former professor of history Elinor Burkett picks up the trail in *The Gravest Show on Earth: America in the Age of AIDS* (Picador, 1995): A medical student at Harvard, Yung-Kang Chow, tooled around with the flop drug, mixing it with the older ones, AZT and its chemical cousin ddI. In February 1993 the test tube action he claimed to have seen was described in a twelve-page press release by Harvard Medical School as the next thing, a likely cure for AIDS. National Institute of Allergy and Infectious Diseases (NIAID) director Anthony Fauci announced on television news, just like an American: ‘You’re the virus. I’m the drug. I’m giving you two choices: either I kill you, or I make you mutate yourself out of existence.’ Reaction was euphoric. The *New York Times*, the television stations, and the rest of the mass media all fell for it. Never mind that Chow was light on proof.

The nevirapine combo idea got its next big boost from a splash in *Nature* later that month. A large-scale clinical trial called ACTG 241 was set up in the US over sixteen centres. But in the April issue of the *Journal of NIH Research*, Chow’s claims were forthrightly picked apart: ‘The experiments are technically flawed,’ the authors said, and went on to detail why – concluding: ‘It is surprising *Nature* published the paper.’ In an address before the plenary session of the 7th International AIDS Conference in Berlin in June, Chow conceded. His supervisor, top ‘AIDS expert’ Martin Hirsch, took another look at his original research. It was a mess, he announced: Chow had made a fundamental blunder vitiating his conclusions. *Nature* was sent a letter of retraction. The *New York Times* and all the newspapers that had written about nevirapine with such excitement in February and March now rained tomatoes on it. Along with *Nature*, which published a disavowal in August:

Chow et al. have sent a retraction of part of their work ... The authors admit that the discrepancies between their data and those of their critics ... invalidate[s] their claim to have proved that multidrug therapy will be effective by avoiding drug resistance.

Now you might imagine that a formal concession that the laboratory study was invalid would be cause to call the clinical trial off. After all, humans were being treated with a very poisonous chemical (we'll see below) for which there was no in vitro warrant, no good evidence of any efficacy in laboratory experiments. But among clinicians facing AZT's manifest failure as an AIDS drug, a lot of enthusiasm had been built up around the concept of trying out combinations of the new drug nevirapine and the older drugs. And widespread belief among experts in the approach meant he didn't see any need to abort the trial, Fauci explained.

On completion of the clinical trial, this is what the investigators reported:

(i) Combined with AZT and ddI in patients who'd taken antiretroviral drugs before, 'nevirapine produced a sustained improvement in CD4 count when compared with ZDV [AZT] plus ddI'. (It didn't seem to matter that CD4 cell counting as a surrogate marker for clinical health had already been discredited two years earlier in the biggest, best and longest AIDS drug trial yet conducted, the Concorde trial in England, Ireland and France.)

(ii) The CD4 cell count boost was most pronounced among patients who'd been on AIDS drugs previously, with cell counts of between 50 and 200 cells/mm³.

(iii) In the case of antiretroviral drug-naive patients (first-timers) with CD4 cell counts

between 200 and 600 cells/mm³, nevirapine plus ZDV and ddI resulted in a 140-cell absolute change from baseline at 52 weeks, compared with a 26-cell increase with ZDV/ddI, and a 2-cell decrease with ZDV/nevirapine.

Looking at the last figure, couldn't they see the futility of it all? You take AZT and nevirapine together and your cell count goes down by the end of the trial.

The trial also involved a 'sub-study' of a small number of patients that looked at the effect of the drugs on so-called 'viral load'. There seems little point in dwelling on these findings (or those reported in subsequent studies) given the manufacturer's qualification of the tentative results in its product information

advisory that ‘the clinical significance of changes in serum viral RNA measurements during treatment with VIRAMUNE has not been established’. Indeed, recently ‘established’ is that they have no ‘clinical significance’ at all. On 27 September 2006 Rodriguez et al. reported in their paper ‘Predictive value of plasma HIV RNA level on rate of CD4 T-cell decline in untreated HIV infection’ in *JAMA* 296(12):1498-506 that, as Jon Cohen summed up in the title of an article about it in *Science* 313(5795):1868, ‘Study says HIV blood levels don’t predict immune decline’. Or put more plainly, ‘viral load’ test results are rubbish. So let’s just move along.

On the strength of this junk (the CD4 data) Boehringer Ingelheim made a pitch for approval by the US FDA. Obviously nevirapine wouldn’t have made it out of the starting blocks in any ordinary drug evaluation process. But this was no ordinary procedure. It was a quickie.

On 21 June 1996, after a fast-track review that lasted just 119 days, nevirapine got its ticket. A qualified one, though. It was not to be used on its own. That’s because even on the worthless measure of efficacy used by AIDS doctors (CD4 cell counting) it was ineffective solo. Get that? It doesn’t work as an ‘anti-HIV’ drug on its own. Moreover, there was no evidence to show that the drug afforded any clinical benefits, which is to say, improved your health and made you feel better. In terms of the Accelerated Approval Regulations Boehringer Ingelheim was required to go home, do some more studies on humans, and come back to describe and verify the clinical benefit that it proposed the drug might have. Cool new system. For drug companies. These times being pro-business ones.

A press release on the same day stated that ‘studies also showed that the virus rapidly becomes resistant when nevirapine is used alone’. Quite how, no one has ever ventured to propose. Let alone suggest more frankly that on a plainer interpretation of the data, the drug is simply ineffective. It’s something like saying: We lost Vietnam because all those frigging gooks became resistant to napalm and saturation bombing and the systematic selective assassination of their intellectuals by our special operatives.

‘Therefore, nevirapine is only recommended for use in combination with at least one other antiretroviral agent’ in the

nucleoside analogue class: AZT, ddC, ddI and d4T. One that the patient hasn't taken before. To modulate the laboratory marker – CD4 cell counts – a bit better than AZT and similar drugs on their own. Not make the patient feel any better. The fact that CD4 cell counts rise for a while in reaction to exposure to metabolic poisons such as AZT even among HIV-negative people (*AIDS* 1996; 10:1444-1445), evidently passed the FDA by. As did the fact that AZT and nevirapine combined was no good, according to the cell-count data.

What's more, the effects of nevirapine on 'surrogate endpoints' were only noticeable among patients 'with HIV infection who have experienced clinical and/or immunological deterioration'. Not for HIV-positive people who were healthy, and whose lab test results were considered normal.

That nevirapine is extremely poisonous is admitted on the drug's label – advising discontinuation 'in patients who develop a severe rash or a rash accompanied by fever, blistering, oral lesions, conjunctivitis, swelling, muscle or joint aches, or general malaise'. And make no mistake, when the manufacturer talks of rash it isn't referring to a brush with stinging nettles; it means a generalised symptom of drug intoxication so severe in some cases that it shows up with thick layers of your skin dying off and peeling away in great chunks. An advertisement for the drug – featuring transatlantic sailor Mike Schmidt's endorsement of 'the dosing convenience of VIRAMUNE' (nevirapine): 'WHEN THINGS GOT ROUGH VIRAMUNE DIDN'T GET IN MY WAY' – explains:

Severe and life-threatening skin reactions have occurred in patients treated with VIRAMUNE, including Stevens-Johnson syndrome and toxic epidermal necrolysis. Fatal cases of toxic epidermal necrolysis have been reported.

The ad also warned of 'severe ... liver toxicity, including fatal cases', apart from the bother of 'fever, nausea, headache, and abnormal liver function tests'.

Stevens-Johnson Syndrome, medical textbooks explain, characteristically involves blistering ulcerations of the cornea, mouth, rectum, genitalia, skin, and urethra, usually accompanied

by a high fever and generalized weakness. Toxic epidermal necrolysis involves the entire skin and all mucous membranes literally sloughing off the victim's body.

The *Physicians' Desk Reference*, a compilation of full drug data that the FDA requires pharmaceutical manufacturers to provide for the information of prescribing doctors, warns in capital letters:

WARNING: SEVERE LIFE-THREATENING SKIN REACTIONS, INCLUDING FATAL CASES, HAVE OCCURRED IN PATIENTS TREATED WITH VIRAMUNE. THESE HAVE INCLUDED CASES OF STEVEN-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, AND HYPERSENSITIVITY REACTIONS CHARACTERIZED BY RASH, CONSTITUTIONAL FINDINGS, AND ORGAN DYSFUNCTION. PATIENTS DEVELOPING SIGNS OR SYMPTOMS OF SEVERE SKIN REACTIONS OR HYPERSENSITIVITY REACTIONS MUST DISCONTINUE VIRAMUNE AS SOON AS POSSIBLE. SEVERE AND LIFE-THREATENING HEPATOTOXICITY, INCLUDING FATAL HEPATIC NECROSIS, HAS OCCURRED IN PATIENTS TREATED WITH VIRAMUNE. RESISTANT VIRUS EMERGES RAPIDLY AND UNIFORMLY WHEN VIRAMUNE IS ADMINISTERED AS MONOTHERAPY, THEREFORE, VIRAMUNE SHOULD ALWAYS BE ADMINISTERED IN COMBINATION WITH ANTIRETROVIRAL AGENTS.

It stands to reason that a drug with this appalling toxicity profile – even worse than AZT – must have some clinical benefit shown; if not by the stage it was licensed, at least by the time it was offered to the public. *Au contraire*, as the ad spelt out, nevirapine is

indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection. This indication is based on analyses of changes in surrogate endpoints. At present, there are no results from controlled clinical trials evaluating the effect of VIRAMUNE in combination with other antiretroviral agents on the clinical progression of HIV-1

infection, such as the incidence of opportunistic infections or survival.

Can you credit this? That a drug so toxic without any proven health benefits should even be on the market? But this is the land of the free. And after AZT, anything.

A sucker for every new offering from the drug industry sponsoring it, Project Inform in the US jumped on it. It promptly released an

ACTION ALERT ... URGE CALIFORNIA STATE OFFICE OF AIDS TO APPROVE THE INCLUSION OF NEVIRAPINE INTO AIDS DRUG ASSISTANCE PROGRAM FORMULARY. ... Please urge the California Department of Health Services to move quickly to make this promising treatment available! Action Needed: Write or fax Kim Belshé, Director of the California Department of Health Services. Urge her to add Nevirapine to the California ADAP formulary immediately.

Project Inform went on: 'Nevirapine may be useful in preventing mother-to-child transmission of HIV.' About which, sailor Schmidt's ad had some interesting things to say in the 'Pregnancy and Nursing Mothers' section. For pregnancy, nevirapine is 'Category C' in view of the absence of 'adequate and well-controlled studies in pregnant women', so the drug 'should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus' – a risk indicated by studies on rodents, which found that 'a significant decrease in fetal body weight occurred at doses providing systemic exposure approximately 50% higher ... than that seen at the recommended human clinical dose'. As far as nursing mothers go, 'a single oral dose' given about six hours before delivery 'readily crosses the placenta and is found in breast milk' so 'mothers should discontinue nursing if they are receiving VIRAMUNE'. So as not to expose the baby to more than it got during delivery. Because it's so poisonous. We'll return to the use of nevirapine to prevent mother to child transmission of HIV in Part Four. You won't know whether to laugh or cry.

It is popularly believed by AIDS activists and their friends in journalism that at recommended doses nevirapine is safer and less

toxic than AZT. In fact, the contrary is the case. Boehringer Ingelheim's glossy 86-page *Viramune Product Monograph version 3.0* states: 'Nevirapine is generally very well tolerated.' After letting us know that people have died of its toxicities. And revealing that in one major study cited, 'The overall incidence of nevirapine related serious adverse events was 4.3% for patients who received combination therapy.' But in an analysis posted on aidsmyth.com, Fintan Dunne in Ireland draws our attention to different numbers in the company's 'Nevirapine data sheet' posted on the New Zealand Medicines Safety Authority website:

The major clinical toxicity of VIRAMUNE is rash ... occurring in 16% of patients in combination regimens in Phase II/III controlled studies. ... 35% of patients treated with VIRAMUNE experienced rash ... severe or life-threatening ... in 6.6% of [cases] ... Overall 7% of patients discontinued VIRAMUNE due to rash. Rashes are usually mild to moderate, maculopapular [*pimpley blemish*] erythematous [*inflamed, red*] cutaneous [*skin*] eruptions with/without pruritus [*itching*], on trunk, face and extremities. Severe and life-threatening skin reactions have occurred in patients treated with VIRAMUNE, including SJS and TEN (toxic epidermal necrolysis). Fatal cases of SJS, TEN and hypersensitivity reactions have been reported. ... Severe and life-threatening hepatotoxicity, including fatal fulminant hepatitis, has occurred.

Dunne rightly deplored the false description of nevirapine toxicity manifesting on the skin as rash, because it is 'not cutaneous' nor 'local' as the word suggests, but is 'systemically driven ... signalling a very serious illness'.

But Boehringer Ingelheim's claim to the New Zealand government that 'rash' occurs in 35% of cases isn't true either. It's an average figure from all the trials combined. Dunne points out that in the clinical trial coded B1-1046: 'In treatment-naive patients, the overall incidence of adverse side-effects is doubled. Serious gastrointestinal side-effects appear.' Concerning the latter he plausibly contends that these are the result of toxic tissue manifestations similar to external ones, quoting a pair of clinical experts defining SJS/TEN's 'definitive characteristics' as being

massive epidermal sloughing at the dermo-epidermal junction ... Gastrointestinal involvement may occur because of mucosal sloughing of the mouth, esophagus, stomach, and rectum [ranging in effect] from anorexia to development of a necrotic [*dead*] bowel.

And finally, Dunne points out the finding in B1 1046 that

Rash affects 50% of subjects – not 35%. Nevirapine and AZT used together produce side-effects at a rate that diverges strongly [upward] from the average of all trials.

A study by Verweel et al. investigating the use of nevirapine among children, reported in *AIDS* (17(11):1639-47) in July 2003, found that

A rash occurred in 20% of patients (15/74), and was severe ... requiring the cessation of treatment in four children (5%). In the other 11 children, the rash was managed with antihistamines ... 5 children experienced ... neutropenia

The ‘adverse events related or possibly related to nevirapine’ included vomiting, diarrhoea, fever, headache, dizziness, hallucinations, hair loss, abnormal nails, swollen liver, muscle pain, gall bladder sludge, elevated cholesterol and triglyceride levels associated with pancreatitis, abnormal liver function, and neutropenia, anaemia and leucopenia (these latter three conditions being manifestations of blood cell poisoning). The stuff they now give African babies.

An investigation of the ‘Incidence and risk factors for rash in Thai patients randomized to regimens with nevirapine, efavirenz or both drugs’, published on 28 January 2005 in *AIDS* (19(2):185-192) by Ananworanich et al., found that ‘The overall incidence of rash in our patient population was high’ – 21% among patients given 200 mg nevirapine twice daily, and 38% of those treated with single daily doses of 400 mg. 2.3% and 19.1% of these cases respectively were of grade III severity, meaning deadly serious. ‘Females and persons with earlier HIV disease or with a large rise in CD4+ cell count after starting therapy are at greater risk for NNRTI-related rash.’

And for pregnant women, the liver toxicity of nevirapine is exceptional, warned Boyle in the October 2003 issue of the *AIDS Reader*:

There is a significant risk of NVP-associated hepatotoxicity in pregnant women, especially those with high CD4+ cell counts ... the progression to severe hepatotoxicity may be explosive in nature and not predicted by the patient's liver enzyme level ... obtained before and during NVP therapy.

Boehringer Ingelheim responded to this liver toxicity finding by issuing a special alert in February the following year:

Women with CD4+ counts >250 cells/mm³, including pregnant women receiving chronic treatment for HIV infection, are at considerably higher risk (12 fold) of hepatotoxicity. Some of these events have been fatal ... The greatest risk of severe and potentially fatal hepatic events ... occurs in the first 6 weeks of Viramune treatment. However, the risk continues after this time and patients should be monitored closely for the first 18 weeks of treatment with Viramune ... In some cases hepatic injury progresses despite discontinuation of treatment.

With reports of serious, sometimes fatal liver toxicity continuing to pour in, the FDA issued a further warning on 19 January 2005, reported on the same day by Reuters under the headline 'U.S. Warns of Safety Risks of Boehringer AIDS Drug':

An important AIDS drug can cause sometimes deadly liver damage ... U.S. health officials warned on Wednesday. The Food and Drug Administration said doctors should weigh benefits and risks before prescribing the drug, Boehringer Ingelheim's Viramune, also known by the generic name nevirapine.

On 5 January 2001 the US Centers for Disease Control's *Morbidity and Mortality Weekly Report* published a report by MedWatch, a voluntary drug toxicity reporting system set up by the FDA, entitled 'Serious Adverse Events Attributed to Nevirapine Regimens for Postexposure Prophylaxis After HIV Exposures – Worldwide, 1997-2000', reporting severe toxicity after an average of just two weeks of treatment given to healthy

medical workers. The *New York Times* summed up on the same day:

Federal health officials advised doctors yesterday not to prescribe a standard H.I.V. prevention drug to healthy health care workers stuck by needles. The drug, nevirapine, can produce liver damage severe enough to require liver transplants, and has caused death in such use, the Centers for Disease Control and Prevention said in its weekly report. But nevirapine should still be used for two other groups, the CDC said. One is in treating people infected with H.I.V., the AIDS virus. The second is to prevent transmission of H.I.V. from mothers to their infants during childbirth. ... The agency said it and the federal Food and Drug Administration had identified 22 cases of severe liver, skin and muscle damage related to nevirapine taken after possible exposure to H.I.V. from March 1997 through September 2000.

Too poisonous for doctors, but great for the rest of us. Excluding rape victims: 'The agency does not recommend nevirapine to prevent H.I.V. infection among people recently exposed to the virus through unsafe sex, [the CDC's Dr Julie] Gerberding said.' But including pregnant women; that's because the 'benefit outweighs the risk, largely because the mother and child take only one pill,' said the CDC's Dr Helen Gayle: 'No serious adverse effects' had been noted in pregnancy studies. (Gayle was flat wrong about that, as we'll discover in Parts Four and Eight.) UNAIDS accordingly supported the CDC's recommendation that the drug be given to pregnant women, and was 'working with Boehringer Ingelheim to start programs in developing countries'. Just in case you never knew that when it comes to pharmaceutical drugs we're all one big happy family.

The speed with which nevirapine toxicity kicks in was confirmed in 2001 by the unfortunately named research team of Fagot et al., who reported in *AIDS* 15(14):1843-8:

Between May 1997 and November 1999, a diagnosis of SJS [*Stevens-Johnson Syndrome*] or TEN [*toxic epidermal necrolysis*] was established in 246 patients ... The reaction began 10-240 days after the introduction of nevirapine

(median, 12 days) ... In 10 patients the reaction occurred with the initial dosage. All but one patient received simultaneously a variety of other antiretroviral agents but ... nevirapine was the only drug significantly associated with ... SJS or TEN in HIV-infected persons ... Because of the severity of these reactions and the long elimination half-life of nevirapine, we suggest discontinuation of the drug as soon as any skin eruption occurs.

Local writer Adam Levin described his experience of nevirapine's severe, acute toxicity in his book *Aidsafari* (Zebra Press, 2005):

Today I begin my first course of nevirapine ... Within a couple of days, I feel quite awful. Nauseous and unable to eat, I lie withering on my bed for days. One night I wake up and need to pee. I stand up and the room begins to spin. I tumble flat on my face, smashing my head on a wooden cabinet. I try to get up, but I can't move. I am stuck and terrified. I yell for help. Shocked, Mom and Dad lift me onto my bed.

After Boehringer Ingelheim secured the US market by getting it past the FDA, the rest was a breeze. As it had been with AZT. The company turned next to the European Medicines Agency, claiming in its submission:

The pharmacology safety programme addressed among others, effects on central and autonomous nervous system, cardiovascular, and renal respiratory systems and did not reveal any severe side effects at relevant dose levels and/or concentrations.

These 'toxicokinetic data' were derived from studies on 'rats and dogs', on the basis of which the company proposed that 'there seemed to be acceptable safety margins' – despite the fact that clinical trials with humans as test subjects had already revealed a shocking toxicity picture. The *Safety* discussion reads like a statement from the Ministry of Truth in Orwell's *1984*. Suffice it to say that it was obvious even then that nevirapine was exceedingly poisonous. As revealed by its effect on the liver, and 'rashes' of such severity that some patients died. Both of which toxic

manifestations had been predictable from the reactions of test animals, discussed earlier in the dossier. But not to worry. Boehringer Ingelheim smoothed things over with this public-spirited precaution:

Therefore having reassessed the risk/benefit profile of nevirapine, the warnings concerning the occurrence of these events have been reinforced. In addition, new recommendations for the liver and cutaneous monitoring of patients ... have been introduced through an urgent procedure.

The EMEA provisionally approved nevirapine on 5 February 1998. On the advice of an expert panel, however, it recommended that it be categorised in its register of approved drugs for prescription ‘under exceptional circumstances’ only. Being a very dangerous drug. And the EMEA required a commitment from Boehringer Ingelheim to conduct further clinical studies, on the basis of which it would make a final risk/benefit evaluation.

The trouble is that new bits of fine print on the paper in the box didn’t make any difference. Inasmuch as poison is poison. Reports continued to flow in of people suffering serious skin and liver damage, some fatal. On 12 April 2000 the EMEA got nervous and issued an urgent ‘EMEA PUBLIC STATEMENT ON VIRAMUNE (nevirapine): SEVERE AND LIFE-THREATENING CUTANEOUS AND HEPATIC REACTIONS’, which it ‘thought ... necessary to provide ... to the public’. The ‘prescribing and patient information’ contained in the package insert was to be substantially revised and amplified further, essentially boiling down to: If you quickly get very sick like other people taking this stuff, with your liver packing in and your skin starting to rot then chat to your quack. Even think about ditching it.

In November 2000 the Americans caught up with the Europeans. The FDA published an ‘Important Drug Warning: Re: Severe, Life-threatening and fatal cases of hepatotoxicity with Viramune’, issued by Boehringer Ingelheim’s US subsidiary, Roxane Laboratories, that extended the monitoring period for liver damage from eight to twelve weeks, after a study found that it resulted in a third of patients having to quit taking the drug – as against the picture painted in Boehringer Ingelheim’s glossy *Viramune*

Product Monograph 3.0 dished out at the 13th International AIDS Conference in Durban a couple of months earlier:

Nevirapine related hepatitis was reported infrequently in clinical trials. The incidence ... was 1.0% ... in BI clinical trials (Pollard et al. 1998) ... In the four controlled trials of combination therapy ... treatment related hepatitis was observed in ... 1.1% ... The occurrence of hepatitis and other liver related events with double and triple therapy regimens including nevirapine from 13 recently completed and currently ongoing clinical trials has also been reported (Pollard et al. 1998). In these 13 studies, the overall incidence of hepatitis possibly related to nevirapine (0.5%) was similar to those in the earlier studies discussed above. ... Fatal cases of hepatitis have been reported.

But Patel et al., reporting in the *Journal of Acquired Immune Deficiency Syndromes* in February 2004, found

Twelve non-HIV-infected individuals developed severe cutaneous toxicity, including 3 with Stevens-Johnson syndrome, after 7 to 12 days of nevirapine containing PEP regimens. Thirty non-HIV-infected individuals developed hepatotoxicity after 8 to 35 days of single-agent nevirapine ... or a nevirapine-containing PEP regimen. ... Findings included ECOG grade 3 or 4 hepatotoxicity ... fevers ... skin rashes ... eosinophilia ... and fulminant hepatic necrosis requiring an orthotopic liver transplant. ... Rates of severe hepatotoxicity (grade 3 or 4) in non-HIV-infected individuals ranged from 10% (4/41) to 62% (5/8).

Is this the same drug we're talking about?

This most toxic of AIDS drugs:

Nevirapine plus efavirenz [*a similar non-nucleoside reverse transcriptase inhibitor*] was associated with the highest frequency of clinical adverse events, and nevirapine once daily with significantly more hepatobiliary laboratory toxicities than efavirenz. Of 25 observed deaths, two were attributed to nevirapine

reported Van Leth et al. in *Lancet* on 17 April 2004. So toxic that on 6 December 2000, in the *Journal of the American Medical Association*, Johnson and Baraboutis had already advised against using it at all:

A severe hypersensitivity reaction is a known complication of nevirapine and can present as a fulminant hepatitis or as a systemic syndrome with predominant cutaneous manifestations referred to as hypersensitivity syndrome (HSS) or drug rash with eosinophilia and systemic symptoms. ... In light of the increased reports of severe ... reactions ... we suggest that this agent not be used ... until the incidence and full spectrum of nevirapine toxicity is clear.

But nobody was listening – not the doctors, not the activists, nor the journalists, and certainly not the businessmen running the nice family firm Boehringer Ingelheim.

Part Two

I am very sensible what a Weakness and Presumption it is to reason against the general Humour and Disposition of the World.

Jonathan Swift

Boehringer Ingelheim had a bit more trouble pushing past the medicines regulators in Canada than it did in the US and Europe. Its licensing application filed on 13 June 1996 had bombed. A second one was wallowing. The Therapeutic Products Programme of Health Canada, a division of the Health Protection Branch, couldn't see any benefit. Only terrible toxicity. But the company wasn't used to taking no for an answer. Who do you red coat naffs think you are? Telling us to bugger off. So its surrogates got the politicians to interfere. Knowing how to get things done.

On 5 March 1998 a mob of TAC types, the Treatment Information Project, an arm of British Columbia People with AIDS, gatecrashed a meeting attended by Health Minister Allan Rock at St Paul's Hospital in Vancouver and began mouthing off that his drug regulators didn't know what they were doing: they 'do not understand how the drugs work', unlike the US FDA which has a 'superior understanding'. Not only stupid, but too independent too – characterised in the BCPWA's report of the day's fun as

ineffective in coordinating its work both internally and internationally. Drug company representatives express enormous frustration that there is little consistency in the personnel [that the Health Protection Branch] assigns to work on a given file. As well, there seems to be little opportunity for fluid, ongoing dialogue during the review process. Add to this the fact that components of a review that could be done concurrently such as clinical and chemistry/manufacturing are instead done sequentially. There are also opportunities for international co-operation that Canada takes little advantage of.

Hell of impressed by the activists, Rock was full of it when stirring things up over at the TPP. A week later, taking a sudden

interest in the drug approval process, he asked the guys how it worked, specifically wanting to know what the hold-up with nevirapine was, since it was already approved in America, Europe and elsewhere. Five days later he got his answer. The TPP mentioned that nevirapine was in the final stages of the review process (in a renewed application) and explained that

Differences in the regulatory status of antiretroviral drugs in Canada as opposed to the United States relate to several factors, namely: differences in submission filing dates, restrictive regulatory provisions [*slightly higher standards in Canada – drug regulators being edgy there in the wake of the thalidomide disaster, particularly bad in that country thanks to regulatory inertia and laxity at the time*], and limited resources. ... Differences in submission filing dates stem from the tendency of pharmaceutical manufacturers to file their new drug submissions in the United States (US) first, primarily to get access to and secure a wider market share.

Working the system in other words.

The TPP memorandum pointed out that in Canada there was none of this ‘conditional approval’ business, with manufacturers being asked to provide evidence of clinical efficacy only after the release of a drug. But they were looking at developing such a scheme. To keep up with the Americans and the Europeans. It then went on about how hard we’re trying but we’re low on dough:

There has been a continual erosion of the appropriated funds ... required for sustaining and enhancing regulatory review activities related to drugs. ... Without infusion of additional resources, the TPP will not be able to respond to the continuing demand for shorter review times for HIV/AIDS drugs.

On 9 April 1998 Rock replied: Get the new conditional approval regime in place. Without delay. We’ll worry later on about drawing up some regulations to deal with drug companies not complying with their obligation to come back with evidence that their drugs out in the market actually work. That’s what he said, he sure did. Now we recall that nevirapine’s benefits, if any, are very modest indeed. Modulating CD4 cell counts slightly better in combo with older drugs than the older drugs alone, but only in the

case of people with low CD4 cell counts. Certainly no clinical benefits shown in terms of improved health. But that's not what the drug lobbyists told him. A swallower evidently, the politician enthused:

As the Department is no doubt aware ... the new antiretroviral drugs are able to cut death and disease rates dramatically ... With respect to the drug Viramune (nevirapine), I am told that this drug is available in 75 countries but not in Canada. I am also told that the drug has been rejected once by HPB [*Health Protection Branch*] and is now under second review. Please advise whether this is true, and if so, the circumstances.

On 22 April 1998 Rock got his next answer, confirming that a conditional approval regime was being implemented as ordered. Also that nevirapine had been approved elsewhere but not at home. The TPP explained why:

the review of the new drug submission for Viramune did not reveal any conclusive effects on clinical end points nor on surrogate marker end points to support the benefit of Viramune in treating patients with HIV disease [*i.e. even the latter were considered too flimsy*]. The efficacy of Viramune was not clinically significant when evaluated against internationally recognised standards of efficacy for drugs used in the treatment of HIV. There are, in addition, safety concerns associated with Viramune use in clinical trials. On March 6, 1997, a Notice of Non-Compliance (NON) was issued by the Therapeutic Products Programme. On July 2, 1997, the manufacturer filed a response to the NON. In the absence of scientific evidence of efficacy and concerns relating to safety, the data available for Viramune are judged to be inadequate to support the clinical benefit of the drug.

On 23 April 1998 Rock's office addressed further questions to the regulators. Their answer the following day reiterated adamantly:

The review of the drug submission for Viramune by the Therapeutic Products Programme found that there was an absence of scientific evidence of efficacy and that there were

also concerns about safety. The data available for Viramune were judged to be inadequate to support the clinical benefit of the drug and a Notice of Noncompliance (NON) was issued on March 6, 1997. This review decision will be forwarded to the Expert Advisory Committee on HIV Therapies for further review.

But with a new conditional approval system rushed into place, the next development was – you guessed it – nevirapine was back on the table for ‘a priority review ... a quick response would be much appreciated’ (per Joyce Pons, Submission Screening Officer in the Bureau of Pharmaceutical Assessment, in an internal memorandum dated 8 September 1998). Following which the drug was conditionally approved with pleasing alacrity on the 17th, just over a week later. But only for use in combination with other old antiretrovirals, not on its own. No good for that. We speak of a drug found to be useless after two unharried assessments – the manufacturer having been unable to come up with any evidence of clinical benefit. Or of any significant effect on laboratory test markers. Despite ample time and opportunity to come up with the goods. In not one but two licence applications. But approved for consumption by the public under the new rules. The process being a quick one. Because look, this is an emergency. The activists say so. So there’s no need to show a drug works anymore. As long as you promise to come back and show us it does later.

A condition was duly attached to the licence, being, that’s right, that Boehringer Ingelheim come back with some evidence of clinical efficacy. Fine, it promised. Just one snag. In the headlong rush to oblige the Germans, the Canadians hadn’t got around to writing the rules concerning the enforcement of such undertakings. Internal communications reveal the confusion: Chris Turner, Manager of the Continuing Assessment Division asked, ‘Who is responsible for following up the conditions? ... We do not have the review staff at present to accept such an assignment.’ Ann Sztuke-Fournier of the Advertising and Promotions Unit replied, ‘As discussed this is still not clear. The conditions are unknown to me and the regulatory impact as well.’ Eric Ormsby, Acting Director of the Office of Science-Risk Management Methods in the agency noted,

We still do not know whether we have the authority to remove an NOC [*Notice of Compliance*] if they do not provide the information agreed upon. Sheila Hills in BPA is writing a guideline or something regarding information required. I don't know much more.

Chris asked, 'Is the NOC with conditions actually finalised yet? I thought there was to be a guideline. What is the regulatory authority for such "limitations" at present?' Ann wrote to Eric:

As mentioned by Chris ... do we have a regulatory authority for these limitations? I am not aware of any formal commitment or agreement to conduct post-marketing surveillance for this drug or under what conditions this drug has been approved.

Vicky Hogan, Head of the Monitoring and Evaluation Unit, set out her agency's 'concerns'. Nothing was being done to 'educate the medical community' about the new conditional licensing policy, she said. And in Boehringer Ingelheim's release about the drug to physicians,

information about the conditions was not highlighted and the prescribing physicians [who] received that information were NOT informed about the outstanding concerns about efficacy associated with this drug. ... physicians are under the impression that this drug ... is considered ... to be both safe and effective.

That nevirapine is in fact neither is frankly conceded by its manufacturer. Robert Johnston of the Canadian NGO HEAL Toronto drew this to Rock's attention in a letter he wrote to him in December 1999:

The manufacturers of nevirapine admit in their own advertising copy that the drug has no proven benefits. All that is clear is the drug's potentially 'life-threatening' side effects: 'VIRAMUNE is indicated for use in combination with nucleoside analogues for the treatment of HIV-1 infected adults who have experienced clinical and/or immunologic deterioration. However, there is no cure for HIV infection. Currently, it is not known whether taking VIRAMUNE in

combination will help you live longer or reduce the number of infections or other illnesses that can occur with HIV. You should also be aware that all antiretrovirals can cause side effects. VIRAMUNE is associated with severe rash, which in some cases has been life-threatening. It should be discontinued when severe rash occurs. Other side effects reported include fever, nausea, and headache. VIRAMUNE is, however, generally well tolerated by most patients' – Roxanne Laboratories Inc. Roxanne also informs us that serious grade 3 or 4 rash occurred in 7.6% of patients on a Nevirapine combination as compared to only 1.2% of patients on other combinations of drugs in the trials they referred to. Grade 3 or 4 rash is considered a serious medical emergency.

Rock didn't reply.

In stating her agency's 'concerns', Hogan pressed on: there was 'deep concern that we do not have [an] active surveillance program in place yet'. She wondered what 'compliance action' will be taken if drug manufacturers do not comply with the conditions imposed on their provisional licences, and concluded by suggesting that

the programme needs to act fast to communicate this new policy to the medical community and to develop some operational infrastructure around it. I am particularly concerned that the vast majority of the medical community does not know the significance of a [provisional licence] and so is left to make prescribing decisions without the benefit of this knowledge and that there seems to be a good deal of confusion in terms of who, in TPP, does the follow through on monitoring conditions set forth in [a provisional licence].

Never mind the Mounties, more like the Keystone Cops.

Once Boehringer Ingelheim had succeeded in stiffing the Canadian government too, its pimps began crooning: driving a shiny new Beamer, no doubt, on his nevirapine trial supervision fees, Julio Montaner, later to become president of the International AIDS Society, enthused: 'We are extremely pleased to see this valuable new treatment alternative in Canada.' Mark Wainberg, then president of the IAS, his back pocket similarly stuffed from overseeing nevirapine clinical trials, applauded in tune:

Nevirapine is a wonderful antiviral drug and its approval now means that Canadian patients, and their physicians, will have increased options for the treatment of HIV disease. I fully expect that people will live longer and enjoy an increased quality of life as a result of this long-overdue decision by Health Canada to approve nevirapine.

Hot on the heels of the nevirapine's registration in Canada, Boehringer Ingelheim spokesman Fred Harris announced a quick marriage of convenience. To a sugar daddy. And guess who:

Boehringer Ingelheim (Canada) Ltd, recognising Glaxo Wellcome Inc. as a leader in the development and marketing of products [*such as AZT*] for the treatment of HIV/AIDS, has decided to enter into a marketing agreement to provide a quicker and more focused introduction of the product into the Canadian community.

So we can get it out there. People are dying.

Part Three

Everything I have written in these lectures underlines the importance to the intellectual of passionate engagement, risk, exposure, commitment to principles, vulnerability in debating and being involved in worldly causes.

Edward Said

When you consider how easily Boehringer Ingelheim rammed nevirapine past the First World Canadians, just think how soft the defences of developing countries are to the predations of such giants with all their financial and propaganda resources. Countries like ours. So predictably there was none of the initial Canadian trouble here, with annoying government pharmacologists saying, Your drug is pure shit. We don't want it here. Take it away. Go and push it somewhere else.

On 22 April 2000 the *Independent Online* quoted Boehringer Ingelheim's local director Kevin McKenna telling us that the approval of nevirapine (in February 1998) had been 'very efficient. It was very quick.' We never doubted it would be. Not a question raised. The South African Medicines Control Council being packed with useless dregs. As they demonstrated by blowing the inquiry into the safety of AZT ordered by President Mbeki in October the year before. Disregarding the key literature. All the latest stuff on AZT's foetal toxicity especially. Not to mention Papadopulos-Eleopulos's et al. exhaustive review of the molecular pharmacology of AZT, published in May 1999 in a special supplement to *Current Medical Research and Opinion* a few months before Mbeki's safety inquiry directive, which concluded that not only is AZT exceptionally poisonous, but also that it cannot and by all conventional measures does not have the pharmacological activity claimed for it by GlaxoSmithKline. But to be fair, the paper dealt with tricky stuff like whether AZT is triphosphorylated intracellularly to its inhibition concentration in vivo, and frankly to expect the MCC's members to exercise their minds around such abstruse technicalities would be asking too much. Because let's face it: we're just a bunch of rubber stamps for the drug industry. And if the FDA hasn't bothered looking into

this, why should we? Just because the President asked us to. Tipped off by some small town lawyer.

Soon after it was licensed in South Africa, nevirapine hit a bump in the road. Approval of the drug by the MCC presented a grand opportunity to Triangle Pharmaceuticals, an American pharmaceutical corporation founded by David Barry, formerly Director of Research at GlaxoSmithKline and a key promoter of AZT. Eager to cut a slice of the AIDS drugs action, Triangle needed some human guinea pigs on which to try out its experimental drug Coviracil (Emtricitabine, alias FTC), ahead of an application to the FDA for a licence. Penurious South African blacks being ideal. Being unimportant and dispensable. Not such a fuss if they get hurt or killed. Nice and cheap too, compared to what such test subjects cost back home in the US: fifty rand to each for every hospital visit – about five dollars. But not bad if you're unemployed here.

Triangle engaged Quintiles Transnational, described at the time by the *Raleigh News and Observer* in the US as 'the world's largest pharmaceutical services company', to conduct a clinical trial with Coviracil in combination with nevirapine and two other drugs, lamivudine (3TC, an AZT look-alike) and stavudine (d4T, another one). Dr Mariette Botes, head of the AIDS clinic at Kalafong Hospital, a teaching hospital of the University of Pretoria where she lectured, was hired to run the trial there, one of sixteen sites at which the study was to be conducted. Its subjects were drawn from Atteridgeville, a largely impoverished dormitory complex outside Pretoria for mostly Tswana speakers. The study was called FTC 302. It was an abattoir.

Here's how they went about it. Barry Hughes-Gibbs, an Anglican priest later punished for his sins, was running a nice lucrative NGO called Mohau, ostensibly a model AIDS charity. By 1999 it was being funded to the tune of more than a million rand a year by several major drug companies, among other donors. So when Triangle Pharmaceuticals went looking for some South African blacks to experiment on, the priest was their man, and he led them in like a Judas goat.

Forty-two patients were enrolled at the Kalafong site in October 1999. One of Rev Hughes-Gibbs's staff was a former Anglican

priest named Johan Viljoen. He was most concerned to hear that four or five people on the trial had died by Christmas. A further six had become very ill on the drugs, two of whom would die the following year. Risking his job, Viljoen blew the whistle and told Pan Africanist Congress MP Patricia de Lille what was going on. At a meeting with the surviving injured parties on 28 March 2000, they described the serious toxic effects that they'd suffered on the trial. Which they'd never anticipated, they said, having regard to the reassuringly light explanation about possible side effects that Botes had given them when she was signing them up. And when they'd approached her over how badly affected they'd been, she'd been unsympathetic, they complained. De Lille recounted to her biographer Charlene Smith in *Patricia de Lille* (Spearhead, 2002): 'They told me that when they were recruited they were told that they were HIV-positive and were going to die in any case.' Well, this is what they teach you in medical school.

On getting wind of things National Minister of Health Dr Manto Tshabalala-Msimang immediately asked the MCC to investigate and report. On 5 April she told Parliament that five women had died

during the course of an ongoing clinical trial involving nevirapine. According to the MCC report, two of the deaths were due to hepatitis. The report further cites the causal association between nevirapine and the deaths as probable in three of the five cases. This meant that, based on what had happened in the trial so far, there was a 1% death rate and a liver toxicity profile of 11%. These are serious findings. As a result, the MCC has halted any further recruitment of study subjects while full reports are being compiled on all serious adverse events, including the five deaths.

The MCC had contacted the FDA in the US, which shared its concerns about the trial, she said. And she'd asked the MCC for detailed information about all reported side-effects reported at all sixteen sites, not only liver toxicity, as well as for information about whether

patients' consent was fully informed and obtained in a language they understood, and for details of the ethics

committees that approved the study, and the names and CVs of all investigators in the trial. In addition I have asked for a comprehensive report on all HIV/AIDS-related clinical trials approved by the MCC that are currently running in South Africa, or that have been completed in the past five years.

Tshabalala-Msimang mentioned that

in recent years there had been a proliferation of clinical drug trials using human subjects, which under normal circumstances were justified. But this was not true in the South African situation, because it was highly unlikely that any but a few South Africans would ever derive any benefits from the drugs being tested here. Once they were patented and registered, they were marketed at prices unaffordable in this country.

She added that her department

had just completed proposals for a national health research ethics council, which would offer significant protection to HIV/AIDS sufferers vulnerable to the hope offered them by drug companies through the promise of participation in clinical trials.

The following day de Lille was reported having told *The Witness* that she'd uncovered

a nest of abuse and exploitation. ... One patient developed a rash all over his body and still has marks on the face. He told Dr Botes that this had happened since using the drugs, but the doctor said it was not the drugs causing the rash, but the HI virus.

Severe skin damage being a brand-new AIDS indicator disease, according to Dr Botes. The AIDS doctor had obviously never heard of Stevens-Johnson Syndrome for which nevirapine is famous.

In a report in the *Independent Online* on the same day, AIDS journalists Lynne Altenroxel and Anso Thom reported that 'Experts have questioned whether nevirapine could have caused the deaths, as the drug had already undergone clinical trials of its

own before being registered for use in 1998.’ To these airheads registration meant it was safe, apparently.

On 7 April the FDA issued a ‘clinical hold’ on the further conduct of the study, which it had approved as a formal licensing trial, sending Triangle Pharmaceutical’s stock into free fall in the US, with more than a third of its value shaved. The company’s executive vice president Carolyn Underwood hastened to exculpate her company’s drug, blathering, ‘The unfortunate part is, it is really hard to sort out how much of this is a political issue. It is escalating and we are caught in the middle of it.’ You would have thought that the deaths were more than a political issue. And that the poisoned test subjects were ‘in the middle of it’. About whom she expressed not a peep of condolence. Instead, after the drug trial was stopped, she said, ‘There are no other drugs in South Africa for them to receive. We are most concerned about the possibility that these patients will be left without therapy.’ Right after the news that it was injuring and killing them. Some of us wondered what gave the Americans the right to come over and experiment on poor black South Africans to get their drugs licensed by the FDA.

Journalist Vivienne Vermaak investigated the ‘rash’ case that de Lille had encountered – a classic case of Stevens-Johnson Syndrome or incipient toxic epidermal necrolysis. A well documented consequence of swallowing nevirapine. Big words for poisoning off skin cells in thick swathes. We’ll call the unlucky subject ‘Joe’, since he’d prefer his real name not be told.

In ‘The mystery of AIDS in South Africa’, published in *The New York Review of Books* on 20 July 2000, American writer Helen Epstein described how Joe’s nightmare began: he

had never been sick before. However, almost as soon as he began taking the drugs, he felt very weak. He mentioned this to [Botes], but ‘she said it was not the tablets that made me sick, it was the HIV, and I should keep taking the medicine.’

This sparkling medical advice flowed naturally from Botes’s membership of the Southern African HIV/AIDS Clinicians Society, the pharmaceutical industry being one of its big financial sponsors. ‘Within a month, [Joe] had to be admitted to Kalafong hospital with vomiting, rash, fever, and painful, bleeding sores that covered his entire body.’

He told Vermaak likewise, and related further: ‘A rash broke out all over my body. I wanted to throw up all the time and had a fever.’ Within days, Joe’s ‘rash’ had developed into suppurating open sores, head to toe. He couldn’t walk. As the toxic reaction began to intensify, he desperately tried reaching Botes on her cell phone, but got no joy. He’d forgotten that his copy of the Informed Consent form contained an emergency hotline number. But it wouldn’t have helped using it either. It was the number of a telefax machine in a small office at the hospital – which didn’t work when Vermaak repeatedly tried it during her investigation. Hardly a fitting medium for a discussion of your life-threatening toxic drug reaction, anyway. And not much use if you live in a shack and don’t own a fax machine. Who in Atteridgeville does? It would have been useless even if he’d had one, because the hospital’s fax machine was unmanned most of the time. On a lucky day it would be staffed by volunteers. Off the street, knowing nothing about the management of drug toxicity emergencies. But you have to understand: we had to contain our costs. This is how capitalism works. And anyway they were only blacks.

Realizing that it was the treatment that had made him sick, Joe staggered into casualty at Kalafong hospital where he showed his pills to the quacks. They had the rare good sense to instruct him to quit the drugs immediately and to book him in, noting on his medical file: ‘Grade 4 skin rash due to nevirapine’ – i.e. life-threatening Stevens-Johnson Syndrome. Botes paid Joe a visit a few days later. Her diagnosis was different: HIV was to blame, she said, not the tablets. Being an ‘AIDS expert’. But then she dumped him from the trial. A funny thing to do, considering: aren’t AIDS drugs supposed to rescue you from the march of AIDS? Two months after Joe stopped taking the drugs he’d recovered his health. Without Botes’s life-saving drugs. Odd isn’t it?

Joe complained to the internal inquiry conducted by the University of Pretoria that he never understood that taking the pills might have caused him to suffer such terrible injury. His grasp of English as a second language wasn’t great, but it wouldn’t have made any difference had he spoken the Queen’s own. The Informed Consent form for the clinical trial, read out to him before he signed it, went:

Side effects that have been seen with nevirapine (Viramune) are rash, fever, nausea, headache, and abnormal liver function tests. These symptoms will be closely monitored.

They weren't, as we know. But the mild ill effects so described are a far cry, you'll agree, from the fate that befell Joe – consistent with the toxicity alert appearing on the nevirapine package insert for whites in the First World, reflecting what had 'been seen' more frankly:

Warning: Severe and life-threatening skin reaction (Stevens-Johnson Syndrome, toxic epidermal necrolysis), including fatal cases, have occurred in patients treated with Viramune.

There was something else about the Informed Consent form that bothered Joe. All recruits to the drug trial were in good health with CD4 cell counts within what AIDS doctors consider normal range, and all had low or undetectable 'viral loads'. But the AIDS doctors had told Joe that he was infected by a deadly germ and had 'HIV-disease'. And that it would be just a matter of time before his health crashed thanks to some or other 'opportunistic infection'. Which surprised him, since he felt as fit as a fiddle. As such news does to most people who light up these tests in good health. Told he was actually diseased, according to the laboratory tests, he was invited to take the trial medicines. He understood that the drugs would keep him well – quite reasonably, having regard to what the Informed Consent form stated:

It is expected that the suggested study treatment will lead to reduced severity and frequency of opportunistic infections (the common diseases that go along with HIV- infection).

Who wouldn't jump at the chance offered by the kind AIDS doctors? They even pay us to take the medicines.

Unfortunately for Joe they didn't share with him the contrary information appearing in the package insert for the drug that nearly killed him:

Information for patients: Patients should be informed that Viramune is not a cure for HIV infection and that they may continue to experience illnesses associated with advanced HIV-1 infection, including opportunistic infections. Treatment

with Viramune has not been shown to reduce the incidence or frequency of such illnesses.

Because had Joe known that, he wouldn't have been so keen to join the experiment. On him.

Apart from suffering terrible fatigue, abdominal cramps and headache on Dr Botes's medicines, one woman, Gladys Mamosodi, went blind for two weeks. The doctor told her it was her AIDS coming on. But strangely she partially recovered her sight after quitting the drugs. Which makes sense, since apart from being neurotoxic, nevirapine is particularly good, Boehringer Ingelheim warns, at rupturing mucosal tissues like those found on the surface of your eyes. And blindness is not an AIDS defining condition. The other symptoms won't be anything new to you, having read *Debating AZT: Mbeki and the AIDS drug controversy*, and knowing what you do now about 'antiretrovirals', two bottles of which Vermaak observed at Mamosodi's home with her name written on them.

Afraid about what was happening to her, Mamosodi approached Botes and asked for her medical case file. It's gone missing, she was told. Unconvinced by this excuse she returned to demand its production again, this time taking her mother along for reinforcement. You can't have it, Botes responded; it's nowhere to be found. When Vermaak put it to Botes that people had a basic right to their own medical information, Botes answered brightly, 'I'm not aware of that. I'm not a legal expert.' I'm an AIDS doctor. I save lives.

Vermaak took matters in hand, masquerading as a nun in a borrowed habit to get through the hospital door. As if to administer the last rites, but really to ask questions and peer into closely guarded medical files when the white madam wasn't looking. In Mamosodi's file she found the entry, 'Patient on HIV treatment trial with Dr Botes', as well as a memo that the serious side effects noted might have resulted from the test drugs.

It wasn't the only missing file; when another trial subject became 'very ill ... tired, depressed' and, like Mamosodi, unable to continue working and needed her case file to support a claim for sick leave she found it missing from the registry – removed, said the clerk, by Botes.

Mamosodi shared her tale with Vermaak kneeling on the floor, emaciated, incontinent in nappies, her head in Vermaak's lap, groaning in agony, on her way out.

Viljoen recalled to Vermaak how she was before commencing the treatment:

I knew her very well. When I started to work there she was a lively, healthy young woman. She was HIV-positive, but she was energetic and certainly if one looked at her you'd say there was nothing wrong with her.

When her health collapsed on the AIDS drugs, she was put in a TB ward. 'They say it's TB,' she told Epstein, 'but I don't believe them.' For good reason: in her file Vermaak saw the results of four TB tests conducted over the preceding two years, and all were negative. De Lille recalled to Smith: 'I saw her the night before she died. She was in a TB hospital, but you could see death in her face – it was very sad.'

Vermaak took the story to the MNet television programme *Carte Blanche*, a show for spilling beans every Sunday night, prime time. Following the broadcast on 22 October 2000 the accused apparently rang their lawyers. There was a set-to. How dare MNet tell such lies? Do you want us to sue you? MNet reacted by repudiating Vermaak's investigation by way of a televised disclaimer, distancing itself from the exposé and apologising for all the hard feelings it caused. Vermaak, MNet suggested, was both incompetent and dishonest: Mamosodi had never been on the antiretroviral drug trial. Said Dr Botes. This was the principal falsehood for which Vermaak was publicly flayed. Yet Mamosodi insisted to Vermaak that she'd been given antiretroviral drugs, nevirapine included. And that it was on these drugs that she started feeling really sick. No, Botes told Vermaak. Mamosodi had been on an antifungal drug trial. She'd been given an 'innocent' drug that 'couldn't cause the side effects [that she'd] complained of'. Except that her signed Informed Consent form, finally produced, warned of some pretty dark ones for the 'innocent' drug too, such as hearing loss and kidney damage.

But it turns out that Vermaak was right about those antiretrovirals after all. At the independent inquiry subsequently commissioned by her university, Botes admitted that she'd put

Mamosodi on two antiretroviral drugs, nevirapine included. Didn't tell her what the drugs were, though. Didn't write a prescription either. Didn't see the need. Not even the legal one. And of course there was no mention of such antiretroviral drugs in Mamosodi's file. All very odd. But nothing odder than Botes's reluctance for that medical file to see the light. First withheld on two occasions and then finally produced with important contents missing – nothing about Mamosodi being given nevirapine and another AIDS drug, and nothing about her blindness that developed after she commenced taking them, but partially reversed when she stopped. Or the uncontrollable diarrhoea and myopathy that caused her to waste away, continuing even after she quit the pills. Until she died on 28 February 2001 at the age of 31, leaving two young children to face the world alone with their grandmother.

The official enquiry into the Kalafong drug disaster – to which we'll return in a minute – found that Mamosodi

had been HIV-positive since 1995 ... during that period she was never ill. In November 1999, Dr Botes put Gladys on a course of two different ARVs; she was not told what they were, nor given an informed consent form to sign. After beginning to take the drugs, Gladys was constantly sick. In February 2000, Dr Botes put Gladys on a trial for drugs, having told Gladys that the drugs were for her throat and that it would be a four-week trial ... Within a week, she developed severe abdominal pain from which she was still suffering on 21 April 2000 ... She tried a week before to get her hospital file, but was told it had disappeared ... [Botes] gratuitously gave Mamosodi ARVs – Hivud [*sic: Hivid (ddC) similar to AZT*] and Viromune [*sic: Viramune (nevirapine)*] – in January 2000 when she began developing loss of vision, but because she was becoming so ill and confused after a month with her ARVs, TB medicines and antibiotics, Dr Botes decided it was more important for her to take her TB medication and other medication regularly and, accordingly, stopped the ARV medicine.

(In fact, Mamosodi's sight began failing after beginning treatment with the AIDS drugs and improved when she quit them.)

Two days after Tshabalala-Msimang's statement in Parliament, Medicines Control Council chairperson Helen Rees contradicted her as to the cause of the victims' deaths, saying that 'no conclusive cause and effect' had been established. What's more, 'many AIDS medications could cause liver and other problems. But the combination therapy can make a huge difference to people's lives.' The kind of thinking we expect from a doctor. Well, most. For whom drug company propaganda passes as medical knowledge – she even speaks as the advertisements do. The deaths were possibly caused by drug interactions, she suggested. The chairperson of the MCC was evidently unaware that all the drugs on the trial taken individually, let alone in combination, were potentially fatally toxic, according to the package inserts supplied by their manufacturers. And that nevirapine was the most acutely poisonous of them all. At Tshabalala-Msimang's insistence the MCC nonetheless ordered the trial called off. Or tried to because Quintiles Transnational just pushed right on with it. Since we just do what we like in developing countries. The media reported 'an uproar in medical circles' over the order to terminate the trials. But of course. To be expected. These are doctors who save lives.

'It's the trials, not the drugs' proclaimed the *Daily Mail&Guardian* on 10 April:

The deaths of five women in HIV/Aids drug trials were more likely the result of flaws in the handling of the trials than problems with the drugs themselves, researchers working on related trials said last week. The researchers were responding to the controversial decision by the government last week to suspend recruitment of new subjects for anti-retroviral drug trials after it emerged that five patients had died in trials testing a new drug, STC, and involving the widely effective Nevirapine [*sic*].

Notwithstanding the horrible drug toxicities that she'd observed among adult clinical trial subjects, de Lille tried winning some cheap political points from the episode by deploring the government's reticence about exposing babies to the drugs that caused them, particularly the most acutely toxic one, nevirapine: 'It is unfortunate that [Tshabalala-Msimang] has used the tragic

event of deaths during the trials to make a political point that justifies her doing nothing to stop mother to child transmission.’ And the government was wasting time talking to AIDS dissidents, she added.

Several people died on the drugs. Five women at Kalafong hospital according to Tshabalala-Msimang, the MCC and Professor Geoffrey Falkson of the University of Pretoria’s Ethics Committee. Only two, Kalafong Hospital sources were later quoted in the press. Actually, only one, a man, claimed hospital superintendent Hanli Dafel. In fact, none, said Triangle’s local man, Dr Ian Sanne, to Vermaak – none at Kalafong Hospital, but seven people at other centres.

Who appear to have died slowly and horribly as the AIDS drug poisoned invariably do, most of them subsequent to Sanne’s report presented as an abstract in late October 2000 at the 5th International Congress on Drug Therapy in HIV Infection held in Glasgow: ‘Severe liver toxicity in patients receiving two nucleoside analogues and a non-nucleoside reverse transcriptase inhibitor’. Within four weeks treatment, about one in ten subjects in the nevirapine treated group suffered

treatment-emergent Grade 4 [*life-threatening*] elevations in liver enzymes ... Two patients developed liver failure and died ... a high incidence of liver toxicity was observed, especially in women. Clinically these events were attributed to NVP [nevirapine] in combination with [nucleoside analogues].

Sanne and his colleagues published further serious liver toxicity findings in the March 2005 issue of the *Journal of Infectious Diseases* under the title, ‘Severe hepatotoxicity associated with nevirapine use in HIV-infected subjects’ – 20% of women and 13% of men. The researchers concluded accordingly: ‘Our data demonstrate a high risk (17%) of early hepatotoxicity associated with the use of nevirapine.’ Skinny people with a low Body Mass Index, especially women, were particularly susceptible to having their livers seriously damaged by nevirapine, they said:

Women with a BMI below 18.5 had a 50% probability of experiencing severe hepatotoxicity, however the probability for women with a BMI above 18.5 was 17%. For men with a

BMI below 18.5 the probability of developing severe liver toxicities was 15% and 7% for men with a BMI above 18.5.

Precisely how many people were killed in the American drug experiment on poor South Africans at Kalafong and other centres we'll never know. When at a chance encounter at an airport, after MCC chair Rees had studiously avoided an interview with her, Helen Epstein suggested five dead, Rees blurted back: 'You have your facts wrong.' But then couldn't remember how many had actually died. When Epstein asked Falkson, his response was: 'They had full-blown AIDS.' (It's what those blacks get, you know.) Epstein called Triangle Pharmaceuticals in the US; only one person had died on the trial at Kalofong, she was told. She phoned Botes about this; none of the dead had been on her trial, she said.

Responding to Tshabalala-Msimang's announcement about the deaths, Boehringer Ingelheim's McKenna ducked and dived at the flashing blue light: 'My information is that the actual link to nevirapine is inconclusive.' He would change his tune a week or so later. His bosses in Germany backed him up concerning his 'inconclusive link' statement with a formal press release on 10 April:

in a clinical trial in which patients are taking multiple drugs, it is not possible to determine with certainty, which drug, if any, may have caused the ... deaths. [*That's the joy of mixing dangerous toxins made by different companies: an escape hatch when things go wrong.*] ... According to news reports, there was a higher than expected incidence of liver toxicity in the study. In fact, the incidence of liver toxicity seen in the study is in line with what is commonly seen in similar studies of triple combination antiretroviral therapies in HIV-infected individuals. As with all potent antiretroviral treatments, there are known side effects of nevirapine as described in the labelling product.

In all, an exercise in wordplay more fascinating than Bill Clinton's about his side-ass jinks in the Oval Office.

Apropos the liver damage observed, since the liver toxicity of nevirapine is the most acute (rapid) relative to the other drugs on

trial, it was a fair bet to blame it – on a preponderance of probabilities, as we lawyers say. ‘Which drug, if any’ suggests doubt that the deaths were the result of fatal drug toxicity. But the causes were diagnosed, and they weren’t AIDS indicator infections or malignancies.

Boehringer Ingelheim seemed to be conceding that, look, a cocktail of arsenic, cyanide and strychnine is more poisonous than single shots. We know this. So what are you complaining about? As for ‘potent antiretroviral treatments’, you’ll rightly be suspecting by now that their only potency lies in their toxicity.

On 12 April the European Medicines Agency released its urgent public warning, mentioned in Part Two, that skin and liver damage caused by nevirapine had killed people in Europe, and that doctors administering nevirapine in EU countries had accordingly been advised to test their patients’ liver function twice a week. McKenna told *Business Day* on the 20th that he’d notified the MCC about this. He said discussions were in progress with the MCC ‘to establish what would be appropriate in this country’ in regard to sharpened liver and skin toxicity warnings. Removing the deadly drug from the market, though, was obviously out of the question.

On 19 April the *Washington Post* reported local reaction to Tshabalala-Msimang’s stated concern about the deaths on its front page. Dissident criticism of AZT and nevirapine

formed part of the basis for a speech Mbeki made to Parliament late last year and for more recent statements by his health minister blaming nevirapine – against the judgment of most South African scientists – for a series of recent deaths in clinical trials. Those remarks came under harsh public attack from South African doctors and clergymen, and some foreign AIDS experts have begun to talk of boycotting the Durban conference.

The angry scientists and priests who couldn’t imagine that their new eucharist might be noxious were dead wrong. The independent investigation found that two of the deceased died of liver failure, one of pancreas failure (both conditions caused by lactic acidosis, a standard deadly side effect of antiretroviral drugs), and two of neurological damage (likewise). Other trial subjects suffered deafness, impaired speech, anal bleeding, sores

that wouldn't heal, abdominal pains, weight loss, fevers, pneumonia, insomnia, vomiting, and depression. The investigation concluded that nevirapine had probably caused the liver damage that had killed two of the women – not surprisingly, since of all so-called antiretroviral drugs on the market nevirapine is top of the pops when it comes to wrecking livers. Even worse than nucleoside analogue drugs in the AZT class, and they're not shy.

At her meeting with the complainants introduced to her by Viljoen, de Lille announced that she would be taking the matter up with the University of Pretoria's Ethics Committee. Which she did, arranging a public meeting with Falkson on 10 April in a lecture hall at the university. Botes spoke first. After claiming to have explained the contents of the informed consent form nicely to everybody, she then objected to anyone speaking next: if they wanted to complain they should do so formally, and not at a public meeting like this. Falkson agreed and stopped the show.

The injured parties duly filed their written complaints with the university Ethics Committee. We live in a constitutional democracy now. We're not apartheid *Untermenschen* any more. We have rights. We've been burned. We expect something should be done.

They were expecting too much. The gist of their complaints was that they didn't understand the Informed Consent forms, and that the drugs caused them to suffer serious adverse effects that they'd not expected. But an internal committee deputed by the Ethics Committee to investigate ripped them up. You people signed; haven't you heard of the *caveat subscriptor* rule? You can't come along later complaining that you didn't know what you were signing. Business is business. An all-clear report was filed with the MCC. It didn't go down well. Particularly since only four of the eight complaints filed had been investigated.

The Ethics Committee got the next report in August. Everyone on the trial was fully informed by Dr Botes about what they could expect taking the test drugs, it found. And funnily enough, the report noted, three complainants had changed their minds. They didn't agree anymore that the drugs had harmed them; no, they wanted to continue being treated by Dr Botes, because, why, the drugs she gave them made them feel better. Even though they were

so toxic that they'd killed some of their friends. Which Botes belatedly admitted: whereas the initial informed consent form drafted on 8 April 1999 warned of headaches, nausea, loose stools, skin rash, vomiting, dizziness and feelings of tiredness and weakness, along with other unknown side-effects that the AIDS doctors promised to monitor, an addendum prepared on 4 January 2000 recorded that it had now been shown that one of the drugs (guess which one) had been shown to cause

severe and life threatening liver toxicity including deaths. To date there have been 53 patients who had serious liver toxicity [*life-threatening in eleven cases*] after receiving treatment (53 out of the 382 that enrolled equals 14% of the patients).

The Registrar of the University of Pretoria, Professor Niek Grové, to whom the report of the internal enquiry was given, appears to have smelt a rat and ordered that an independent investigation be performed. The venerable 'Sas' Strauss, Emeritus Professor of Criminal and Medical Law at the University of South Africa, was called in to conduct it. Strauss remarked that 'very puzzling questions arise' from the volte face of three of the eight complainants. So did a High Court judge who had cause to review the history of the matter in May 2005. As for the other complaints, Strauss found no fault. But then it never was his brief to look beyond petty questions of professional conduct and into the possibility of an immense corporate fraud. Like the marketing of arsenic for the treatment of syphilis during the first half of last century. Bayer called it Salvarsan and made a killing from it.

Smith's biography of de Lille cited some of Strauss's findings, including those concerning Mamosodi set out above. A month after starting on the drugs one woman

began to feel sick with fever and pain. In November 1999, she was told she had cervical cancer and began to experience dizziness, muscle spasms and fits.

Another woman said that within three weeks of commencing treatment, 'I vomited, had diarrhoea, developed an itching rash, had a fever and terrible mood swings.' Another said that she'd been HIV-positive since 1983, but after going on the test drugs she'd suffered muscle cramps, muscle spasms and fits.

Strauss recorded that two complainants had died before his enquiry commenced: Gladys Mamosodi, and Maggie Maake, who died on 21 April 2000. Concerning the latter he recorded:

Two weeks after being put on the drug trial she developed severe symptoms ... She was admitted to Kalafong hospital ... On 10 March 2000, she was admitted to Louis Pasteur Hospital with complaints of bronchitis and liver problems.

But since she 'did not improve [she] was sent home'. By the doctors. To die.

All and any complaints about the 'misplacing or inaccessibility' of medical files were 'outside my mandate' to investigate, Strauss held. And as for our AIDS doctor:

The picture that emerged of Dr Botes in the course of this inquiry is that of a dedicated doctor who, in collaboration with other medical experts, is in the forefront of medically combating, to the best of her ability, the terrible epidemic of HIV that has hit South Africa.

Doctors get away with anything when there's a fearsome disease to stamp out, especially one they claim is spread by Africans having too much sex.

A striking thing about the Kalafong affair was how the mostly white AIDS activists, journalists and human rights campaigners in South Africa, who clamour for AIDS drugs for blacks at every chance, were strangely mute for a change. We didn't see a single one of them with their tee-shirts and placards and banners at the funerals.

Most noteworthy was then MRC president William Makgoba's silence about it all. The guy who'd presented a paper at the 13th International AIDS Conference in Durban in July 2000 entitled 'Ethics of AIDS Research in a Developing Country – Balancing Power in Disguise'. Making such points as:

temptations may remain to subordinate the welfare of the volunteers ... and treat human beings as a means to an end. Research may also be motivated by financial gains where expediency obscures ethics to the detriment of volunteers and the integrity of science. ... Informed Consent has become one

of the major ethical transgressions of our time – particularly in developing countries. Informed Consent has four essential components: disclosure of all relevant information about the research; comprehension by the prospective participant of this information to make an informed decision ... However codes and requirements alone do not guarantee protection ... In South Africa ... most of our subjects speak ... a different language from the languages of the researchers and practitioners; secondly most subjects in our countries are poorly informed with substandard education. ... The weak and the powerless in our society require a different form of approach ... in order to fully understand the magnitude and implications of signing an informed consent form. ... the tendency is for power to prevail over protection.

Finely spoken, William, we all agree. So what did you have to say to your masters in the drug industry when these people were dying poisoned, others badly injured? Apart from yes sir, no sir, three bags full sir. Except in this country you say baas.

Part Four

Father, forgive them for they know not what they do.

Jesus Christ

In 1996 Brooks Jackson, an American pathologist working as chairman of the history department of Johns Hopkins University School of Medicine in Baltimore, Maryland, decided he wanted to save Africa – specifically African babies from their mothers bedevilled by the fearsome HI virus. He mooted trying out nevirapine, just approved by the FDA (under very restrictive conditions), compared with a short blast of AZT, with the effect of both drugs commencing at labour and followed by treatment of the newborn baby. No matter that Boehringer Ingelheim warned in the *Physicians' Desk Reference* that 'the safety profile of Viramune in neonates has not been established'.

The following year Jackson persuaded the National Institute of Allergy and Infectious Diseases (NIAID), an arm of the US National Institutes of Health (NIH), to approve his proposal that such a trial be conducted on African mothers and babies in Uganda, and to pay the cost of it. No one in NIAID was bothered about the fact that Jackson had no training in public health or in infectious disease epidemiology, much less in clinical drug trial research. To run the study hands-on Jackson recruited two doctors from Makerere University in Uganda and fellow Johns Hopkins staffer Laura Guay, who'd been working in Uganda since 1988 and who'd just been promoted to associate professor of pathology and paediatrics. None of them had any clinical trial expertise either. But they'd be experimenting on Africans, so no worries.

Everyone was keen to help. NIAID put up the cash and got its own people involved. Boehringer Ingelheim had a man in there too, because if this thing worked out the company would have struck a gusher.

The results of the study – named HIVNET 012 – were spectacular. Characteristically in the AIDS age, they were announced to the world, not in any scientific or medical journal, but in the newspapers and on TV, with more puffing around them than in a used car shop.

A press release on 14 July 1999 by the US Department of Health and Human Services quoted Jackson announcing,

In this study, the short-course nevirapine regimen resulted in a 47 percent reduction in mother-to-infant HIV transmission compared with a short course of AZT. The implications of this study for developing countries, where 95 percent of the AIDS epidemic is occurring, are profound.

The press release also quoted NIAID director Anthony Fauci: 'This study represents the most promising advance to date toward the goal of finding strategies that can be used worldwide to prevent the spread of HIV from infected mothers to their infants.' Health and Human Services Secretary Donna Shalala purred full of stars and stripes:

This extraordinary finding is the most recent in our efforts to bring an end to AIDS, not only in the United States but in countries around the world. American scientists along with our international partners are committed to developing treatments that not only work, but that are also feasible in other health care settings. These results achieve both those goals.

On the same day as the press release, Fauci told CNN:

This is going to open up an entire new avenue now of approach towards prevention of transmission of HIV from an infected pregnant woman to her infant in countries that previously could not afford it. ... It might come in handy [in rich countries such as the US as well] when people come into a clinic or emergency room not having any prenatal care whatsoever, and they come in just about to go into labor. You won't be in a frustrating situation of saying, 'My goodness, you should have come in 25 weeks ago or 30 weeks ago when you first knew you were pregnant.'

To CBS Evening News later in the day he said the wide-scale use of nevirapine could

potentially prevent 300,000 to 400,000 newborns each year from beginning life infected with HIV. ... We were hoping

that nevirapine would be at least as good as the AZT. [But it turned out to be] significantly better than AZT.

So why then, no one thought to ask, wasn't AZT being dropped in the US in favour of 'significantly better' nevirapine? Particularly because, as the *New York Times* pointed out the next day, it was so much cheaper as well:

The cost for the two doses of nevirapine was \$4, compared with \$268 for the AZT regimen now used in developing countries and \$815 for the much longer and more complicated course used in the United States and other developed countries, Federal health officials said in releasing the findings yesterday.

Fauci summed up later on: 'You're talking about the possibility of preventing infection in up to a thousand babies per day for a cost that is really very minor.' So his statement to the *Times* that 'there was no need to change the United States recommendations until more studies are completed' was inexplicable – if HIVNET 012 really did prove what he claimed it did: that it saves babies from being killed by their mothers' sex germs even better than AZT does, and at a minute fraction of the cost. 'No need'?!

In a press statement released simultaneously with the NIH's, US Vice President Al Gore said that while

drugs alone are not the solution for countries that lack the systems to adequately provide them, all of us who have been searching for hope in this terrible epidemic should be encouraged by this promising news.

Ugandan Minister of Health Crispus Kiyonga trumpeted the HIVNET 012 study in similar hopeful terms in Kampala on the same day: 'This research provides real hope that we may be able to protect many of Africa's next generation from the ravages of AIDS.'

The following day the *Seattle Post-Intelligencer* both paraphrased and quoted Thomas Fleming, a member of the HIVNET 012 research team: '

With little treatment available, most HIV-infected infants in developing countries die within two years. 'It's devastating,' Fleming said. ... 'Until now, we've not been able to

meaningfully reduce the risk [of mother to child transmission of HIV] in countries where risk is the highest. Now we think we have a way.'

The *Los Angeles Times* quoted Jackson on the same day excitedly suggesting that 'in high-risk regions [*where Africans live*], the drug could even be administered to all women giving birth'. But as Jackson was gushing over the possibilities, UNAIDS director Peter Piot was expressing a much more circumspect view to the *New York Times*; while the HIVNET 012 regimen was 'a major gain' because it 'approaches ideal prevention therapy', it was 'unrealistic to introduce it on a large scale in developing countries without first using pilot programs', he said. But please don't go mistaking Piot for that rare breed of doctors with brains; he's one of those total medical dickheads who tell African mothers that breastfeeding their babies can kill them, and who advocate formula milk instead. The *Times* quoted him further:

It is still a logistical, economic and cultural challenge to develop programs to encourage H.I.V. testing, counseling and baby formula as a substitute for breast-feeding for infected mothers.

Even before the MCC had accorded nevirapine its special registration as an experimental perinatal HIV prophylactic, the Americans were barging in and pushing the drug on us. On 29 March 2000, in a report critical of the South African government's reluctance to burn the country's unborn young with AZT (after reading my exposé *Debating AZT: Questions of safety and utility*), *Newsday* reported that

U.S.-based groups such as the Elizabeth Glaser Pediatric AIDS Foundation and the Global Strategies for HIV Prevention had offered free nevirapine to South Africa, a safer alternative to AZT that also blocks HIV transmission to newborns. That offer, too, was rebuffed because Dr. Ian Roberts, special adviser to Tshabalala[-Msimang], said, 'We are not satisfied that it is proven safe. We must test its safety, by South African standards.'

Which sounded perfectly perverse when there were babies to be saved. What the report left out was that the South African government was not alone in harbouring such reservations. AIDS doctors in the US shared them too – in regard to the use of the drug back home anyway. In subsequently licensing the drug provisionally for this bold new indication, the MCC wasn't just slavishly following the FDA in the normal course. Because the exceedingly toxic drug wasn't approved in the US for giving to mothers and babies, and for reasons we're about to read probably never will be.

You might want to buckle up for this story, because it's a tale of medical incompetence and official corruption that beggars belief. And needless to say, in covering it local journalists blew it completely.

Tshabalala-Msimang had first learned about the possible use of nevirapine as an anti-HIV perinatal prophylactic as an alternative to AZT during a visit to Uganda in the first week of August 1999. On her return on the 6th she told reporters tentatively:

There's no conclusive evidence, but we're testing it. There's also a cost issue here and we don't want to raise the expectations of our population yet.

On a matter of price, though, nevirapine was appealing: about twenty-five rand a mother-child pair, a speck of the cost of AZT treatment for pregnant women.

To Quarraisha Abdool Karim, professor of epidemiology at the Nelson R Mandela School of Medicine in Durban, Tshabalala-Msimang's cautious remark was the start of the end.

It was the beginning of our downward spiral. ... When Tshabalala-Msimang came back, that was when we started to hear the Duesberg-type pronouncements.

(Peter Duesberg PhD, Professor of Cell and Molecular Biology at the University of California at Berkeley and member of the National Academy of Sciences of the United States of America, is a prominent critic of AZT and the HIV theory of AIDS.) So Karim complained to Michael Specter, writing his apologia for the AIDS industry, 'The Denialists: The dangerous attacks on the consensus about H.I.V. and AIDS', in the *New Yorker* in March 2007 – his

flaccid endeavour to patch the holes blown through the AIDS business by the publication of Celia Farber's nuclear strike in *Harper's Magazine* a year earlier, 'Out of Control: AIDS and the Corruption of Medical Science', focussing closely on HIVNET 012.

Specter put it this way:

Tshabalala-Msimang took a delegation to Uganda and looked at a study, called H.I.V.NET, which found that just a few doses of Nevirapine, an antiretroviral given to the mother at the beginning of labor, and then to the infant within the first three days of life, dramatically reduced the risk of passing on the virus. The regimen is cheap and easy to use, and is now in place throughout the developing world. In just a few years, it has saved the lives of hundreds of thousands of infants.

Shortly after Tshabalala-Msimang's return, and even before the full report of HIVNET 012 paper had been published, Boehringer Ingelheim was banging on the MCC's door armed with the 'Executive Summary' of the study findings that had been released in July. In 'The facts about Nevirapine' published later on its website, the MCC recorded:

1999 August: An application was received to fast track the approval of nevirapine as a single agent (monotherapy) for the reduction of HIV transmission from mother to child, based on a single study conducted in Uganda (HIVNET012).
1999 November: The Clinical Committee of the MCC presented its recommendations to Council.

On 4 September 1999 the first report of the study finally appeared – in *Lancet*, under the title, 'Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial'. Which sounded promising, although you might have wondered why the essential terms 'placebo controlled' and 'double blind' were missing from the title of a report of a pivotal clinical drug trial, purportedly showing the efficacy of a new indication for the drug.

Jackson's co-principal investigator Laura Guay wrote the paper in pleasant formal medical prose, pregnant with solemn purpose.

That seems to have got it past its peer-reviewers, because as we're about to learn the study itself was an unbelievable mess. To read Guay referring to the drug's 'potent antiviral activity' and its 'safety profile', i.e. very effective and safe too, contrary to what was already known about it, was just a foretaste of what was to follow.

It's elementary that a drug trial should be randomised, placebo-controlled and double-blind – meaning that its subjects should be treated or not treated on the basis of a random assignment; test drugs and dummies should be equally distributed; and neither the doctors nor the patients should know who's on what. There should also be an untreated control group in the trial, given neither test drugs nor placebos, to exclude the possibility of outcomes hoped for by the researchers showing up without any intervention at all – since the administration of placebos can have the strangest effects, as we're about to see. And of course there should be a large enough number of test subjects on the trial from which to draw meaningful conclusions.

Guay apparently knew most of these basics when she began, because she stated in her paper that the trial

was originally designed to be a randomised, placebo-controlled, double-blind phase three trial of 1500 mother-baby pairs to investigate the safety and efficacy of oral zidovudine and oral nevirapine for the prevention of vertical mother to child transmission of HIV-1 from pregnant women to neonates in Uganda.

A fair start, except that Guay didn't think to study an untreated control group. A not insignificant omission, seeing that in 1999 the American CDC, studying the effect of AZT for the same purpose, reported in *Lancet* (353:773-80) that placebos apparently reduced the transmission rate (18.6%) when compared with untreated controls (24.2%), leading the researchers to observe:

The lower than expected background transmission rate highlights the importance of having included a randomised, concurrently enrolled, untreated control group. Had the test regimen been inactive, a transmission rate of 18.6% may have suggested some efficacy when compared with historical data.

The study began falling to pieces on the day it began. The system devised to keep the trial blinded collapsed immediately. Guay reported this fundamental breakdown of control with face-saving delicacy:

After randomisation, on-site study staff and investigators became aware of the treatment and infection status of the mother-baby pairs. Mothers also knew to what study group they had been assigned after randomisation and were told the infection status of their babies during the study.

She concluded accordingly: ‘Limitations of our study were that investigators and mothers were not masked to treatment status or outcome after randomisation.’ She could have put it more plainly: We fucked it up from the word go.

That the unblinding of the trial would have affected its outcome is certain, given the terror of the diagnoses and the inevitability that at least some of the pregnant women given the news that their babies might die would do anything to reduce the chances: resort to pill sharing between groups, for instance, or swallow other drugs by the handful, or traditional potions not necessarily benign. Those on experimental nevirapine might have taken ‘proven effective’ AZT as well – unseen by the trial overseers, because ‘many doses [of AZT] were given unobserved. Mothers were identified before labour and given the drug to take at home.’ And one must consider the possibility that those on AZT might have gone to any lengths to obtain the hyped new drug instead. The kind of stuff that FDA inspectors discovered went on behind the scenes in the chaotic licensing trial that preceded AZT approval in the US. The key one that became thoroughly corrupted (detailed in my essay *Licensing AZT*, online), but on the basis of which GlaxoSmithKline still claims AZT extends lives.

Subjects for the study were drawn from pregnant

women attending antenatal clinics at Mulago Hospital in Kampala, Uganda ... screened for HIV-1 infection by EIA [ELISA] for HIV-1 antibody. If a woman tested positive, she received post-test counselling about her infection status and was informed about the opportunity to enrol in HIVNET 012.

In other words, women lighting up a single ELISA HIV antibody test were considered infected, told so, and offered the chance to save their babies with free medicine if they joined the drug trial. In her next sentence, however, Guay stated that ‘Women were eligible for the study if they ... were positive on EIA and Western blot for HIV-1 antibody.’ So which is it? By what criterion did Guay define ‘HIV infection’?

Nearly all AIDS doctors agree that a single reactive ELISA antibody test is insufficiently reliable a basis upon which to make an HIV-positive diagnosis, notwithstanding that the manufacturers of these state-of-the-art, third-generation, recombinant protein-based test kits typically claim 99.6% specificity for HIV, i.e. only four mistaken positive diagnoses per thousand, as the figure would suggest. It’s a claim made on an essentially fraudulent basis, however, because the sensitivity and specificity of these tests has never been assessed by observing how they perform in relation to groups of confirmed HIV-infected individuals, as against confirmed uninfected ones – HIV-infected meaning having the virus in, and isolated from, the HIV-positive patient’s blood or tissue.

The reason is startlingly simple: HIV has never in the history of the AIDS era been isolated from anyone – by ultracentrifugal purification and then electron photomicrograph verification (the standard, universally accepted procedure for isolating viruses). The existence of the most feared pathogen in history is inferred instead from indirect and ambiguous biochemical clues.

Guay’s ‘Trial Profile’ schematic tells us that 13 839 women were ‘tested for HIV-1’. 2 144 were described as ‘with positive HIV-1 test’. Whether Guay meant positive according to a single ELISA or positive according to an ELISA ‘confirmed’ by Western blot is simply left in the air. Leaving us to wonder. 1 499 of those 2 144 women were excluded from the trial, leaving just 645 mothers and not the 1 500 originally intended. Among the reasons for excluding the 1 499, Guay mentions ‘an indeterminate or negative western blot’. But since women lighting up a single ELISA ‘received post-test counselling about [their] infection status and [were] informed about the opportunity to enrol in HIVNET 012’, it’s quite possible that some of these women came aboard the trial without further

testing. And since further Western blot testing always leads to the exclusion of the majority of single ELISA positives, the necessary conclusion is that most of these single ELISA positive women were not infected. We are staring into a massive crack in the trial's foundations that nothing can patch.

Simple logic dictates that repeating an ELISA can't confirm the initial positive result, because whatever triggered the first test (such as TB bacilli and about seventy other documented conditions) can just as well set off the second one. Even if it's made by a different manufacturer. (This point has never occurred to University of Cape Town 'AIDS expert' virologist Dianna Hardie, because according to her two positive ELISAs do just fine – so she said on John Perlman's prime-time *AM Live* radio show 'for the well-informed' on 4 April 2002.)

Guay may or may not have been alive to the problem just stated, because we see that she wasn't content with a second reactive ELISA:

We screened plasma from mothers for HIV-1 antibody with a licensed assay (HIV type 1 Vironostika, Organon-Teknika ...). If the test was reactive, a second HIV-1 antibody test was done on the same sample with the Murex 1+2 assay ... For women with blood samples that were reactive on both tests, we took a second sample and did an HIV-1 western blot analysis (Cambridge Biotech ...) for confirmation of HIV-1 infection.

As your doubts begin rising like bile, you might wonder whether those mothers 'confirmed' infected by Western blot retesting were really 'living with HIV' anyway. See, you can't intelligently confirm positive ELISAs with a Western blot either. Most AIDS doctors regard Western blot results for HIV antibodies as decisive, as the absolutely reliable last word. Not in England and Wales, though, where Western blots are not used to confirm positive ELISAs precisely because they are regarded as too unreliable. (Welcome to AIDS medicine.) The spuriousness of a 'confirmatory' positive Western blot test for one or more positive ELISAs got a close look in a lengthy landmark review, 'Is a positive Western blot proof of HIV infection?' by Papadopoulos-Eleopoulos et al., published in a prominent scientific journal,

Bio/Technology (now *Nature Biotechnology*), in June 1993, and it makes a staggering read. (It's archived on the internet).

The authors point out that all the proteins used in these tests as antigens to fish for 'HIV antibodies' are not unique bits of 'HIV' as had always been imagined by AIDS doctors, but are actually ubiquitous cellular proteins or clumps of them (oligomers). Bits of us, in other words, or bits of common bugs. What's more, the performance of the tests has never been gauged by reference to the gold standard of confirmed viral infections. Because oddly enough, as just mentioned, 'HIV' has never been isolated from the blood or other tissue of anyone.

But we don't have to get into all that. It's surely enough to know that AIDS doctors apply completely different criteria from place to place when interpreting Western blot test results. In their Western blot paper Papadopulos-Eleopoulos and colleagues describe eleven distinct currently applied official sets of criteria for diagnosing 'HIV infection' with Western blot tests, varying radically from continent to continent, institution to institution and even between laboratories in the same city. So that whether you're 'infected' or not, and condemned by doctors to die soon, or told to your great relief that you've a long life ahead, is really the luck of the draw. Being all about how your test result is interpreted. Which criteria are applied. Infected with a deadly virus here, but free of it according to a different interpretation there. It's unbelievable but true. But as I say friends, this is AIDS, and in AIDS anything goes. Don't bother asking AIDS doctors about any of this stuff, though, let alone your family doctor. They'll huff and puff with haughty dismissals and assurances, but in truth won't have a clue as to what you're even talking about. (Been there, got the cap.) You'll have to read up for yourself.

Although recruitment had started in November 1997, by February 1998 only 49 women had been enrolled on the trial – 19 of whom were assigned placebos, 15 AZT and 15 nevirapine – when Shaffer's pleasing report came through of the results of his short-course AZT trial in Thailand (*Lancet* 353: 773-80).

The activists now took over. In November 1999 Peter Lurie and Sidney Wolfe, two American doctors working for the powerful consumer lobby Public Citizen, wrote a scathing letter to the

British Medical Journal deploring how very unethical the researchers were to continue with a placebo arm. It didn't strike them that there might be anything unethical about treating HIV-positive pregnant African women with the experimental drug nevirapine to see whether it worked or not.

In 'The Pathologist Who Struck Gold', published in the Spring/Summer 2001 issue of *Hopkins Medical News*, Anne Bennett Swingle recounted:

Jackson felt strongly that he didn't want to drop the placebo part of his protocol. Testing the two drugs against nothing, instead of only against each other, was the only way to make a valid scientific assessment of the worth of both medications. ... As pressure mounted, Jackson dropped the two placebo arms of his clinical trial, a step that still riles him today. ... 'No researcher,' Jackson says, 'can assess a drug's effectiveness with scientific certainty without testing it against a placebo. That's the only way we can know for sure if a short course of AZT or nevirapine is better than nothing.'

So the abandonment of the placebo control was indefensible, and Jackson and his colleagues knew it. But this is the sort of thing that happens when powerful lobby groups claiming to be human rights champions get to call the shots.

There's another reason why the placebo control shouldn't have been abandoned: Schaffer's study in Thailand involved the administration of AZT to pregnant women for a few weeks before birth. The AZT arm of HIVNET 012 involved a completely different experimental drug regimen: AZT given at commencement of labour, during it, and to the baby for a week after birth. So there was no justification for relying on Shaffer's findings as a basis for abandoning the placebo arm of the study. Before she did so, however, Guay noted that the transmission rate among women given placebos was 26.1%. But also that the rate among women given AZT was a 'similar' 25%.

Amazing: when it comes to saving babies, placebos are as good as AZT. That's not what AIDS doctors tell you, though. Indeed, recording these substantially identical numbers, Guay said in the same breath that 'short-course zidovudine may have had some benefit'. Except that placebos wouldn't have caused the kind of

toxic shock resulting in vomiting and premature labour contractions that Guay reported among some of the women given AZT. Let alone the harm caused to the babies. We'll return to deal with her toxicity data shortly.

Dropping the placebo wing of the study made it impossible to claim a benefit for the test drug – nevirapine being the new one under investigation – since not only do untreated mother to child transmission rates vary hugely from place to place according to all the reports (ranging from approximately one in two cases to one in ten), but even placebo administration has magical reported effects. For instance, in the Shaffer study of the effect of short-course AZT administration on mother to child transmission, placebo administration was reported to have reduced ‘transmission’ at one hospital 14.3% and at another 23.7%.

But not only does placebo administration have mysterious benefits, so does taking nothing at all. A study by Ladner and Leroy published in the *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* in 1998 (18:293-8) reported that the transmission rate among 561 African women given neither antiretroviral drugs nor placebos was 12%. That's lower than the 13.1% rate triumphantly claimed by Guay as the benefit of administering nevirapine. Which is to say the Ladner study supports the conclusion that pregnant African women left to have their babies unmolested by white missionary AIDS doctors like Jackson and Guay actually do best of all.

Apart from a theoretical grasp of some of the basics for the proper conduct of a clinical drug trial – even as she watched her study fall apart – Guay was wise to a couple more things. Such as

maternal viral load must be substantially decreased by the time of labour or the baby must have systemic concentrations of active drug present at the time of HIV-1 exposure to successfully lower risk of transmission.

But then without batting an eyelid she went on to report: ‘Maternal plasma HIV-1 RNA levels were ... not significantly different at delivery from baseline.’ Which is rather hard to reconcile with her claim that the drug worked as hoped. To lower transmission risk by lowering the concentration of viruses in the mother. Since it turned out not to.

We'll just accept for now that a 'viral load' count indicates the number of HIV particles in your blood. We'll block our ears to Nobel Laureate biochemist Dr Kary Mullis's complaint that it doesn't, and that the test is an abuse of the PCR technology that he conceived, for which he won the Swedish honour.

With the effectiveness of nevirapine for the purpose of reducing maternal 'viral load' in the can – Guay's first condition for efficacy – let's turn to the second one: '... the baby must have systemic concentrations of active drug present at the time of HIV-1 exposure to successfully lower risk of transmission.' What she meant by a 'systemic concentration' is enough of the drug in the blood to equal or exceed its inhibition concentration (IC50), i.e. a concentration high enough to inhibit viral replication by half, as determined by the usual indices. Guay whimsically picked a generous figure of 100 ng/ml, being ten times the IC50 of nevirapine asserted by the manufacturer in 1990 – although two years later other scientists reported nevirapine's IC50 value as being double that, with both values being determined, however, in highly artificial laboratory conditions with no relevance to the real world.

Guay happily told us that a pill of nevirapine given to pregnant mothers going into labour achieved drug concentrations surpassing her arbitrary 100 ng/ml concentration. The trouble is that Havlir et al. reported in the *Journal of Infectious Diseases* in 1995 (171: 537-45) that in vivo (as opposed to tricks in test tubes) the minimum concentration of nevirapine for a virological response is 3.4 to 8 µg/ml. But in no case did the nevirapine plasma concentrations that Guay achieved come anywhere even close to that. Meaning that with the dose that she gave Guay was unable to achieve systemic concentrations of nevirapine in the babies sufficient to prevent HIV replication and thereby reduce the risk of HIV transmission from mother to child. Either before or during birth. Or after it during breastfeeding. Which is another way of saying that nevirapine given as described couldn't possibly be doing what Guay claimed it was.

Nonetheless, at the end of the study Guay's exciting bottom line was this: the transmission rate (assessed at 14-16 weeks) among mothers on AZT was 25.1%. On nevirapine it was 13.1%. On this

basis nevirapine was declared 48% more effective than AZT. And Christ we've never heard the end of it.

Since it's accepted by everyone that babies inherit their mothers' antibodies when born, and AIDS doctors therefore forswear HIV antibody tests for ascertaining mother to child transmission, you would be right to wonder how the 'transmission rate' was determined in HIVNET 012. Guay explains:

HIV-1 infection [*among babies*] was defined as a positive qualitative HIV-1 RNA assay confirmed by a quantitative HIV-1 RNA assay or HIV-1 culture on a second blood sample. If babies died after only one positive RNA assay on the sample, we classified the baby as being infected.

No matter what caused the baby's death – an adverse drug reaction, a bad heart, whatever.

It's just a pity that Guay never got around to reading the instruction manuals that came with her PCR-based RNA test kits. Had she done so she would have read Roche Diagnostics stating in regard to its qualitative RNA test used in her study: 'For research use only. Not for use in diagnostic procedures.' Not for diagnosing whether babies are infected or not. And the quantitative RNA test used by the researchers on babies to confirm the result of the first improperly used qualitative test carries an explicit prohibition against just that: 'The Amplicor HIV-1 Monitor test is not intended to be used as a screening test for HIV or as a diagnostic test to confirm the presence of HIV infection.' This is because it's non-specific – too hit and miss. Not reliable enough to hang a diagnosis on. Our very own National Institute for Virology (now sexily renamed 'for Communicable Diseases') goes along with the FDA about this, which has accordingly licensed Roche's quantitative Amplicor HIV-1 Monitor test in the US for prognostic purposes only, i.e. to monitor people already diagnosed HIV-positive by means of a completely different kind of testing technology.

Roche's RNA assays for HIV are hopelessly inaccurate for HIV diagnosis, the US Centers for Disease Control agrees with everyone; they're not reliable enough even for screening donated blood for possible infection and rejection by pouring it down the sink. Let alone telling someone that they've got the sex virus in them and are going to die. But inexplicably, without rhyme or

reason, and unable to explain why when asked, the CDC relaxes the rule for babies. For them, the CDC says, RNA assays are as true as an atomic clock. Sometimes anyway: for keeping count of babies putatively infected by their mothers the RNA test is fine, says the CDC, but not in cases of suspected infection by blood transfusion or in any other way, in which cases the CDC reverts to its ban on the use of RNA assays to determine whether babies have the virus in them.

But the final nail in the coffin of HIVNET 012 is the fact that the CDC supports the exceptional use of RNA assays in possible mother to child HIV transmission cases for ‘surveillance purposes’ only, and not for making a ‘clinical diagnosis’ of HIV infection – just as the HIVNET 012 researchers proceeded to do, ignoring as they did so: (a) the explicit prohibitions of the manufacturer of the tests against using them for making diagnoses; (b) the specific, circumscribed licence for RNA test use issued by the FDA, which limits its use to prognostic monitoring of confirmed infections; and (c) the qualified exception cooked up by AIDS doctors in the CDC, in defiance of the manufacturer and the FDA’s aforementioned restrictions, allowing the use of RNA tests for determining HIV infection in mother to child transmission cases, but not via blood transfusion or any other route, and ‘for surveillance purposes’ only, and not for making a ‘clinical diagnosis’.

On the strength of clinical diagnoses of HIV infection among babies made on the basis of results they got from the prohibited tests, the HIVNET 012 researchers staked their claim that nevirapine is effective in preventing mother to child transmission of HIV. But hang on, we’re AIDS doctors. Are you suggesting we’re illiterate and incompetent clots?

In his answering affidavit filed in the TAC’s nevirapine case (coming up) the MCC’s Jonathan Levin alluded clumsily to some of the trouble with diagnosing babies using PCR (RNA) tests – in doing so, missing all their basic non-specificity problems. On the use of such tests for diagnosing babies, the statistician shared his wisdom with us as follows:

It is also possible that the PCR test used at 6 weeks gave some false positives. A study by Glenda Gray on the influence of breastfeeding on MTCT found a number of indeterminate PCR

results. A paper by Zijenah et al. states that the use of PCR for diagnosis of HIV infection has been hampered by a lack of suitable primers for clade C viruses. In addition in September 2000 (after the Petra and SAINT PCR tests were done) Roche announced the development of an improved PCR kit. Thus virologists should be consulted to comment on the reliability of PCR particularly at 6-8 weeks.

As if they'd know better than the manufacturer of such tests. The fact is, all you have to do is read the instruction book that comes with any PCR-based HIV-RNA assay. It says it all. You cannot diagnose HIV infection with PCR tests. Period.

These most basic problems aside, let's dwell for a moment on the sense of giving pregnant women nevirapine as they go into labour in order to prevent mother to child transmission of HIV. A very poisonous chemical, it's well known. Even a little bit, the CDC warned doctors and nurses on 5 January 2001 – contraindicating it for just a couple of weeks of prophylactic treatment in the case of needlestick injury.

AIDS doctors tell us that unlike other viruses HIV is a retrovirus with especially scary powers: it burrows into and becomes part of our DNA; that infected pregnant women can infect the babies they are carrying; and that a single pill of nevirapine administered to the mother during labour can prevent this. But if the mother's virus has had nine months to reach the baby through the placenta, the umbilical cord, and all those shared fluids, and thereafter ingratiate itself into the baby's DNA, would someone care to explain the value of the magic pill? How it can possibly prevent anything? Particularly since administration of nevirapine alone has no effect on CD4 cell counts and no significant effect on 'HIV RNA'.

Since nevirapine's alleged pharmacological activity is reverse transcriptase inhibition, the drug is notionally only able to prevent the infection of new cells, not eradicate HIV from already infected cells, or prevent such cells from expressing new HIV particles. So if the child is 'infected' by the mother while in the womb during the nine months it is being carried, administering nevirapine to the mother as she goes into labour is completely pointless. As is giving it to the baby: the drug concentration in the baby's blood achieved by the recommended dose of 2 mg/kg following birth is much

lower than the concentration determined to be necessary for an antiretroviral action. Likewise the concentration of the drug found in breast milk, so it can't prevent infection via breastfeeding either.

But irrespective of this Guay claimed: 'Most vertical transmission occurs during active labour because of maternal blood transfusions to neonates and direct exposure to virus during passage through the birth canal', citing a couple of speculative studies proposing that mothers infect their babies during labour and birth. Which makes it difficult to understand why in the West AZT is administered for many weeks before it. Especially since it doesn't reduce maternal 'viral load' either.

British AIDS doctors aren't too sure about this last-minute infection story anyway. Certainly not in all cases. A report put out in April 1998, *Reducing Mother to Child Transmission of HIV in the United Kingdom*, by the Royal College of Paediatrics and Child Health, hooked up with other top boffs, states: 'Indirect evidence suggests that in the absence of breastfeeding about two thirds of infections are acquired around the time of delivery.'

Part One of this book noted that the ostensible benefits of administering nevirapine (per CD4 counts) were observed only in people 'with HIV infection who have experienced clinical and/or immunological deterioration'. But the overwhelming majority of pregnant women who light up HIV antibody tests are healthy. (In fact, Guay pointedly excluded women with health problems.) And nobody looks at whether their CD4 cell counts are within what AIDS doctors consider (arbitrarily) to be a normal range.

What's more, 'nevirapine is only recommended for use in combination with at least one other antiretroviral agent in the nucleoside analogue class'. Because notwithstanding how allegedly 'potent' it is (according to Boehringer Ingelheim's *The Role of Nevirapine in HIV Therapy* information release) the manufacturer admits that it's ineffective on its own no matter how much of it and for how long you take it. Yet it's claimed by AIDS doctors to work its magic solo with a single dose when given to pregnant women and their babies. Irrespective of the mothers' CD4 cell counts or clinical health status. Brilliant.

In *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence*, a

monograph published on 1 October 2001 and submitted to the South African government the following month, Papadopulos-Eleopulos and her colleagues (me included) point out another basic problem with giving nevirapine to women entering labour: it takes an average of 4.6 hours for an oral dose of 200 mg to reach its maximum concentration in the blood. Since women generally deliver at between 0.9 and 10.5 hours after dosing, and nevirapine takes between one and eight hours to reach maximum plasma concentration, an unascertained number must give birth before the target concentration can be reached. In fact, as we've discussed, it never is.

Nevirapine may be completely useless, but does it do any harm to give it? Guay's take on it was this:

Although the zidovudine and nevirapine regimens we used seemed safe, long term follow up of the babies remains a high priority to find out about possible long-term toxic effects.

But what did her data say? About the immediate short-term ones? About the safety of the drugs? About evidence of poisoning with the poisons?

Nevirapine, we read in Part One, is extremely toxic. Would it come as a surprise then to learn that in HIVNET 006, the toe-in-the-water trial that preceded HIVNET 012, a chilling four African babies out of the twenty-two treated with nevirapine by Guay and her associates died? Twelve 'serious adverse events' were reported, but the researchers didn't connect them with the drug. But then we've read enough already to know that this bird wouldn't recognize a toxic reaction if it hit her between the eyes.

In HIVNET 012,

The rates of maternal serious adverse events were similar in the two groups (4.4% in the zidovudine group, 4.7% in the nevirapine group). One mother in the zidovudine group died 2 weeks after delivery and had bronchopneumonia. One serious event, anaemia, was possibly associated with zidovudine, but excessive blood loss at delivery may have accounted for the anaemia. The occurrence of clinical or laboratory abnormalities in mothers was similar in the two groups (82.2% in the zidovudine group and 80.7% in the nevirapine group had

at least one such event). The most frequent adverse clinical event was bacterial or viral infection, occurring in 18.2% of women receiving zidovudine and 20.4% of those receiving nevirapine, followed by parasitic infection in 12.4% and 15% respectively, followed by anaemia in 10.5% and 13.1% respectively. Nine mothers (four in the zidovudine group, five in the nevirapine group) had maculopapular rash, but no case was serious.

The sky-high incidence of ‘laboratory abnormalities’ detected after the drugs were given were not specified in the report; Guay didn’t think it important to identify them. The development of infectious illnesses in about one in five women on the trial following ingestion of the general metabolic poisons didn’t draw any comment either – even though the FDA itself pointed out in a press release concerning AZT on 5 March 1990 that it ‘may reduce white blood cell counts to the point where the drug has to be discontinued to avoid infections’.

As for the effect of the poisonous drugs on the babies, Guay reported that

The rate of serious adverse events in the two groups [*of babies*] was similar up to the 18-month visit (19.8% in the zidovudine group. 20.5% in the nevirapine group), with the median age at last visit being 183 days ... The most frequent cause of serious adverse events within 56 days of birth were sepsis, pneumonia, fever, congenital anomaly, asphyxia, and dyspnoea. [*Eighteen babies were reported to have suffered maculopapular rash, and twenty-two anaemia.*] The frequency and severity of laboratory-detected toxic effects, including neutropenia [*depleted immune cells*], thrombocytopenia [*depleted clotting platelets*], and abnormalities in creatinine [*energy metabolism*] or bilirubin [*breakdown product of haemoglobin*], were similar in the two groups.

But again, Guay didn’t think to share the numbers with us.

38 babies (6.8%) died (22 (7.9%) in the zidovudine group, 16 (5.7%) in the nevirapine group). The most frequent causes of death were pneumonia, followed by gastroenteritis, diarrhoea, dehydration and sepsis.

None of this would have come as a surprise to any switched-on toxicologist. Haddad et al. point out in their textbook *Clinical Management of Poisoning and Drug Overdose* (W.B. Saunders Company; 3rd ed., 1998):

The physiology of the newborn is unique [in the manner in which ‘drugs are absorbed, distributed, metabolized and excreted’], and organs that have an important role in susceptibility to and the moderation of toxic reactions, such as the liver and kidney, are immature in their function. As a result, the manner in which the neonate handles a toxic exposure is frequently quite different from the response of an older child or adult.

In short, babies are incomparably more susceptible to drug toxicity than adults, so reducing an adult dose of a dangerous drug per body weight for a baby does not result in a correlative reduction of risk for drug injury or fatality.

Of the ‘long-term toxic effects’ that Guay considered a ‘high priority to find out about’, one she never thought of was the effect of dosing a baby just entering the world with a neurotoxic chemical good at damaging tender brains, particularly in the light of the *Physicians’ Desk Reference’s* note that ‘Animal studies have shown that nevirapine is widely distributed to nearly all tissues and readily crosses the blood-brain barrier.’

Writing in the *British Medical Journal* on 13 April 2002, Wise et al. reported ‘Neuropsychiatric Complications Of Nevirapine Treatment’ in three adults, all of whom attempted suicide following the development of ‘delirium, an organic affective state, and an organic psychosis’ evidenced by

low mood ... cognitive impairment and clouding of consciousness ... impaired consciousness ... visual hallucinations ... persecutory delusions and depressive thoughts.

The ‘nevirapine treatment was clearly related to the evidence of symptoms’, the psychologists found. The sort of drug sure to give babies a nice sunny start.

A further report in *AIDS* in September that year by Morlese et al. discussed similar case studies with the title of their paper asking

tellingly: ‘Nevirapine-induced neuropsychiatric complications, a class effect of non-nucleoside reverse transcriptase inhibitors?’

The particular vulnerability of babies to neurotoxic chemicals is illustrated by the hexachlorophene debacle in the middle decades of the twentieth century, in which an antiseptic in the dioxin class considered safe for decades was finally banned in the US in 1976 from soaps and other products when it turned out to be a neurotoxin causing seizures and death in numerous babies washed with it – thirty-four killed in a Parisian hospital in 1972 alone.

But anyway, on the basis of a one in five incidence of serious adverse events and an almost 7% death rate among the babies treated with nevirapine and AZT in the HIVNET 012 trial, would you also have deduced – especially without placebo and untreated controls for comparison purposes – that the ‘zidovudine and nevirapine regimens ... used seemed safe’? Being a person in your right mind? In your sound and sober senses? Compos mentis? Having a normal IQ?

And a person with any kind of ordinary moral sense? Remember that in recommending the administration of nevirapine to mothers and their babies, the HIVNET 012 researchers cautioned that ‘long term follow up of the babies remains a high priority to find out about possible long-term toxic effects’. In other words, without having first conducted conventional animal studies to determine the safety of nevirapine administration to babies, the researchers were evidently unconcerned about the ethical implications of conducting an experiment on African children to ‘find out’ whether they might be seriously and permanently injured by nevirapine’s ‘possible long-term toxic effects’.

The risk that South African babies born mostly to poor Black mothers might suffer ‘possible long-term toxic effects’ from even a single dose of a drug as extremely poisonous as nevirapine cannot be underestimated. Thalidomide, the most notorious pharmaceutical drug disaster in the modern era, provides an object-lesson in this regard, even if the toxic drug exposure in question occurred a few months earlier in the child’s development (and the incidence of deformity was relatively rare having regard to how many millions of doses of thalidomide were consumed). Goth recounts in *Medical Pharmacology* (Mosby, 9th ed., 1984):

The piperidinedione hypnotic thalidomide was responsible for thousands of children with disastrous defects such as absence of limbs. This occurred especially in Germany. Pregnant women ingesting a single hypnotic dose of the drug between the twenty-fourth and thirty-sixth day of their pregnancy have delivered severely deformed babies.

And whether South African children suffer liver and other organ damage, and or brain damage and or impairment – initially sub-clinical and therefore not apparent to doctors – on account of their exposure to nevirapine as babies, will be only be evident in time, which is to say when the experiment upon them is complete and the damage is already done.

Another lesser-known drug disaster serves as a precedent for the potential in this regard: hundreds of thousands of women were urged by their doctors to take the synthetic hormone diethylstilbetrol (DES) between 1938 and 1971, advertised by its manufacturer

for routine prophylaxis in ALL pregnancies ... 96 per cent live delivery with desPLEX in one series of 1200 patients – bigger and stronger babies, too. No gastric or other side effects with desPLEX – in either high or low dosage.

Thousands of women exposed to diethylstilbestrol in utero later developed ordinarily rare clear-cell adenocarcinoma of their vaginas and cervixes in adulthood, and suffered structural changes in their reproductive organs (virilization), infertility, ectopic pregnancies, miscarriages, and preterm labour and deliveries. The damage caused by the drug was only evident decades after administration.

As word of HIVNET 012 got about in South Africa, AIDS doctors, activists, pharmaceutical regulators, health officials, opposition politicians, journalists and human rights lawyers all became tremendously excited. Here was rock-solid proof that nevirapine would effectively save our babies' lives. Our black ones. AZT for pregnant women was dropped like a hot plate. Now the roar was for nevirapine. In just about every newspaper just about every day.

On 16 November 1999 Tshabalala-Msimang mentioned the drug in Parliament, reporting that a

clinical trial was done, both with AZT, and with a new drug called Nivirapine [*sic*]. The trial was done as a joint Uganda/United States study. The drugs were given to the women once during labour and delivery and the babies were given one dose within three days of being born. The final results of the study have not been published yet, but in the interim analysis, the team looked at 308 women who had taken AZT and 310 who had taken Nivirapine, and the Nivirapine was markedly more effective. Nivirapine was also safer, less expensive and more practical than AZT or any other drug tested so far, in preventing MTCT. Nevertheless, Nivirapine is still not registered in Uganda for mass administration for the prevention of MTCT. In terms of affordability

though, she said nevirapine would cost ‘R30 per mother and child’ versus ‘R400 per mother’ for ‘the short course of AZT, as given in the Thai study’.

This will mean that many countries that could not adopt drug strategies that involved AZT, because of the cost, could now adopt a strategy with Nivirapine, that could lower the rate of MTCT. Comparative studies are currently underway in South Africa to look at Nivirapine as compared to the short course in AZT (the Thai Trial) and the short course in AZT plus 3TC (the PETRA Trial). The findings of these cost-effectiveness studies are expected in March 2000. They will provide critical information for policy making around MTCT of HIV in South Africa. Until then, we simply do not have enough information, either on the affordability or on the appropriateness of the drugs to make any decisions that might have long term health effects on the lives of children born to HIV positive mothers.

Glenda Gray, director of the Chris Hani-Baragwanath Hospital Paediatric AIDS Unit, naturally went for it like a barbel for a blob of *phutu*:

It’s your magic bullet. One pill to the mother, one pill to the baby, and you halve your transmission rates. ... The scientific

evidence we now have is dramatic. We can, without any doubt, block transmission of the virus from infected mothers to their children. The only question to me is why aren't we doing everything we can to do it?

The MCC's Dr Jonathan Levin later spoke the same stupid way in an answering affidavit that he made in the TAC's nevirapine case: 'NVP would save 10 out of every 100 babies born to HIV-positive mothers ... HIVNET 012 provides conclusive evidence of the efficacy of NVP.' With friends like these on your side, who needs enemies? Is it any wonder the government lost the case? As we're still to read, Levin backtracked after the case was over, but by then of course the damage was done.

On 7 July 2000, two days before the start of the 13th International AIDS Conference in Durban, Boehringer Ingelheim issued a press release, offering to supply nevirapine free of charge to South Africa and other developing countries for five years. It 'can fill a critical need in the developing world', the company said. 'We hope that our initiative for the prevention of mother-to-child transmission will help make an impact on the HIV/AIDS epidemic.' International AIDS Society president Mark Wainberg was delighted: 'I don't think that anybody expected [the offer]. I think that industry is absolutely prepared to change its view.'

Instead of acclaiming Boehringer Ingelheim's heart-warming philanthropy, ACT UP New York, Philadelphia and Paris condemned it in a joint statement the next day:

An announcement of a donation, with no plan at all for providing for the care of the mother or child is completely unethical. Multiple issues are not substantially addressed, including informed consent, voluntary counselling and HIV testing, and breastfeeding.

It's completely unethical not to tell women not to breastfeed.

Rejecting Boehringer Ingelheim's offer, Tshabalala-Msimang rightly pointing out that the drug hadn't been licensed for perinatal use in South Africa; and anyway, she added at the conference, 'We don't believe that the only way to prevent mother to child transmission is by using AIDS drugs.' The TAC reacted to this by threatening litigation against the government to force it to believe

differently. Actually it was just posturing at this stage. Behind the scenes its lawyers had advised it that since nevirapine wasn't yet registered for this indication it didn't have a case.

'Do we sentence children to death by applying an all-or-nothing principle?' responded International Association of Physicians in AIDS Care president José Zuniga to the government's decision.

It will require a great deal of political and social courage to address the rationing issue. The sooner South Africans have that public conversation, the better off the nation will be. The longer you defer, the more lives are at stake.

But what had rationing got to do with it?

Three days later some AIDS doctors at the University of KwaZulu-Natal's Nelson R Mandela Medical School announced that they would be presenting proof at the conference that one dose of nevirapine each for a pregnant woman and her child worked just as well as multiple doses of AZT and 3TC. Salim Karim, the MRC's AIDS research head and Durban AIDS Conference Scientific Programme director, described this as 'amazing'. Like, wow.

Celebrities scrambled to join in the campaign for the drug in South Africa: Nelson Mandela, Desmond Tutu, Jimmy Carter and Bill Gates among them. But it was only in South Africa that this unreal drive took off, because American and European AIDS doctors didn't see it the way the aforementioned nevirapine fans did – as the ANC pointed out later on in a press statement on 10 March 2002, deploring Carter's deprecation of the government's reservations about the drug, after meeting Mbeki and Tshabalala-Msimang the day before during his tour with Bill Gates's father to turn up the heat on the government to supply it.

Timothy Trengrove-Jones reported the TAC's then empty threat to sue in the *Mail&Guardian* on 8 September 2000:

In the bleak days of intensifying crisis, [the TAC's] courageous move is early evidence of the development of a concerned population willing to tell this country that if the government won't take the lead in addressing what the government itself sees as our pre-eminent emergency, there are the skills and the means to force our leaders to realise their obligations.

(Wits University actually employs this arse to teach English.)

Tshabalala-Msimang responded in Parliament on the 18th: because the drug was not registered by the MCC for perinatal administration, the government would be increasing

research on operational challenges of providing the drug for free in all provinces [but] I wish to stress that it is very important for us to grasp some of these international concerns [about nevirapine] so that we do not in our passion and determination to act start conveying messages that are inaccurate.

Nobody outside was listening.

On 18 April 2001 the South African Medicines Control Council finally approved nevirapine on a conditional basis for experimental use to prevent mother to child transmission of HIV. A few weeks later, on 8 June, Tshabalala-Msimang approved the administration of the drug to HIV-positive women in labour and to their newborn babies at eighteen pilot sites around the country (two in each province), in a cautious exploratory trial to be conducted over two years and supervised by the Medical Research Council. This was in line with a resolution taken in August the previous year by Health Minmec, a committee made up of Tshabalala-Msimang and the country's nine provincial health MECs, that government policy not to use AZT would continue and that nevirapine would be tried out on a limited scale instead.

The Minister resisted the call for a large-scale roll-out:

It would be immoral and unethical for government, despite numerous requests it had been receiving, to make policy decisions on using the drug in South Africa until the full results of the clinical trials were available. This is true for any country in the world, and I am at a loss to understand why South Africa should proceed with any less caution than any other country does.

The logic was crystalline. But the judges wouldn't see it.

On 22 June, in a special hour-long multimedia 'Face to Face with the President' interview broadcast over national television, thirty-five radio stations, and online, Mbeki responded to callers' questions on a range of subjects. There'd been 'hundreds of calls on HIV/AIDS', said anchor Tim Modise sitting with Mbeki in the SABC's Cape Town studios, and from the way the issue was

prioritized in the interview, evidently many more than on any other topic. Linked by satellite in the Johannesburg studios, John Perlman distilled a caller's question by asking:

Mr President, there are lots of questions on HIV/AIDS. I want to focus on the general area of treatment, on the issue of mother-to-child transmission. In mid-August last year, the government made a commitment to set up research sites for the administering of the drug nevirapine across the nine provinces. Ten months later only three provinces have actually put that into practice. Why is that?

Mbeki's reply revealed his interest in and knowledge about the drug, and his concern about it. Masterfully deploying the AIDS doctors' own mumbo jumbo about the disadvantages of giving nevirapine to mothers and babies, and emphasizing their own uncertainty about its use, he responded:

You are indeed quite correct; we took that decision and announced it. The Minister of Health and the MECs for Health have been working on this issue. I have had a meeting with them on this particular question, and we agreed that they must go ahead and roll out the programme. We must understand, John, that it is actually a complex matter. One of the questions that has been raised with regard to nevirapine, is that the mother who gets this drug should not breastfeed for a certain period of time, because if they breastfeed, then this child will become HIV positive two years on. So the question that we need to ask with regard to a rural mother living in a poor area with no clean water as yet, no electricity and so on is, how are they going to feed this child? If you have given her nevirapine, it means that she must feed the child on food that she buys from shops and which has to be prepared. How do you sustain that? It certainly is a question. When the Medicines Control Council licensed nevirapine in this country, it said there remained unanswered questions about the use of drug and said various kinds of scientific work had to continue in order to deal with these questions. One of the issues I have raised is about mothers who are not allowed to breastfeed under the conditions I have been describing. But there are also the

scientific questions. Then as I say, in certain circumstances it is said that if the child becomes HIV positive again, he/she won't respond to other medicines. So the trials that are being done have also got to attend to matters like that. Therefore you need equipment, qualified personnel, the necessary controls and so on, to be able to do a proper controlled scientific experiment to find out what the truth is. So it is not simple.

Perlman pressed:

No, it is not a simple matter, Mr President, but may I ask, how much is your view on these things conditioned, to some extent, by your own belief in the science around HIV/AIDS. I ask that because in an interview in April you were asked whether you will consider taking an Aids test. Your response was: "It's setting an example within the context of a particular paradigm." You went on to say the following to your international panel: "One of the things we have to do is determine the following – when we do an HIV test, what is the test testing, what is it measuring?" Now if you are expressing doubts about the efficacy of an AIDS test, it would logically follow that you will have doubts about drug interventions in dealing with HIV/AIDS. Is that a major factor in all of this?

Mbeki made clear that his personal scepticism about the entire AIDS drama was one thing, formal government policy another:

Not at all. You know what the government policy is. The government policy is that there is HIV/AIDS, and various things follow from that. That is the basis on which the government in acting with regard to the development of vaccines, testing of nevirapine, and so on. It is based on that. Whatever I think won't impact on what the government is doing, and the government is doing what the rest of the world is doing with regard to this matter. But nevertheless, as you can see, I was saying just now that when the Medicines Control Council licensed nevirapine it said there are unanswered questions. I am sure not many people in the country know that. So they will say I won't give out nevirapine when the medical authorities themselves are expressing concern about various matters, which you have got to try and

follow. You have got to pursue this. Earlier this year, the US medical authorities radically changed the instructions with regard to the prescription of antiretroviral drugs.

Perlman tried cornering him: ‘With regard to adults and adolescents though.’ But unsuccessfully; Mbeki pointed up the general implications:

Yes, surely with regard to adults and adolescents. What I am saying is that arising from their own experience in the United States, they said that these particular regimes that we have been following in the past, are no good. Let’s change them. The scientists must do their work, and I don’t think it is correct to say that science must freeze up.

Modise:

If I may come in, Mr President, and ask for a brief response to this question – the Secretary General of the United Nations, Kofi Anan, has announced that he wants to raise about \$10 billion for what he calls the Global Aids Help Fund. Now if the United Nations raised this money and bought some of these drugs and made them available to South Africa, would we accept them, would we use them?

Mbeki responded, ever the statesman:

These drugs are licensed and there is no problem in using them. They are all of them licensed. Whether it is nevirapine or AZT and so on, they are licensed. They are available. They are legal and they are in the health system, they are in the public health, in the public hospitals. I mean people who for instance get needle stick injuries and so on, medical personnel, they have access to these. So there would be no problem about that.

Modise sought to drive home to checkmate: ‘Even if it were to be used for mother-to-child HIV?’ But Mbeki skilfully sidestepped a show-down:

Yes, I mean the reason we are doing these trials with regard to nevirapine is to be able to see how we overcome the problems that have been indicated by scientists. You solve these

problems and therefore say that we have got the capacity in fact to dispense.

On 20 September Mbeki responded to further questions on AIDS from the Opposition in Parliament, and specifically regarding the provision of ARV drugs to pregnant women. Again, he underscored the distinction between his own private views and government policy, and highlighted medical uncertainty over nevirapine, which, he said, had not been registered anywhere in the world for giving mothers and babies and was still under consideration by the WHO.

Guay herself seems to have entertained some quiet doubts about the drug. The single-shot nevirapine treatment – safe she claimed – would spare mothers and babies in the First World the horrible AZT toxicities suffered following longer exposure that have been showing up in paper after paper in the medical journals. But Guay pulled back from recommending nevirapine instead:

we cannot judge the efficacy of the nevirapine regimen used in our study compared with the full three-part zidovudine regimen that is currently the standard for prevention of transmission in more-developed countries. The data from our trial do not change recommendations in the USA and Europe for ... use of the three-part zidovudine regimen for prevention of transmission.

Why not, if one dose of nevirapine was so effective? And perfectly safe too. Why not? Guay concluded the report of her drug trial with some self-promoting sales-spin:

Single-dose nevirapine given to the mother and the baby is likely to be one of the few deliverable and sustainable strategies for prevention of perinatal HIV-1 transmission in resource-poor settings. The challenge is to rapidly translate our findings into public-health policy to bring an effective HIV-1 intervention within the reach of millions of HIV-1 infected pregnant women.

We see it differently, Laura. We think you and your colleagues should be struck off for dangerous incompetence. And the identities of the anonymous peer-reviewers, who approved your

dismal paper for publication in *Lancet*, should be revealed, so that they can be publicly shamed for doing so. Perhaps marched down the journal's nearest high street in dunce caps, along with those twenty-two 'top names in South Africa's scientific and medical community', reported by the *Cape Times* on 22 March 2002, including 'AIDS experts' 'Slim' Karim, 'Jerry' Coovadia and Carolyn Williamson, who co-signed a 'declaration' published in *Lancet* in the same week to the effect that 'the fundamental scientific evidence in favour of nevirapine is incontrovertible' and that the government should accordingly 'distribute the drug without delay'.

Joined in the parade in the same hats we'd like to see Zackie Achmat, Nathan Geffen and Mark Heywood of the TAC (they like marching), Nicoli Natrass and the rest of the mediocrities who supported the TAC's application to the High Court to force the government to supply the drug, followed by Edwin Cameron, Costa Gazi, Glenda Gray and James McIntyre, along with Howard Barrell, Belinda Beresford, John Perlman, Sally Burdett, Lynne Altenroxel and their fellow white journalists who've had so much to say, and who love getting righteously indignant in radio and television interviews and articles knocking recalcitrant black health officials who don't share their enthusiasm for giving cell-poisons to black babies. Not forgetting former Catholic priest and struggle hero Father Cosmas Desmond, who asked in the *Mail&Guardian* on 8 March 2002, 'Can Manto Tshabalala-Msimang really be as abysmally stupid as her actions suggest?' in view of her reservations about nevirapine toxicity in the long term (shared by the HIVNET 012 researchers) in the absence of any available data.

In the meantime, the rather short-term effects of her – and puppeteer-in-chief Thabo Mbeki's – policy of not providing the drug to all HIV-positive pregnant women is killing tens of thousands of babies every year.

Really?

The extraordinary thing about this widely believed notion, publicly expressed by Desmond and privately at white suburban dinner parties at the time, is that there is nothing in the medical literature to support the idea that babies born to untreated mothers have a worse prospect of surviving than those who are treated. Nor

is there any good evidence for the root belief among most whites that babies born to HIV-positive mothers are doomed to die early. To the contrary, numerous studies (canvassed in my book *Poisoning our Children: AZT in pregnancy*, online) show that babies exposed to these chemicals in utero have far higher rates of death, disease, brain damage, immunological disorders and birth defects than the unexposed. An unpalatable reality, but not a surprising one to people who take the trouble to look at the pharmacology of such drugs for themselves. Instead of asking the doctor. Whose knowledge of such matters derives from what the visiting bimbo in the red BMW from the drug company told him, or what he read in the newspapers and in the glossy advertisements in his professional journal.

The real ‘challenge’, we think, is to keep American AIDS doctors like Brooks Jackson and Laura Guay out of our country. And as far away from our people as possible. According to Guay’s report, ‘During screening for our trial, many women refused to be counselled or tested or did not return for their test results.’ Good on them. Spurning the doctors’ inherently ridiculous new dogmas, just as their ancestors did the equally horrible, morbid ideas being sold by missionaries before them.

In her *Hopkins Medical News* article ‘The Pathologist Who Struck Gold’, Swingle claimed cluelessly that the HIVNET 012

data proved stunning. It showed that nevirapine was 47 percent more effective than AZT and had reduced the number of infected infants from 25 to 13 percent. Best of all, nevirapine was inexpensive – just \$4 for both doses. If implemented widely, the drug could prevent HIV transmission in more than 300,000 newborns a year. Jackson’s findings were announced jubilantly in Kampala, by the Ugandan Minister of Health. In the United States, on July 14, 1999, Vice President Gore broadcast the news around the world. Today, Hopkins AIDS researcher Tom Quinn, of the Division of Infectious Diseases, defines Jackson’s study as a breakthrough in the prevention of mother-to-infant transmission. ‘Make no mistake about it,’ he says. ‘What made it so important is that nevirapine is affordable and sustainable.’ Many would call the study a perfectly constructed clinical trial by a superb academician.

Swingle quoted Jackson on his involvement in HIVNET 012: 'For me, it's personally been very satisfying. But you know, we were just so lucky. We struck gold with nevirapine.' Indeed he had. At an Alpha Omega Alpha honours dinner at Johns Hopkins Medical School that year he was introduced as the highest funded researcher there, having attracted 'more than \$30 million as a principal investigator'.

Part Five

Clearly the constitution must protect the normal rights to criticise ... government public officials, to take part in free public debate over issues confronting the country ... As Thabo Mbeki, member of the National Executive of the ANC, has pointed out, freedom of expression will have a special significance in a new South Africa.

Albie Sachs, *Protecting Human Rights in a New South Africa* (Oxford University Press, 1990)

On 21 August 2001 the TAC launched an application in the Pretoria High Court for orders declaring the government's policy on the use of nevirapine at pilot sites unconstitutional, and compelling the government to forget about the pilot trial and 'to make Nevirapine available to pregnant women with HIV who give birth in the public health sector, and to their babies' without further ado.

Three days later Boehringer Ingelheim alleged that the government had accepted its offer to donate the drug to the country's maternity wards. Offering it free at first, in the style of any sharp drug dealer.

The TAC's strike against the government was smartly planned and carried out, you must admit. It got the Children's Rights Centre and a couple of paediatricians lobbying for nevirapine under the winsome moniker 'Save Our Babies' to join in as co-petitioners, backed by a list of 150 general practitioners wanting the same fix. With organizations like those twinkling at the top of the papers, could the judge really be expected to refuse to save our babies by denying the children's rights to treatment with nevirapine?

In his founding affidavit, paediatrician Haroon Saloojee spun out his abracadabra like a wizard casting a spell:

as doctors who place the health of our patients first, we would act against our constitutional right to freedom of conscience and against our ethical duty of clinical independence, if we were to deny women the right to use anti-retroviral therapy to prevent mother to child transmission of HIV. The current

policy ... denies women this right and undermines the doctor-patient relationship.

Gee, it would take a whole book to decode and deconstruct all this shit. But cringingly deferential to the wisdom and authority of doctors of divinity and of medicine alike, the judges would swallow it whole, every chunk.

On 4 November, a couple of weeks before the case was heard, Judge Edwin Cameron engaged in some thoroughly improper heavy breathing over the trial judge's shoulder during an interview on the MNet television programme *Carte Blanche*. Announcing his view of the matter, and implicitly that of his judicial brethren on the appeal court as well, he declared nevirapine to be

a very good drug. It's been offered free to our government to give to mothers who are about to have babies, and our government has not yet taken up that offer, which is a tragedy, I think.

We trial lawyers call this 'giving an indication'. Of the direction the wind is blowing in a case – and in the nevirapine one, the way it would likely go on appeal, where it was certainly to end up, whoever won. Was the trial judge really supposed to cock a snoot at Cameron and the rest of the Supreme Court of Appeal and throw the TAC's case out after this?

Amping up the moral temperature, the TAC bussed in a crowd to stand overnight vigil outside the High Court on 25/26 November before the hearing started, and then to go into court in their 'HIV Positive' tee-shirts to show the judge what for.

At another TAC demonstration in Durban on the day of the hearing, Richard Pithouse, who bills himself as a

music critic, factory worker, cashier at the Smith Street tote in Durban, trade union educator, sales assistant at WH Smith in Fulham, philosophy lecturer, and door to door salesman in the small rural towns of KwaZulu-Natal

and finally AIDS activist – sort of inevitably for a cosseted suburban white in his angry young man phase, getting involved in like really relevant politics – made the momentous announcement that he wouldn't be lighting a candle on World AIDS Day in a

couple of days time, because there was no point in lighting candles while people are dying of HIV-AIDS. 'We want nevirapine now for women who have HIV.'

In tune with Cameron's tragic sentiments, TAC counsel Gilbert Marcus SC argued before Judge Chris Botha that the pilot study policy was 'arbitrary, unreasonable and irrational ... This case is about life and death. It raises concerns about whether the newly born child will live or die.' Health Director General Ayanda Ntsaluba was trying to 'defend the indefensible' in claiming in his affidavit that the provinces didn't have the resources to expand the pilot programme to provide free nevirapine to all HIV-positive pregnant mothers. South Africa was 'in the grip of a catastrophe', he said, quoting a member of the Medicines Control Council, and without the drug about 20 000 babies would die every year. The government's position was 'not only a manifestation of irrationality', it was 'nothing short of insanity'. It was totally insane. Talk about crazy coons.

Marcus cited an affidavit by Andrew Grant, acting superintendent of Bethesda Hospital in Ubombo in rural northern KwaZulu-Natal: 'It is an easy drug to administer and we have seen no side effects on this regime (except extreme gratefulness).' The angry lawyer's next card invoked Orwell and pigs in charge: the government seemed to regard all babies as equal, except in the provinces where nevirapine programmes were being extended; there the babies 'were more equal than others'. Like in separate development: the democratic government was as foul as the apartheid one.

In his opposing argument the government's counsel Marumo Moerane SC emphasized the government's reservations about the safety of nevirapine for babies. First of all the drug's long-term efficacy had yet to be proved, he said. And

In order to give maximum benefits to pregnant women and children, you have to have phased implementation. We are trying to be responsible. ... What the health authorities are doing is reasonable and in line with international approaches. You have to adopt the cautious approach. You have a focused field in which you can do research before you send it out in the wide field. It's a reasonable approach. ... When you're dealing

with a new and potent drug like nevirapine, you have to adopt a cautious approach. We do not know what the long-term effects are. The only sensible way to deal with the issue is the present system. ... The constitution provides for a right to reasonable health services, not a right to nevirapine. That is the critical distinction. There is no established right to Panado. ... The public's demand for quick solutions would lead to extremely negative consequences. ... This is a completely new drug which necessitates the health department's progressive expansion of the frontiers of rights to health care.

But even before Moerane was done, the judge interjected to disagree. The provision of nevirapine 'should be extended all over the country as soon as practically possible', he announced. The government's practical problems with this had seemed to him impossible – until he'd read the Western Cape's papers filed in the case on how the province had succeeded in making it generally available. The light shining out these papers 'was like going into the promised land. What they did is what actually should have been done' by the other provinces. The promised land run by the New National Party relics of the apartheid regime.

Reserving judgment, Judge Botha said it 'would definitely be delivered before Christmas'. Obviously no problem with that; he'd already made up his mind, hadn't he? About how to lead the rest of the country to the promised land. For Christmas.

True to his word, Botha J gave judgment on 14 December. The *Saturday Argus* in Cape Town reported this the next day in a fat, front-page headline, 'At last: good news on HIV':

Champagne corks popped and loud cheering and hugging followed the victory judgment in the Pretoria High Court which lifted the death sentences hanging over thousands of babies born to HIV-positive mothers.

In his 'victory judgment' Botha J held:

I am of the view that the policy ... prohibiting the use of nevirapine outside the pilot sites in the public health sector, is not reasonable. It is an unjustifiable barrier to the progressive realisation of the right to health care. It is a breach of their

negative obligation to desist from impairing the right to health care.

The article reported the judge saying,

This breach could be remedied by supplying HIV-positive mothers-to-be, as well as their babies, with nevirapine. 24% of pregnant women in South Africa were HIV-positive and 70,000 children were infected each year through mother-to-child transmission of HIV. About 4.68 million people, or 10% of the population, are HIV-positive. Based on the evidence before court HIV/AIDS could be treated with antiretroviral drugs such as AZT and nevirapine. ... about one thing there must be no misunderstanding: a countrywide MTCT prevention programme is an ineluctable obligation of the State.

Here was the government being ordered by a judge to do trade with a multinational corporation, to buy its merchandise (pressed on it free at first), on the back of the successful marketing propaganda that it was essential, that it saved lives. Here was a judge declaring nevirapine to be a human right. But with Supreme Court of Appeal Judge Edwin Cameron having repeatedly promoted nevirapine and AZT from every public platform, implicitly supported by Chief Justice Arthur Chaskalson and other top judges by their attendance at the University of the Witwatersrand's special General Assembly on AIDS on 7 March 2001 to mobilize for action against AIDS (for drugs, basically), backed by hundreds of medical and allied academics at the Universities of Cape Town and the Witwatersrand, and with the general legal convictions of the community (as we lawyers say), or 'the healthy sentiments of the people' (as the Nazis did), on display on banners and placards borne by TAC demonstrators bussed in for the TV cameras, the decision was hardly a surprise. What judge would want to be universally pilloried and watch his judgment almost certainly torn up on appeal, rather than be carried out of court, so to say, on the shoulders of all those cheering AIDS activists and be praised in every newspaper? The human rights guy. Not some baby killer – like Mbeki, as *Mail&Guardian* cartoonist Jonathan Shapiro suggested in a lampoon of him ascending a Golgotha hillock of their corpses in place of a stairway

as he boarded his jet. A modern-day Herod. Except busy with a massacre of his own.

‘We’ve made history today,’ swooned TAC treasurer Mark Heywood. ‘The judgment brings hope to potentially tens of thousands of women who have HIV.’ The repeated personal tragedy in Heywood’s own life driving his drugs-to-save-babies campaign, and cluttering any kind of dispassionate, intelligent appraisal of the miraculous medicines he’d devoted to his life to selling, was revealed in a confessional article he wrote in the TAC’s newsletter on 22 August 2000:

Two of my children died shortly before or after birth. So I can remember their faces. I also know the look of a mother when she is told that her child is dead – the harrowing cry of ‘give me back my baby, it’s not true’ as it echoes through a maternity ward that is suddenly emptied of life and promise. And years of pain that follow it. ... Each year now, 70,000 infants are born with HIV. Each day, many babies and children die of AIDS. ... It is a tragedy that our government now allows this to happen hundreds of times a day.

But not to worry any more:

Every child born free of HIV as a result of this week’s decision will be living proof of the wisdom our society showed in opting for this form of democracy

proclaimed the *Sunday Times* in an editorial in the weekend. ‘The outcome shows that even strongly dominant political opinion cannot stand in the way of a Constitution that is supreme.’

Four days after judgment was delivered, Tshabalala-Msimang met with eight of the country’s provincial health MECs to discuss it. A press statement by her the following day announced:

we felt we could not allow the court judgment to remain unchallenged. ... Government takes the view that policy, including policy on HIV/AIDS, may be guided by firm principles but that it is not cast in stone. We decided at yesterday’s meeting to conduct a further appraisal of the current MTCT programme at the Health Minmec in January next year, taking into account the latest data from the current

MTCT sites. ... When it came to the legal issues, we were quite clear that an appeal against Justice Botha's judgment is unavoidable. Having examined the reasoning of the judgment and the orders made, we came to the conclusion that this judgment could have far-reaching implications in defining our constitutional democracy and in shaping the State's responsibility for the delivery of social services. We have therefore instructed our legal counsel to appeal the judgment to the Constitutional Court as soon as practicable. We consider it critical, in order to create certainty in the public policy domain, to seek the wisdom of the Constitutional Court on this matter. We would like to emphasise that this appeal is not an attempt to obstruct the development of the MTCT Programme. Rather it is aimed at clarifying a constitutional and jurisdictional matter which – if left vague – could throw executive policy making into disarray and create confusion about the principle of the separation of powers, which is a cornerstone of our democracy.

To which Heywood retorted that 'if government had responded to the ruling immediately', instead of appealing, 'as many as 50 000 lives could be saved next year'. As many as 50 000 babies were being made to die by the government. (When in business a salesman makes grand claims in round figures that decrease over time, you know he's not to be trusted. Especially when qualifying them with 'as many as', so he can get off, scuttling away like a crab, when you accuse him of lying.)

At its national executive committee meeting a couple of weeks later in January 2002, the TAC resolved to answer the government's move to appeal with an application for an interim execution order, requiring compliance with the interdict forthwith, irrespective of the pending appeal, which in the ordinary course suspended the judgment's operation. 'The justification for this,' Heywood later explained in a résumé of the case for the *South African Journal of Human Rights* (2003, 19), 'was that it could save up to ten lives a day during the period in which the legal process around the appeal took place – approximately six months.' (10 lives x 30 days x 6 months gives me 1 800 lives, not 50 000; but then maybe it's because I'm not as good at arithmetic.)

On 5 February the Colleges of Medicine of South Africa, representing 7 000 specialists and 2 000 family practitioners, implicitly threw its weight behind the TAC's legal victory in a public statement claiming it was 'unethical and against medical principles to withhold preventative treatment for mother-to-child transmission of HIV', and 'unethical to create in the minds of the public the belief that proven effective treatment is useless or even harmful'. It's unethical to think beyond the propaganda.

The United Democratic Movement sought some political mileage from the case by putting up posters in the centre of Cape Town the night before Mbeki's opening of Parliament on 8 February, featuring UDM leader Bantu Holomisa's visage captioned with a demand that the government 'stop AIDS killing' – by providing nevirapine. But they were taken down by municipal workers before the arrival of Mbeki's cavalcade (presumably because they hadn't been authorized and stamped by the municipality). About which Western Cape party spokesman Pieter van Pletzen blustered, 'We find it appalling that the Democratic Alliance city council is suppressing our constitutional right of freedom of expression.' The DA should rather concentrate on Mbeki's 'continued support of a campaign of genocide', he said. Like in Rwanda? 'If the DA doesn't have the balls to attack Mbeki's lunacy, they shouldn't prevent those who do it as a matter of conscience,' he said. He's a dictator, a mass-murderer, and a lunatic, you know. And another brandy and Coke please, George.

Opening Parliament, Mbeki confirmed Tshabalala-Msimang's statement on 19 December that the government's 'policy on HIV/AIDS ... may be guided by firm principles but that it is not cast in stone' by noting that

continuing work will be done to monitor the efficacy of anti-retroviral interventions against mother-to-child transmission in the sites already operational and any new ones that may be decided upon.

But he wasn't going to be railroaded by the people making the most noise, he said: 'Any focus on one [health] issue, at the expense of the others, may have the effect of undermining what we all seek to achieve.'

Delivering a backhanded reproof for the TAC and its supporters in all the newspapers, ANC Secretary-General Kgalema Motlanthe commented that he was 'very happy' with Mbeki's 'relaxed and balanced way' of dealing with the matter. 'It was very encouraging to hear him engage with the issue in an unemotional fashion.' If only everyone could. Like Cameron, quoted in the *Daily Dispatch* on the same day: government faced 'a moral and practical challenge ... on the provision of ARVs to pregnant women'. It 'should change its obstructive policies on mother to child transmission'.

Interviewed on SABC 3 *NewsHour* on the 10th, Mbeki reiterated the government's flexibility: 'provinces with the resources to extend the [nevirapine pilot] programme should not be delayed by provinces that did not have the resources'. Gauteng Premier Mbhazima Shilowa read this as an invitation to do just that, and announced at the Opening of the Gauteng Provincial Legislature a week later that his province's two nevirapine pilot sites would be increased: within 'the next financial year, we will ensure that all public hospitals and our large community health centers provide nevirapine,' he said, and named nine further hospitals that that would do so 'within the next hundred days'.

An almighty row broke out when Tshabalala-Msimang criticized this departure from agreed national and provincial policy as being 'contrary to the resolution'—namely to use the drug cautiously at a limited number of sites in order to establish whether it was safe and effective before widespread administration. The left and the right all joined hands to condemn her. UDM leader Bantu Holomisa called on her and Mbeki to resign; they were

only interested in semantics, dodging responsibility and undermining the efforts of others who cannot in good conscience sit by and watch a nation being decimated by a preventable disease.

Tshabalala-Msimang's objection was 'unbelievable', said the DA's Jack Bloom. Yes, said the Inkatha Freedom Party, it showed her lack of interest 'in tackling this national crisis while our people are dying like flies'. COSATU was

shocked and disappointed at the minister's statement that seeks to condemn a move that only yesterday gave HIV-positive mothers hope in Gauteng. The federation condemns the minister's stance and attitude. She should know that the time for politicising the issue of Nevirapine and anti-retroviral drugs is over.

Her criticism of Shilowa's breach of the Minmec resolution was an 'embarrassment ... a stumbling block in the fight against the pandemic'. The SACP was 'dismayed' too, denouncing her for 'the hesitancy, prevarication and lack of decisive leadership' that had characterized government policy on 'HIV/Aids in general and the prevention of mother-to-child transmission in particular'. The communists called on the government to enter into a 'full discussion' with it and with the workers in COSATU. Why, they had the answers, the answers supplied by the bosses running the foreign pharmaceutical corporations.

Notwithstanding Tshabalala-Msimang's objections to Shilowa's move, Eastern Cape Premier Makhenkesi Stofile announced alike two days: nevirapine would be made available at all clinics and hospitals in his province. Commenting in East London, PAC Health Secretary Dr Costa Gazi criticized the government's reticence over providing the drug, and claimed that in KwaZulu-Natal, wherever it was not possible to provide counselling, it would simply be administered to all pregnant women across the board:

This method has been recommended by researchers where resources are limited. The prevalence of HIV is so high – one in five mothers have HIV – that it is fully justified to do this. It is already so late in the day that not a single baby should die because of slowness in implementing mother to child transmission everywhere.

Or any other kind of slowness.

The ANC released a formal statement by Head of Presidency Smuts Ngonyama two days after Shilowa's move, making clear that he was out of line:

In the ANC's view, the Gauteng Province jumped the mark in announcing a full roll-out programme ... The ANC respects

the Health Minmec resolutions that all provincial MECs for health in ANC-led provinces, based on the preliminary report, go back to their provinces to study and further consult on the report with a view of formulating an appropriate response.

None had been drafted at the last meeting between Tshabalala-Msimang and the provincial health ministers at the last Health Minmec meeting on 31 January, he said.

Thus, any approach that deviates from this position defeats the objectives set out in Minmec in order to come out with a well-thought out, comprehensive national position on this issue.

The statement regretted the TAC's 'cheap political point scoring ... As the ANC, we refuse to be drawn into trivializing and politicising an important issue like this.'

Cabinet met to discuss the nevirapine judgment on 20 February. A statement released by Joel Netshitenzhe, director of the Government Communications and Information Service, the next day announced that

The meeting was informed that, with regard to the programme against mother-to-child transmission in particular, communication would be stepped up in the coming period to ensure that there are no ambiguities.

The text of an intended newspaper advertisement was provided, describing in some detail the 'Government's programme to reduce HIV infection in babies'; 'What happens at the research sites?'; 'What have we learned from the research?'; 'When will this service reach more people?' and 'Why is Government appealing against the court ruling?'. Apropos of the latter, it explained:

In December 2001, the Pretoria High Court said Government should make Nevirapine available to pregnant women in all public health institutions, beyond the pilot sites. Government is appealing against this judgment. This is not because we are against expanding the mother-to-child programme – that process continues. It is because we need to gain clarity on whether the courts or the elected government decides on the detail of providing health services. This is a critical question about the division of powers in our democracy. The wisdom of

the Constitutional Court should be applied to it. The appeal process will not stand in the way of health authorities expanding the programme. Any expansion of the pilot sites will continue to be guided by research results and by available resources – including human resources and the standards we have set for comprehensive care.

In his *South African Journal of Human Rights* piece, Heywood revealed that the TAC's interpretation of the government's explanation of its decision to appeal was that it was mere subterfuge – false in other words. In reality, in the TAC's view, the case was all about

the President's denialist AIDS policy ... TAC believed that the MTCT policy was based upon a political decision taken at the highest level of government. ... This case, because ultimately it was a manifestation of the President's AIDS policy, was therefore fiercely defended.

Botha J heard the cross applications for leave to appeal against the interdict and for interim compliance with it on 1 March. Again, the TAC bussed in crowds to dance on TV to create an illusion of mass popular support for its cause. TAC executive committee member Sipho Mthati alleged in her founding affidavit, on oath, that 'every day in which the implementation of [the order] is delayed results in unnecessary infection and death of ten children'. Not nine, not eleven, not approximately ten: ten dead children. Normally when you make things up in court, it's called perjury. And you go to jail. But Miss Mthati's dreadful fib wasn't challenged by the government in its answering papers – and the result was that the judge would treat it as an agreed fact, the pivotal fact on which his decision swung. It was 'not denied' by the government, he held, that the execution of his interdict could save ten lives a day. Ten babies a day, saved. From dying.

While the judge was wondering what to do, Mandela decided this was now a good time to get involved and weigh in with his sage advice. At a press conference in Johannesburg on the 3rd, attended by top ANC notables Zuma, Pahad, Motlanthe and Ngonyama, Mandela announced:

My proposal, both to the government and the ANC, is that [people be told]: We are busy conducting this research, but people who feel they can't wait for these findings must be free to consult with doctors if they wish. We can't afford to be conducting debates while people are dying. We have to ensure that our people are given the drugs which are going to help them. This is a war. ... [While the government's] important research [was being conducted], People who want to consult [a doctor] and any other person who they think can give them a drug which is going to be useful, which is going to cure their condition, must be free to do so. ... But it's important from the view of the government as a responsible organisation that if a drug is given it is safe from the point of view of toxicity. ... My view is that a perception has been created that we [*the government and ANC*] don't care for lives; we don't care for the babies that are being born almost every day by women with HIV. I am concerned that we should clear that impression. To me the only way of clearing it is to say: We are conducting these scientific researches; when we have concluded our research, we will then publish our findings ... but in the meantime people who want to [get the drugs] must be free to do so.

No doubt gratified to know he was on the side of the country's living patron saint, Botha J gave judgment a week later on the 11th, granting both applications: the government was given a certificate allowing it to take its appeal directly to the Constitutional Court, but it was ordered to comply with the interdict in the meanwhile. Were his execution order to be 'implemented,' the judge held,

and the appeal succeeds, the result will be that health facilities will have suffered some inconvenience here and there and that resources, especially human resources, will have been strained. In many cases that will be an inconvenience that ethically motivated health workers will gladly assume. At the same time there will be a gain in lives saved which cannot be considered a loss even if the Constitutional Court should find that parallel access to Nevirapine should not have been granted at all. If the order is suspended and the appeal were to fail, it is manifest that it will result in loss of lives that could have been saved. It

would be odious to calculate the number of lives one could consider affordable in order to save the respondents the sort of inconvenience they foreshadow. I find myself unable to formulate a motivation for tolerating preventable deaths for the sake of sparing the respondents prejudice that can not amount to more than organisational inconvenience.

Back on earth, though, there was no actual evidence, as opposed to fervent moral conviction all round, that any ‘loss of lives’, any ‘preventable deaths’ would result from not providing nevirapine to mothers and their babies by ‘ethically motivated health workers’—and there still isn’t.

And as for just how many ‘preventable deaths’ could be averted with nevirapine, luckily for Achmat and his TAC the judge didn’t read the blue-collar magazine *You* after work. Because in ‘Zackie Achmat – Why I won’t back down’ just over a week earlier, Achmat asserted quite different figures from those alleged by Marcus about how many babies were allegedly dying without the drugs:

If Mbeki is in denial, fine. But why put the country through it. ... And while politicians debate and ponder, South Africans – as many as 2000 a day – are dying like flies. Every month as many as 8000 babies die of AIDS.

(Again, the weasel words ‘as many as’, giving the liar away as distinctly as a badge.)

Just as the TAC’s dying babies line won the judge, it had also worked like a charm for George Bush the elder in 1991 to rally Congressional support for the first US invasion of Iraq. In ‘Remember the “dead baby” lies of ’91? The U.S. propaganda machine is back’, in the *Toronto Star* on 22 December 2002, Maggie O’Kane recounted how

the daughter of the Kuwaiti ambassador in Washington, Nijirah al-Sabah, tearfully described how, as a volunteer at Al Adnan Hospital in Kuwait City, she had watched Iraqi soldiers looting incubators to take back to Baghdad, pitching the Kuwaiti babies on to ‘the cold floor to die’. Except it never happened. The Filipino nurses who worked in the Al Adnan maternity ward, Frieda Construe-Nag and Myra Ancog Cooke,

had never seen Ms. al-Sabah in their lives. Amnesty International admitted it had been duped and Middle East Watch confirmed the fabrication, but it was too late: a marginal U.S. Congress had been swung to vote for war. Bush mentioned the ‘incubator babies’ seven times in pre-war rallying speeches. It was months before the truth came out. By then, the war was over.

Telling lies about babies dying carries the argument, apparently. (Coincidentally, Hill&Knowlton, the PR firm that invented the utterly fictitious ‘incubator babies’ story for the CIA, is one of the world’s leading marketing agents for the pharmaceutical industry and spins for Boehringer Ingelheim.)

A few days after the judgment, Mandela again lent his moral heft to the TAC’s nevirapine campaign. Opening a clinic at Qawukeni near Lusikisiki in the Eastern Cape – built by AZT manufacturer GlaxoSmithKline at a cost of R2 million in response to his challenge to do so two years earlier – Mandela urged: ‘

Many young people and babies are dying in large numbers every day. The people who are well must give them support and love, and we must make sure we give them the proper treatment.

About the proper treatment, clinic matron Nomvelo Batakati was more specific, telling the *Sunday Times* that the clinic would be dispensing nevirapine to HIV-positive pregnant women and babies ‘the moment we get our hands on it. Once it’s available to us, we will do it.’ Mandela’s spokeswoman Zelda le Grange confirmed: ‘This will be in keeping with Madiba’s proposals to the ANC that nevirapine and any drug that helps should be made available to any person who needs it’ – adding that Mandela supported the Provincial Premier’s remark that ‘nursing staff and midwives should be trained in how to treat mothers with nevirapine’.

The government promptly applied for leave to appeal against Botha J’s interim implementation order. A government press release on 17 March, announcing the appointing of 2 and 3 May as court dates for the argument of the main appeal, explained the reason for its appeal against the interim compliance order too:

At the heart of the main appeal is the argument of the Minister and the MECs for Health that the High Court stepped into the realm of policy-making in its original judgement and acted unconstitutionally in terms of the separation of state powers. The Minister and MECs decided to appeal against the recent execution order because they believe that the same principle is at stake here.

Dissenting from the *Sunday Times*'s earlier celebration of the TAC's victory, deputy editor Ray Hartley also thought the 'Judge oversteps the mark in a fit of wisdom' in a piece published under that title on the same day – to which the AIDS Law Project's Jonathan Berger responded the following week, hissing that Hartley's criticism of the judgment 'appears to be an attempt to provide succour to President Thabo Mbeki and the HIV denialists in his party and Cabinet'. Tshabalala-Msimang summed up in an article she wrote for the *Sunday Times* on the 30th:

Government not courts must decide on HIV/AIDS and other social policy. [The judgment] amounts to a position that policy should be in the hands of the judges.

WITS Law School lecturer Kevin Hopkins expressed a supporting view in 'Shattering the Divide – When Judges Go Too Far' in the attorneys' journal *De Rebus* the same month. The judgment, he agreed, was an example of what happens

when judges forget themselves and exceed the powers that they are entrusted with in performing their judicial functions ... Government policy is a political creature and this is why it is governments which make policy, not judges. The remedy for unpopular policy should rightfully be political, not legal.

Right on, except that the policy had not been unpopular, other than with the drug propagandists and the drug propagandized.

The ANC National Executive Committee endorsed the government's decision to appeal against the immediate execution order, explaining in a statement on the 20th that it was

driven by the desire to clarify the critical matter of the role of the judiciary in relation to detailed matters of public policy. It

is incorrect for anyone to prescribe a specific drug from the Bench, let alone one whose efficacy is still under investigation.

Obviously, although in their human rights enthusiasm the point would be quite lost on the learned justices of the Constitutional Court. The statement concluded by outing the TAC as a marketing agent of the pharmaceutical industry:

Where there is prophesising for doom, we stand for hope. Where there is mobilisation for despair, we call for measured, effective and sustainable programmes. Where there is focus on one issue, we draw attention to the whole gamut of actions required to fight HIV and AIDS. We are not populist. And we shall always strive to act with honesty. Not once in its history has the ANC been corrupted into acting as an agent for any force, no matter how powerful. Not once in its history has the ANC sought short-cuts when faced with difficult problems. Nor shall we mislead our people in search of an adulatory news headline.

On 22 March, the same day that Botha J heard the government's application for leave to appeal against his order for immediate interim compliance with the interdict he'd granted the TAC, the shit hit the fan in the US.

Looking forward to cashing in on the vast market opportunities generated by the publication of the HIVNET 012 findings in *Lancet*, Boehringer Ingelheim had lodged an application to the FDA for authority to market the drug in the US for the new indication they supported. It probably wished it hadn't. A look at the trial data by NIAID staffers in the Division of AIDS (DAIDS) found big problems – described by FDA spokesman Jason Brodsky as 'potentially quite serious'. As the company put it in a press release on the day the news broke,

Boehringer Ingelheim is aware that questions have been raised regarding reporting and documentation in a study conducted in Uganda for prevention of the transmission of HIV from mother-to-child during birth called HIVNET 012.

A simultaneous press statement by NIAID put it this way:

Although no evidence has been found that the conclusions of HIVNET 012 (the Uganda trial) are invalid or that any trial participants were placed at an increased risk of harm, certain aspects of the collection of the primary data may not conform to FDA regulatory requirements.

This statement was an obvious snow-job having regard to NIAID deputy director John La Montagne's disclosure that there were often 'professional differences of opinion' between the American researchers and the Ugandan hospital staff concerning what constituted a 'serious adverse event'. The 'irregularities', as Reuters called them, appear to have concerned in part the under-reporting of toxic reactions to the test drugs. So NIAID's soft soap line didn't wash; La Montagne's revelation about 'differences of opinion' concerning the critical issue of toxic reactions was indeed 'evidence that the conclusions [*of HIVNET 012*] are invalid' – calling as they did the claimed safety of nevirapine for babies very pertinently into question.

Following NIAID's press release, probably authored by him too, La Montagne made several press statements to keep the sinking boat afloat:

There is absolutely no evidence that I know of that the effectiveness of nevirapine ... has been compromised ... Nevirapine is a very, very safe drug. It's an extensively used drug. ... There is no question that the drug works. ... We believe the studies were done to extremely high standards and that they were done properly and ethically. ... I don't think that anyone is alleging that anything was improperly done. ... When dealing with the kind of hospital records they're having to deal with, it becomes a logistical problem.

The reason why La Montagne should have gone out on a limb in defence of the indefensible was because considerable national and institutional prestige was at stake. NIAID had sponsored the cost of HIVNET 012 and some of its officials participated in the conduct of the study. USAID had subsequently pitched in with a whole lot of cash too. The Bill Gates Foundation also. Relying entirely on HIVNET 012, the WHO and UNAIDS had made a joint statement in October 2000 supporting the perinatal use of

nevirapine and claiming its benefits outweighed its risks. Jesper Morch, UNICEF's representative in South Africa at the time, added:

The most important implication is that these drugs are safe to use and that no one can any longer use concerns about safety as an excuse to not have schemes with drugs that will reduce mother to child transmission.

Relying on the WHO's endorsement in turn, nearly three score developing countries implemented perinatal nevirapine administration programmes. The 'potentially quite serious' problems with the HIVNET 012 data were consequently likely to be a source of considerable embarrassment to the American government.

As could be expected, the TAC uncritically echoed NIAID's spin. A SAPA report on 23 March quoted Nathan Geffen

who claimed to be in constant contact with both BI and NIH ... BI's withdrawal in the US was due to the FDA's stringent requirements for registering medicines and had nothing to do with the safety and efficacy of the nevirapine. 'The safety and efficacy of the drug were not questioned by the FDA. The application was withdrawn entirely for administrative reasons. This is not unusual in the difficult FDA registration process,' he said.

It was just a minor bureaucratic snafu, according to the TAC; don't hassle.

In a joint statement, the WHO and UNAIDS denied that there was any cause for concern about the safety of nevirapine for babies; questions over HIVNET 012 were confined to 'reporting and documentation irregularities' that didn't warrant any change to their support of the drug for such little patients. 'We are aware of no information that would cause the WHO and UNAIDS to change its recommendations.'

According to a report in the *Kampala Monitor* on 3 April 2002, Guay's Ugandan collaborator Professor Francis Miro had been able to find only a hundred of the source documents sought by the FDA for auditing; the rest, he said, were 'stacked up in a container due to the ongoing rehabilitation at the hospital'. Which sounded

like lost. La Montagne implied the same too, if you read between his lines: there are ‘differences in the way hospitals in Uganda keep records and the requirements of the FDA’, which, he said, ‘quite rightly has a rigorous standard’. The records, he said, would have to be ‘reconstructed’ – suggesting they didn’t exist. But the study was conducted by American AIDS doctors, so his attempt to blame the Ugandans for the shambles was insupportable. And then in a separate press statement La Montagne contradicted himself, claiming the original records were scattered over three different sites in ‘Seattle, Baltimore and Uganda’. This was plainly untrue: if the records were simply packed away they could have been produced for the FDA to audit.

They should have been easy to produce if they existed: the study’s *Performance Site Establishment Plan* gave the

Location of central coordination for this performance site (e.g. where data are processed and/or regulatory and other study related files are maintained)

as ‘MU-JHU Research House ... Old Mulago Hill Road, Mulago Hospital Kampala, Uganda’.

The upshot of it was that on 22 March Boehringer Ingelheim withdrew its license application to the FDA, at the latter’s suggestion, to avoid seeing it formally rejected. Nevirapine is not licensed for marketing to prevent mother to child HIV transmission in the US or in Europe or in any other country of the First World. But in developing countries it’s different. Where lower standards apply. Boehringer Ingelheim spokesman John Wecker said, ‘Boehringer Ingelheim continues to donate nevirapine to programs in some twenty-three countries where the drug is used to help prevent mother-to-child HIV transmission.’ (A figure soon to treble.) That’s how the company operates to penetrate new markets in the Third World: it gives its drug away, until such time as the routine use of it establishes it in doctors’ minds as the standard of care. Then of course everything changes. Do you think we’re in this for charity?

The high frequency of severe toxic reactions in HIVNET 012, disclosed in the first *Lancet* report – those that were actually recorded – we’ve noted already. But the TAC’s activists evidently didn’t get as far as reading the ‘Adverse events and toxic effects’

bit on page 799. Because in response to a contemporaneous public announcement by Tshabalala-Msimang concerning the reported trouble with the integrity of the study data, the TAC released a frantic press statement containing this fake gem: ‘Not a single serious side-effect to mother or child has been reported from this study.’ The TAC statement went on:

In a speech today in Alexandra, Johannesburg, the Minister of Health once more called into question the safety and efficacy of nevirapine. Yet again she has done so without any scientific basis. The inflammatory nature of her speech and the continued baseless attacks on life-saving medicines that have been proven safe and effective are highly irresponsible. This is a desperate attempt to create smokescreens and red herrings to divert public attention from her department’s failure to accept the Pretoria High Court’s decision on mother-to-child transmission prevention.

Arguing the government’s application for leave to appeal against the interim execution order, Moerane informed the judge that Tshabalala-Msimang had just received a letter from the Medicines Control Council two days earlier, notifying her that questions had been raised by the American authorities about the integrity of the Ugandan HIVNET 012 study on which the TAC’s entire case had been based, and that ‘We are to review nevirapine in the light of these developments and will inform you of the decision as soon as information is available.’ Compounding this, he contended, was the news in that very day that Boehringer Ingelheim had withdrawn its application to the FDA for a licence to market nevirapine for use by pregnant women and their babies in the US. This was all the more reason not to administer nevirapine to pregnant women and their babies outside the pilot sites at which they could be closely monitored until such time as the MCC had concluded its investigations: ‘The new circumstances demand caution and limitation to exposure to the drug.’ The judge asked whether in the light of the American developments the government intended suspending the administration of nevirapine at the pilot sites. Moerane replied:

We will certainly do so if the investigations that the MCC conducts in the light of the information of the FDA reveals that there was fraud in the reporting and documentation of that Ugandan study or that information submitted to the MCC on closer analysis and scrutiny was incorrect or, if on the basis of what the MCC will have known by then, they have withdrawn the registration. The probabilities are there that the pilot sites will be closed down.

When it was his turn to talk, Marcus moved to neutralize the grave ramifications of the sudden very bad news from America reported by Moerane to the judge, along with the MCC's response to it, by asserting that the TAC had no reason to believe that the MCC would cancel nevirapine's special registration for mothers and babies – stretching it a bit one might say, since when he made that assertion the facts about the serious trouble with the Ugandan study weren't yet known to him. He assured the judge that the WHO considered nevirapine both safe and effective, that the WHO supported its use outside the pilot sites, and said he hoped the MCC would take the WHO's endorsement of the drug into account in reviewing the drug. (Yes, but the WHO was relying on NIAID's self-serving damage control statements.) That awkward hiccup in the case behind him, he was soon whipping up a right moral lather. What sort of savages were running the government?

The government and co-respondents deliberately turn a blind eye to the unpalatable truth that their opposition to the execution order will result in the sanctioning of the preventable deaths of children and the sanctioning of the psychological devastation of the mothers concerned. ... It is quite intolerable to weigh the lives of children up against anything else.

Issues such as whether the study on which he based his case was sound; whether it really did show that nevirapine protected babies from an early death – indeed, that they were going to die without it as the TAC claimed; and whether the drug he was punting so hard was safe for them. In the six months or so that the appeal would take to be heard, more than 400 lives would be saved if the execution order sought by the TAC was granted, he claimed. (A different news report had it as 900.) When Moerane challenged his

play with numbers as ‘rather alarmist’, Marcus backed off; it didn’t matter whether ten lives or one life a day was saved, he said. Lives that would be lost without the nevirapine baptism, he told the judge: ‘The respondents say this is a sacrifice you should endorse. We say it would be unspeakably horrific to do so.’

When all the arguing was done, the judge said he’d take a couple of days to mull over it. As he was doing so, the ANC Youth League smarted in a statement issued the following day:

We would like to point out that judges are not elected to govern the country, they are not qualified to make political decisions about government, not to mention prescribing policies to the people’s government. We wonder why does the court reduce itself to become an agent to drum profit for multinational pharmaceutical companies, whose only interest is to make money out of sick people.

News of the FDA’s scowl at the trouble with the HIVNET 012 study data, and of our own MCC’s in turn, sent the TAC into a flat spin. On the 24th it frantically issued, ‘FOR WIDEST DISTRIBUTION’, ‘Five Critical Statements on the Safety and Efficacy of Nevirapine for Mother-to-Child Transmission Prevention’ by the WHO, NIAID, CDC, Elizabeth Glaser Pediatric AIDS Foundation and Boehringer Ingelheim ‘that affirm the safety and efficacy of nevirapine for the prevention of mother-to-child transmission’.

Interviewed on SABC television that evening, Tshabalala-Msimang told Sally Burdett,

My own view is that the judiciary cannot prescribe from the bench – and that we have a regulatory authority in this country that is interacting with the regulatory authority the FDA in the USA, and I think we must allow them to assist us in reaching conclusions.

Burdett asked, ‘Will you stand by whatever the court decides?’ The Minister replied: ‘No, I think the courts and the judiciary must also listen to the medical authorities, both in this country and in the US.’ ‘So are you saying no?’ ‘Yes, I’m saying no. I am saying no.’ But three days later, responding to an uproar over this, she reassured everyone that in fact ‘we have no intention of

circumventing the courts. ... We stand ready to abide by the final decision of the courts on the execution order.'

In an op-ed piece in the *Sunday Independent* on the same day, Professor Gideon Knobel, chief forensic medical specialist at UCT, declared that 'the deaths of thousands of children could have been prevented by nevirapine' and that 'withholding life-prolonging and life-saving medication' could lead to a successful prosecution for

the death of a person through an act or omission which prima facie amounts to an offence. ... [With the government] preventing doctors from treating their patients with antiretroviral drugs, and, even more seriously, preventing the administration of nevirapine to HIV-positive pregnant mothers, doctors ... are being forced to practise unacceptable and unethical medicine.

The result was that South Africa faced "genocide" that ... may well exterminate millions more South Africans in the next few decades'. (Especially since 'There is no way to persuade sexually active people [*i.e. Africans, he meant*] to restrict the number of partners' when the President himself isn't a believer.)

And in the same issue of the newspaper, PAC chief whip Patricia de Lille declared: 'I support Mandela in his call for the provision of nevirapine to HIV-positive pregnant mothers. I am part of a group that works for this.' The South African Medical and Dental Association should strike Tshabalala-Msimang from the roll for ethical reasons, she added. And as for Mbeki: 'The old struggle cry "*Phansi [down with] PW Botha*", is now "*Phansi Thabo Mbeki*". Mbeki is a dictator who rules by fear.'

Also interviewed on SABC television that evening, retired Anglican Archbishop Desmond Tutu deplored the government's hesitancy over extending the nevirapine pilot study:

I would have hoped ... that we would invoke the same spirit, the same passion, the same commitment to fight this pandemic as we had when we were fighting apartheid – and that is to use all available information and knowledge. The WHO and UNAIDS are organizations that on other scores are held in high regard. The things they promote would normally be regarded as safe and acceptable. They say that despite some

questions about what happened in Uganda, in the experiments and tests in Uganda, nevirapine is something they would recommend as being able to deal with the onslaught. My view is then ... that these drugs do have an important impact, especially in the prevention of mother to child transmission.

Judge Botha found Marcus's hysterical oratory about babies being deliberately sacrificed like lambs in the temple by unspeakably horrible people more appealing than Moerane's sober reservations, and on Monday the 25th dismissed the government's application for leave to appeal against his order for interim compliance with the interdict pending the outcome of the main appeal. He wasn't having any truck with the argument that the continued special registration of nevirapine for babies looked uncertain:

In my view the fact that there may be a revision of the registration of Nevirapine is irrelevant. Until that happens, there is no reason to review the order or to discontinue the work at the pilot sites. What is conspicuous is that the [government has] not produced any evidence, after almost a year of dispensing nevirapine to approximately one tenth of the affected population, of any deleterious effects encountered in its programme.

In fact, there was already 'evidence' of a high rate of 'deleterious effects' in the first report of HIVNET 012 in *Lancet* (and much more would emerge in appalling detail two years later) but neither the TAC nor the government had brought this to the judge's attention in their affidavits.

As for the government's argument against the immediate implementation of his order on practical grounds:

In essence I had to balance the loss of lives against prejudice that could never amount to more than inconvenience. I find it unlikely that another court will conclude that the choice that I made was wrong. [The government's argument that the number of 10 lives a day lost was merely speculative] was no more speculative than the fears of chaos and disruption. The figure of 10 lives a day was a modest projection based on figures that were common cause in the main application. If

fewer lives will be saved, there will be less inconvenience and vice versa. In the end the choice was between tolerating the loss of life and tolerating inconvenience, no matter how many lives were at stake.

The day after Botha J's refusal of leave to appeal against his grant of an interim order for immediate implementation of the nevirapine interdict pending the main appeal, the government filed an urgent notice of appeal in the Constitutional Court. Having regard to the withdrawal of Boehringer Ingelheim's licence application in the US, and the 'safety' questions that had arisen, it was 'not in the public interest that an order as prescriptive as the execution order be enforced', it said in a statement. 'It is not inconceivable that ... the registration of nevirapine may be withdrawn altogether.'

The TAC protested:

The effect of the announcement is an appeal on an appeal on an appeal. We are involved in endless litigation and that has the consequence of denying a life-saving medicine to mothers and children

said Heywood. Geffen added:

The frustration is that the more delays there are, the more cases there will be of women who cannot get nevirapine and therefore this places more babies at risk of becoming infected.

To which Tshabalala-Msimang responded:

I would like to emphasize that we have no intention of circumventing the courts or simply delaying matters by endless litigation. We have ... indicated that the matter should be treated on the basis of urgency and should be heard either when the appeal on the main application is heard – on May 2 or 3 – or before that date, as the Constitutional Court may direct.

Reconvening especially to hear the matter during its recess, the Constitutional Court heard the appeal on 3 April. Achmat contended in an affidavit that the government was motivated merely by an attempt 'to stultify the execution order', which is to

say it was dishonestly abusing the court process for an undeclared ulterior purpose.

In his argument, Marcus framed the core issue in terms of saving lives:

From one thing there is no escape. [Providing nevirapine] will result in the saving of lives – how many doesn't matter. ...

Nevirapine is the closest thing we have to a vaccine. ... Saying to a mother, 'You can't get the drug', is a form of irreparable damage. ... [It would result in] psychological devastation.

Dusting his gown off as he emerged from the ruins, Moerane stated the real issue: the clinical trial evidence that nevirapine was beneficial was insecure, and the drug might be deregistered accordingly. Madala J was interested in whether there was any evidence documented of adverse events in the year that nevirapine had been used at pilot sites; 'No,' replied Moerane. But answering a question later on by O'Regan J as to what harm would be caused by immediately complying with the interdict to provide nevirapine nationwide, he said there was the 'potential for great, great harm'. Obviously.

Black Britain quoted Tutu on the day of the appeal:

I hope the government will abide by the court decision and the rule of law. Since we live in a democracy that is what we would expect. The government's stance on nevirapine has made South Africa the laughing stock of the world.

And sometimes our grip tends to slip in our retirement.

Six doctors – Professor Louis-Jacques van Bogaert, chief gynaecologist at Mpumalanga's Philadelphia Hospital, Dr Ames Dhai, senior consultant in obstetrics at the Nelson R Mandela School of Medicine in Durban, Professor Graham Howarth of the departments of obstetrics, gynaecology and bioethics at the University of Pretoria, David Hanekom, assistant professor of medicine at the University of North Dakota, Professor Ghoyga Ogunbanjo of Medical University of South Africa's department of family medicine and Dr Donna Knapp van Bogaert, bioethics lecturer at the same place – published a statement in the *South African Medical Journal* in the same month, warning their colleagues not to become accomplices to a new wave of 'atrocities'

by refusing antiretroviral drugs to pregnant women, which, they said, they had a moral duty to prescribe. Alluding to the earlier sacking of Rob Ferreira Hospital superintendent Thys von Mollendorf by Mpumalanga Health MEC Sibongile Manana for allowing the NGO GRIP to distribute AZT to rape victims treated there, contrary to government policy at the time, the professors made their argument by pricking the guilty consciences of South African doctors morally and politically indolent in the apartheid era. Health care workers who spoke out against apartheid abuses were victimised, they said (in fact, a tiny handful, and none of the professors):

We will not accept history repeating itself. More than a decade after the official end of apartheid, we wonder how some of our colleagues became involved in atrocities. Was it cowardice or complicity? Over and over we say ‘never again’. . . .
fundamental principles of medical ethics were in issue, and the state’s intervention in the antiretroviral debate opened the way to more human rights abuses.

It was cheap talk but damn good propaganda. If the doctors were so hot for it, why was the government abusing human rights by withholding it? When the manufacturer was giving it away free. The noise masked the real merits: was nevirapine given to pregnant women and their babies safe? Did it do any good?

Dismissing the government’s interlocutory appeal on the 4th, the Constitutional Court reserved its reasons for delivery together with its judgment in the main appeal, but its *ratio decidendi* could be surmised from a question asked of Moerane during argument when he alluded to the practical difficulty of doling out nevirapine outside the government’s eighteen pilot sites. Underscoring the premise from which the whole case proceeded – that nevirapine saves babies’ lives – Justice Sachs asked rhetorically: ‘What one is asking for is a generation of mothers to be sacrificed in the name of scientific planning. Isn’t that asking too much?’ Which all goes to show. How AIDS turns the best men’s minds to mush. No one has ever claimed nevirapine ‘saves mothers’. No one ‘asked’ for the ‘sacrifice’ of any women. No one suggested that ‘a generation of mothers’ be lost; the main appeal was just a month away. An

utterly ridiculous thing to say. But nice and showy, a perfect sound-bite for the news, epitomising the intellectual level of the public discourse in the controversy, and foreshadowing the standard of the debate in the main appeal.

Reporting the judgment in the *Sunday Times*, Carmel Rickard claimed that ‘over the next few months at least, many infants otherwise denied a chance at life could survive’. In fact, the core assumptions that untreated babies are fated to die and that nevirapine gives them ‘a chance at life’ has no basis in any paper in all the vast research literature on AIDS. It’s pure myth. But as Salman Rushdie has observed, ‘Sometimes legends make reality, and become more useful than the facts.’ Who can blame Rickard though when top American AIDS doctor Lynne Mofenson, chief of the paediatric and adolescent AIDS branch of the National Institute of Child Health and Human Development, says things (at the 14th International AIDS Conference at Barcelona in July 2002) such as giving nevirapine to all pregnant women of unknown HIV sero-status is

feasible as an interim strategy where there is no voluntary counselling and testing (VCT) infrastructure in place. ... To wait until a proper VCT program was in place in resource-poor settings could cost thousands of babies’ lives.

It’s a marvel how AIDS doctors kick caution, reservation and dissension to touch by simply claiming that it will cost lives. And are never challenged to prove their claim. Least of all by journalists, who imagine they’re contributing to the War on AIDS as message carriers for the good guys. Feeling all warm inside as they do. Being on the side of good, truth and light. And of the natives. When their chiefs are no good.

The day after Judge Botha’s ruling, the Americans phoned. In a teleconference with US consulates in Cape Town, Johannesburg and Pretoria, NIAID deputy director John La Montagne

said the Ugandan study ... was successful and demonstrated clearly the value of nevirapine in interrupting mother-to-child HIV transmission. ... He said the scientific research in Uganda was of high quality and that the only problems lay with gathering raw data, which was in three locations in both the

US and Uganda, to satisfy the US Food and Drug Administration. ... 'There is no evidence that the effectiveness of nevirapine in preventing mother-to-child transmission has been compromised. The data is solid and we are very confident that things will work out quite well in the end. ... No one is alleging that anything has been improperly done. It is an issue of basically constructing records, and when you're dealing with the kind of hospital records that they're having to deal with, it becomes a bit of a logistical problem. The drug company wouldn't have pursued this unless they were sure the drug study was done to very high standards.' ... After the conference call, Zackie Achmat, head of the Treatment Action Campaign, appealed to Tshabalala-Msimang to issue a statement 'to inform people the drug is safe'.

Why, 'The prestige [*sic*] US research body, the National Institutes of Health, had come out in strong support of the use of nevirapine to prevent mother-to-child transmission of HIV,' said Di Caelers in her piece reporting the affair in the *Cape Argus* on the 27th, quoted above.

Mbeki was livid over the Constitutional Court's dismissal of the government's appeal against Judge Botha's interim compliance order. And responded in his *Letter from the President* posted on the ANC's website the next day. Emphasizing that 'the predominant feature of illnesses that cause disease and death among the black people in our country is poverty', he fumed:

some in our society and elsewhere in the world, seem very determined to impose the view on all of us, that the only health matters that should concern especially the black people are HIV/AIDS, HIV, and complex anti-retroviral drugs, including nevirapine. ... We will not be intimidated, terrorised, bludgeoned, manipulated, stampeded, or in any other way forced to adopt policies and programmes inimical to the health of our people. That we are poor and black does not mean that we cannot think for ourselves and determine what is good for us.

In an article entitled 'So much power, so little rule', AIDS Law Project attorney Jonathan Berger threw a screaming queen fit equal

to any of Achmat's in the *Mail&Guardian* on the same day, attacking on the government's bona fides. The government's appeal against the interim execution order was an 'Abuse of court process', 'an abuse of the courts', and 'an assault on the Constitution ... the state has vigorously sought to undermine judicial independence and integrity', it had tried to 'engage every legal process and technicality to delay the inevitable provision of health-care services', and it 'values control at the expense of human life'. Yes, Jonny. Those barbarians. Do you need a fan?

As the date of the main appeal in the Constitutional Court drew nearer, Tshabalala-Msimang wrote to the MCC to ask what it had decided. Its response was to make a public announcement on the day before the appeal (a public holiday in between) confirming that its registration of nevirapine for perinatal use was under review.

The first day of the appeal on 2 May was celebrated with the usual festivities. The TAC hired a fleet of busses to ship in thousands of unemployed Africans from the townships to demonstrate outside the Constitutional Court in Johannesburg in return for a free 'HIV Positive' tee-shirt to wear (even if they weren't) and to keep to take home afterwards, as well as plenty of food and drink during the day's outing in town. Simultaneous demonstrations against the government were staged in Cape Town and Durban, with the African poor from the outlying peri-urban barrios there attracted by the same inducements. 'Stand Up For Your Rights' was the theme of the show, meaning your rights to pharmaceutical drugs being foisted on your government.

Before the commencement of argument in the appeal, Professor Sam Mhlongo of the Medical University of Southern Africa applied for a hearing as an *amicus curiae* (a friend of the court) to bring the American licensing problems to its attention, as well as the radical flaws in HIVNET 012 that had been identified by the Perth Group in its 130 000-word monograph, *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence*, amplified by a PowerPoint slide show they'd prepared, *A Critical Analysis Of The Evidence Considered Proof That Nevirapine Prevents Mother-To-Child Transmission Of HIV*. In sum, he said,

It is incredible to contemplate that a notoriously very toxic drug, approved as a therapeutic agent in the First World on a provisional basis only should be judicially prescribed in our developing country for an indication not licensed anywhere else in the First World.

After an adjournment to consider the application, Chief Justice Arthur Chaskalson ruled that notwithstanding what he described as Mhlongo's 'compelling argument' in his affidavit, the unanimous decision of the court was to decline his application for an audience, for reasons to be given with the main judgment later on. Actually, as his affidavit made clear, Mhlongo was not merely making an 'argument', but was setting out

profoundly important developments ... unsettling [the] factual substrate [of the case], and re-agitating what had been common cause between the parties

namely the founding premise that nevirapine had been shown to save babies; but as we were to see from the delicious moral feast they made of the case the court was in no mood to listen to the party-pooper. The appeal was 'urgent' said the Chief Justice; it needed 'urgent attention'. Why, the court had lives to save, lives the government wouldn't, and they weren't going to let some spoiler derail their plans to do this at the last minute. The court held later:

The applicant's purpose in seeking admission as an amicus was to enable him to challenge the scientific integrity of the clinical trial that led to the approval by the Medicines Control Council of nevirapine for the prevention of mother-to-child transmission of HIV. The applicant wanted to introduce a substantial body of new evidence in support of a challenge to the decision of the Council to approve the use of nevirapine for this purpose. The evidence was untested and the submissions based on it would have opened an entirely new issue on appeal. It was therefore inappropriate for the amicus belatedly to try to introduce the challenge to the approval of nevirapine as a new issue in the case. Moreover, allowing the applicant to raise this new issue on the first day of a protracted hearing would have been both disruptive and prejudicial to the parties. It would

have necessitated the postponement of an otherwise urgent matter and inevitable delay in resolving a matter that required urgent attention. It would therefore not have been in the interests of justice to admit the applicant as an amicus in these circumstances. That is why the application was refused.

That is why we weren't interested in taking time to consider all the available information, why we conducted the case like any ordinary commercial one, with a premium on expeditiousness, and why we weren't especially alert to new evidence of apparently profound, fundamental importance, before doing something as drastic as usurping the elected government's power to make policy for the country in accordance with its mandate, and making it on its behalf instead, in regard to the countrywide provision of an experimental new treatment for mothers and babies with a drug known to be exceptionally toxic. And not permitted for babies by any drug licensing body in the First World. It wouldn't have been convenient.

Glenda Gray at Chris Hani-Baragwanath Hospital said on television news that night that she was annoyed by the MCC's public announcement that its registration of nevirapine for mothers and babies was under review: 'Mischievous ... mischievous,' she complained. The *Mail&Guardian's* Belinda Beresford was also sour at news of the MCC inquiry, commenting on its 'exquisite timing'. Threatening to spoil the party atmosphere in court. Because have a party they surely did. Judges and lawyers, knowing their every word was being noted by the local and international media, competed in their blandishments to the press gallery like the first fifteen all vying for the same school floozy.

Evident from the endless grandiloquent rhetoric was that not a word of Mhlongo's affidavit had penetrated the estimable minds of the jurists at play in that courtroom. Not one. Moerane SC for the state agreed with the court's opening proposition that the issue was one of life and death. Which it wasn't, but that sealed the outcome of the case, and from there on it was downhill all the way.

'What could be more basic [*a right to healthcare*] than a free drug that can save a life?' asked Chaskalson CJ gravely. As if there's even a shred of evidence that nevirapine can 'save a life'. Moerane countered: 'You are giving a drug to 70% who do not

need it'; only 30% of babies born to HIV-positive mothers were infected, he said. (Actually, there's massive variation in the 'infection' rate from study to study.) 'And you are introducing a drug of which you do not know the long term effects,' he continued – just as the HIVNET 012 researchers had expressly cautioned, emphasizing the need for such an investigation as 'a high priority'. On the other hand, he said, 'If we had major safety concerns we wouldn't even consider expanding sites, we wouldn't even consider having a national rollout.' He was referring to the Cabinet decision days earlier to provide antiretroviral drugs in the public health system. 'There don't appear to be any major concerns about safety,' he added, not having been briefed properly. 'But safety concerns cannot be ruled out.'

Goldstone J couldn't see it: 'What is the relevance of long-term toxicity?' he asked. To which Moerane didn't reply. So O'Regan J did, assuaging Moerane's worries with the news that the 'WHO study', which he'd mentioned, referred to a study on the long-term effects of nevirapine. Mystifying us all, sad to say, because there's never been any 'WHO study' or any other 'study on the long-term effects of nevirapine'. On God's earth. As Sax had noted back in the October 1999 issue of *AIDS Clinical Care*, 'studies on the long-term safety and efficacy of the nevirapine therapy have not been done'. Still haven't.

Kriegler J took issue with the state's inflexible approach of not allowing any hospital to administer nevirapine outside the pilot sites. Forgetting that the drug was still on test he commented: 'You either have a Cadillac or you don't.' Sharing in the American dream? The judge's fabulously witty remark reportedly had the gallery in stitches.

If a woman is given the choice, what would she choose?
Second best [*nevirapine without counselling and powdered milk*] or dead baby. Because the policy does not give her the choice. ... Save the kiddies that are dying now and come up with a programme for what is happening three months down the line. What is wrong with that as an interim measure?

If you get the drift. Flashy cars! Nestlé formula milk! The kiddies! Dying! Saving them! With a pill! Jeepers!

Appearing for both the Institute for Democracy in South Africa (IDASA) and the Community Law Centre of the University of the Western Cape as appointed friends of the court, Trengrove SC strained to outdo everyone in flamboyant high talk:

This is a case in which thousands of babies die in misery. A single dose can ensure a life of health and well-being. Not providing [nevirapine] is a violation of the right to dignity. It says that the mother and baby are not worthy citizens.

So the TAC story goes. But nice and rousing, like the Storm Troopers' marching song: 'When Jewish blood spurts from the knife, things go twice as well.' As Trengrove spouted ridiculously before the country's top justices, none of them interjected to reprove him: 'Please, Mr Trengrove, spare us. What's this Golden Nostrum, this miracle new medicine that you're trying to sell us? Do you really think we're all fools?' Because none of them voiced any such reservations as they all listened in wonder. None paused to doubt before buying it.

Carrying on long after the normal time for the court to adjourn the day's session, Marcus SC for the TAC entertained his enthralled audience, on both sides of the bench, with a sorry tale of how a pregnant woman who 'knew' that she was HIV-positive, who 'knew' that nevirapine would reduce the risk of transmitting the virus to her child, who was too poor to afford private treatment, and who lived far away from a pilot site, went to a public hospital where she told the attending doctor that her 'informed choice' was for nevirapine, only to be told that state policy precluded his prescribing the drug. A policy that 'does not even meet the minimum requirement of rationality', he fulminated. It put doctors to an 'utterly intolerable' ethical dilemma, and was 'an invitation to civil disobedience'. It was the government's 'utter rigidity and inflexibility' that had led to the TAC's lawsuit. 'It drives doctors of conscience to do what their life's calling trained them to do and, in so doing, to take the law into their own hands.' It forced doctors to 'take a conscious decision to allow a child to die, or face disciplinary action' for providing nevirapine in contravention of government policy. For mothers 'already afflicted by the deadly disease' it was 'nothing short of an assault on their psychological integrity'. It led to 'the beginning of a process of acute suffering

and premature death'. There was too much 'foot-dragging and vacillation' and not enough urgency to the government's approach to AIDS. 'Death is different,' he said thoughtfully.

Are you done now? Carrying on like a holy roller saving souls. Is this trial advocacy? For which you are so well paid. Has it anything whatsoever to do with the Constitutional point in issue? About the reach of judicial power. About whether a court has the power to prescribe a particular medicine. For the Department of Health to compulsorily go out and buy. When the freebies are over. Because to us it sounds like rhetorical gimmickry of the most boorish sort. The kind to try on an inexperienced magistrate when you don't have a case.

These were South Africa's best legal minds on display. This was the standard of the forensic debate in our Constitutional Court, the quality of legal reasoning in the great nevirapine case.

The Democratic Alliance wasn't going to be left out of the farce: the government was condemning between 192 and 274 babies to an early death for each day it spent arguing its nevirapine appeal in the court, it said in the newspapers. On a high moral horse, always. Even as it was taking a million bucks in secret contributions from major-league German fraudster fugitive Jürgen Harksen. Buying friends in high places. In the DA.

The DA and the TAC even found a natural friend in Dr Wouter Basson, former head of the apartheid government's chemical and biological warfare programme, Project Coast. Just-acquitted by an apartheid era judge of murdering freedom fighters with poison, among other sins, he urged that instead of appealing his acquittal at a likely cost of about two million rand, the state should rather spend its money on nevirapine. This sum would buy enough of the drug for 250 000 pregnant women and their babies, he said; and the cost of the trial itself would have paid for five million doses. 'I'm not sure what the population needs more – medication or some kind of retribution?' he asked. As if he's the kind of guy who actually gives a damn. But the medication in question would have appealed to him.

And when it was all over, judgment in the nevirapine appeal was reserved, but it was obvious from the way the judges and the drug lawyers had been waxing in unison that the government had lost.

The doyenne of South African AIDS journalism Belinda Beresford reported the first day of the appeal in the *Mail&Guardian* on 3 May in her piece, ‘On the road to recovery’. Her opening lines set the tone: ‘

God joined the minister of health in court this week, to gaze at 11 of the finest legal minds in the country deciding on the fate of thousands. The almighty, in the form of Archbishop Njongonkulu Ndungane, had come to watch the government appeal that it not be forced to curb mother-to-child transmission of HIV by providing nevirapine.

The following week she reported Mhlongo’s endeavour to inform the Constitutional Court about the fatal trouble with HIVNET 012, the study on which the entire case was based. I read her article over and over, just amazed. To be frank, it had always been obvious from her writing that the woman was pitifully thick, but this took the cake. Her piece, ‘Medunsa Aids dissident “advises health minister”’, had apartheid journalist Cliff Saunders’s poison-pen style, ridiculing Mhlongo for describing nevirapine as ‘notoriously toxic’, by omitting to cite paragraph after paragraph in his affidavit establishing just that – on the official version, not his.

Although Mhlongo’s affidavit made clear that most of the HIVNET 012 clinical case files were reportedly lost, rendering auditing by the FDA impossible and the trial consequently worthless by First World drug licensing standards, Beresford crookedly fudged the gravity of the problem, describing it as ‘issues with paperwork for the notoriously pedantic and rigid FDA approval’. She also slapped down Mhlongo’s contentions about the untenable claims made by the trial overseers concerning the drug’s safety. ‘All indications are’ that the withdrawal by Boehringer Ingelheim of its licence application related only to ‘paperwork’ problems, she wrote. Mhlongo’s argument was evidently too complex for her to follow: since NIAID had revealed frequent differences of opinion between the American and Ugandan researchers concerning the incidence of serious toxic reactions, and most of the files were said to be missing, apparently discarded or lost, the FDA would not be able to resolve the disagreements – placing the toxicity profile of the drug in doubt, if the shocking

nearly 6% mortality rate among nevirapine-exposed babies born to clinically healthy mothers still left any.

Not only dim, ignorant too: ‘Pregnant women with HIV in the First World are usually on some form of chronic antiretroviral treatment throughout their pregnancy.’ Not according to the official American *Guide to the Clinical Care of Women with HIV* (2000): AZT, the most popular drug given to pregnant women, should only be given ‘after the first trimester’. Stuff to do with its mutagenicity and teratogenicity, causing ‘squamous vaginal tumours’ and ‘fetal malformations’ in animal studies.

But what really got Beresford’s pretty head in a tizzy was that

Mhlongo questions the existence of the virus that causes Aids, saying that HIV has ‘never in the history of the AIDS era been isolated by the classical procedure for the isolation of viruses, namely by purification and electron micrograph verification. The specificity of such tests for the presence of the putative virus is consequently unknown.

She hadn’t heard that one before, and didn’t understand it either, so the best she could do was to giggle:

Mhlongo’s affidavit provides another interesting insight into the world of Aids dissidents, similar to that given by the now notorious ‘Castro Hlongwane’ document, which effectively calls Aids a racist plot.

She concluded with a my-daddy-said-so affirmation:

Five major international health bodies [*all relying on NIAID’s damage control statements*] had said there were no questions about the safety and efficacy of nevirapine for mother-to child transmission.

Therefore, to this gaga chick, there aren’t any. And that’s it.

Beresford’s equally simple AIDS journalist colleague, Lynne Altenroxel, wrote a similarly obtuse piece for the *Sunday Independent* on 5 May: ‘Supposedly “toxic” nevirapine used around the world’, she headlined – in 53 countries for preventing mother to child transmission of HIV. Places such as Botswana, Brazil, Thailand, China and Taiwan – none of them countries in the First World. Developing World countries where Boehringer

Ingelheim gives the drug away free. All the better to establish it in hearts and minds as the standard of care. So that when the charity ends the company steps into a nicely established market. Not having to lay out a pfennig on marketing. ‘The suggestion that all these countries are playing with peoples’ lives is ludicrous,’ Altenroxel quoted Heywood. Not that anyone had suggested they were. Altenroxel was also put out by the MCC’s decision to review the registration of nevirapine for perinatal use, because a week earlier Boehringer Ingelheim had furnished it with a list of countries that had registered nevirapine for this indication.

Yet, on Tuesday night, just 36 hours before the constitutional court case over nevirapine started in Johannesburg, the MCC released a statement saying that it was investigating the drug’s registration

she pouted.

On 17 May the US CDC published its latest revised guidelines on interventions to prevent mother to child transmission of HIV, and they conspicuously omitted nevirapine – implying that in the view of the CDC the HIVNET 012 study, squarely relied upon by the TAC and the courts, did not establish the efficacy and safety of nevirapine for American pregnant women and their babies. Nobody saw fit to comment on the implications for South African mothers and their newborns, mostly black, mostly poor.

Writing in *Z Magazine* on 20 June, lefter-than-thou poseur and fawning TAC groupie Professor Patrick Bond, Director of the Centre for Civil Society in Durban, claimed in “‘Nepad? No thanks’”, say African activists’ that ‘the department of health continues to prevaricate on providing AIDS treatment, including inexpensive nevirapine for pregnant women and rape survivors’. It continues to tell lies instead of just saving lives. But in his eager posturing to sound hip and look cool, the sloppy economist got his facts wrong: due to its acute, severe toxicity, no medical authority anywhere recommends nevirapine for giving rape victims.

The Constitutional Court dismissed the government’s appeal on 5 July. The heart of the judgment went:

The provision of a single dose of nevirapine to mother and child for the purpose of protecting the child against the transmission of HIV is, as far as the children are concerned, essential. Their needs are ‘most urgent’ and their inability to have access to nevirapine profoundly affects their ability to enjoy all rights to which they are entitled. Their rights are ‘most in peril’ as a result of the policy that has been adopted and are most affected by a rigid and inflexible policy that excludes them from having access to nevirapine. ... It is clear from the evidence that the provision of nevirapine will save the lives of a significant number of infants. ... In evaluating government’s policy, regard must be had to the fact that this case is concerned with newborn babies whose lives might be saved by the administration of a ... single dose of nevirapine to both mother and child at the time of birth. ... The prospects of the child surviving if infected are so slim and the nature of the suffering so grave that the risk of some resistance manifesting at some time in the future is well worth running.

In fact – and this was the core fallacy from which the entire case sprung – there is no evidence that babies diagnosed HIV-positive nearly all die, and that like Jesus on the cross they do so exceptionally painfully.

Government policy was an inflexible one that denied mothers and their newborn children at public hospitals and clinics outside the research and training sites the opportunity of receiving a single dose of nevirapine at the time of the birth of the child. A potentially lifesaving drug was on offer and where testing and counselling facilities were available it could have been administered within the available resources of the state without any known harm to mother or child.

‘Without any known harm to mother or child’? As Mhlongo had pointed out in his affidavit – the one the learned justices threw out – the first report of HIVNET 012 in *Lancet* recorded a ‘maternal serious adverse event’ rate of ‘4.7% in the nevirapine group’. The rate of ‘serious adverse events’ among babies treated with a single dose of nevirapine after birth was 20.5%. Of the babies so treated 5.7% died – from sepsis, inability to breathe and other illnesses, all

consistent with metabolic poisoning, and not from ‘AIDS-defining’ conditions. But Ugandan doctors, who’d participated in the study, disputed the accuracy of these figures, presumably on the basis that the American AIDS doctors clamouring over their alleged success with the drugs under-reported the incidence of serious adverse events and the number of deaths. (That this was indeed so publicly emerged in December 2004.)

‘Once a drug that has the potential to reduce mother-to-child transmission is available,’ the court held, ‘it is desirable that it be made available without delay to those who urgently need it.’ The court concluded:

The question in the present case, therefore, is not whether socio-economic rights are justiciable. Clearly they are. The question is whether the applicants have shown that the measures adopted by the government to provide access to health care services for HIV-positive mothers and their newborn babies fall short of its obligations under the Constitution. ... In the circumstances we agree with the finding of the High Court that the policy of government in so far as it confines the use of nevirapine to hospitals and clinics which are research and training sites constitutes a breach of the state’s obligations under section 27(2) read with section 27(1)(a) of the Constitution.

In short, it was unconstitutional not to give nevirapine to African mothers and babies, the court held. ‘The anxiety of the applicants [*i.e. the TAC and its supporters*] is understandable because one is dealing here with a deadly disease,’ Chaskalson explained sympathetically. Like Zackie, I’m also in a big flap about saving lives. It’s quite exciting, actually. Thinking about Africans having so much sex that they’re all dying from it, and their babies too.

Achmat responded to the judgment obviously: ‘Obviously we’re elated, we feel vindicated ... We call on the government to work with us in making comprehensive HIV care a reality for all.’ We call on the government to do what we tell them to do. They must accept the opium being pressed on them from abroad. They must accept the forced trade with foreign merchants. And like the liberal judges, we know what’s best for the natives. Better than their own leaders do.

The judgment ‘broke the dam wall,’ he commented later on.

It broke the dam wall, in the sense that the country realized that government’s denialism is not invincible, and that people unified in action can achieve things.

With a war-chest of millions from corporate funders overseas.

In giving judgment the court slipped in a blessing for the TAC, remarking that the

regrettable degree of animosity ... contention and emotion ... spilt over into this case ... bedevil[s] future relations between government and non-governmental agencies that will perforce have to join in combating the common enemy ... the catastrophe we confront.

Cluck-cluck-clucking like Henny-Penny: ‘The sky is falling! And we must tell the king.’ What to do. (‘Sounds good to me,’ said Foxy-Loxy.) Achmat took the Constitutional Court’s wet kiss on his cheek very much to heart. Four years later on 30 August 2006, addressing the Cape Town City Council at DA mayor Helen Zille’s invitation, and calling for Tshabalala-Msimang and Health Director General Thami Mseleku to be sacked, he claimed, ‘The city has a constitutional duty to work together with us to make this work.’ (The DA-led council agreed, and voted to do so.)

Cheering broke out in the gallery as the judges filed out of court. TAC demonstrators toyi-toyied and ululated outside. ‘This is a judgement that saves lives,’ gushed TAC attorney Geoff Budlender. ‘It is a victory for pregnant women with HIV and it’s a victory for the constitution. It shows that our social and economic rights are real and powerful. I am very happy. I hoped for this.’ Underscoring his subscription to the root fallacy of the case – that nevirapine saves babies’ lives and that they will die without it – he’d told a meeting of the Harold Wolpe Memorial Trust several months earlier on 21 August 2001:

It is very difficult to contend that it is reasonable to refuse to provide a medicine which is effective, safe, and available for free, and which doctors want to administer, to children whose lives will be saved by it. In this matter, government policy adversely affected the poorest people, because the rich can buy

access to nevirapine. It is plainly unreasonable for government effectively to say that poor babies can die, when there is a simple and inexpensive way to prevent their deaths.

In a victory speech in the *Mail&Guardian* on 12 July, Budlender said the Constitutional Court judgment ‘was simply the conclusion of a battle that TAC had already won outside the courts, but with the skilful use of the courts as part of a broader struggle’. The moral of the case was that ‘social and economic rights are only as strong as the willingness of civil society to enforce them’.

That Budlender, the quintessential paternalistic white South African liberal, had himself uncritically bought into the whole farrago; that he fancied himself to be a Very Good White Man for getting involved in the TAC struggle to save Poor Little Black Babies – in the virtuous tradition of the radical white lawyers defending freedom fighters during apartheid; that he considered that he was in it for a high moral cause and not just for the money, like any other lawyer who’ll say and do anything for it, especially when it’s a lot; and that he thought his client Achmat to be a paragon of human rights activism, was also evident from his commentary on the case during an interview that Achmat conducted for a documentary film on some famous human rights court cases, broadcast on local television on 21 February 2005:

What TAC shows is that the constitution can be enforced in many ways. It’s enforced in the streets, it’s enforced in the press, it’s enforced in Parliament, and it’s enforced in the courts. And TAC shows that when you have a social movement with a strategy which understands the constitution and which plugs in the legal work in an appropriate way then the constitution is very powerful in the courts.

No wonder the Judicial Services Commission has repeatedly bounced Budlender’s yearning pleas to be appointed as a judge.

At a media conference afterwards, TAC Western Cape co-ordinator Thembeke Majali said wistfully, ‘We will never again have a Nkosi Johnson who had to die because his mother did not have access to preventative medication.’ At least 40 000 babies had suffered unnecessarily since the start of the case, added

Haroon Saloojee of Save Our Babies. Speaking elsewhere, Anglican Archbishop Ndungane agreed:

While the outcome is a tribute to those who have persevered against severe odds ... we cannot lose sight of the time and lives that have been lost and will continue to be at risk until our state hospitals shift into gear.

The South African Medical Association released a happy statement: ‘We believe that wherever there is a doctor, there is also the capacity to provide nevirapine.’ A lobotomy also.

Judge Cameron naturally loved the judgment too, thinking and speaking similarly in his address to a satellite meeting at the 14th International AIDS Conference in Barcelona the following day. *Business Day* quoted him in paraphrase three days later:

The nevirapine judgment holds out the hope that health rights can indeed be justiciable and made real. Thanks to the South African example of efficient and principled activism around HIV/AIDS, it is now possible ... to convey ‘a sense of possibility’.

The failure of the government’s lawyers to take issue with the TAC’s claims – passing up my free offer of assistance to refute them – resulted in the Constitutional Court buying them one and all: HIV-positive means infected with a deadly virus from which you’ll surely soon die. Your baby too if you’re pregnant. Without the magical potion. Just a sip will do – ‘a single tablet of nevirapine to the mother and a few drops to her baby at the time of birth’. Like sacramental wine? Matching Sigma Chemical Company’s deadly orange skull and crossbones label on the AZT it provides researchers, GlaxoSmithKline serves the drug to kids as a citrus-flavoured syrup. Boehringer Ingelheim doesn’t say in its package insert whether its nevirapine suspension comes tasting like wine-gums.

Newsday quoted Tshabalala-Msimang’s bitter reaction on the 9th:

We will implement because we are forced to implement. The High Court has decided [*and the Constitutional Court has confirmed*] the Constitution says I must give my people a drug that isn’t approved by the FDA. I must poison my people.

Exactly.

The *Cape Argus* derided her on the same day by way of a cartoon adapted from Sigma's lethal toxin label for AZT, with Tshabalala-Msimang's face substituting for the skull above the crossed bones. Below it the caption read: 'POISON: KEEP FAR AWAY FROM HIV/AIDS TREATMENT DECISION-MAKING.' The following day, in reaction to an outcry from AIDS doctors and activists against her complaint, Tshabalala-Msimang claimed that the only 'concern' that she'd raised with *Newsday's* journalist was that she'd been unable to establish from the FDA why Boehringer Ingelheim's licence application to market nevirapine for perinatal administration had been withdrawn.

Equally put out by the decision, Justice Minister Penuell Maduna suggested on television that it was 'the decision of just one court and purely on the basis of our legal system it is not binding on the rest of the country'. 'Utter rubbish,' Mark Heywood responded, right for once. Maduna then set his gaffe straight by speaking nicely: the judgment

demonstrates the crucial role of the courts in maintaining commitment to the Constitutionalism that underpins the vision of a new South Africa. [The nevirapine judgment] represents a new depth and maturity in our new democracy. It shows that the Constitution creates a powerful tool in the hands of civil society, to ensure that the government gives proper attention to the fundamental needs of the poor, the vulnerable and the marginalised.

The TAC clapped.

Even legal academic Kevin Hopkins, who'd criticized the High Court judgment, and who'd consequently been instructed to provide a nice lucrative opinion on the government's prospects on appeal, loved the Constitutional Court one: 'The judgment, which reads well, is extremely clear', he wrote in the November issue of *De Rebus*. He was blown away by their Lordships' 'exceptionally insightful and brilliantly articulated reasoning'. He was now happy that 'the peculiar facts of this case did require judicial intervention' after all. He didn't want to sound like a denialist anymore. Better to be on the winning side with the progressive lawyers, the 'brilliantly' clever human rights guys.

In his characteristically extravagant, intellectually slack prose, Patrick Bond rejoiced garrulously over the judgment on his Centre for Civil Society website in ‘Johannesburg Lefts Prepare to Summit Against the Global Elite’:

Closely allied with Cosatu, the Treatment Action Campaign (TAC) has done exceptionally powerful advocacy work to gain access to Aids medicines for five million HIV+ South Africans, resulting in formidable pressure against the government’s ongoing Aids-denialist, genocidal policies. Although TAC’s victory in a precedent-setting constitutional court case in early July forces Pretoria to provide the drug nevirapine to pregnant HIV+ women and rape survivors, the roll-out process is slow and subject to central government sabotage. Health minister Manto Tshabalala-Msimang was quoted at the recent Barcelona Aids conference calling nevirapine ‘poison’, and she hijacked a grant to KwaZulu-Natal province from the UN-administered Global Fund last week so as to centralise funding into programmes that don’t emphasise treatment as much.

‘Aids drug could be banned’, headlined the *Sunday Times* on its front page on 4 August, reporting a statement by the MCC that it had ‘serious concerns’ about nevirapine’s efficacy and toxicity, regarding which it had

grilled the drug’s manufacturer, Boehringer Ingelheim, in a heated meeting two weeks ago. The company was asked to explain alleged deaths from the drug in Uganda and why it had withdrawn an application for approval in the US.

The report mentioned further that the MCC had set up a ‘Pharmacovigilance Unit to monitor adverse events related to antiretroviral therapy’, and that the MCC would be making a decision on perinatal nevirapine in mid-September. MCC Registrar Precious Matsoso confirmed to the *New York Times* on the 8th that

the council would not be swayed by the flood of criticism from advocates for AIDS patients. ‘We are not going to promote bad

science. ... If someone challenges the data's credibility, we have to make sure it is correct.'

To which TAC's Nathan Geffen responded:

There is overwhelming evidence that nevirapine is safe for mother-to-child transmission. Not a single serious side effect has been reported when nevirapine has been used for this purpose. We are very concerned that Precious Matsoso and [MCC chairperson] Peter Eagles are not acting on the basis of ensuring access to safe and effective medicine, but rather with political motivation. They are trying to scuttle the process. [The MCC] is clearly losing its independence.

In truth, not only was there a high incidence of severe side effects reported in HIVNET 012 – and many more unreported ones, some fatal, emerged later – there was local evidence in South Africa of the drug's toxicity in perinatal applications too. In 'It's the trials, not the drugs' in the *Daily Mail & Guardian* on 10 April 2000, David Le Page had written:

The mother-to-child trials, also called the Saint trials, have involved extremely low doses of Nevaripine [*sic*], two to the mother before giving birth, and one to the newborn infant. The Saint trials, run by Jerry Coovadia at the University of Natal, involved more than 1 000 patients, and while the results have yet to be fully analysed, have demonstrated few immediate side effects other than dermatological problems.

For the reasons discussed in Part One, however, 'immediate side effects' such as 'dermatological problems' following drug administration, particularly in infancy, are a very serious matter, signaling a general systemic toxic reaction. And as for Geffen's claim that 'There is overwhelming evidence that nevirapine is safe for mother-to-child transmission', it's basic to lawyers that a paucity of evidence early in an investigation doesn't amount to 'overwhelming evidence' the other way. So if, for instance, the police haven't collected sufficient evidence for a judge to nail a serial killer, his lawyer can hardly claim after the trial that there's 'overwhelming evidence' that he's innocent. But Geffen, the office computer technician, wouldn't know this. As we're still to read,

the independent auditors of HIVNET 012 discovered that the principal investigators conducting the trial had had no training in Good Clinical Practices, and had accordingly failed to keep a proper tally and record of the incidence of adverse events, serious adverse events, and deaths during the trial. They had failed to properly collect and report the evidence that the exceptionally toxic drug was harmful. To Geffen and his TAC this meant it was harmless.

The launch of the MCC's review ruffled feathers all round. Coovadia obviously thought the deregistration of nevirapine would be 'quite disastrous' for the country's HIV/AIDS programme. Side effects from the drug were rare and anyway reversible, he claimed. Also,

The fact that the drug is only given once also makes the occurrence of side effects very unusual. ... In my professional opinion the pros of nevirapine far outweigh the cons. The consensus is that nevirapine is safe and effective for mother-to-child transmission and is appropriate for developing countries because it is affordable and the administration is very simple. ... The withdrawal will also create a wider gap between the government and the country's people and the population will gradually lose faith in the government's public health policy.

Glenda Gray couldn't understand what the fuss concerning safety and efficacy was all about when these things had been 'addressed during a study of nevirapine in South Africa in 2000', and told *Lancet* that it was right that the MCC should weigh up the risks and benefits. Then again, maybe not: 'But surely it's criminal to undermine a safe drug when there is an epidemic and children are dying like flies.' The native children. Like little black flies everywhere.

Quoted in 'Aids drug safe says company' in the *Daily Dispatch* on 5 August, Gray's hospital colleague James McIntyre said,

I think the MCC has the duty to review all the information. In my opinion I feel it is a safe and very effective drug and to withdraw it will be a detriment. I think that although some concerns have been raised about the administrative paperwork of the Ugandan trial, the World Health Organisation hasn't

changed its recommendation, and the US Public Health Department haven't changed their recommendations either.

McIntyre evidently hadn't noticed that just two and a half months earlier, following the withdrawal of Boehringer Ingelheim's licence application to the FDA, the CDC had loudly left nevirapine out of its revised guidelines for the prevention of mother to child transmission of HIV in the US.

New National Party leader Martinus van Schalkwyk was quoted on air saying that deregistering nevirapine would be

a massive human disaster for the Western Cape and South Africa as a whole. It is our view that the benefits far outweigh the possible negative effects.

Not that he knew anything about it apart from what he'd read in the newspapers, but anyway he said his party's lawyers were looking at legal options to stop the MCC from such mischief. He added later: 'The overwhelming preponderance of scientific and medical opinion, advice and evidence is that nevirapine is safe, and the province's decision to use the drug was based on this advice.' Donated, Western Cape AIDS chief Fareed Abdullah confirmed. Like elsewhere in the Third World. Given away by Boehringer Ingelheim. The kind uncle. Caring.

The DA's Western Cape provincial leader Helen Zille gave van Schalkwyk a cheer: 'We strongly support his defiance of the ANC government's disastrous policies on HIV-AIDS.' Rather missing the point; wasn't this all about a resolution by the MCC? The workers chimed in too, with the Western Cape branch of COSATU issuing a press statement saying, 'Premier Martinus van Schalkwyk should be commended for providing the drugs.'

PAC whip Patricia de Lille said her party was giving 'notice to the Minister of Health': 'She must just try to ban nevirapine. We will definitely defy the ban.' IFP health spokeswoman Ruth Rabinowitz reckoned 'This is unbelievable – just another smoke screen of the government finding another way not to roll out nevirapine.'

But Eastern Cape peoples' doctor and PAC health secretary Costa Gazi outdid them all: the MCC's 'announcement ... that it is revisiting its licensing of nevirapine for use against mother to child

transmission of HIV is nothing less than a Sharpeville massacre', he said. Examining the supporting data for the drug's special registration was just like shooting dozens of unarmed Africans in the back.

Notwithstanding the MCC's non-committal, guarded comments about the review underway of its perinatal nevirapine licence granted to Boehringer Ingelheim – explaining perfectly reasonably on its website that the

MCC wants to ensure that the HIVNET 012 study data that was submitted by the manufacturer in support of the application approval of MTCT is valid and that there are no data integrity problems

– the TAC went on the attack, accusing the MCC without any cause at all

of losing its independence and of not seeking to ensure access to safe and effective AIDS medicines. Nevirapine is registered in 53 countries for the prevention of mother-to-child transmission of HIV-Aids

it said, neglecting to mention that not a single one of them was a First World state. 'In the United States it is considered safe enough for mothers to use throughout their pregnancies to prevent transmission of HIV-Aids.' It is?

A day later the TAC's Heywood was quoted on the radio threatening litigation against the MCC if it deregistered the drug.

On 6 August the *Cape Argus* reported Achmat taking a further 'swipe at the government, saying that since they'd lost in court, they were using the MCC to undermine the court decision' – once again, without a jot of evidence to support his claim that the MCC were doing the government's bidding.

Achmat said there was no scientific evidence that nevirapine was unsafe, and called on the MCC to hand over any data it may have to the contrary. 'The government has not been able to produce a single person who has suffered any ill-effect,' he said.

That's because to AIDS doctors, drugged babies falling ill and sometimes dying are being taken by the virus. And didn't the first

Lancet report of HIVNET 012 claim nevirapine to be safe and effective?

Heywood's TAC comrade Nathan Geffen told *Lancet* that he believed that

the MCC, with the backing of the government, has a hidden agenda to undermine the constitutional court's judgment on July 5, which forced the government to provide nevirapine to all HIV-positive pregnant mothers. 'We believe they continue to cast aspersions on nevirapine because they do not want to roll out. This is because there is strong support for AIDS denialists by government.'

Kevin McKenna, Boehringer Ingelheim's South African technical director, disputed the *Sunday Times*'s report that the MCC harboured 'serious concerns' about the safety and efficacy of nevirapine. MCC approval would not be withdrawn, he said, because nevirapine's effectiveness and toxicity were not in question. Claims that nevirapine might be deregistered for perinatal prophylaxis on those grounds were incorrect, he added:

I was not informed about any moves of the MCC to do that. They would only do that if they had great concern about the safety and effectiveness of it and there is absolutely no basis to question the safety or effectiveness of the drug.

Absolutely none. He wouldn't say what had transpired at his company's meeting with the MCC, but he mentioned that the withdrawal of the application to the FDA in March had led to the MCC's investigation. 'Nothing has changed since then. The only thing that has changed is that the National Institutes of Health is in the process of actively recording the trial. They are putting their administrative problems in order.' Their administrative problems. As for allegations that there had been unreported deaths during the HIVNET 012 trial, 'The unreported deaths are rumours that the NIH refuted some time ago. I had seen in writing a letter that the NIH sent to the MCC that the rumours are unfounded.' Only they weren't; stand by.

The pivotal significance of the MCC's review of its special registration of nevirapine for perinatal administration lay in the fact that, with the help of the TAC, South Africa had become a key

marketing portal for its German manufacturer, Boehringer Ingelheim. A red flag from the MCC after a review of all the available data would probably mean the end of the drug's advance in the Third World – but a green one, Open Sesame.

On 6 August Mhlongo filed a submission to the MCC concerning the perinatal use of nevirapine, a list of one hundred points that we drew summarising the case against this special indication (see Appendix 1). Clinical Trials Director Dr Rajen Misra telephoned him two days later to confirm receipt, and thanked him for them. 'They made sense', he remarked, saying they would be given due consideration. Misra said that it was obvious from the submission that Mhlongo knew more about the issues in question than any member of the council – to which Mhlongo retorted: 'That's because you people don't read. It's time you stopped approving drugs on the basis of tee-shirts', alluding to Misra's revelation that the Perth Group's definitive monograph on AZT and nevirapine for preventing mother to child transmission of HIV, a copy of which he'd delivered to the MCC, had gone unread, and to the TAC's 'HIV Positive' tee-shirts always worn for the TV cameras. Misra was evidently bowled over by the comprehensiveness of the 100-point critique, because he took no umbrage at the gruff rebuke and went on to tell Mhlongo that he intended proposing to the council that he be invited aboard it. (Never did; soon afterwards, to avoid trouble for the drug business, the MCC took in one of Mhlongo's very junior white colleagues Roy Jobson instead.)

On the same day that Misra called, a bloc of eighteen members of the executive committee of the Health Sciences faculty at the University of Cape Town shared the TAC's dismay at the MCC's investigation in a letter to the *Cape Times*: 'Show proof, or stop implying that nevirapine is dangerous.' The very title was notable for its scolding of the MCC merely for reviewing the drug's registration – thereby 'implying' it to be dangerous. The academics thereupon set out selling nevirapine as a drug proven safe and effective; the Ugandan study established it, they said – even if the FDA and CDC didn't think so. And a South African study confirmed it – although no one, including our MCC, took it seriously. And then:

Deregistering nevirapine on unscientific grounds will be a devastating blow to our evolving Aids prevention programme and will be morally and ethically indefensible. If the council has any evidence to suggest that nevirapine is indeed toxic or not effective, then they should make such information available immediately. If not, they should refrain from creating the belief in the minds of the public that this proven and effective treatment is useless or even harmful.

As useless as the medical experts whose lazy letter, so very typical in tone and ignorance, creates the belief in the minds of the public that the drug works and that it's safe?

Two days later *Lancet* ran an implicitly critical report, 'South Africa soaks up pressure to change HIV/AIDS policy':

South African doctors, activists, and politicians have vowed to fight plans by the country's drug regulatory authority to withdraw nevirapine for the prevention of intrapartum HIV transmission.

And so on.

The *Sunday Times* published a half-page opinion piece the next day in which Achmat elaborated his wild charges:

It's not just lives that are at risk. The political manipulation of the Medicines Control Council is a threat to our democracy, says Zackie Achmat.

Nevirapine, he said, 'is a life-saving medicine that keeps people with HIV living longer and healthier lives'. Not that there's any evidence supporting this claim, the manufacturer itself openly admits, but who was going to dare challenge his lies? Nor did he present a single fact to back his claim that the MCC was being politically manipulated or was itself doing any manipulating. Unable to brook any debate, any inquiry, any doubt about his line, Achmat frothed in a melodramatic broadside:

The Medicines Control Council is contributing to anguish, fear and confusion among people living with HIV/Aids. At the root of this confusion is its mishandling, since November 1999, of the registration status of nevirapine for the purpose of preventing the transmission of HIV from mother to children.

And on he flapped in his article, the usual weak-minded waffle, the whole thing as feeble as his facial expression in an accompanying photograph. But ending in stamping feet:

Any attempt to change the registration status of the drug without clear, scientifically verified information will undermine the MCC. Should it suspend registration of or deregister nevirapine for mother to child transmission prevention without sufficient reason, the TAC will take legal action to ensure that more unnecessary HIV transmissions and deaths do not occur.

As its executive had formally resolved to do, a week earlier, on the 5th. It wasn't just talk: a Legal Resources Centre press release 'Government Reminded of Constitutional Obligations Regarding Nevirapine' on 20 February 2004 revealed that

When the Medicines Control Council threatened to deregister Nevirapine, the Constitutional Litigation Unit of the LRC, once more stepped in to act on behalf of the TAC. An appeal was lodged against the council's decision and preparations were made for litigation. Ultimately the MCC rescinded its decision.

Responding to Achmat's performance, *Sunday Times* editor Mathatha Tsedu thought the 'Arrogance of TAC is nauseating' in a piece under that title in *The Star* two days later:

The activists have become so self-righteous that nothing they disagree with can ever be right. These critics pontificate and rubbish the credentials of honest scientists simply because their own organisations rely on funding dependent on anti-government stances. The abundant threats of defiance will most definitely open the donor doors. It is time someone told the TAC that it is contradictory to say science rules but then to rubbish any scientists who want to be thorough in their work. The TAC should be told it is ironic that its leader encourages other people to use nevirapine but will not use it himself! The point is that the TAC is a useful organisation, but needs to grow up and accept that not everyone who differs with it is a lackey of the government.

The Parliamentary Health Portfolio Committee got the jitters. On 16 August it summoned the MCC to appear before it to explain its decision to appoint a special committee to review its registration of nevirapine as a perinatal prophylactic. Achmat and a group of TAC members and supporters were permitted to sit in at the hearing – dressed not in formal gear for the occasion, but instead like children in their ‘HIV Positive’ tee-shirts to make their point. Except that, Achmat aside, the TAC’s top brass aren’t. MCC statistician Jonathan Levin told the committee that there was no basis for the belief that nevirapine halved the HIV transmission rate during childbirth. (A belief treasured by Judge Cameron: ‘Medicines exist that, now, can reduce [the infant infection rate] by half.’ And shared by the Bill and Melinda Gates Foundation’s Helene Gayle (formerly of the CDC): there was ‘clear evidence’ that nevirapine ‘would cut transmission of HIV from mother to child by half’.) On Levin’s reading of the data, if a hundred HIV-positive pregnant women were given nevirapine, twelve or thirteen would infect their babies as compared with sixteen to eighteen if untreated – an insignificant difference, he said. Nobody on the Health Committee pointed out to him that this conclusion (very different from what he’d asserted in the High Court) obviously warranted the immediate deregistration of nevirapine for use in maternity wards. No one asked why then the drug was still on the books.

Under interrogation by the Health Committee, MCC registrar Precious Matsoso hedged: ‘Nevirapine is not banned in this country’, having said earlier on radio that she did not ‘know where this thing of banning comes from’. And later: ‘Firstly, we are not deregistering. Secondly, we are not banning. Thirdly, we are not withdrawing.’ Asked whether the drug might be deregistered for administration to pregnant women and their babies, she answered, ‘It will be difficult to predict given what we have so far. We don’t want to pre-empt the outcome of the committee’s decision.’ Fair enough. But disheartening was her announcement, in as many words, that the committee would probably just be going along with the Americans rather than exercising any independent judgment. The MCC had already received an audit of HIVNET 012 carried out by Boehringer Ingelheim and the US National Institutes of

Health, she said; it was now awaiting a curiously named ‘re-monitoring report’ from the NIH, expected in September, which, the *Daily Dispatch* reported on the 19th, ‘would be used to finalise the matter’.

Matsoso concluded with an ass-kissing compliment for Father Christmas handing the drug out free: Boehringer Ingelheim had acted ‘very responsibly’, she mewed, although quite how she didn’t say. ‘We have not had any problem whatsoever with the company.’ Make trouble for it, Precious, and you soon will have, I promise you. And you’ll no longer be talking like a kitchen maid: My master is a very nice somebody. When I shine his shoes and bring him his tea.

Achmat’s advice after the meeting was that if there was any doubt about the effectiveness of nevirapine the government should immediately switch to AZT or ‘triple therapy’. The TAC had wanted AZT from the start, he said, but the Health Department had picked cheaper and simpler nevirapine (for pilot research use) instead. Claiming to understand the maths better than Levin the statistician did, Glenda Gray drew from her wide vocabulary to slam Levin as ‘mischievous’ for furnishing the disappointing figures. The *Weekend Argus* on the 17th sided with ‘acclaimed Aids expert’ Gray, reporting: ‘Boffin blasts Aids drug claims by MCC’.

Getting his thoughtless word in too, as usual, was Patrick Bond. In ‘Alliances and conflicts prior to Cancun’, posted on his Centre for Civil Society website on 18 September a year later, he wrote:

The state Medical Research Council [*sic: Medicines Control Council*] further complicated matters by threatening the deregistration of the drug Nevirapine, which TAC says has saved more than 50,000 babies from getting the HIV virus from their mothers.

Small wonder John Pilger finds Bond’s writing unreadably tedious and his company unbearably boring.

On 15 October 2002 Boehringer Ingelheim granted local drug maker Aspen Pharmacare the right to manufacture nevirapine for administration at public hospitals and clinics. By the 21st of that month, according to Public Works Minister Stella Sigcau, speaking at the launch of her department’s new HIV-AIDS awareness policy

for the construction industry, 10 043 mothers and 6 947 babies had been dosed with the drug. She didn't say that they would have been almost exclusively black.

In early November MCC Registrar Matsoso announced that we wouldn't be getting the MCC's long overdue decision concerning the registration of nevirapine for perinatal use before the end of December. The MCC was awaiting a report from the US NIH concerning the Ugandan nevirapine study that 'will guide its decision', she said. Since we're unable to make up our own minds. We just follow the Americans. Matsoso added that an interim report from the NIH was 'subject to a confidentiality agreement between the MCC and the NIAID, on the latter's insistence'. Meanwhile, she said, nevirapine remained the 'drug of choice' for preventing mother to child transmission of HIV.

Edmund Tramont, director of NIAID's Division of AIDS, issued a statement claiming that proper records had not been kept by the HIVNET 012 overseers, because the trial had not originally been intended as the basis of an application to the FDA to market nevirapine for perinatal administration in the US. But Boehringer Ingelheim had changed its mind about that, he said, when it saw the reported results of the trial. All of which, we'll later read, was completely untrue.

The MCC met on 5 November to consider the NIH's interim report concerning the HIVNET 012 shambles. A journalist for Health-e who asked Matsoso what had been discussed was fobbed off by reason of the secrecy agreement. Not only was the NIH report blacked out from public scrutiny, so were the minutes of the MCC meeting. Incredibly, in his address to the Portfolio Committee on Health in July, the MCC's vice chairman told the committee in a memorandum that during the previous month there had been a

Meeting with US official (Health attaché of the US embassy) in MCC offices. Discussion on the conditions in which we can obtain the data from NIH. To sign confidentiality but can only view the data at the US embassy and not obtain a hard copy!

This was the contemptuous view that the Americans took of South Africa's MCC.

Not a single one of our AIDS journalists saw anything remiss in the American gag on the MCC's deliberations, its blockade of news flow in relation to a matter of considerable national importance and public interest. All that was on the table for review was a commercial licence application granted in South Africa – but not in the US – to a German drug manufacturing corporation to market its product for a special indication: to administer to women in labour and to their newborn babies. And to profit thereby in the ordinary course. Of the drug business. No national security interests were on the line to justify the information embargo imposed by the US. But very much at stake was the reputation of the US NIH, which had funded the study that the FDA rejected at the door, and whose scientists had participated in conducting it, according to the first *Lancet* report. The WHO, the drug licensing boards of dozens of developing countries (by July 2004, seventy of a hundred and twenty targeted, and currently still about the same number), and AIDS doctors everywhere had gone on to rely on HIVNET 012. And let's not forget our Constitutional Court, which had likewise. If the study was thrown out there would be egg all over America. Another US rocket ship disintegrating into scrap. Everyone watching. And talking. About American science.

On World AIDS Day, 1 December 2002, Boehringer Ingelheim placed a big fat advertisement in the *Sunday Times*, headed in underlined capital letters:

WE HAVE DONE MORE THAN JUST CREATE
VIRAMUNE (NEVIRAPINE). BOEHRINGER INGELHEIM
IS AT THE FOREFRONT IN THE FIGHT AGAINST
HIV/AIDS. THAT IS HOW VIRAMUNE (NEVIRAPINE)
CAME INTO BEING, NOW SAVING LIVES AND ALSO
ADDING QUALITY TO LIVES OF THOUSANDS OF
OTHERS LIVING WITH HIV.

What we have done:

- Provided nevirapine free of charge to the developing world to reduce the number of children being born HIV+
- Provided nevirapine for those living with HIV, at a price in South Africa, that is amongst the lowest in the world
- Offered nevirapine to countries of the developing world at low prices

- Granted a non-exclusive licence to allow generic production of nevirapine in South Africa
- Funded a national campaign of continuing medical education for doctors treating people living with HIV/AIDS. Our future commitment:
- Continue to provide nevirapine free of charge to reduce the number of children being born HIV+
- Continue to research new medicines to manage HIV/AIDS
- Support governments, NGOs and larger employers by providing nevirapine at low prices
- Continue our programme of investment in clinical research to learn more about nevirapine and HIV.

Try to imagine a world where there are no new medicines for the treatment of disease. We want to ensure that this does not happen. Boehringer Ingelheim.

Well, thanks a whole lot. For looking after us. Especially our little black babies. Spoken under oath, the lies in the headline would have landed their authors in prison.

A press statement on the same day, issued from the company headquarters in Germany, pressed the government to join forces with it and with the company's local marketing agent, the TAC:

‘The constantly rising figures of HIV infection and the high death toll AIDS is causing, call for more combined efforts of governments, NGOs, pharmaceutical industry and other partners in health care than ever before,’ said Professor Rolf Krebs, Chairman of the Board of Managing Directors of Boehringer Ingelheim, in view of World AIDS Day 2002. With a stronger political commitment from heads of governments in developing countries and the possibility to use their often scarce health infrastructure more efficiently, more progress could be made in addressing the devastating effects of this disease.

By buying our goods.

On 17 December the TAC filed an application in the High Court asking for the imprisonment of Mpumalanga Health MEC Sibongile Manana for contempt of court and the compulsion of

Tshabalala-Msimang, on account of the former's alleged failure to provide nevirapine in that province to pregnant women and babies in compliance with the interdict it had won. Manana was to be made an example of. Claiming that only KwaZulu-Natal, Gauteng and North West provinces had complied with the order, TAC attorney Geoff Budlender warned, 'We hope this will make it clear to other provinces that haven't complied fully that if they don't get their house in order they will face court proceedings.' We'll show these stubborn, lazy afs who's boss.

On 10 February 2003 Tshabalala-Msimang publicly responded to the TAC's application against Manana: 'If she goes to prison, I'm going with her.' UDM party health spokesman Nonhlanhla Nkabinde's answer was that since she was determined

to continue with the genocide against people who are living with HIV or AIDS ... Going to jail in solidarity with her MEC is the first constructive proposal she has ever made in her entire term of office.

The application fizzled out.

The nevirapine litigation, Tshabalala-Msimang told Parliament on 12 March, had cost the government a total sum of R2.88 million, the TAC's legal costs included.

In April the NIH released its final report concerning the HIVNET 012 trial. Lynne Altenroxel reported the news in the *Mercury* on the 23rd.

A year-long investigation into the anti-Aids drug nevirapine has found beyond doubt that the treatment is safe and effective. The finding is made in a report by the United States National Institutes of Health and is to be discussed by South Africa's Medicines Control Council on Friday at a special meeting about nevirapine's possible deregistration. Panic over reports about the possible banning, which surfaced during last year's Constitutional Court battle over the drug, were fuelled by the political debacle over Aids dissidents and the government's insistence that nevirapine was dangerous. But the 50-page report, which scrutinises the standards of the 1997 Ugandan drug trial where nevirapine was first tested on pregnant women, recommends that the treatment continue to be used. Its

findings are pivotal for the council, which based its registration of nevirapine for prevention of maternal transmission on the Ugandan study and has been waiting for the report to be completed before deciding whether to withdraw its approval.

What Lynne hadn't noticed was that the NIH was giving its own trial the all clear. We lawyers have a tiresome old rule against this; translated from Latin the maxim goes: 'No one should be a judge in his own case.' But whatever, one thing's for sure. Nevirapine will never be pushed past the FDA for giving to American mothers and their babies. Because there's still no accounting for all that missing clinical trial data, and without them it's no go. Only it's different in Third World countries. Where anything goes. Bumped along by the cream of the legal world sometimes.

The cream of the legal world like Constitutional Court Justice Albie Sachs. Who on 3 July brought his one-eyed, one-armed, one-man AIDS revue down to the National Arts Festival in Grahamstown. Addressing the enrapt audience from the pulpit of a church, Sachs stoked the intimate emotional atmosphere of the occasion by bobbing his head foolishly and pausing ponderously after his phrases in a totally artificial, ridiculous delivery, bloated with lugubrious sentimentality, like a *koeksuster* dripping in oil and syrup:

We were about to go into court in the nevirapine case. Eleven judges of South Africa's Constitutional Court. And my colleague Sandile Ngcobo said to me: 'Albie, would you like a handkerchief?' And my colleagues knew why he offered. Because in a previous case involving HIV-AIDS, this is what happened. The court was jam-packed to hear the outcome of a case concerning a Mr Hoffmann, who'd applied for a job as a steward aboard a South African Airways plane. He passed all the tests with flying colours, but he turned out to be HIV-positive. And SAA said we will employ you in any capacity, but not serving passengers on the plane – they might go to another airline. Sitting in the court were people young, old, black, white, male, female, wearing tee-shirts saying HIV-AIDS, HIV-positive. I don't even know if Mr Hoffmann was there. And my colleague Sandile read out the judgment of the court. And he said people living with the virus need all the

support from agencies of the state like South African Airways. To refuse them employment simply because of the prejudice of passengers is to give in to that prejudice and constitutes unfair discrimination, and it's against the new South African Constitution that protects them and everybody. And he said the fact that foreign airlines for commercial reasons would refuse to employ someone like Mr Hoffmann cannot be a basis for deciding a fundamental right of a South African. The people in the court were completely silent. But as we moved into the corridor behind the court, we heard cheering. And I cried. I might say I had a good precedent – Archbishop Tutu cried. [*Smiles sweetly for empathy.*] And I used to say the difference between the TRC and the court is that bishops can cry; judges can't cry. [*Smiles some more.*] But I cried. And I cried with emotion that wasn't sorrow. It was a much more powerful and very positive emotion. The weight of the affection, but also the sense that we have a constitution. And I have the great honour to be on the court, where we can do something about humans' inhumanity to fellow human beings. That's what brought the tears to my eyes. Now at the end of the nevirapine case, the court jam-packed once again with people wearing tee-shirts saying HIV-positive, people from the Ministry of Health, journalists from all over the world, intense emotion in the court, we're about to go in, Sandile says, 'Albie, would you like a handkerchief?' [*Another fey smile.*] And I said, 'Sandile, it's OK, I'm prepared this time. It won't be necessary.' And we went into court. And we gave what we like to believe was a very balanced judgment, granting pregnant women living with HIV the right in the public sector to get to doctors who are in a position to provide counselling and access to the nevirapine, to have that, to give their babies a much, much better chance. It was a beautiful judgment. Again the court was silent when we delivered the judgment. We went out into the corridor at the back and I cried.

And after this wrenching testimony there was a thunderclap of applause as the judge walked from the pulpit to the pews to fellowship with the congregation, which loved him with the same 'weight of affection' as the gallery did in the Hoffmann case – for

having shared with us how he sobbed with joy after his ‘beautiful judgment’ was read out, enforcing African babies’ human rights to nevirapine, and how great it was that thanks to him and his colleagues doing ‘something about humans’ inhumanity to fellow human beings’, babies had ‘a much, much better chance’. And it was like Jesus feeding the five thousand. And healing Lazarus with a single touch. And suffering the little children to come unto to him. And in a country saddled with a haughty and uncaring Marie Antoinette. And it was enough to bring a lump to the throat. A lump of vomit. And Tutu then followed Sachs to the pulpit to tell us ‘What an incredible icon Albie is!’ And we all felt just so incredibly pleased with ourselves, since there’s nothing more morally fulsome than being an AIDS drug activist. In the pulpit and on the bench. And it’s rather like having a marvellously unending moral orgasm. So that when in church we try describing how it feels we do so in a kind of dazed, silly reverie. As if still a bit drunk or stoned from the big party the night before. And still high on saving the picaninnies.

And at his Inkatha Freedom Party’s AGM on 12 July, Chief Mangosuthu Buthelezi joined the snivelling; referring to the nevirapine case he said,

I have no words to explain to myself the absurdity and tragedy of a court of law having to order a recalcitrant government to do what basic conscience dictates ... to ensure that the children could be saved.

The little children.

Part Six

*Take nothing on its looks; take everything on evidence.
There is no better rule.*

Jagers the solicitor to Pip in *Great Expectations*
Charles Dickens

On 29 July 2003 MCC Registrar Precious Matsoso went on air at noon on national radio with a bombshell announcement: the MCC had rejected the Ugandan HIVNET 012 study on account of ‘data integrity’ problems. She said that Boehringer Ingelheim had not fulfilled the conditions under which nevirapine had been provisionally registered for perinatal use, and that the company had been given ninety days within which to come up with evidence of efficacy for that indication: ‘We have to be cautious. If information is available that meets rigorous scientific standards, we will look at it.’

Well, hello! That HIVNET 012 was a complete mess had been detailed extensively in Professor Mhlongo’s urgent application to the Constitutional Court. On the morning of the government’s appeal, he’d applied for a hearing to set out the glaring trouble with the study on which the entire case was based. But the eminent justices were so intent on gorging themselves at their drunken moral banquet that they kicked him out the door. And as we’ve just read, one of them, tired and emotional when the do was over, actually burst into tears. Feeling so sad with happiness. Had the judges properly considered what Mhlongo was saying, before they turfed his application out, they’d have saved everyone a lot of trouble. And thousands of poor black women and their babies pointless exposure to an extremely poisonous, useless chemical.

‘Thousands of HIV-positive mothers are to be denied a chance to save their babies’ lives if a Medicines Control Council (MCC) ruling leads to the banning of nevirapine,’ cried Lynne Altenroxel on the front page of the *Cape Times* the following day:

Activists and scientists are outraged at the MCC’s decision. ... Last night Dr Fareed Abdullah, head of the [Western Cape] provincial Aids programme, hit out at the MCC, saying the confusion it was creating was ‘completely unhelpful. The news

astounds me ... The safety of the drug is well-established and that should be their main concern.'

The MCC's dramatic decision flew in the face of the NIH's fifty-two page final report filed on 30 March, which had concluded:

In summary, the re-monitoring of the study determined that nevirapine, 200mg orally given to the mother at delivery and 2mg/kg given to the neonate within 72 hours, is safe and effective. However the conduct of the study lacked the necessary documentation to support a request to the FDA to consider this study as a stand alone pivotal trial.

In other words – to cut the crap – the recording and reporting of the study had been too poor to satisfy the FDA that the drug 'is safe and effective' for American mothers and babies (and the US Centers for Disease Control did not consider it fit for them either), but American AIDS doctors in the NIH nonetheless considered it up to scratch for 'a developing country' (per the NIH report) like ours.

Interviewed on radio by John Perlman on 30 July, an American spokeswoman for UNAIDS responded to the news of the MCC's announcement by reiterating UNAIDS's endorsement of the NIH's support for the perinatal use of the drug. In Africa where the coloured people live.

The MCC's thumbs-down for perinatally administered nevirapine was a most surprising development – and against all expectation, considering how it had buggered Mbeki's AZT safety enquiry three years earlier. It appeared to signal that the body was willing and able to exercise an independent judgement and not simply kow-tow to the Americans, and that it was prepared to weather the intense political fallout that would inevitably follow such an extremely unpopular decision. Risk a lawsuit from the TAC too.

In a brief statement accounting for its decision, the MCC noted that the NIH report reflected that patient records did not support the published results; there were problems with the manner in which the study was conducted; records did not account for how the drug was stored, handled and distributed; records indicating which treatments were allocated to trial participants were missing;

and the obtaining of voluntary informed consent for the trial participants could not be confirmed in all cases.

It is therefore no longer valid for the MCC to continue to approve the use of nevirapine as a single agent in reducing the risk of HIV transmission from mother to child. The MCC has requested that the company responsible for the application provide further evidence of nevirapine when used on its own in reducing the risk of mother to child transmission of HIV, within 90 days. This decision of the MCC does not affect the use of nevirapine as part of combined anti-retroviral regimens in HIV and AIDS. Nevirapine is still recommended for that indication. The MCC reiterates its commitment to fulfilling its statutory obligation to ensure that medicines which are made available to the South African public are safe, have been shown to be effective and are of the required quality.

But what appears to have finally swung it for the MCC was the statement in the NIH report's covering letter that 'at the outset, it was never considered that such a trial could be used as a stand alone pivotal trial ... for [FDA] licensure'. Which was a barefaced lie (we'll see), told to conceal the hard fact that the study had not been conducted to IND (Investigational New Drug) standards – i.e. to the standards expected and applicable in a clinical trial of a test drug, but which, through gross incompetence, had not been observed. But then again, if the Americans can get away with lies about weapons of mass destruction in Iraq, they can get away with lies about anything.

Unfortunately, it was evident from the MCC's reasons that it had not considered or not understood the 100-point submission delivered by Mhlongo in August the year before. Summarising the trouble with HIVNET 012 described in Part Four above, the memorandum we drew pointed out root problems with the study that went way beyond unsatisfactory record-keeping and the like; it was fatally flawed for a host of other reasons going to the fundamentals of the design, conduct and interpretation of the study. None featured in the MCC's statement. The MCC's relatively superficial criticism of HIVNET 012 rendered its decision vulnerable to attack in the courts. As the TAC immediately threatened.

Boehringer Ingelheim's Kevin McKenna confirmed Matsoso's announcement:

We received a letter from the MCC on Monday [*the day before the MCC's public announcement*] which said it had rejected the HIVNET study and gave us 90 days to submit new evidence from other studies. Their reasons are technical and relate to problems to which we've already drawn their attention. They're problems with technical issues in the documentation and reporting on the Ugandan trial. But we [*in a restricted, confidential submission in June*], the World Health Organisation [*in a statement a week earlier on the 16th*] and the National Institutes of Health [*in its preliminary and final reports*] have all accepted that these concerns don't in any way invalidate the findings. ... We shall continue to try to work with the MCC to clarify these technical issues. But it will be very difficult for us to produce that evidence ... there are no other studies. There is no other information available.

The look of it then was that as a perinatal antiretroviral prophylactic, nevirapine's number was up.

MCC chairman Professor Peter Eagles explained that after studying the NIH's preliminary and final reports,

We are no longer able to continue accepting HIVNET [012] as a basis for registering nevirapine for single-dose use in preventing HIV transmission from mother to child in South Africa.

Disagreeing with the NIH's conclusion that the study's findings stood firm, notwithstanding all the problems it had uncovered, the MCC evidently considered the problems found to be more serious than mere 'technical issues', as McKenna had tried discounting them.

Nono Simelela, head of the government's HIV/AIDS directorate, responded to the MCC announcement, saying:

We'll discuss the implications of the decision with the Director General, Dr Ayanda Ntsaluba, and with the Minister, Dr Manto Tshabalala-Msimang. They could be serious.

Yes, honey, they really could. In another statement made a day or two later, Simelela said she'd been

spending sleepless nights asking what we are to do with mother-to-child-transmission if we can't have nevirapine. I have 80 000 women on this programme. I have to have an answer for them.

This is because I've been telling them that they need the special medicine made by those clever white people in Germany, or their babies will all die. As I'd told the Health Minmec meeting in August 2000, 'Ethically, it is important to provide nevirapine to these women while strengthening existing health services.'

'What is going to happen to all the thousands of babies exposed to the virus?' fussed Glenda Gray in the same way. A quarter of a million HIV-positive women give birth annually in South Africa, she said:

There's enough published and unpublished information to confirm that nevirapine reduces the spread to 12%. It is unethical to conduct tests with placebos, but everyone knows the spread without intervention is nearly 25% in developing countries.

Her colleague James McIntyre agreed:

The experience of other trials and many other women, probably more than fifty thousand worldwide, has demonstrated the efficacy and safety of nevirapine. I can see no reason to deregister it.

Of course Gray and McIntyre should talk like this, both being in Boehringer Ingelheim's pay (GlaxoSmithKline and Bristol-Myers Squibb's too, according to a disclosure in the *British Medical Journal* (2002; 324:218-21)) and hired by the company the month before to write a secret submission to the MCC to try to save the drug from losing its special registration as a perinatal anti-HIV prophylactic. It contained everything they could scrape up to rescue the fast dissolving HIVNET 012 report, every scrap of new research data they could gather. But the MCC was unimpressed. As it was with Glenda's plaudits included among her credentials cited at the end of her report:

1997: Awarded the Femina magazine 'Woman of the Nineties' national award ... 1999: June: Edgars Club Magazine: Everyday Hero ... 2000: Longevity Magazine Millennium Collectors Issue: Profiled as 'one of five people that the magazine considered icons of the century'. ... 2000: The Mail&Guardian: Listed in South Africa's Top 10 Movers and Shakers making their mark in the new millennium ... 2002: Winner of the 6th Annual Rapport/City Press Prestige Award: South Africa's most inspiring woman.

Was the MCC really supposed to give a damn about what women's magazines and clothing merchants thought of her as a pop celebrity? In conducting a review of scientific data supporting the particular use of a drug, paid for by its manufacturer?

In a radio interview on 1 August McIntyre told John Perlman that there was no new evidence for efficacy that Boehringer Ingelheim could put up. His and Gray's report said it all, he said. For nevirapine it looked like countdown to game over.

Keith Bolton, chairman of the South African Paediatric Association, spoke as dull doctors do: 'I am convinced that millions of lives would be lost if this bungle is allowed to happen.' In a formal statement that followed, his association said nevirapine had already saved

many hundreds or perhaps thousands of infant lives. ... The executive committee of Sapa believes the efficacy and safety of Nevirapine usage, as part of a strategy for the prevention of transmission of HIV from mother to child, has been adequately established beyond reasonable doubt. We believe that failure to continue to administer Nevirapine at this time would constitute a dereliction of the ethical duties of individual health care professionals as well as an unconstitutional abdication of responsibilities of our health authorities. We appeal to the MCC to immediately repeal their decision that is out-of-step with the extensive reviews and statements of authoritative bodies such as the US National Institutes of Health, the US Federal Drug Administration and the World Health Association. [*The stupid doctors hadn't noticed that the basic point of the MCC's objection to the continued registration of nevirapine for perinatal use, based on HIVNET 012, was that*

the study wasn't acceptable to the FDA – nor was it to the CDC. Nor was any other study.] We urge our members in the field to follow their conscience by utilising the accepted practice of providing Nevirapine as part of the PMTCT programme. In doing so they will dramatically and significantly lower the risk of transmission of HIV from mother to child and thus prevent most cases of childhood Aids.

‘Jerry’ Coovadia said of the MCC’s decision to reject the Ugandan study:

I think this is just such a dreadful mistake. The implications for the country’s programme to prevent mother-to-child transmission, and for the reputation of our country, are really very profound. I think we are now going back to the stage from which we thought we had advanced – that is, all the controversy around HIV/AIDS. I’ve read the [*NIH*] report, and I didn’t need anything else. The conclusions of the report were that there was no question about the scientific validity of the findings. That means the safety and efficacy of the trial was not questioned – in fact it was confirmed.

Coovadia summed up his sort of thinking at the first South African AIDS Conference in Durban at the start of the month:

The AIDS epidemic has been bedevilled by unscientific, irrational, unreasonable and downright perverse attitudes. I really am left breathless by the decision of the MCC to question the validity of the scientific results around nevirapine.

It’s all so confusing to me that I just don’t know what to say.

Missing the point – that the unpopular decision was the MCC’s not the government’s – Coovadia added later that there was a danger of ‘democratic anarchy’ unless government had recourse to ‘the best available science’. Uncritically defer to experts like him, in other words.

His colleague Andrew Gray, senior lecturer in the Department of Experimental and Clinical Pharmacology at the same university, attacked the MCC’s integrity – treating us on the way to a further lesson in medical logic:

what is clearly necessary now is a very detailed account of the reasons for the decision by the MCC – a level of detail that would bring the whole secrecy issue in the workings of the MCC into the spotlight. So, as momentous as this decision is, moving popular opinion away from the obvious conclusion – that political pressure was brought to bear – will require a major overhaul of MCC processes.

NAPWA deputy director Thanduxolo Doro similarly claimed that there were ‘sinister motives’ behind the decision. PAC health spokesman Costa Gazi also accused the government of ‘using the MCC, which is supposed to be an independent body’. The DA’s Eastern Cape spokesman on health, Athol Trollip, complained: ‘South Africa is one of the worst-hit AIDS countries, and still our political leadership clings to its dissident attitude.’ DA national spokesman on AIDS, Michael Waters, likewise accused the MCC of succumbing to political interference:

Given the lack of medical basis for its decision on nevirapine, the only possible conclusion is that the MCC is bowing to political pressure from the Minister ... without any regard for the consequences to babies born to HIV-positive mothers. This demonstrates clearly how the capacity of the MCC to provide South Africans with an absolute guarantee about the safety and efficacy of the medicines that we rely on is being compromised by interference by the executive in pursuit of political objectives. South Africa needs a truly independent MCC, free from the Health Minister’s control. The DA believes the council is in serious need of an overhaul.

So vote for us next time. We’ll make sure the drug companies doing business here don’t have problems like this again.

Tshabalala-Msimang dismissed the allegations and said South Africa cannot be party to

double standards ... We can’t have something that’s only good for Africa and not good for developed countries. ... We must be convinced based on the research data available to us, which is not at the moment convincing.

Quite.

MCC Registrar Matsoso also repudiated all the political interference talk; HIVNET 012 simply didn't meet the MCC's standards, she said:

It would be irresponsible of us to make this a political issue. A letter was written by Boehringer to alert us to the problems in the Uganda trial. How can this be a political issue if they wrote to us? We are not a banana regulatory authority, to forget it [*the reported trouble with the study*] because of an emotive issue.

TAC chairman Zackie Achmat threatened more litigation, claiming

the MCC has chosen to play games with this issue instead of an open and honest approach that takes public interest and public health into account. TAC will issue a full statement after consultation with our lawyers and a teleconference of our secretariat on 30 July 2003.

A press statement from the TAC meanwhile claimed that the MCC had been playing 'political games' with the registration of nevirapine from the start:

Regrettably, the MCC has played political games with the registration of nevirapine for mother-to-child-HIV transmission since November 1999. Unfortunately, the MCC's questioning of science appears to coincide with the conversion of President Mbeki and Minister Tshabalala-Msimang to HIV denialist science. Despite their protestations, the MCC cannot deny the enormous political pressure brought to play on it during the registration process and in the MTCT court case. ... Many thousands of pregnant women and communities have already been confused by the forays of the MCC into the politics of medicines and anti-retrovirals. HIV/AIDS denialists misuse the MCC's authority to cause further confusion and harm in our communities. The MCC has not provided the public with any new scientific information to support its inexplicable position. The recent work of the MCC to register generic ARVs including nevirapine is being undermined by its fork-tongued approach.

All data showed that the drug was safe and effective, claimed the TAC:

If the MCC has information to the contrary, it must make this available because of the public interest in this issue. In the meanwhile the TAC will seek legal opinion from its lawyers on how to proceed on this matter.

‘We think that it would be wrong of the government to simply withdraw nevirapine,’ said TAC national treasurer Mark Heywood. ‘What the government needs to do is to introduce, as soon as possible, access to double drug regimens or triple drug regimens for pregnant women.’ Including AZT.

Interviewed on radio, Mbeki pointed out that the MCC’s decision was squarely within its jurisdiction; its function was to ensure the safety of licensed drugs. And in his *Letter from the President* posted on the ANC’s website that week, he commented incidentally on the decision, scorning the TAC as he did so:

Some questions burst suddenly over our heads, such as ... the decisions of the Medicines Control Council (MCC), about the anti-retroviral drug, nevirapine. This announcement illustrated the challenge we face, to ensure that even on this vexed question, we honour our commitment to let a hundred flowers bloom, and a hundred schools of thought to contend, refusing to allow the never-ending search for scientific truth to be suffocated by self-serving beliefs. Critical to the success of the historic African transformation project is our courage to stand up for what we think and feel is correct. We must have the confidence in ourselves to say and do what we believe is right, and openly to admit and correct any wrongs we might commit. We must free ourselves of the ‘friends’ who populate our ranks, originating from the world of the rich, who come to us, perhaps dressed in jeans and T-shirts, as advisers and consultants, while we end up as the voice that gives popular legitimacy to decisions we neither made, nor intended to make, which our ‘friends’ made for us, taking advantage of an admission that perhaps we are not sufficiently educated.

The drug industry’s white bunnies in AIDS journalism all scampered out to expostulate in protest at the MCC decision to

require acceptable clinical trial evidence supporting the perinatal administration of nevirapine:

Thousands of HIV-positive mothers are to be denied a chance to save their babies' lives if a Medicines Control Council ruling leads to the banning of nevirapine

wrote Lynne Altenroxel on the front page of the *Cape Times* on the 30th; 'The fight against Aids in South Africa does not need another setback.' 'What about the babies?' wrote Antoinette Pienaar for the news service News24:

The manufacturing company, Boehringer Ingelheim and scientists were astounded on Tuesday to hear the MCC was re-considering the registration of the drug for use in countering mother-to-child transmission of HIV/Aids.

Di Caelers wrote in the *Cape Argus* on the same day:

Another state threat to halt the use of nevirapine to prevent mother-to-baby HIV transmission could mean Western Cape taxpayers forking out R300 for a drug [AZT] for each mother and child – instead of the R16 it costs now

'HIV experts' report trashes nevirapine doubts', claimed Jo-Anne Smetherham in the *Star* on 1 August, referring to Gray and McIntyre's submission to the MCC: 'A confidential report has demonstrated conclusively that nevirapine prevents mother-to-child transmission of HIV.'

A typically partisan editorial published in the *Mail&Guardian* on 1 August, 'Don't crow too soon over Nevirapine', tried in characteristic hauteur to douse any satisfaction that nevirapine critics in government might have enjoyed seeing their position vindicated by the MCC. The liberals talking down, as ever, to the natives. Telling them, as Mbeki put it in Parliament on 6 June,

what to think, feel and say. My advice to these is they should desist from telling us what to feel, think and say. I would like to advise them that we fought for our liberation precisely because we refused that anybody should tell us what to feel, think and say. We did not achieve our liberation in order to perpetuate a master-servant relationship in our country.

But it was deaf ears at the *Mail&Guardian*:

Aids dissidents in official circles should be careful about crowing too loudly about the threatened demise of Nevirapine. To ensure the government will not be shackled to the drug if better remedies become available, the Constitutional Court ordered the provision of Nevirapine or 'an adequate alternative' in mother-to-child cases. The implication is that if Nevirapine is de-registered, public health institutions will have to supply something at least as effective to pregnant mothers with HIV. That is likely to be AZT, or a cocktail including AZT, Minister of Health Manto Tshabalala-Msimang's pet bogey. AZT is far more effective than Nevirapine in checking the transmission of the virus from mother to baby. But it will be expensive for the government, and more complicated to administer.

The extraordinarily emotive and prejudiced reaction of South African journalists was pointedly noted by the BBC in an article posted on its website on 1 August, 'SA media alarm at Aids drug move':

The South African media is expressing outrage at a recent decision by the country's Medicines Control Council (MCC) to reject the findings of a study into the anti-Aids drug Nevirapine.

On the same day, the US Elizabeth Glaser Pediatric AIDS Foundation announced the launch of a global petition to be delivered to the MCC, which it sent to thousands of organisations and individuals around the world:

As researchers, health professionals, advocates and organisations working to prevent and treat HIV/Aids throughout the world, we are writing to express our strong support for proven interventions to prevent mother-to-child transmission (MTCT) of HIV, including the use of Nevirapine. There is clear scientific evidence from multiple authoritative sources that a single-dose of Nevirapine, given once to the pregnant woman at the onset of labour and once to her infant in the first three days after birth, substantially reduces the risk of

transmission of HIV from mother to child. The efficacy and safety of Nevirapine in preventing MTCT has been clearly demonstrated ... in highly regarded international studies, including the SAINT trial in South Africa. In addition, the World Health Organisation (WHO) and the National Institutes of Health (NIH) recently re-stated their continued support for using Nevirapine to prevent mother-to-child transmission of HIV.

The drug had been used safely in thousands of cases, it said. 'We urge you to continue to expand the availability of this lifesaving intervention.'

The uncertainty over the registration of nevirapine for perinatal administration threatened poor black women and their babies with a frying-pan-into-the-fire menace. In putting Boehringer Ingelheim on terms to come up with evidence of efficacy, MCC Registrar Matsoso said,

The council's decision has grave implications if the manufacturer doesn't provide information within the next 90 days. Luckily there are other treatments, such as a short course of AZT, which can prevent the spread of the disease.

An MCC statement said much the same thing: 'It must be noted that nevirapine is not the only agent available for reducing the risk of transmission of HIV from mother to child.' As did the Cabinet in its statement on the 6th:

It should also be noted that the decision of the MCC does not affect the use of Nevirapine as part of general antiretroviral regimens; nor is Nevirapine the only drug (or combination of drugs) that can be used for reducing the risk of mother-to-child-transmission.

The statement added:

The [Cabinet] meeting noted that this was an independent decision taken on scientific grounds by the MCC, and urged that public discourse on this matter should take into account the mandate of the MCC and its responsibility to the South African people.

In alluding to the alternatives to nevirapine, the MCC's members clearly hadn't yet read the very latest research papers reporting the serious foetal toxicity of AZT and the terrible harm it causes. Indeed, at least one of them later confessed as much privately to Tshabalala-Msimang.

It is so that paragraph 4 of the Constitutional Court's mandatory interdict directing the state to provide nevirapine to HIV-positive women 'does not preclude government from adapting its policy in a manner consistent with the Constitution if equally appropriate or better methods become available to it for the prevention of mother-to-child transmission of HIV'. But the phrase 'if equally appropriate or better methods become available' appears to contemplate a newly discovered drug intervention, not an older one such as AZT. When trying the TAC's application neither the High Court nor the Constitutional Court considered the issues of AZT's efficacy and safety in pregnancy. Nor was there any consideration of the much greater cost to the state of providing pregnant women with four to six weeks of daily AZT as opposed to a couple of doses of nevirapine to mother and child. In fact, AZT wasn't even mentioned in the judgment. But as the *Mail&Guardian* editorialised, quoting IDASA's Richard Calland opining alike, the thinking was that AZT stood in line for compulsory substitution should nevirapine be knocked out.

In 1999 the clinical and research literature cited in *Debating AZT* concerning the toxicity of the drug to babies in the womb especially, which I'd sent up to government, irrevocably set Mbeki and Tshabalala-Msimang's faces against AZT for use in pregnancy. Many more such reports had since been published. A new front of struggle was opening. We were back to square one.

With the Anglican Church in the frontlines: 'How can our government not acknowledge that nevirapine is recommended in dozens of countries in the world, including our own, as a safe chronic medication?' fumed Anglican Archbishop Ndungane against the heretics. The big one especially. 'Denialist twaddle' was the *Mail&Guardian's* supercilious lead editorial theme on the 8th.

If anyone was in doubt that this country's leader remains an Aids dissident, they should read last week's ANC Today ... In

an essay, *A hundred flowers under the African sun*, President Thabo Mbeki [delivers] his bombshell: [*quotation, as above*]. This is classic denialist twaddle – the president wants his Aids advisory panel to continue its dissident research (it hasn't properly been dissolved yet); he still thinks anti-retrovirals are poison. We were not surprised when the Minister of Health Manto Tshabalala-Msimang parroted the self-same conspiracy theory a few days later ... These two are, after all, our liabilities in the battle against Aids. [*The front-page headline for that issue of the newspaper read: 'Mbeki and Manto hamper Aids indaba' – Mbeki simply by not attending the first South African AIDS Conference in Durban the previous week.*] ... Politically, [the Cabinet's April 17 statement] required the president to dissolve the panel and cut ties with the silly dissidents who sit on it; to submit his individual minority belief to the will of the collective and allow government to play its leadership role in the matter. A year later, it's clear he has not done so and that he won't let the government assume its correct role at the head of the anti-Aids fight.

What both the pontiff and the newspaper missed was that the row concerned a decision taken by the MCC, not the government. Which the Department of Health promptly pointed out in reaction to Ndungane's confused public fussing.

Five schools in the University of Cape Town's health sciences faculty released a statement on the same day expressing their 'extreme concern' over the MCC's decision:

We urge the Medicines Control Council to consider very carefully the implications of its decision and hope that it will not lead to the deregistering of a safe, cost-effective drug for the prevention of mother-to-child-transmission of HIV.

It didn't matter to the teaching doctors that the study on the basis of which nevirapine had been claimed safe and effective was defective by FDA standards. Yet it was supposed to satisfy our MCC. As it did the academic doctors at UCT. Barking mindlessly together like suburban dogs. And then wagging their tails for one of their faculty's big donors: the underwriter of their splendid Boehringer Ingelheim Lung Institute.

Part Seven

The responsibility of intellectuals is to speak the truth and expose lies.

Noam Chomsky

At a meeting on 5 September 2003 at which it considered a flurry of protests and entreaties from the TAC on 25 August and 2 and 4 September, along with what it described as ‘studies presented by [local] researchers’, the MCC decided to rescind its resolution of 25 July ‘in order to clarify the intention of this resolution’. The first resolution had resolved:

1. To reject the study HIVNET-012 as a pivotal study for the approval of the use of Nevirapine for the reduction of risk of intrapartum transmission of HIV-1 infection.
2. That the applicant be requested to submit in 90 days any new evidence (other than previously submitted evidence on HIVNET-012 and SAINT information) to convince the MCC of retention of this indication.

This resolution was recalled and substituted by a second one:

1. That it be brought to your [*Boehringer Ingelheim's*] notice that Council can no longer rely on HIVNET 012 as a pivotal study.
2. That Council will consider all available evidence demonstrating the efficacy of Nevirapine as a single agent for the reduction of risk of intrapartum transmission of HIV-1 infection from mother to child, and,
3. That in terms of section 19(2) of the Medicines and Related Substances Act, you furnish Council with the information set out below within six months of this resolution.
4. That the information be presented in a manner to be decided by the Registrar in consultation with yourselves, namely:
 - (a) such data that you have in your possession, or which you are in a position to obtain, regarding the efficacy of Nevirapine

as a single oral dose of 200mg to the mother during labour preferably more than 2 hours before delivery and a single oral dose of 2 mg/kg to the infant within 48 to 72 hours after birth or before discharge, whichever is earlier, to reduce the risk of intrapartum transmission of HIV-1 from mother to child in pregnant women who are not taking antiretroviral therapy at the time of labour.

(b) any other information which you may wish to submit and which may serve to support the use of Nevirapine for the reduction of risk of transmission of HIV-1 from mother to child.

(c) any information regarding the use of Nevirapine in combination with other antiretroviral agents for the reduction of risk of transmission of HIV-1 from mother to child.

(d) and that you submit regular progress reports in a manner determined by the Registrar.

In effect, the new resolution simply extended the ultimatum to let some steam out the pot and stave off the evil day. Of deregistration, when things would get extremely hot. Even hotter than they already were. Lawsuits on top of derision and universal condemnation. HIVNET 012 was still unacceptable to it, the MCC noted, as was the unconvincing locally conducted SAINT trial.

But a week after the second resolution was passed to give Boehringer Ingelheim more time, everything changed. On 12 September the MCC released a press statement, as dramatic as it was incoherent. All of a sudden the MCC's doubts were gone:

Nevirapine has been shown to be effective in reduction of the risk of intrapartum transmission of HIV-1 infection from mother to child. Scientific evidence was provided to the MCC to support this.

This 'scientific evidence' consisted of 'additional data from South African researchers ... that may support the continued use of Nevirapine for this indication'.

None of the data, local and foreign, tabled in Gray and McIntyre's secret submission to the MCC in June had counted for anything before the first ultimatum was issued. So what was this

‘additional data from South African researchers’ now pulled from the hat that had impressed the MCC? A report on the 19th in *Healthlink*, a bulletin published by the Health Systems Trust, citing PLUSNEWS four days earlier, revealed that it comprised findings

presented at the country’s first national AIDS conference, held in Durban last month, [providing] new evidence that the drug works. Of 600 HIV-positive women at Chris Hani-Baragwanath Hospital who received Nevirapine, only 11.9 percent transmitted HIV to their babies, while in a study of 300 HIV positive mothers at Coronation Hospital, the transmission rate was 8.9 percent.

In its statement on the 12th, the MCC said it ‘recognised the importance of the new information’ – on one hand categorically affirming that the drug had been ‘shown to be effective’ as a perinatal anti-HIV prophylactic, but on the other giving Boehringer Ingelheim more time to produce proof that it was. It was all very confusing. Or maybe under the immense political pressure it was under the MCC was just losing it.

The MCC also noted in its press statement that

Additional information regarding the original study has also now been published. Recognizing the importance of the new information, the MCC, on 5 September 2003, adopted a new resolution, which extends the time period for Boehringer Ingelheim (the supplier of Nevirapine) to review existing evidence, and to submit additional data for expert assessment by the MCC

such as data on nevirapine ‘in combination with other antiretroviral agents for the reduction of risk of transmission of HIV infection from mother to child’. Other antiretroviral agents like AZT.

The ‘additional information regarding the original study’ was a second paper by the HIVNET 012 research team, evidently made available to the MCC for preview, and published in *Lancet* the following day: ‘Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow-up of the HIVNET 012 randomised trial’. This time the lead author of

the paper was the study originator and co-principal investigator Brooks Jackson.

The gist of it was captured in a paragraph headed 'Findings':

Estimated risks of HIV-1 transmission in the zidovudine and nevirapine groups were 10.3% and 8.1% at birth ...; 22.1% and 13.5% by age 14-16 weeks ...; and 25.8% and 15.7% by age 18 months ... Nevirapine was associated with a 41% ... reduction in relative risk of transmission through to age 18 months.

And that, seriously, was it: according to the test results, nevirapine was relatively better than AZT. There was no comparison of the 'HIV-1 infection status' of treated and untreated children at eighteen months. Nor was there any mention of whether the babies treated with nevirapine or AZT did any better or worse than untreated ones. The American doctors didn't think of anything as obvious and basic as that. None paused to wonder how 'risks of HIV-1 transmission' could increase as the babies got older. Wasn't the risk of transmission from the mother supposed to be during birth? Or was it just that study authors Jackson, Guay, Musoke, Owor, Bakaki, Mirochnick and Miiro had

received honorariums and/or travel expense reimbursement over the past 2 years for giving talks at scientific meetings partly or wholly sponsored by the maker of nevirapine

according to a notice at the foot of the paper, all saying what great stuff nevirapine is for saving African babies, and so couldn't see even the most obvious problems with their claims?

The US State Department, no less, saw fit to issue an extraordinary press statement concerning this second HIVNET 012 report under the headline: 'Findings could help prevent 800,000 annual infections' – casually doubling Fauci's claim of 300-400 000 saved, made to CBS Evening News on 14 September 1999. With this sort of political muscle pumping above the NIH's own simultaneous press release, right after a statement supporting perinatal nevirapine issued by the Pharmaceutical Society of South Africa, it's not surprising that the MCC buckled.

It's just a pity that the MCC didn't think to ask the FDA what it thought about it all. Not that the FDA regulates drugs for the whole

world, but if a drug or the particular use of a drug is considered no good by the FDA for administration to Americans, one would think that is something for another drug licensing agency to take account of. Because when in March 2004 Dr Valendar Turner, a consultant emergency physician with the Western Australian Department of Health, enquired of the FDA's Division of Drug Information whether nevirapine is approved for the treatment of mothers and their newborn babies to prevent mother to child transmission of HIV, the answer he got was No:

Viramune [*nevirapine*] is not FDA approved: 1) for the prevention of HIV in mother-to-child transmission, by itself or in combination with other drugs. If used in this fashion, it would be an off-label use. 2) Viramune is FDA approved for HIV infected, pediatric patients 2 years and above. It is not approved for use in the newborn at their time of birth to prevent whatever HIV is transmitted from the mother establishing itself as infection in the newborn.

Everywhere in the second HIVNET 012 report, repeated like a mantra over and over, is the grimly impressive word 'survival'. To ordinary people 'survival' means not dying, especially in a medical context. But not to the HIVNET 012 researchers. For them the benchmark of drug efficacy is 'HIV-1 free survival', and never survival in the usual sense. This is because, surprise, surprise, the drug-treated children fared no better than the untreated.

In a rambling gloss on the Jackson paper published in the same journal, 'Long-term findings of HIVNET 012: the next steps', Karen Beckerman of New York University School of Medicine complained with feminist indignation that

It is disturbing that no man would be intentionally exposed by his caregivers to nevirapine or zidovudine, either alone or in a dual combination. Why should this ever be an acceptable strategy for any infected individual?

(If guys can get three drugs, why should we sisters and our babies settle for one or two? It's disturbing.) But buried in Beckerman's asinine commentary was an awkward fact omitted by the HIVNET 012 researchers whose ringing significance didn't seem to register on her as she reported it:

The HIVNET 012 protocol did not affect child survival. Overall infant mortality at 18 months was 12% and did not differ significantly between groups (10·6% with nevirapine and 13·6% with zidovudine).

Beckerman wondered ‘what can be done to improve the survival of infants of infected mothers if transmission prevention alone has no effect on 18-month mortality?’ – instead of asking herself the obvious question: if the ‘HIV infection status’ of a child demonstrably has no bearing on his or her prospects of making it through infancy, and children treated with nevirapine or AZT don’t do any better than untreated children, why give African mothers and their babies nevirapine or AZT in the first place? What’s the point? Other than to keep AIDS doctors busy. And the drug industry in business.

A clue to what Beckerman correctly called the ‘high mortality’ rate of Ugandan babies, around 12%, whether ‘effectively’ treated or untreated, whether HIV-positive or HIV-negative, lay in its real cause – poverty – ascribed in Beckerman’s medical jargon to the ‘debility of the caregiver’, understanding of which ‘is extremely limited’. By visiting pill-popping white American doctors fixated on sex germs, yes. But not by Africans such as Mbeki and Tshabalala-Msimang who understand it all too well – to the chagrin of liberal journalists, AIDS doctors and professional drug lobbyists more interested in fantasizing about African sexuality than pondering the political challenges of mass African poverty. In 2001 the *State of Uganda Population Report* published by the Ugandan Department of Health found that 39% of Ugandan children were undernourished in 2000. UNICEF’s *World Summit for Children End-Decade Indicators: Uganda 2000-2001* reported that one hundred and fifty one children per thousand died before reaching the age of five – 15% of them. Of those surviving 38% were stunted, and 22% underweight by a factor of two deviations from the norm.

Back on 13 July 1999, when the provisional findings of HIVNET 012 were released in Kampala, Jackson had boasted to the *Washington Post* the next day that

In terms of its ability to save lives, this single-dose regimen [of nevirapine] will potentially save more lives than any other HIV intervention to date in developing countries.

As Beckerman pointed out in her commentary four years later, it didn't.

So would you people just please all go home now?

In June 2004, more than three months after the expiry of the time that the MCC had afforded Boehringer Ingelheim to table fresh clinical trial evidence to convince it that it should retain its registration of nevirapine for perinatal use, things drifted on unresolved. And then a whole lot happened.

First of all, 'resistance' flared up again. Initially raised when the drug was being considered by the MCC for special registration for perinatal use in the period August 1999 to April 2001, the issue re-emerged in March 2004 when at a press conference on the 16th Italian AIDS-fighting NGO *Sant'Egidio* condemned nevirapine, saying it left too many babies infected, didn't extend the lives of mothers and caused resistance to other AIDS drugs. Which anyone with any sense knows is code for inefficacy – inefficacy in modulating the bogus surrogate markers claimed to evidence HIV infection, such as antibody and 'viral load' test readings and CD4 cell counts. None of which has anything to do with being well or sick, now or later. 'It has no future in Africa,' said spokesman Mario Marazziti; pregnant women should be given traditional triple therapy during pregnancy, in which nevirapine was one of the medicines. Back to AZT in other words.

On 29 June, following a meeting attended by Tshabalala-Msimang, Boehringer Ingelheim representatives, MCC members, provincial health officials and drug researchers, the Ministry of Health announced that according to preliminary results of a study conducted by government and Boehringer Ingelheim researchers, some mothers were becoming 'resistant' to nevirapine, and that a conference was being planned to look into this.

Another issue coming up at this time was the drug's deadly toxicity – for adults. Sally Satel, a physician and resident scholar at the American Enterprise Institute, mentioned insouciantly in an article in the *Los Angeles Times* on 1 July that

In rural Africa, where sophisticated medical care is lacking, a calculable percentage of patients will become very sick or even die from the nevirapine component of this three-in-one drug [*Triomune*].

That the other two components of the combo, AZT look-alikes lamivudine (3TC) and stavudine (d4T), were just about as deadly she didn't say. Locally, PlusNews reported on the same day that according to Hannie Dlamini, president of the Swaziland AIDS Support Organisation,

members of his group, which counsels people living with HIV and AIDS, and dispenses ARVs, have died of liver poisoning, allegedly due to Nevirapine. ... No autopsies have been conducted to determine the cause of death, but AIDS activists are adamant that Nevirapine was to blame. 'It's so painful to me. People are given ARVs, and two weeks later you see in the papers they are late [*dead*]. If it were my country, I'd stop distribution now. There must be a six-month public education campaign before they are reintroduced,' Dlamini said.

It appeared that AZT was being groomed for a comeback for the treatment of pregnant women in the Developing World, and that GlaxoSmithKline was intent on capitalising on the remarkable marketing beachhead established by Boehringer Ingelheim in getting nevirapine accepted as a standard of care in developing countries for HIV-positive pregnant women and their newborn babies. The low-cost argument in favour of two doses of nevirapine didn't count anymore, now that Bush's \$15 billion had been approved 'to turn the tide against AIDS' in Southern Africa, as he put it (in black Haiti and Guyana too). The US taxpayer would be coughing up, not the governments of the South. Since a single-dose nevirapine treatment of the mother-child pair cost a measly \$4, a much greater profit potential lay in wait to be exploited by GlaxoSmithKline hawking AZT for administration during several weeks, even months, of pregnancy.

On 22 June I sent the MCC a detailed enquiry about the status of its review (Appendix 2). MCC Registrar Precious Matsoso, to whom the letter was addressed, didn't respond in the two weeks that I suggested, and packed her bags for the 15th International

AIDS Conference in Bangkok instead. Where, opening the government's stand on 11 July, Tshabalala-Msimang said that there was an 'ever-growing resistance against the prescription of nevirapine' for pregnant women. The government had been 'forced by the courts and the TAC' to provide it to all HIV-positive pregnant women in the country, despite the fact that the drug had been conditionally approved for further research use only. The government had acted 'under pressure from some civil society organisations'. There was a growing body of research supporting breast-feeding over powdered milk, she added. And that it was a pity that none of the official conference sessions were covering research being done into the value of traditional medicines in AIDS. Also that she would soon be arranging 'a national summit' to discuss AIDS drugs: 'We must ensure that the government's programme is safe.' She revealed that only about six thousand people were taking AIDS drugs under the general rollout programme. Not much interest, in other words. Or lost quickly after a bitter taste. She mentioned too that the Actuarial Society of South Africa had found the AIDS figures here over-estimated by 33%. All of which naturally upset everyone, Zackie Achmat most of all.

The time had come for government to choose, he announced, between Tshabalala-Msimang and the world, which wanted to support us in the fight against AIDS. Her questioning of nevirapine had been 'a sideshow' and 'a tragedy', he said.

Scientists were not confused. They were laughing at us at the conference. South Africa is a laughing stock – not only the Health Minister, all of us are. ... The Minister chooses to remain ignorant and misuses scientific information for politics. ... She does not understand the science, nevirapine, or AIDS statistics. I hope the medical authorities scrap her from the roll.

A bit rich coming from a guy who'd described himself during an interview in *Rapport* on 10 February 2002 as 'scientifically illiterate'. Lacking even the rudiments of high school biology and general science, having quit school with a Standard Six. (Just as Mark Heywood, TAC treasurer and director of the AIDS Law Project, a law firm, boasts an English degree.) 'South Africa does not have a problem with nevirapine,' Achmat said. 'The problem is

with the Health Minister.’ Yes, she was misinforming the public about the problem, charged South African Medical Association chairman Kgosi Letlape, ‘putting the [*perinatal nevirapine*] rollout programme in jeopardy’. Why, there was ‘considerable data showing the efficacy and safety of nevirapine,’ responded UNAIDS, Unicef and the Elizabeth Glaser Pediatric AIDS Foundation in a joint press release.

But the day after Tshabalala-Msimang’s perplexing statements about nevirapine, Matsoso followed with one from the MCC:

The council believes the risk-benefit profile of nevirapine has changed and therefore no longer recommends the use of monotherapy for the prevention of mother-to-child-transmission (PMTCT) of HIV.

The MCC had met on the 2nd, she said, and had recommended that nevirapine and AZT, previously approved as ‘monotherapy interventions ... to reduce the risk of transmission of HIV from mother to child during labour’ should henceforth be used only in combination: ‘The council feels combination therapy should be considered for this indication.’ She explained where the MCC got its feelings from:

A number of recent studies, including an expert consultation report of the World Health Organisation in February this year, confirms the view of the MCC that nevirapine monotherapy is less efficacious than combination regimens.

Had the members of the MCC stopped to think instead of feel, they might have wondered about the absurdity of the suggestion that a single pill of nevirapine administered to pregnant women in labour will cause them to become drug resistant later on. But as a diversionary tactic it was an effective one: the MCC was seen to be moving responsibly and acting independently – at no political cost, at no risk of being sued by the TAC as promised by resolution passed in August 2002 should the MCC mess with Boehringer Ingelheim’s licence, and without dealing with any of the efficacy and safety considerations raised in my letter.

On the same day that Matsoso was announcing the MCC’s new feelings in Bangkok, Boehringer Ingelheim was hopping into bed with GlaxoSmithKline: a press release from the former on the 12th

announced that the companies had signed a 'letter of intent' to develop a 'co-package' (single pill) containing AZT, 3TC and nevirapine 'for the treatment of chronic infection in the developing world'. But handy for dosing pregnant women and their babies in developing countries too, of course. The groundwork was being laid, said the statement; the US FDA had already been consulted. And two days earlier the *New York Times* reported that

A combination of two inexpensive drugs ['nevirapine and AZT'] is the best way to keep mothers in poor countries from passing the AIDS virus to their children, new studies have found. ... The studies, which will be published in the *New England Journal of Medicine* next week, were released yesterday because they will be presented at an international AIDS conference at Bangkok. The World Health Organisation, aware of the promising results beforehand, has begun to recommend the use of the two drugs together.

The piece could have been written by a PR firm. As for the studies, we'll be onto them in a minute.

The WHO responded to the MCC statement the following day, issuing, as the *New York Times* put it on the 14th, 'a pointed statement supporting the treatment of pregnant women with nevirapine alone'. 'Progress,' said the WHO,

in implementing programs to prevent mother to child transmission based on single-dose maternal and infant nevirapine or other short course regimens should not be undermined.

By people in developing countries thinking for themselves? Achmat was quoted in the report commenting further that 'limiting the use of nevirapine was another sign of how the South African government had sowed confusion over AIDS'. And added later: 'The confusion our Minister sows is undermining prevention programmes around the world.'

But it was Achmat who was confused; Health-e cited his response to Tshabalala-Msimang's negative mention of nevirapine: 'We all know that the best drugs to use is [*sic*] a combination of drugs – all three for treatment or a dual therapy of nevirapine and AZT' for pregnant women and their babies.

The co-chairman of the Bangkok AIDS Conference and president of the International AIDS Society, Joep Lange, condemned the MCC decision too: 'It sends out a totally wrong message,' he said – taking a swipe at Mbeki on the way for 'not showing leadership'. As if any of this stuff had anything to do with him. But then again, the conference slogan, 'Access for all', evidenced its pro-drug, industry-serving agenda more openly than ever before, and as everyone knows, Mbeki isn't so keen on that. Unlike Thai Prime Minister Thaksin Shinawatra, who announced at the conference: 'I will never cease my commitment to support universal coverage of antiretroviral treatment to people with HIV and AIDS.' Now that's what we like to hear. In the drug business. Paying for these events.

Matsoso tried cooling the heat by confirming that the MCC had not deregistered nevirapine for solo use in perinatal applications, but that it was merely recommending a better alternative, she said: nevirapine mixed with AZT. Sure, but since, as the MCC pointed out at Bangkok, 'The approval of nevirapine as monotherapy for this indication, in April 2001, was conditional upon monitoring of resistance and its impact on efficacy', it seemed that Boehringer Ingelheim would never get its final ticket from the MCC to sell its drug to pregnant women and their babies. Practically though, it didn't matter to the company; the conditional licence allowed it to hawk nevirapine unhindered, just as if it had been fully licensed. This being the new way of the world in the drug business in the case of fast-track-approved drugs. With licensing boards just laughing off the ordinary need to prove safety and efficacy, when enough people in tee-shirts shout angrily: No time to lose on the usual approval procedure. This is an emergency!

Department of Health spokesman Sibani Mngadi told the press on the 14th: 'We will have to comply with the decision by the MCC. We are going to have a national consultative meeting immediately after the Bangkok conference.'

Tshabalala-Msimang moved to calm things down the next day:

The Department of Health will continue providing nevirapine as monotherapy to mothers and babies at public health facilities until agreed upon treatment regimens are available. It must be emphasized that the MCC did not recommend that the

use of nevirapine be stopped altogether, but that it should be used in combination with other drugs, because it is showing a significant resistance of up to 50%. Also, the drug has not been deregistered as indicated in media reports.

I tried finding out what had become of my letter to the MCC via a contact who was friendly with one of its members. He confirmed that the MCC was running scared of being sued by the TAC.

Tshabalala-Msimang forthrightly criticized Achmat on the 26th, in response to another attack on her by him at a meeting of the Centre for Conflict Resolution earlier in the week. By resorting to legal action, she said, the TAC had

forced government to extend the use of the drug beyond limited research sites where the possibility of resistance was being monitored. ... Achmat should be more honest in this matter. His main worry about nevirapine being discussed openly at this particular conference stems from the wrong decision being taken by the TAC on this matter. TAC should reflect objectively. The organisation should be asking itself whether the constant threat of legal action is always the best route in pursuing its narrow objective.

On 12 August a consultative workshop was held to discuss the resistance story, attended by Tshabalala-Msimang, provincial Health MECs, and delegates and representatives from the MCC, the Medical Research Council, the Essential Drug List (EDL) Committee, the Perinatal HIV Research Unit at Chris Hani-Baragwanath Hospital and the National Institute for Communicable Diseases. The upshot, announced by Tshabalala-Msimang's spokesman Mngadi, was that the Department of Health would 'continue to recommend nevirapine until another approach has been decided upon'. It had been agreed all round that further research was necessary, he said.

Then again, to anyone hip to a 'Research Letter' by Quaghebeur et al. in press at the time for publication on 3 September in *AIDS*, any more research into 'resistance' would be a waste of time. Under the title 'Low efficacy of nevirapine (HIVNET012) in preventing perinatal HIV-1 transmission in a real-life situation', the researchers stated:

Since 2001, the unrestricted use of HIVNET012 has been recommended for the prevention of mother-to-child transmission in low-resource settings, despite the lack of validated efficacy data outside research settings. We implemented the nevirapine regimen in a real-life situation in Kenya. The perinatal HIV-1 transmission rate at 14 weeks was 18.1%, similar to the 21.7% before the intervention. These data call for further evaluation of the simple nevirapine regimen in field conditions, and underline the need for alternative strategies.

Which is to say, as scientists do, the Ugandan findings were not reproducible, and are consequently worthless. More plainly put, ‘in a real-life situation’ the drug was a total flop:

Our findings question the usefulness of the current prevention of mother-to-child transmission recommendations based on HIVNET012, which have been implemented in resource-poor settings, based on just one observation in a clinical research setting. ... These data, suggesting a rather limited effect of the widely recommended HIVNET012 intervention, call for further research on the long-term efficacy of the HIVNET012 regimen in a field setting. Taking into account the low coverage of the nevirapine regimen, the lack of benefit for maternal health, the concerns about resistance, the enormous deployment of resources needed to provide nevirapine within the current voluntary counselling and testing paradigm, and the reported lack of efficacy in real-life conditions, the true health gains of the intervention should be reconsidered.

And it wasn't as if Ann Quaghebeur and her colleagues had gone in with a negative bias against the use of nevirapine. On the contrary, in reporting their study (led by Marleen Temmerman) published in the same journal in May the year before, ‘Mother-to-child HIV transmission in resource poor settings: how to improve coverage?’, they regretted that ‘The coverage of perinatal MTCT was low as a result of a variety of programme elements requiring urgent improvement at different levels.’ So many more

mother-infant pairs could have received a preventative intervention with a hospital policy of antepartum as well as intrapartum testing and treatment in place

they lamented.

But anyway, after Quaghebeur's et al. findings of perinatal nevirapine's 'lack of efficacy in real-life conditions', who was still interested in 'resistance' – especially since Recsky et al. had just reported in mid-June in the *Journal of Infectious Diseases* concerning 'Antiretroviral resistance among HIV-infected persons who have died in British Columbia, in the era of modern antiretroviral therapy' that 'treatment failure due to antiretroviral resistance was not a major factor influencing mortality in this cohort'? Other than a whole lot of pious, self-important AIDS doctors and activists – once noisy champions of the useless drug, but now worrying about the collapse of their reputations. Especially in South Africa, where they'd deceived the country's top judges, pulling them into their stupid mania like Titus Oates and his Popish Plot.

Part Eight

[Negroes are] beings of an inferior order, and altogether unfit to associate with the white race, either in social or political relations, and so far inferior that they had no rights which the white man was bound to respect.

US Chief Justice Roger Brook Taney in *Dred Scott v Sanford*, 1857

In July 2003 the Division of AIDS (DAIDS), a wing of the National Institute of Allergy and Infectious Diseases (NIAID) in the US, appointed Dr Jonathan Fishbein MD to a newly created post: Director of the Office for Policy in Clinical Research Operations. This was a very senior position specially created to fix some serious problems. How serious they were he'd soon be finding out, and what they were would emerge very publicly a year and half later. Fishbein's formal brief was to create and enforce research policy, because things were in a parlous state at DAIDS when he hit the scene. Before his appointment, he had been vice president of North American Medical Services at PAREXEL International, 'one of the largest pharmaceutical services companies in the world' with 'more than 5,100 employees worldwide' and 'offices in 36 countries', according to its website. Clearly for some reason DAIDS needed a heavyweight fixer.

Upon Fishbein's arrival at DAIDS, director Edmund Tramont placed entire sections of the division under his jurisdiction: Contract Research Resources Branches, Pharmaceutical Affairs and Regulatory Affairs. Fishbein's first inkling that there was something seriously remiss was hushed talk about some drug trial in Uganda that DAIDS had run, and that hadn't gone at all well. And Mary Anne Luzar, head of Regulatory Affairs, the branch of DAIDS responsible for communications with the FDA, was still sitting in the division's dog-box, he heard, having been reprimanded by Tramont in April for sending an embarrassingly negative safety report over to the FDA. About which we'll be hearing more anon. But which had been perfectly proper, Fishbein decided after looking into it; and on 6 August he persuaded

Tramont to expunge the black mark against her. Despite DAIDS deputy director Jonathan Kagan's strenuous objections.

Things were going well. The only thing a bit worrisome to Fishbein was Tramont's talk to him of wanting DAIDS running like 'a virtual drug company'. Yes, that's exactly what he said – repeatedly. Four months into his new job, NIAID director Anthony Fauci presented Fishbein with a 'Certificate of Appreciation' with Tramont's support, awarded 'In Appreciation of Outstanding Contributions and Efforts in Support of the NIAID Mission'. Tramont continued to hold Fishbein in good regard, and was sufficiently impressed by his achievements in improving research safety and compliance to recommend that he be awarded a salary bonus two months later.

But deputy Kagan didn't like the newcomer changing things and rocking the boat. He wasn't becoming part of 'the gang', he griped to Tramont, and carped that the latter's good opinion of him was undeserved. Things began to sour, Fishbein told me in September 2004, three months before his story exploded in the world press, when 'Shortly after joining DAIDS, it soon became apparent that I was hired not so much to change things at DAIDS but to give the appearance that I was.'

By 3 February Kagan's harassment and obstruction had become serious enough for Fishbein to go and see Tramont and make a complaint, which he confirmed by email the following day:

The incessant interference and distraction of Jon Kagan is jeopardizing my work. By creating a hostile working environment for me and other members of my staff, Jon is trying to destroy my chance at success for this office and the entire division.

When Kagan got wind of this the next day, he told Fishbein that his number was up; he was going to see to it that he was thrown out.

Kagan's antipathy arose from the fact that Fishbein had become aware of serious, possibly criminal scientific misconduct in DAIDS in relation to the HIVNET 012 nevirapine study, and felt threatened by his persistent, dutiful investigation of it. He promptly began plotting to oust him. To one of DAIDS administrative staff he emailed a 'Blunt question. Does Fishbein have a probationary

period? I beg you to say yes. I assume he has an indefinite T-42 contract, right? How hard would it be to terminate that?’ Kagan got the affirmative answer he wanted, along with the explanation that Fishbein could be fired if underperforming. But twenty minutes later the smile was wiped off his face by a further piece of news from the same staffer: ‘If you are thinking about moving on termination you may want to pull the award recommendation.’

Kagan hadn’t yet heard about this obvious major stumbling block to early dismissal proceedings on the grounds of alleged professional incompetence: ‘Whatever it is, please HOLD!!!! Thanks for the heads-up on that!!’ What ‘it is’ was then explained to him: ‘Ed [*Tramont*] recommended a 2500 SRA.’ Being a special bonus of \$2,500 cash for outstanding performance.

As Kagan was looking for fault despite this, going through Fishbein’s timesheets, scratching like a chicken for something to stick on him to justify kicking him out, Tramont reassured Fishbein in an email on the 14th:

It has not been lost on me that the most complaints I heard from our constituents when I arrived revolved around what are now your functions. And since you have arrived, I have NOT heard a single complaint, and when I inquired about that, the answer has been the change brought about by you.

But within a week Tramont had done an about-turn and joined Kagan in a conspiracy to fabricate a false case against Fishbein for his dismissal. In an email to Kagan on the 23rd he wrote:

Jon Let’s start working on this. Tony [*Fauci*] will not want anything to come back on us so we are going to have to have ironclad documentation, no sense of harassment or unfairness, and like other personnel actions, this is going to take some work. In Clauswitzian style, we must overwhelm with ‘force’.

Tramont’s first move was to place Fishbein under Kagan’s supervision, a manifestly vindictive act, and contrived to create an intolerable work situation for him. The day after Tramont’s email to Kagan, the latter told Fishbein that he was going to be dumped for bad performance. Having just pocketed a bonus for good performance. True to his promise Kagan drew and filed a performance assessment in late February that found Fishbein

useless and recommended that he be fired. When in April Fishbein received a notice of intention to terminate, he appealed. A senior advisor to NIH chief Elias Zerhouni saw what was going down and wrote a confidential memo to him on 9 August 2004, warning that sacking Fishbein in the circumstances gave the ‘appearance of reprisal’, to say the least of it. Word then came down and the notice was withdrawn, although Fishbein remained on compulsory ‘administrative leave’.

Well you might wonder why Tramont suddenly changed his mind and figured that it would be better were the troublemaker to be taken out on a bogus pretext with maximum prejudice, the all-American way, in an operation planned and executed with German military precision. Here’s why.

NIAID director Fauci and his deputy Clifford Lane are royalty-earning joint inventors of recombinant interleukin-2 (rIL-2), a drug covered by a US government patent. Its potential against AIDS was being tested in a major long-running clinical trial called the ESPRIT study. By early 2004 cardiovascular problems, diabetes and suicide/suicidal ideation were showing up as serious side effects. FDA regulations required that the study protocol and the informed consent documentation be updated to reflect this, and that all trial subjects be told, i.e. ‘reconsented’. When the ESPRIT medical officer responsible, Lawrence Fox, informed principal investigator James Neaton to attend to this, he got no joy. So he turned to Fishbein, who as the overseer of AIDS research policy formally issued a peremptory sixty-day notice on 6 February, ordering compliance. Naturally, Neaton and his executive committee colleagues, including Lane and Sandra Lehrman of NIAID, were outraged. Fishbein was jeopardizing the study, because telling people on the trial about the serious known risks of taking rIL-2 could frighten them into dropping out of it. Thereby threatening Fauci and Lane’s visions of early retirement, awash in patent fee millions.

Here was Fishbein playing it by the book, but in the corrupt culture of the NIH that sealed his fate. What likely happened next you can imagine. Tramont got a furious phone call: Ditch this guy. By now Fishbein’s fortunes at DAIDS had already changed. He had just formally complained to Tramont about Kagan’s

obstruction of his work and about his sexual harassment of female colleagues. Under written NIH policy the latter charge was an especially serious matter, and even more so if not acted upon and formally resolved by the boss. Fishbein's professional penchant for making sure that things were done properly was starting to make Tramont nervous, because Fishbein was on to secrets Tramont didn't want told, secrets concerning his own misconduct in relation to – you guessed – HIVNET 012, the Ugandan nevirapine trial on the strength of which the WHO recommended the drug for giving HIV-positive pregnant women and their newborn babies in the Developing World, the South African MCC had specially registered it, and the South African government had been forced by the Constitutional Court to provide it for this purpose.

In the course of his work Fishbein had a close look at that study, and was more appalled the more he read. What he 'discovered', he recounted to me, was 'considerable documentation demonstrating frighteningly poor research practices in HIVNET 012 and serious scientific misconduct by the Division to hide that fact'. In view of the NIH Policy Manual's stipulation that

All NIH employees have a responsibility to assist in efforts to combat fraud, waste and abuse in all NIH programmes and have the responsibility to report such matters to the appropriate official

Fishbein diligently endeavoured to see that the gross irregularities he'd uncovered were addressed. But, as he told me,

In February 2004 after enduring considerable resistance to bringing about reform to DAIDS, I reported allegations of wilful obstruction to my work ... The reward for these disclosures was immediate demotion followed by termination

of his responsibilities pending final dismissal.

Stymied by his own department, Fishbein took his findings regarding HIVNET 012 upstairs. None of the several offices of the NIH that he approached were interested. Nor were any in the NIH's parent Department of Health and Human Services that he tried next. So in March Fishbein went to Congress, specifically to the Oversight and Investigations Subcommittee of the Energy and Commerce Committee, where he and the smoking documents he

carried under his arm were taken more seriously. The politicians called the NIH in, and between them they brokered a deal in May to bring an end to the embarrassing fuss: the Institute of Medicine (IOM), a part of the National Academy of Sciences, a quasi-governmental organization that advises the government on scientific matters, would look into it.

Had Fishbein seen the IOM's recently published report, 'Dietary Reference Intakes for Macronutrients', he might have predicted what was to come. A testament to its members' competence, integrity, and independence from special interest groups, in short their professional reliability, the IOM asserted – in stark defiance of WHO and UN Food and Agriculture Organization (FAO) recommended limits – that up to 25% of our daily calories can safely be got from refined sugar – about 40 teaspoons of it. So pack four cans of Coke into your kid's lunch bag every day, no problem.

The NIH agreed to conduct an internal investigation of Fishbein's complaints too, but appointed to head it was Joan Schwartz, married to senior NIAID staffer Ronald, Chief of the Laboratory of Cellular and Molecular Immunology in the Division of Intramural Research, who was tight with NIAID chief Fauci. This guaranteed the outcome: a cursory enquiry found nothing out of order, no wrongdoing at all.

Imagine how disappointed Fishbein was again when he read on the IOM website who had been appointed to its investigating panel: a whole bunch of guys funded by the very department that had sidelined him. Hardly the sort to give his complaints an unbiased hearing. And the terms of reference for the enquiry didn't even touch sides with the issues he was raising. Needless to say, not a single expert critical of HIVNET 012 was invited to testify, least of all him. The National Whistleblowers Center in Washington, which had taken up his case, reported these most basic problems to Congress. In response to the NWC's charge of conflict of interest on the panel, two members promptly resigned – but only two.

So what was it all about? Following the publication of the first bright report of the HIVNET 012 study in *Lancet* in September 1999, Boehringer Ingelheim started shipping nevirapine free of

charge into maternity wards all over the Developing World – but not in the First. Before it could do this it needed to get past the US FDA, after which it would be smooth sailing getting approval for this special new indication in Europe and in other industrialised countries. And in South Africa too, the model for the rest of the Developing World, but whose Medicines Control Council was being difficult and holding things up.

After filing its special licence application, and knowing the kind of things the FDA would be scrutinising, Boehringer Ingelheim flew a crew out to Mulago Hospital in Kampala, Uganda, to see whether the HIVNET 012 records were in order. They found a complete shambles, documented in a sixteen-page summary of their findings. The company's Kevin Dransfield telefaxed it to DAIDS on 24 January 2002 – with a confidential request: 'Controlled distribution from BI. BI stated not to copy.' This request, recorded in a hand-written memo on the face of the report, was coupled to an even graver one, also duly annotated: 'Sensitive information. Asked for it to be destroyed when audit is upon us.'

That is to say, Boehringer Ingelheim's own inspectors' findings were so damaging that on no account did the company want the FDA to see their report, because if it did, and all the skeletons fell out, bang would go the company's chances of getting its special licence in the US, and thereafter in the rest of the First World. Nevirapine's future in the Developing World would be doomed too. So the bad news about its drug was not to get out. This, my friends, is the pharmaceutical industry. And that's how incestuously tight the company is with the NIH – that it could even ask such a thing, confident that DAIDS would collude with it in a criminal conspiracy to destroy evidence, to keep it from the FDA and the world.

In fact, DAIDS officials already knew that HIVNET 012 was a disaster: three weeks before Boehringer Ingelheim faxed through its audit summary, they held a meeting to discuss some huge basic problems of which they were aware. The minute of the meeting recorded that the trial protocol had been changed mid-course repeatedly, but the principal investigators had refused to file amendments.

There should have been continued safety monitoring of deaths, but the site staff thought they did not have to ... Also, they do not know GCPs [*good clinical practices*] – apparently neither does Laura [*Guay*] or Brooks J [*Jackson, the principal investigators*].

Under ‘SAFETY’ the minute noted that

there were more deaths that were not on the CRFs [*clinical report files*] and this was found on only a sample of forms – At least 16 deaths—possibly 5 others or more ... 11 NVP grp [*in the nevirapine group*] & 5 AZT grp – and 19 missed SAEs [*serious adverse events*]. ... there are differences in #s [*numbers*] of SAEs & deaths ... site used their own criteria for grading SAEs, No lab normal values, & serious under-reporting of SAEs ... no Med Officer involved, no MO [*medical officer*] AE [*adverse event*] over-sight @ the site. Etc, etc. Other Problems – Data Integrity: Are deaths Drug related – it was felt it was too early to tell. There is a murky picture of what happened at the site. Dr. Mike Hensley is still there & feels with some work it may be possible to salvage study??

Under ‘Efficacy Issues/Ops issues’ the DAIDS officials noted:

3-4 databases not reconciled, pharmacy issues, drug repackaging, storage & access issues. Randomization procedure unclear etc. ... No master log, stolen file cab with IC docs—lost IRB [*institutional review board*] docs etc. Not reported to DAIDS ... How much is salvageable? Unknown at present time.

Another issue that compromised the HIVNET 012 drug findings and rendered them worthless by FDA standards was that

over 50% of HIV+ babies co-enrolled in another vitamin A trial. (Laura [*Guay*] & B Jackson in mid Feb said there were no other ongoing studies at site??) Missie and Laura said that MG Fowler of DAIDS was aware of vitamin A trial.

It emerged from the schedule of clinical trial protocol violations later submitted by Fishbein to the IOM enquiry that Guay had initially lied about her knowledge of the concurrent vitamin A trial.

Because it was only

when confronted [*by the Westat auditors; see below*] with findings in source records of references to an apparent concurrent study (Attachment 11) [that] Dr. Guay acknowledged that 1/2 of the HIV positive infants in the 012 trial were entered into a CHS trial. This double blind trial evaluated the therapeutic potential of high dose vitamin A, compared to placebo.

You are running a clinical trial to test nevirapine and you allow the babies to be treated with a high-dose micronutrient likely to affect clinical outcomes substantially. First you deny it, and then when shown the incontestable documentary proof you admit it. Unbelievable. But not really, once you've heard the rest of this tale.

DAIDS didn't actually tear up Boehringer Ingelheim's confidential report as the company had requested, but it deliberately withheld it from the FDA for several critical weeks with the same fraudulent intent. 'It shouldn't have happened that way,' said NIAID deputy director Lane later, after the cat was out the bag. It was naughty of us.

In fact, this sort of criminal scientific misconduct was par for the course at NIAID, a cesspool of rotten ethics permeating the organisation right to the top. Tipped by Fishbein, Associated Press filed a Freedom of Information request with NIAID in early January 2005 concerning conflict of interest, specifically probing the secret financial stakes that NIAID researchers have in the success of official drug trials that they are running, financed by millions of dollars in public funds. And making millions on the side, it emerged, a few days after AP's nosing, when the NIH suddenly implemented a disclosure policy, requiring its researchers to tell patients on test drugs: Look, if this thing works, I'm in for a mint. So is it OK if we experiment on you? Obviously we'll be biased to find that it works great, and downplay whatever harm it causes you. Since we've got all these patents to cash in on once we're done with you.

The disclosure policy was well overdue. When the scandalous practice of government researchers secretly profiting from official drug trials first hit the news in May 2000, Health and Human

Services Secretary Donna Shalala promised that policies would be implemented requiring ‘that any researchers’ financial interest in a clinical trial be disclosed to potential participants’. Guidelines were issued by HHS in January 2001, and again in May 2004 concerning ‘compensation that may be affected by the study outcome’ and the disclosure to patients of ‘proprietary interests in the products, including patents, trademarks, copyrights or licensing arrangements’. But for five years the NIH did nothing to comply, while its officials sneakily lined their pockets.

Two culprits flushed out by AP’s probe, among more than fifty researchers, were none other than NIAID director Fauci and his deputy Lane. ‘I’m going to give every penny of it to charity ... no matter what the yearly amount is,’ said Fauci, protesting too much and trying to slither out the net. But not Lane, who brazenly stood on his right to pocket his secret benefits. He ‘occasionally gave patients scientific journal articles’ that noted him as drug patent-holder, he said, expecting us to believe this – as if it was good enough anyway. ‘I believe patients should know everything that might influence their desire to be participants in research,’ he lied further – in the same breath stating with Fauci that they were ‘unwilling to tell’ patients about their financial interests in the outcome of the drug trials because, why, the NIH hadn’t yet formally promulgated any policy requiring it. Until AP started asking awkward questions, and suddenly the disclosure policy was set in place. ‘We were reluctant to make a formal policy until the broad policy came down from the department and NIH,’ Fauci explained lamely. Even though he was head of ‘the department’.

NIH spokesman John Burklow squirmed over AP’s exposé of the NIH’s rotten ethical norms: ‘Quite frankly, we should have done it more quickly. But as soon as [NIH] Director [Elias] Zerhouni found out about it, he ordered it done immediately.’ As soon as Zerhouni learned that AP had found them out, and the game was up, he meant.

Anyway: passing Boehringer Ingelheim’s thumbs-down report about HIVNET 012 on to DAIDS director Tramont, the division’s FDA liaison chief Luzar scribbled on its cover-page: ‘Ed – Here is B.I. summary of their audit. M.A. Has a lot of problems uncovered too.’ Given how things turned out, and the fact that our MCC was

later to reject HIVNET 012, it seems idle to recount the whole ‘lot of problems’ found by Boehringer Ingelheim’s audit team, other than in one respect still crucially relevant, drug safety:

‘Information describing adverse events was most thoroughly collected during the first eight weeks after delivery.’ After that ‘the safety data are incomplete’. Among the ‘fatal and life-threatening’ adverse events experienced by babies exposed to the trial drugs that ‘were reported late’ were ‘pneumonia ... worsening’ three days later when the baby was readmitted to hospital, but not recorded and reported as a serious adverse event. The serious adverse events, some ‘life-threatening’, some ‘fatal’, included

Grunting respiration ... Pre-eclampsia ... Neonatal sepsis, vomiting ... Intrauterine fetal death ... Fatal ... Hemorrhagic disease of newborn ... Hypertension ... Respiratory distress, cephalohematoma ... Transient tachypnea of newborn ... Infectious dermatitis ... Birth asphyxia ... Fatal ... Fresh stillbirth ... Fatal ... Severe anemia ... Life threatening.

There were also ‘two serious, unexpected SAEs, where the relationship is stated as unable to determine ... diarrhea and ... pneumonia’ which ‘should [have been] reported as IND [*investigational new drug*] reports’.

But even where the adverse event data were recorded, ‘The primary difficulty with these data are [*sic*] the arbitrary definitions of seriousness and severity that were employed.’ Again it was noted that ‘the sub-investigators and PI’ (the principal investigator, Guay) were ‘not actually seeing the patients whose events they are evaluating’. Imagine that.

The dismal state of the record-keeping in HIVNET 012 was synopsisized in the report:

A core issue for the Mulago site is an absence of documented internal procedures. Reliance on memory and precedent is useful but likely to be associated with inconsistencies in data collection.

In plain speech, useless.

On 11 February, in a pickle over the serious problems that it had discovered concerning the integrity of HIVNET 012 (whose

reported results NIAID director Fauci had publicly praised), NIAID contracted Westat, a firm of professional drug trial auditors,

to conduct a site visit and assist staff in preparing for an upcoming FDA inspection for the HIVNET 012 clinical trial. ... The FDA approach to a pre-approval inspection covers all the major requirements, although typically the focus of a foreign inspection is on verification of safety data and data supporting primary efficacy endpoints.

Yes indeed.

Odd that the American government should have involved itself in helping a drug company, Boehringer Ingelheim, to obtain an extended licence from the FDA, but there we are. In fighting AIDS we're all in it together.

Things backfired when Westat's 'review team' described the sewer they'd waded into in a fifty-seven page report. Considering that our MCC eventually rejected HIVNET 012, our only remaining interest is in the safety of nevirapine for South African babies, so again we'll stick to this aspect:

Looking at the examination for discharge, for Mothers, more than 1/3 were marked abnormal. ... On a similar note, looking at infant weights, it was apparent that a weight of less than 7Kg at 12-month follow-up was not an uncommon finding, despite the generally robust size of most infants at that visit. It was thought likely that some, perhaps many, of these infants have serious health problems. A sample of 43 such infants from the larger sample of 93, showed adverse events at 12 months. Of these 43, only 11 were HIV positive, suggesting that upon audit of the site files we would find more pathology than had been reported. More to the point, most of the SAEs reported for infants were in the newborn period, which was incompatible with the large number of infants with apparent Failure to Thrive past six months of age. ... Additionally, there was the matter of the Lancet paper, which mentioned 59 Serious Adverse Events in infants less than two months of age. Both the data sample described above, and the Lancet report, suggested more serious adverse events in infants than had been

reported to FDA under the IND [*investigational new drug report*]. Taken together, it appeared likely in fact, that many adverse events and perhaps a significant number of serious adverse events, for both mother and infant, may not have been collected and reported in a timely manner to the FDA, under the IND. ... Safety reporting therefore became a primary focus for the site audit team.

Again it was noted that

For the most part, neither the Principal Investigator nor any sub-investigator actually saw the patient experiencing an AE or SAE. Completion of this form, as well as decisions on seriousness, causality, relation to study drug and severity were made on the basis of second hand information.

Cases where mothers brought their ailing babies back to hospital in unscheduled visits for treatment within six weeks of delivery and nevirapine or AZT exposure, or anytime after that, were not routinely recorded as severe adverse events and were generally inappropriately classed as ‘non-serious’ adverse events instead. Fishbein summed up the Westat finding on this aspect for the IOM panel: ‘Since patients were kept out of hospital by very aggressive therapeutic approaches, many events are recorded ... as adverse events rather than SAEs.’

Where serious adverse events were noted, there was no follow-up of the patient to clinical resolution – a basic FDA requirement – opening the possibility of fatal outcomes not being recorded.

The high number of ‘Failure to Thrive’ cases among treated babies is chilling. We speak of irrecoverable toxic shock at birth manifesting many months later. Not taken into account, and not reported by the HIVNET 012 researchers in their glowing papers in the medical journals.

The Westat auditors found and described numerous other serious anomalies in the records of adverse events, and, what’s worse, uncovered ‘deaths not reported to the FDA’ in notes kept by visiting nurses. Guay

was surprised, however, [that] any death might have been missed. ... Although initially Dr. Guay described strict adherence to protocol specified endpoints for collection of

safety data, interpretations of seriousness and severity were not actually made according to the protocol or according to 21CFR. ... On several occasions Dr. Guay stated that there were probably ‘thousands’ of such missing [*unrecorded serious adverse*] events. ... Taking into consideration the decision by Dr. Jackson, Dr. Guay, et al., to coin their own local definitions of seriousness and severity, and keeping in mind the under-reporting of SAEs which resulted from that (‘thousands’), then the entire safety reporting system can be seen to have been significantly different from that expected in an IND study. In explanation, Dr. Jackson and Dr. Guay cited a need for consistency in a somewhat chaotic and very busy clinic system. Regarding the definition of ‘Serious’ they cited ignorance of the 1997 safety reporting regulation, although the protocol, as amended in 2000, included a clear statement of the new rule. They also reported that they had never had ‘GCP’ [*good clinical practice*] training, and had never attempted a Phase III trial.

Which made them too ignorant, too inexperienced and too incompetent to run a drug trial on Americans, but which equipped them just fine to experiment on Africans.

In their ‘Summary of Discussions with PI and Sub-investigators’, the Westat auditors noted that

All acknowledged the [audit] findings as generally correct. ... Both Dr. Guay and Dr. Jackson expressed concern regarding statements made regarding safety and efficacy in the *Lancet* paper, and resolved to review the data.

Which is to say they conceded that their claims in *Lancet* in September 1999 that nevirapine had been shown to be safe and effective were wrong. But they quickly forgot what they promised the Westat auditors: in their second HIVNET 012 report in *Lancet* in September 2003 they were silent about it.

In summing up Westat noted that

a remarkable lack of understanding of Good Clinical Practices, as applied to a Phase III, IND trial was apparent. ... Finally, it was not at all clear, even in the last hours of the last day of the audit, that the PI and Sub-investigators fully understood or

appreciated the significance of the observations. Their assessment appeared to be that they had attempted to do too much with too few resources. The issues of oversight, management, and personal responsibility within a highly regulated environment did not yet seem to have been appreciated.

These were the clowns assumed to be the experts by the TAC and by the judges whom it co-opted to compel our government to give nevirapine to women giving birth and to their newborn babies in South Africa, mostly black, mostly poor. (At the request of the TAC, Jackson and Guay actually made affidavits to persuade the Constitutional Court that all was well with HIVNET 012 and with the administration of nevirapine to mothers and babies.)

Given its own and Westat's dreadful findings, Boehringer Ingelheim's chances of getting an extended licence out of the FDA to market nevirapine to pregnant women in the US were obviously zero. So, with the connivance of FDA and NIH officials, the company arranged to withdraw its licence application – because formal public rejection by the FDA of nevirapine for pregnant women and their babies would be the end of the Developing World's confidence in the drug. The safety of mothers and babies in developing countries was plainly the least of the company's concerns. But again, these are the ethics of the pharmaceutical industry.

Celia Farber described the moves behind the scenes in 'Out of Control: AIDS and the corruption of medical science', published in *Harper's Magazine* in March 2006:

On March 14, 2002, the FDA called a meeting with DAIDS, Boehringer, and the trial investigators. 'They reprimanded the whole gang,' says Fishbein. [']Then they said to Boehringer: Withdraw your application for extended approval, if you want to avoid a public rejection.'

The chaos discovered by both the Boehringer Ingelheim and Westat auditors was alarming enough to DAIDS officials to order the Mulago Hospital site shut down for further research by American researchers. But instead of disclosing the dire trouble with their study, Tramont deliberately sat on the information, even

concealing it from the White House, with the result that, kept in the dark about the questions now hanging over the safety of nevirapine for babies, George Bush II announced a \$500 million mission to fight AIDS in Africa on 19 June 2002, centring on the provision of nevirapine:

This major commitment of my government to prevent mother-to-child HIV transmission is the first of this scale by any government, anywhere. We will support programs that administer a single dose of nevirapine to the mother at the time of delivery, and at least one dose to the infant shortly after birth. This therapy reduces the chances of infection by nearly 50%.

Tramont justified his deceit – what we lawyers call a fraudulent non-disclosure – in a note to NIAID director Fauci on 14 March 2002: ‘Everyone has recognized the enormity that this decision could have on the use of nevirapine to interrupt mother-to-child transmission.’ No matter that the drug’s sunny reputation as safe and effective had been completely blown.

Determined to see a happy ending to the saga, notwithstanding that HIVNET 012 had been found to be a bucket of puke by his own staff, by nevirapine’s manufacturer and by the independent professional auditors hired by the NIH, Tramont summed up the situation in a ‘DAIDS summary of March 19 Westat debriefing’ minute, which grossly wrested the findings of the audits and painted the problems uncovered as trivial, concluding: ‘There is presently no evidence that the study’s scientific results are invalid.’

In ‘Out of Control’ Farber mentions that

DAIDS officials was so dismissive of the Westat report that Westat’s lawyers eventually put officials on notice that they were impugning Westat’s reputation.

Deceived by Tramont, if not complicit in his fraud, NIAID deputy director John La Montagne dismissed the Westat findings in similar terms: ‘There is no question about the validity [of the HIVNET 012 results] ... the problems are in the rather arcane requirements in record keeping.’

Tramont’s next ploy in the cover-up was to send a third team of his own DAIDS staffers to Kampala to write another review report,

a sweet one. Its examination of the hospital records of a probe sample of eighty mother-child pairs resulted in the ‘Remonitoring Report’ that was given to our MCC a year later – a crass attempt to whitewash the trouble with HIVNET 012 that had led Boehringer Ingelheim to pull its extended licence application to the FDA, an attempt that failed when the MCC finally rejected the study findings.

As Fishbein related to me:

What you and the public know from the Remonitoring Report is a very watered down version of what really went on in Kampala. Well before the remonitoring was done, the NIAID had already decided that the data, the results, and the conclusions of the 1999 Lancet paper were valid. Too much was at stake to have ever let that be questioned, so what the report stated was a foregone conclusion.

In other words, the premeditated, fraudulent object of Tramont’s ‘remonitoring’ exercise had been to deceive our MCC. Reassure the WHO. And dupe all and any other suckers such as the leaders of the TAC.

Led by paediatrician Elizabeth Smith, DAIDS’s ‘HIVNET 012 Safety Review Panel’ comprised specialists with ‘extensive experience in safety monitoring for both government and industry sponsored HIV clinical research treatment or prevention trials’, as the introduction to the ten-page summary of their findings noted. Their report tore the study to pieces:

Acceptable or required timeframes for reporting SAEs and deaths were not followed. ... The safety reporting quality for the HIVNET 012 study does not meet levels expected in perinatal trials sponsored by DAIDS. ... The supervision or monitoring of the willing and capable Ugandan site personnel in all aspects of safety, including subject information regarding treatment risks, verification of eligibility criteria for mothers and infants as well as safety reporting does not appear to have been in place and raises concerns about the study conduct. ... Site records for safety monitoring and subject visits were of poor quality and make safety statements very difficult from the perspective of a review process. ... Monitoring during the trial

for safety and clinical trial management was not in evidence. ... Safety reporting did not follow DAIDS reporting requirements during the conduct of HIVNET 012. Safety conclusions from this trial should be very conservative.

Among the critical problems with safety reporting was the fact that the principal investigators ‘used less stringent toxicity grading scales and created a team-defined reporting algorithm for the study with the admitted goal to report fewer AEs and SAEs’ among babies, as Fishbein put it in his submission to the IOM enquiry. Meaning that Guay and company had contrived to make sure that the adverse event data would come out looking better than they were. Which they’d admitted under interrogation.

Fishbein cited Smith’s findings further:

Grading for rashes and decreased hemoglobin did not follow the grading tables as described in the HIVNET 012 protocol and in general were graded more mildly than commonly seen in perinatal trials sponsored by DAIDS.

Rendering useless all data on the incidence of ‘rash’ (symptomatic of a general systemic toxic reaction) and haematological toxicity. Crucially relevant data in a trial on babies involving nevirapine, but useless.

On 23 January 2003, smelling trouble coming, Tramont called for Smith’s report to be given to him when complete, before it was submitted to the FDA: ‘I need to see the primary data – too much riding on this report.’ Strangely enough, the report the FDA got a couple of months later read entirely differently from the one Smith’s team of safety experts had drawn:

There was some concern expressed by one of the American physician monitors about the adequacy of standards of clinical care in Uganda. ... During the full review of 80 mother-infant charts, the reporting of AEs was found to be generally complete. The discrepancies that were found between the database and the source documentation were due to some missing information in the adverse event report. ... The remonitoring of review process undertaken by the safety review panel has shown that there was a consistent attempt throughout the study to document AEs and SAEs as evidenced

by the large numbers of such reports ... and the small numbers of missed events in the remonitoring process. ... HIVNET 012 has demonstrated the safety of single dose nevirapine for the prevention of maternal to child transmission of HIV infections. Although discrepancies were found in the database and some unreported AEs were discovered during the remonitoring process, these were not clinically important in determining the safety profile.

Aghast, Tramont's staff enquired how this had happened. Easy, he answered casually: 'I wrote it.' Associated Press later quoted him explaining that 'Africans in the midst of an AIDS crisis deserved some leniency in meeting U.S. safety standards'. Which is to say we lower our safety standards in drug trials on those Negroes over in Africa. We rewrite our safety reports to suit local conditions. We airbrush out all the bad stuff.

But the Office for Human Research Protections (OHRP), a branch of the Office of Public Health and Science in the Department of Health and Human Services, didn't see it as Tramont did. On 5 and 12 April 2002 Drs Nyiira and Sewankambo of the Ugandan National Council of Science and Technology had filed complaints concerning

allegations of serious non-compliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects ... at Makere University (MU) and Mulago Hospital (MH)

as the OHRP's response on 16 July that year put it. And which office, in a nine-page analysis and decision, found in favour of the complainants on all scores: the HIVNET 012 trial had violated American federal clinical trial rules for the protection of human subjects.

When Smith and her team saw that Tramont had deliberately omitted their damning safety findings from the 'Remonitoring Report', they passed their 'The HIVNET 012 Safety Review: Findings and Summary: Final Report_3 April 2003' onto DAIDS Regulatory Affairs chief Luzar, who was in charge of liaison with the FDA. Particularly worried about the final report's note of hyperbilirubinaemia among drug-exposed babies – evidence that

they had suffered liver damage and/or red blood cell poisoning – she dutifully passed it up to the FDA. Tramont, Kagan and Jackson descended on her like a ton of bricks for this, with Tramont issuing a formal reprimand, as if she'd done something wrong.

Who wouldn't have been alarmed by the hyperbilirubinaemia findings?

The results of the bilirubin review by treatment, approximately 310 infants on each treatment arm, show that on day 7 post treatment, the number of infants on ZDV [AZT] with grade 3 was 132 (44 with other concurrent AEs, 40 without). The number of infants on NVP with grade 3 was 64 (24 with additional concurrent AEs and 90 without) and with grade 4 was 28 (9 with additional concurrent AEs and 19 without). ... The infants who had the grade 4 bilirubins have not been followed up to determine if any difference in morbidity [*disease*] and mortality was conferred by the difference in the risk of grade 4 bilirubin levels.

And having mentioned in the introduction to their 'Safety Review' that it was 'not designed to address missing information or bias in reporting results', Smith and her team cursorily touched on the entirely unscientific manner in which the researchers had worked, making bias inevitable:

Conversations with HIVNET 012 team members reinforce the often repeated fact that they all worked very closely together and decided most things by consensus with the FHI and DAIDS team members. In fact, all served as authors of the Lancet article published after the interim review for HIVNET 012.

(Family Health International ('FHI') is another of these AIDS-drug pushing NGOs.)

Farber tells in 'Out of Control' how, ever more flagrant in his deception, Tramont 'was considering HIVNET researchers Jackson and Guay for an award', as if their performance in HIVNET 012 had been fabulous rather than dismal. His chicanery was too much even for Kagan, however, who balked in an email on 19 June 2003:

Ed – I’ve been meaning to respond on this – the bit about the award. I think that’s a bit over the top. I think that before we start heaping praise on them we should wait to see if the lessons stick. We cannot lose sight of the fact that they screwed up big time. And you bailed their asses out. I’m all for forgiveness, etc. I’m not for punishing them. But it would be ‘over the top’ to me, to be proclaiming them as heroes. Something to think about before pushing this award thing

Despite the millions spent by the NIH during the shut-down for improving conditions at Mulago Hospital before continuing with drug testing on Africans there, professional safety monitors hired by the NIH were still not satisfied that things were up to scratch the following year. Just appointed to his post at DAIDS, Fishbein was dismayed when Tramont pressed for the site to be re-opened nonetheless. Tramont dismissed Fishbein’s concerns in an email to him:

I am convinced that this site is ready to resume given the limitations of doing research in any resource-poor, under developed country. I want this restriction lifted ASAP because the site is now the best in Africa run by black Africans and everybody has worked so hard to get it right as evidence [*sic*] by the fact that their lab is now certified. ... The site was shut down for 15 months. It was stupid and bureaucratic not to reopen it.

In truth, the real reason Tramont wanted the site hurriedly re-opened for drug research was because President Bush was due to visit it, and he didn’t want him finding out what a total cock-up HIVNET 012 had been, and moreover how he had deliberately concealed this from him – since losing his head would be a distinct possibility if this got out.

Picture the possible scene at Mulago Hospital that Tramont feared:

Bush: Howdy folks, real nice to be here. But where are all our famous American doctors saving African babies with the swell new medicine we bought for them?

Ugandan hospital matron: They were suddenly called home in early 2002, sir. We heard that it was because of all the

unreported deaths and serious adverse reactions in the big nevirapine trial that they ran in our country a few years ago. Bush: Is that right, Ed? Why didn't you tell me about this? I mean before I made a total jackass of myself by publicly committing America to supplying nevirapine to Africans? \$500 million dollars worth. This was a high-profile foreign policy position that we took. We understood from you that this stuff had been shown to work safely. What's the fucking deal?

In an email to Kagan in July 2003, copied to Tramont, Fishbein expressed his 'several concerns' about Tramont's intention to re-open the site, pointing out that 'experienced and credible safety investigators' still had reservations about it. DAIDS's letter to Guay and Jackson 'removing the suspension' had been 'poorly written', he thought; 'I am not convinced that the site is indeed prepared to become active.'

Kagan responded by supporting Tramont: he didn't want the NIH 'perceived as bureaucratic but rather thoughtful and reasonable'. Popular impressions counted for more than the rude facts, in other words. And

As our involvement in resource-poor under developed countries grows, we have the responsibility to develop a system that the FDA is comfortable with – and they are anxious for us to do that. Finally, the epidemic in Africa is out of control, the countries which embraced research first, Senegal and Uganda, have curtailed their epidemics the most – we must continue to encourage them – especially when the president is about to visit them! Bottom line, this letter must go out on Wednesday, poorly written or not.

But soon afterwards Kagan had a change of heart. He emailed Tramont: 'You know, I've given more thought to your responses to Jonathan [*Fishbein*] re Kampala ... and I've begun to think a bit differently.' It wasn't only DAIDS staffers who thought it premature to re-open the site: Kagan's email mentioned a team of European monitors with the same concerns, whose report Tramont had withheld from Fishbein:

I realize that this might be one of the best sites in Africa, but Jonathan does, I believe, deserve a chance to review the data.

Your dismissal of the monitoring reports, based on the opinions of the Europeans ... and their ... ‘cultural’ shortcomings, is, on reflection, very superficial. I think Fishbein deserves to see what those reports said and what evidence there is that the deficiencies were corrected. If we have the data, it shouldn’t take a long time for him to review this and I believe that both he and DAIDS deserve the time to do this. ... He’s a scientist. He’s also good, Ed, at what he does. Better than anyone in DAIDS ... including you (with all respect). This IS why we brought him on. ... From his vantage point, Ed, it must almost look like we have something to hide – let him find out what was wrong and what was done about it. What’s the harm? Ed, what your note is essentially saying is that you want that site opened. ... It’s not going to matter if the site opens this week or next or even the next. We should not be motivated by political gains and it’s dangerous for you, of all people, to be diminishing the value of our monitors.

But undaunted and over-riding the objections of all his staff, Tramont ordered the Mulago Hospital site reopened later that month. With everything now smelling sweetly of lavatory spray, Bush visited Uganda on 11 July 2003. At a joint press conference with President Museveni, Bush went to town:

Mr. President, you have been a world leader – not just a leader on the continent of Africa, but a world leader in the fight against HIV/AIDS. You have shown the world what is possible in terms of reducing infection rates. You have been honest and open about the AIDS pandemic, and therefore have led your people to seek prevention and treatment and help and love.

Unlike Mbeki, he meant, who didn’t honestly and openly share the American view that nevirapine and AZT were the same as love.

Basking in the political glory, Tramont emailed his staff two days later, ordering them to cease debating the problems with HIVNET 012 and whether its results were worth anything:

Folks, HIVNET 012 has been reviewed, re-monitored, debated and scrutinized. To do any more would be beyond reason. It is time to put it behind us and move on. Henceforth, all

questions, issues and inquiries regarding any aspect of HIVNET 012 [are] to be referred to the Director, DAIDS. Dr. Tramont.

Where he'd kill them, he implied. Fishbein couldn't live with that, and his diligence and integrity in performing the work he'd been contracted to do, in compliance with the NIH's own codes of conduct, led to his ejection from 'the gang'. But it also resulted in the world learning the shocking truth about HIVNET 012 and what went on around it.

Tramont's folksy email belied its menace. Fishbein later told Celia Farber: 'People send me emails every day from inside DAIDS, telling me they're right behind me, telling me what's going on in there. But they can't go public. It's terrible in there now. Everybody is terrified.'

On 13 December 2004 Associated Press broke the story in the first of a series of articles by John Solomon to follow in the next few weeks (he interviewed me too). It was major news, with the scandal reported by more than a thousand newspapers worldwide. The South African government was gratified. The whole idea of setting up pilot studies in South Africa had been to confirm that the drug was both safe and effective, said the Health Department in a statement:

That decision was made to allow us to gather our own evidence regarding the use of nevirapine in monotherapy. Most unfortunately, a court order issued to us by the Constitutional Court did not allow us to proceed in a more-cautioned [*sic*] manner. As the general public will also recall, we appealed against the court's decision on two occasions, but were ultimately compelled to abide by the ruling.

'This news is not new to us at all,' said Government spokesman Joel Netshitenzhe. 'That's why the Department of Health is working with the relevant institutions to establish the facts and to find alternatives' – referring to a combined task team made up of representatives of the Department of Health, the MRC and the MCC, set up earlier in the year to reassess nevirapine's safety and efficacy, and to look at alternative options.

AP quoted Michael Hensley, one of the auditors hired by the NIH, who'd 'first helped disclose the problems' with HIVNET 012:

NIH officials were in a rush to declare that things were OK. It seemed to me we were drawing conclusions too quickly across the board, especially the implementation of nevirapine in South Africa.

As the controversy took flame here, the MCC's reaction was to say nothing, pull the blankets over its head, pretend nothing was happening, and hope the trouble would just go away – vaguely remembering that it had been informed as early as 6 August 2002 in a 100-point submission that the safety data in HIVNET 012 were insecure and that the study was otherwise complete junk. And reminded in a detailed letter about this in June the following year. Advice it had simply ignored.

Throwing another of his familiar tantrums the TAC's Achmat yelled in a press release that the

Department of Health has once more issued an unscientific, irresponsible and inaccurate statement on nevirapine aimed at undermining public health. ... The criticisms levelled by the parties involved in the NIH news story, that broke two days ago, do not provide evidence questioning the safety or efficacy of short-course nevirapine. It is false, as has been reported in some places and by the Department of Health, that short-course nevirapine has been associated with thousands of adverse events. There is to date not a single reported life-threatening adverse event associated with this regimen which is used widely in the developing world. The criticisms of the NIH management relate to the conduct of the trial and the NIH's communication of the problems associated with the HIVNET 012 trial. The TAC is angry and considering legal advice on the Department of Health's continued misinformation campaign on nevirapine. Today, yet again, the Department issued a statement misrepresenting the safety of nevirapine.

And so he went on, adding later:

We have had hundreds of phone calls from patients. It's enormously disconcerting for those with a life-threatening illness who is [*sic*] beginning to feel well and suddenly worry if they're killing themselves off.

No doubt it is.

James McIntyre reminded us how extremely fortunate we are to have a white expert of his calibre looking after our African babies:

The messages out here in Africa are that somebody has said the drug is bad. The other side of it, which is that there are allegations about the way the National Institutes for Health have handled this, are somewhat lost. The message that comes over very strongly is that there may be concerns about this drug. I think that's unfortunate. ... In my country this has been seen as a US and pharmaceutical company conspiracy. ... Fishbein's story has really created so many mixed messages that it is diverting attention away from more important issues. The Uganda study has become irrelevant.

McIntyre's colleague Glenda Gray piped up from the same slow class: news reports of unreported deaths and complications were unfounded, she said, but anyway 'Many of those findings were not drug-related.'

US Senate Finance Committee chairman Charles Grassley, on the other hand, appreciating 'the serious nature of these allegations and the grave implications if the allegations have merit', formally called for an investigation of the conduct of the NIH officials involved in the scandal by the Inspector General of the US Department of Health and Human Services, and simultaneously by the US Attorney General for possible criminal indictment.

Placed on the spot by AP's revelations, the White House called a press conference to try to put them to bed. Aping his boss, White House spokesman Wayne McClellan's answers to media questions on 15 December were completely incoherent and uninformed – confusing nevirapine's provisional registration by the FDA for use only in combination with nucleoside analogues as an AIDS treatment of last resort with its use solo in maternity wards, for which it was certainly not licensed in the US:

A couple of things. One, the President's emergency plan for AIDS relief is about saving lives. The United States does more than any nation in the world to combat AIDS. The President made an unprecedented commitment to addressing the pandemic and helping those who are suffering in our most afflicted areas of the world. That was the \$15 billion commitment over a five-year period. In terms of the specific drug, nevirapine, it's been approved in the United States since the 1990s, and it's been a proven – a drug that's been proven to be effective in stopping mother-to-child transmissions of the AIDS virus. And the NIH has stood behind its effectiveness. But because some questions had been raised, they've also asked that the Institute of Medicine do a further analysis of the drug. And so we look forward to seeing what that analysis is. But the President remains committed to doing all that we can to stop the spread of AIDS and prevent – and implement preventive measures to help those in the most afflicted areas.

Q: And is he satisfied with the way NIH handled [not] disclosing the information about the risk?

A: Well, I don't – in what term – in what ways? The NIH referred the matter to the Institute of Medicine for further analysis. It's a drug that is approved for use here in the United States. It is a drug that can help save lives. And the U.S. Public Health Service guidelines continue to recommend short-term therapy with nevirapine as an option for women who enter care late in pregnancy.

Q: You're talking about – the President is talking about saving lives, but this drug has lethal effects to include liver damage. How are you saving lives one way, and then letting somebody die from a lethal effect another way?

A: I take exception to the way you characterize that ... The President's plan is about saving lives. And we want to make sure that people who are afflicted have lifesaving drugs available to them, or people in those afflicted areas have lifesaving drugs available to them. I just pointed out that the NIH, because of the questions that have been raised, has referred to the Institute of Medicine for further analysis. We want to see what that analysis is. But we will always work to

improve medicines and treatments on all diseases, and that includes HIV/AIDS. In the meantime, though, we're pursuing the available treatments that have shown to be effective, and it is something that is approved for use here in the United States of America. And it can have very important, positive effects when it is used in the proper dosage.

Q: Isn't there a concern at the White House that the President was not made aware of these lethal effects of this drug when he signed off on sending the drug there? And two, what does the White House say to some African Americans saying this looks like, if you turn your head one way and close your eye another way, it looks like....

A: In what sense? It's approved for use here in the United States. But there have been questions raised, and the NIH is taking an appropriate step to ask for further analysis of the drug. That's what their role is in this. In terms of the review and testing of medications, the White House is not involved in that. That's something that the FDA is involved in.

And on he dithered, repeating himself idiotically.

The NIH went into full defensive spin mode, lying flagrantly, claiming that

throughout multiple reviews, the overall conclusions regarding the safety and efficacy of single-dose nevirapine in the setting have remained intact. ... It is conceivable that thousands of babies will become infected with HIV and die if single-dose Nevirapine for mother-to-infant HIV prevention is withheld because of misinformation.

A NIAID statement claimed the agency was 'confident' that previous studies indicating that nevirapine is safe for mothers and babies

will be upheld. ... Nevirapine has been used in developing countries to prevent HIV infection in thousands of infants. It represents a major public health advance and is one of the true success stories in HIV prevention.

And there's nothing to 'suggest that current recommendations regarding use of this regimen should be changed'.

A major reason why the NIH was so anxious to defend the indefensible in HIVNET 012 was because it was DAIDS's one and only glory. American medical science could save the world. Congress loved it. All that expensive AIDS research was finally paying off. In the five years since the first findings of the study were published in *Lancet*, Congressional funding for the NIH doubled – from \$14 billion to \$28 billion. But Fishbein's whistleblowing on HIVNET 012 cooled Congress's enthusiasm like a cold shower: in 2005 the NIH got an insignificant 1% funding increase over the previous year.

On 17 December, four days after the story broke in the world press, the NIH jammed Fishbein's website for access by NIH employees, and then later in the day gave him the sack – kept on salary, but expelled from his office, forbidden to communicate with his colleagues, and sent home with a play-play assignment to write a report on how they could all do their job better. (No kidding.)

After a thorough résumé of the scandal under the fitting title 'Nevirapine, drugs & African guinea pigs' on the same day, *ANC Today* commented that

Dr. Tramont was happy that the peoples of Africa should be used as guinea pigs, given a drug he knew very well should not be prescribed. In other words, [NIH officials] entered into a conspiracy with a pharmaceutical company to tell lies to promote the sales of nevirapine in Africa, with absolutely no consideration of the health impact of those lies on the lives of millions of Africans. [The AP article] implied that there had been numerous deaths due to nevirapine that had been covered up by the U.S. authorities to promote their own ends.

The author of the commentary then gored the TAC, with a bitter dig at the courts on the way:

We too agree that these disclosures have grave implications. But obviously, the TAC does not agree. It is determined to continue to pursue its mission to promote the widest possible use of anti-retroviral drugs in our country, at all costs. In this regard, despite the fact that it is a mere NGO, and not a body of suitably qualified scientists, it is quite ready even to deny

the reality of established scientific truths. Consequently, despite and in the face of everything we have reported in this article, it issued a statement which said, among other things: ‘The criticisms levelled by the parties involved in the NIH news story, that broke two days ago, do not provide evidence questioning the safety or efficacy of short-course nevirapine. It is false, as has been reported in some places and by the Department of Health, that short-course nevirapine has been associated with thousands of adverse events. There is to date not a single life-threatening adverse event associated with this regimen which is widely used in the developing world.’ Desperate to ensure that the truth does not undermine its drug marketing campaign, the TAC said, ‘The TAC is angry and considering legal advice on the Department of Health’s continued misinformation campaign on nevirapine.’ Intent to sustain public pressure for the expansion of the market for anti-retroviral drugs in general, and nevirapine in particular, the TAC also said: ‘Reporting in South Africa over the last 24 hours regarding this (NIH) news story has been sloppy, with many journalists failing to understand the content or context of what is being debated. This has the potential to undermine public confidence in nevirapine unnecessarily. Science reporting in South Africa is generally poor and the TAC will endeavour in the future to work with journalists and other organizations to improve the quality of science reporting.’ And so, to guarantee and improve the sale of anti-retroviral drugs, this being the central mission of the treatment campaign of the Treatment Action Campaign, the TAC boldly proclaims that it is a Science Institute that is capable of improving the quality of scientific reporting in our country, and undoubtedly especially ‘scientific reporting’ about nevirapine and other anti-retroviral drugs! It counts our courts as its ally, which, presumably because of past experience, it is confident would adjudicate the scientific and health controversy that has arisen concerning nevirapine, in its favour. Perhaps our judges will have to decide whether they are a scientific review panel or an institution that has oversight over the faithful implementation of our Constitution and our laws. But to make doubly sure that

it achieves its objective of marketing anti-retroviral drugs at all costs, the TAC also pledges to position itself as the central adjudicator of what should appear in our mass media as quality science reporting! And the quality science reporting it seeks should be such that it does not unnecessarily ‘undermine public confidence in nevirapine’. Naturally! Michael Hensley said it seemed to him that despite the known adverse effects of the drug, the NIH was very keen to expedite ‘the implementation of nevirapine in South Africa.’ Jesse Jackson wrote that ‘We should stop discounting the lives of Africans.’ Strangely for an organisation that presents itself as African, passionately concerned about the health and the lives of Africans, the TAC seems quite happy to ‘discount the lives of Africans’, and to ensure ‘the implementation of nevirapine in South Africa’, regardless of ‘the significant number of serious adverse events for both mother and infant (that) may not have been collected or reported in a timely manner during the course of the Uganda study’. Whose interests does the TAC serve?

This was all too much for Zackie Achmat. Demanding an apology he spluttered: ‘Several of us want to sue the ANC for defamation. We have to consider that very carefully, and we will put it to our executive committee for a decision in early January.’ But the ANC shot back, right on the mark: ‘He should rather deal with the issues raised in the article.’

Irrationally personalizing them, and unable to conceive that there was serious trouble in the air over HIVNET 012, that any intelligent person could see, Achmat got it into his silly head that the critical article in *ANC Today* could only have been written by one man – but anonymously, because

President Mbeki does not have the courage to publicly declare his views on HIV. ... I am ashamed that the power of the President’s office, the resources of government and the prestige, power and strength of the ANC is used to sow confusion among people who are sick and dying.

It wasn’t Mbeki, pointed out ANC Head of Presidency and Communications Smuts Ngonyama; the ‘opinion piece’ had been

submitted by a party member. Well then, said TAC treasurer Heywood,

Since it was carried in the ANC's weekly newsletter it certainly has his endorsement, so we hold him responsible unless another author comes forward. The TAC doesn't mind taking knocks here and there, but it is very inappropriate for the President of the country to speak a language that threatens a major public health program.

Asked to comment on the article, Mbeki's spokesman declined to give the President's view of the matter. But he hardly needed to tell us that Mbeki agreed with it heartily.

Achmat's failure to have grasped the facts, much less understood the ramifications of AP's revelations about HIVNET 012 and Tramont's whitewashing of the negative safety data, was apparent from a statement he put out on his TAC website:

The writer of the article [*in ANC Today*] is either confused or deliberately trying to mislead; his or her views contradict ANC and government policy. It is true that there were problems with the trial in Uganda, but an audit was conducted to examine the trial's shortcomings. The conclusion from this was that the scientific results of the trial remained unaffected.

This was the 'conclusion' of DAIDS's fraudulent 'Remonitoring Report', rejected by the MCC – the one, it turned out later, containing all the fake safety conclusions. This ignorant view propounded by the TAC, that 'an audit' had concluded that the HIVNET 012 findings were just fine, was repeated on P4 Radio in Cape Town on 27 January 2005 by the organization's Nathan Geffen, purporting to refute my statements about the trouble with HIVNET 012 on the same station in early December. Here was the TAC selling the official NIH line to South Africans on behalf of the American government: the false, corrupt one. Thanks kids.

The TAC website statement went on:

Single-dose nevirapine is safe and effective for preventing mother-to-child transmission of HIV. This is not merely the opinion of the TAC. It is the opinion of the South African Medical Association, the Rural Doctors Association, the

Southern African HIV Clinicians Society, the World Health Organisation and every reputable HIV research and activist organization in the world. Denouncing it as unproven and dangerous therefore contradicts government programmes and policy.

The one forced on it by the TAC and the judges.

In early March 2005, in an article ‘Activists angry at fallout from AIDS drug trial allegations’, *Nature Medicine* quoted Geffen repeating his complaint about me:

advocates are fighting to convince pregnant women in developing countries that it still safe to take nevirapine – a drug they say has prevented thousands of women from passing HIV on to their babies. [*Only it doesn't.*] They say the Associated Press articles have reignited confusion and fear among AIDS patients. ‘There are people going on the radio and telling people to stop taking nevirapine,’ says Nathan Geffen, national manager for the Treatment Action Campaign, an advocacy group based in South Africa. ‘This is having consequences for public health.’

Not that he could actually demonstrate any.

Reacting to the scandal as it broke, Boehringer Ingelheim Pharmaceuticals, Inc. in the US skirted all the issues and ascribed the fundamental problems with HIVNET 012 to mere ‘procedural deficiencies’. At the end of its statement the company reaffirmed its ‘commitment to the fight against HIV/AIDS’, as a

steadfast partner to professionals, patients, government and non-governmental organizations (NGOs) ... With our partners we are working toward a goal of ensuring that the next generation of infants in the developing world are born HIV-free. It is important that media reports preserve accuracy to ensure that people in AIDS-ravaged countries are not unnecessarily discouraged from continuing to use nevirapine and other treatments to prevent the transmission of HIV during childbirth.

A friend and partner of the TAC, talking like the TAC, and likewise pretending that AP’s exposé was somehow inaccurate.

DAIDS went into denial right away. Reports that Tramont had doctored his division's safety report were 'completely false'; he'd merely 'edited' the data given him and 'included more extensive and comprehensive information in his omnibus report'. DAIDS was 'deeply concerned about the consequences of the distortion of facts', namely that

there is a real possibility that physicians and health care providers in developing countries will not use the lifesaving single-dose nevirapine regimen to block mother-to-infant transmission of HIV ... It is conceivable that thousands of babies will become infected with HIV and die if single-dose nevirapine for mother-to-infant HIV prevention is withheld because of misinformation.

Except that the data reported in the second report of HIVNET 012, published in *Lancet* on 6 September 2003, showed that giving the drug to mothers and babies had no clinical benefit whatsoever, let alone a lifesaving one. Nor does nevirapine 'block mother-to-child transmission of HIV' reported Quaghebeur et al. in *AIDS* in September 2004, when they tried the HIVNET 012 regimen out in Kenya, 'in a field setting' without any bias to come up with favourable results.

NIAID deputy Lane went on television, ours included, lying through his grinning American teeth:

It sounds like there's something wrong and you look at it in, you know, great detail, and there's no technical inaccuracy, that there's just spin, and you so have a headline, you know, 'NIH official changes report'. Well that's part of his job to edit the work of his subordinates. ... I don't think there's any new information coming out that would change the fundamental conclusion that single-dose nevirapine is effective and safe.

AIDS doctors involved in HIVNET 012 defended it shamelessly and witlessly to the end. A press conference called by the Ugandan Department of Health had Phillipa Musoke, head of Pediatrics at Makerere University Medical School, bamboozling journalists with American medical lingo:

There is considerable scientific data demonstrating that a short-course nevirapine regimen is safe and effective and should continue to be used to prevent mother-to-child transmission in settings where more complex regimens are not available.

‘It’s an issue affecting people’s lives,’ said her Ugandan colleague, Saul Onyango, to divert attention from the real point. ‘A lot of damage has already been done and we need to do damage control.’

A statement issued by the lead author of the first HIVNET 012 report in *Lancet* in 1999, Laura Guay, and co-signed by Musoke, tried just that, promising to ‘clarify the scientific facts, based on the full body of evidence’, but then didn’t, perhaps because ‘the full body of evidence’, concealed until Fishbein went public, was so awkward. Instead of addressing his revelations that AP had published, Guay waffled about the usual red herring:

It is true that resistance has been shown to occur in those receiving short-course nevirapine. The problem of drug resistance has partly been as a result of violations in prescription rules. However, to date, there is no evidence of negative clinical outcomes as a result of subsequent antiretroviral therapy.

In the teeth of the unreported adverse event and fatality revelations, their colleague Francis Miiro likewise persisted in asserting that nevirapine is safe.

A joint statement by ‘Makerere University, Johns Hopkins University Research Collaboration Investigators’ dismissed the

current allegations made by a dismissed and disgruntled NIH employee. ... Let us not be derailed in our efforts to prevent the children in resource poor settings from becoming infected with HIV as we continue to look for more effective PMTCT regimens.

Then again, revealing themselves to be ignorant cretins, they added: ‘Studies have shown a low risk of toxicity with long term use of Nevirapine in combination with other antiretroviral drugs for HIV treatment.’

We should continue using it on African women and their babies, urged Ashraf Coovadia, head of the paediatric HIV clinic at Johannesburg's Coronation Mother and Child Hospital:

I'm of the view that we should use nevirapine till a better situation can be created. To halt the program would cause damage to what we have already achieved.

It's clearly unsafe, but as one of the doctors who went to court with the TAC to get this stuff out there, it would be embarrassing to openly admit that I made a dreadful mistake.

Another really bright spark, his namesake 'Jerry' Coovadia thought

the controversy is more manufactured rather than being real. First of all, there is no new evidence, which has arisen, which might account for the news item, which appeared in the Associated Press. Whatever we've known, we've known for some time. And what we've known is that nevirapine is a safe drug. It's tolerated well in mothers and in infants. And most important, it is highly effective in reducing transmission of the virus from mothers to children. So that remains unchanged.

To think this person marks exam papers.

Speaking a little later, however, Coovadia was outdone by another big-time local AIDS doctor, Professor Robin Wood, co-director of the Desmond Tutu HIV Centre at the University of Cape Town. In an affidavit he made on 17 April (Case no. 2807/05, Cape High Court), he claimed: 'There is not a single recorded incident of a serious adverse event associated with the single-dose nevirapine regimen.' But then this is the same expert who also said that 'the toxicity of [AZT and similar drugs] is very low indeed', so you'll be pardoned for bursting out laughing. Or shuddering when you ponder that the public, including judges, takes people like these seriously. Especially when speaking under oath.

Giving women and their babies single shots of nevirapine was 'often the only way to save a baby's life ... the only chance to save a baby from infection', said *Médecins Sans Frontières*'s Rachel Cohen. 'The truth about nevirapine is getting widely misrepresented.' That's for sure.

The Elizabeth Glaser Pediatric AIDS Foundation defended the continued use of nevirapine in the same language:

It would be premature and inappropriate to withdraw nevirapine as an option for mother-to-child transmission at a time when so many pregnant women throughout the world have no other option to save the lives of their babies.

Obviously the foundation would talk this way; it's paid to. In 2001 Boehringer Ingelheim gave it a million dollars. And it got fifteen more from the Bill and Melinda Gates AIDS Foundation to promote the implementation of mother to child prevention programmes in the Third World. (Gates is heavily invested in the pharmaceutical industry.)

Likewise, 'Articles criticising nevirapine trial may endanger babies' lives', headlined one Dr Roehr in the *British Medical Journal* on 8 January – as John James had put it in *AIDS Treatment News* the week before: 'Nevirapine Misinformation: Will It Kill?', faithfully echoing the NIH line to silence criticism.

In a report wired four days after its exposé of Tramont's whitewashing of the nevirapine toxicity data, AP quoted Achmat's scintillating take on it:

I don't see a problem with nevirapine at all. ... NIH may be guilty of a cover up of bad protocols, in which case we would be the first to want them held accountable. But there is no doubt in my mind about the safety of nevirapine.

Mostly because as a self-admitted 'scientifically illiterate' person who never made it past Grade Eight at school, I have no idea what a protocol is. Since it wasn't 'bad protocols' that had been covered up, but evidence of nevirapine's toxicity for the African babies in the Americans' drug experiment on them.

Achmat's American treatment activist comrades took to insulting Fishbein by email: Gregg Gonsalves of the TAG in New York dismissed his likening of HIVNET 012 to the Tuskegee experiment as 'biased crap from a disgruntled NIH employee – you know nothing about AIDS and are doing tremendous damage'. Like the TAG, Project Inform in San Francisco is also funded by Boehringer Ingelheim; so little surprise when director Martin

Delaney slagged Fishbein off as having ‘psychological problems’, of being

an unbalanced and reckless individual who is putting his own interests above those of people worldwide who are affected by the spread of HIV. In all my 20 years of working in this field, I have never seen a package like you. Shame, shame, shame.

As for the subject of the fuss, HIVNET 012 itself, ‘nothing has been hidden here’, Delaney wrote; the ‘deficiencies in record keeping were addressed. The only thing that strikes me as odd here is your own behavior.’ Reacting a few weeks later to Fishbein’s reference to Tuskegee, Delaney emailed him again, calling him a ‘crackpot’ who should be

banned from making further false claims over the internet. You obviously have no understanding of the issues facing developing nations or the challenge to implement such protocols. You just sit on your lazy ass somewhere in the US, pontificating, attacking, and denigrating the work of others, all in hopes of, of...of what? Vindication? A big settlement? Another shot at fifteen minutes in the media spotlight? You disgust me as a human being and you are clearly ill.

And then, on 20 December, Fishbein suffered a personal blow. A judge of the Merit Systems Protection Board dismissed his legal claim to protected whistleblower status on the technical ground that having been hired as a special consultant medical expert, a Title 42 employee, he enjoyed ‘no appeal rights’ during his probationary period in which he’d been dismissed – for ‘non-performance’, claimed the NIH, having judged him a star performer a year earlier. Before he started causing trouble. Which meant that his honesty and courage had cost him his position.

The *New York Times*, which, like liberal newspapers everywhere, had consistently advocated giving AZT and nevirapine to pregnant women in Africa as the liberal thing to do, immediately jumped to nevirapine’s defence, rather than reconsidering its position in the light of the revelations:

A series of articles critical of past trials of an important AIDS drug has created a furor in Africa, causing many public health

experts to worry that some countries will stop using the drug, which prevents mothers from infecting their babies with the virus that causes AIDS. On Friday, the National Institute of Allergy and Infectious Diseases, an arm of the National Institutes of Health, sharply criticized the articles, saying, ‘It is conceivable that thousands of babies will become infected with HIV and die if single-dose Nevirapine for mother-to-infant HIV prevention is withheld because of misinformation.’

So ‘Don’t block this drug’, pleaded the headline of an editorial in the *San Francisco Chronicle*.

In South Africa the *Mail&Guardian*’s reaction to the disclosures wired to it by AP was not to publish them, but to discredit them instead by giving vent to its darling human rights crusader Zackie Achmat’s histrionics about what nonsense it all was – a predictable response in the light of editor Ferial Haffajee’s statement to me on 12 December, the day before the AP exposé: ‘Our newspaper has been at the forefront of the push for antiretrovirals in this country.’ So it would be tricky for us now to face up to the fact that we have been pushing a bad drug on the country’s most vulnerable people: poor pregnant African women and their babies.

The world’s leading science journals, *Science* and *Nature*, joined in the damage control effort, with both journals taking the NIH’s side and closing ranks around the AIDS establishment and its favoured chemicals. A piece in *Nature* on 23 December, ‘Activists and researchers rally behind AIDS drug for mothers’, quoted Brooks Jackson slapping backs:

Ed Tramont is a man of integrity and common sense, and he has probably done more than anybody at the NIH to improve the infrastructure for conducting these trials in developing countries. ... There’s no question in my mind that single-dose nevirapine is safe and efficacious, and now that’s been supported by several other studies independent of ours.

(On the contrary, Quaghebeur et al. had just reported in *AIDS* in September that the HIVNET 012 nevirapine regimen didn’t work.) And then he really piled on the BS:

You get criticized because some people feel you should provide the same exact standard of care as you do in the United

States, and it's just not feasible. On the other hand, you get criticized for doing regimens that are too difficult or cost too much or are not realistic, so you're sort of caught in the middle.

This is why we need to be lenient about drug safety in Africa.

The subtitle of the piece spelt out *Nature's* view of the matter: 'Nevirapine trial was not flawed, say researchers'. The article quoted Arthur Ammann, president of Global Strategies for HIV Prevention: 'There are already mothers who are refusing to take nevirapine. This is the most successful therapy in the entire Aids epidemic. It should not be attacked.' It offends our funders; as our website reveals, among 'our many donors ... Boehringer Ingelheim and GlaxoSmithKline' are our two 'Corporate Sponsors ... Thank you'. Sure. Keep it up and there'll be plenty more.

On 24 December the first paragraph of 'HIV TRANSMISSION: Allegations Raise Fears of Backlash Against AIDS Prevention Strategy' in *Science* set the tenor of the rest of the piece:

Much to the dismay of AIDS researchers and clinicians around the world, the Associated Press (AP) ran a series last week that has reignited debate about the safety of one of the most heralded interventions in AIDS prevention: use of the drug nevirapine to prevent HIV transmission from an infected mother to her infant. This treatment likely has spared tens of thousands of children from the disease. Experts insist that, although the drug is not problem-free and some irregularities occurred during one clinical trial, nevirapine's benefit far outweighs the risks.

Science quoted NIAID's deputy director Lane claiming to have 'worries that "this particular news story may cause people to stop using nevirapine, and infants could be infected and die needlessly"'. The journal also quoted Jackson talking about Boehringer Ingelheim's audit in January 2002: 'A Boehringer representative said the audit turned up "a lot of pin pricks but no show stoppers," recalls Jackson.' Which, of course, was a blatant lie. The findings were so bad that they indeed stopped the show: the drug testing site in Uganda was closed down.

As distinctly honest as Fishbein is, however, he never did grasp

the core fallacies of the entire research project that he'd exposed – as was evident from two garbled interviews he gave as the AP reports were breaking. On 14 December he told ABC television news:

You may save the child, but you – in a sense – sentence the mother to death because there are no other AIDS drugs that are probably affordable that that woman will be able to get, so you've created an orphan.

As if nevirapine saves children and AZT their mothers. And that without the drugs they die. *Science* quoted him making a similar statement ten days later: 'Meanwhile, Fishbein says he is "not in disagreement" that nevirapine saves lives. "My issue is not nevirapine, but the process."'

On 4 January 2005 he at last got his day to say so. In all the heat generated by the AP reports, the IOM decided to grant Fishbein an audience after all. 'HIVNET 012 is a study so poorly conducted that its data must be rendered invalid as a matter of law, policy and human health,' he argued. 'We can ill afford to entrust the lives of people to invalid data.' Even the test results to determine whether babies were infected should be disregarded, he urged: the tests were done 'often by individuals that didn't have the training'. (Not only that, but completely inappropriate, unreliable, non-specific tests were used.) He pointed out that because they were focused only on trying to show nevirapine works, the principal investigators overlooked its 'often dangerous side-effects'.

Fishbein gave a roundup of his appearance before the IOM in a third-person report on his website run by his brother:

Several independent audits of the HIVNET 012 study found numerous violations of established procedure that appear to have had life threatening consequences for African AIDS patients. Documents now being reviewed by Congress clearly show that senior officials from the NIAID sanctioned a cover-up of the false and misleading test data in an effort to promote the popular AIDS drug, nevirapine. ... 'The safety, well-being and lives of African patients are being put at unnecessary risk because of the negligent, slipshod and careless behaviour of researchers for whom there is little or no accountability.

Despite its goal to advance medical research to benefit all peoples, the actions of the NIH reveal that it does not value African lives as highly as American lives,' said Fishbein. 'The implication of this double standard is that it is permissible to visit upon people in third world countries research too substandard for the treatment of Americans. And that is why people who are outraged by this double standard have made the "Tuskegee" and "guinea pig" analogies. ... The consequences of their failure not only strike deeply at the heart of NIH and its commitment to scientific integrity, but have grave and sometimes fatal implications for the lives of real patients. Here is where our duty as doctors "to do no harm" comes into sharp focus.'

Although alerted to the corruption of the HIVNET 012 data, the NIH was too 'heavily invested in the trial's outcome' to respond appropriately and reject the findings, he said. Such behaviour 'would never be tolerated in the private sector. ... The old adage "garbage in, garbage out" is apt'. Unfortunately, instead of throwing out HIVNET 012, the NIH threw Fishbein out.

The result was that by February – according to a Reuters report on the 10th – thirteen thousand Ugandan women and their babies had been given nevirapine or a combination of AZT and 3TC in 2004 alone. But the harm caused by the drugs the doctors administering them wouldn't be able to tell you; the report quoted Phillipa Musoke complaining: 'It is frustrating when these mothers come for a single dose of nevirapine to protect their unborn babies, but when they are discharged and told to report back, they don't.'

The US State Department put out a statement on the 14th whose title said it all: 'Exaggerated Concerns About Anti-AIDS Drug Nevirapine: Media allegations that anti-AIDS drug causes severe reactions disproved'. This was the second time the State Department had come out in support of nevirapine – a reflection of the extent to which the US administration was committed to the drug as a token of US foreign policy benevolence.

Speaking for the WHO, Charles Gilks, director of AIDS treatment and prevention, commented on Fishbein's revelations: 'We are aware of the toxicity profile, but at the moment we believe

the benefits outweigh any problems.’ This is because we’re committed too.

The FDA’s reaction to the new stench around HIVNET 012 was to issue yet another toxicity warning about nevirapine’s serious liver toxicity on the 19th. Other than to make the elliptical claim that no death had ever been reported to it from taking a single dose of the drug, the FDA was silent about the implications of AP’s disclosures, but then no comment was due: it does not permit the administration of the drug to American mothers and their babies. Nor does the US Centers for Disease Control, which had nothing to say either.

Boehringer Ingelheim responded to the FDA alert by stating that it wouldn’t be changing its policy of donating nevirapine to developing countries for giving to such patients (coloured ones):

There is no consequence for our donation or for supply of the drug for continuous treatment at reduced prices in developing countries. We do not expect any major effects on the behavior of doctors or on our sales as a result of the FDA warning.

Sales of nevirapine were indeed unaffected: doctors prescribed 288 million euros (\$372 million) worth in 2005.

But the ANC’s Smuts Ngonyama took the FDA’s point: ‘Our position is the same, that ARVs have serious side effects and the FDA is confirming that.’ A point disregarded by *Médecins Sans Frontières*’s Campaign for Access to Essential Medicines coordinator Daniel Berman:

This is a formalization of something known in the medical community. All of the drugs have side effects and should be monitored at the beginning of treatment. Other drugs have other issues, none of them is perfect.

As if nevirapine is in the same league as a disprin.

In the first week of February 2005 Fishbein got some good news. Under the glare of all the adverse publicity that his case was attracting, the Department of Health and Human Services (HHS) changed its tune and filed a legal brief with the Merit Systems Protection Board (MSPB), supporting his appeal to the full board in his claim to protection from official retaliation under federal whistle-blower laws. ‘There is nothing in the record indicating that

there was ever any Congressional intent to exclude the Petitioner from the protections of the WPA [*Whistleblower Protection Act*],’ said HHS attorney William Biglow, contradicting the ruling of the MSPB judge who’d tried Fishbein’s case in December and thrown it out on jurisdictional grounds.

A voice notably mute during the furore in South Africa over AP’s revelations about the abusive human experimentation on African mothers and babies that went on in HIVNET 012, and about the NIH’s suppression of the negative safety findings that had been reported, was TAC patron Judge Edwin Cameron’s. The decent thing to do, we would have thought, would have been to take a tip from Alexander Pope – ‘A man should never be ashamed to admit that he has been in the wrong, which is but saying, in other words, that he is wiser today than he was yesterday’ – and to have issued a public statement along the following lines:

We meant well, but we were wrong; we weren’t thinking, and in our misguided moral enthusiasm we all got completely carried away. We uncritically accepted a bad American study and all the propaganda spun around it, and in so doing we endangered the lives and health of babies born to poor black African mothers in public hospitals. I would like to offer my personal apologies to President Thabo Mbeki and Minister of Health Dr Manto Tshabalala-Msimang for having been at the forefront of local and international condemnation of their well-justified concerns about nevirapine. And about AZT too. I realize that by suggesting that they’ve been both lacking in judgement and uncaring, I’ve needlessly besmirched their personal reputations, and indeed I’ve damaged our new democracy’s standing in the eyes of the international community by implying that our country’s independent-minded African leaders are unfit to rule. I especially rue my repeated insinuations, in speeches given locally and abroad, that for their reservations about AIDS drug toxicity they’re in the same moral league as Nazis. I feel most embarrassed about the role I’ve played in the nevirapine fiasco, and particularly for having abused my status as a senior judge to promote this poisonous and harmful chemical (which I used to call ‘a very good drug’) for giving to African mothers and their babies, and

to cast our government's concerns about it as 'a tragedy, I think'.

You must be wondering why I haven't been quite as chatty about AIDS drugs recently as I used to be. Well, as I've pointed out before, 'I have no doubt that I have natural intellectual gifts.' I have to admit, though, that they're not particularly obvious in my dreadfully badly written, narcissistic, and self-adulatory book, *Witness to AIDS*. Anyway, I've recently been applying my special gifts to pondering what my AZT, 3TC and nevirapine combo that made me 'feel blessed' and that gave me such 'a zest for life' is doing to me – particularly nevirapine, which by all accounts is exceptionally rough on the liver. You might remember what I said in the interview I gave my friend Khopotso Bodibe in 2003, broadcast on SAfm in two parts on 18 and 25 September: 'My tummy is getting a bit larger and people tell me I'm putting on weight. In fact, I'm not putting on weight. My liver and some of the other inner organs are growing a bit larger from lipodystrophy.' I referred to the problem lightly as 'organ thickening', a 'minimal side effect'. Well I'm not so sure about that anymore, because I've since learned that hepatomegaly – swelling of the liver resulting from fatty degeneration – is no joke, and that according to the findings of a major study by Justice et al., first reported to the 14th International AIDS Conference in Barcelona in July 2002, the 'most common cause of death among HIV positive people' on antiretroviral drug treatment is not from AIDS-defining diseases, but from 'liver failure'.

And I got quite a fright to hear that on 19 January 2005 the FDA in America issued yet another warning about the deadly liver toxicity of nevirapine, probably the most poisonous of all the AIDS drugs. What I've realised is that my ballooning liver means I'm on the high road to liver failure and early death.

On top of that, I was even more worried to read the draft new treatment guidelines issued by the British HIV Association (BHIVA) on 26 April 2005, drawn by a team headed by top English AIDS doctor Professor Brian Gazzard. The guidelines drop nevirapine as a favourite component of AIDS drug

combinations – as they do AZT, due to the latter drug's 'propensity to cause lipoatrophy', which means wasting away as my cells die off.

Whenever I run into people while cruising the trendier shopping malls in Johannesburg and Cape Town, people stare at my now very gaunt, skeletal face. After which their eyes drop down to my paunch, now so grotesquely swollen that they wonder silently when's the baby due.

All this set me wondering to myself: exactly what have I been swallowing? And encouraging others to. As doctors slowly wake up, like they did after half a century of injecting arsenic, with the support in 1934 of the Health Organization of the League of Nations, right up until the mid-1950s. Salvarsan, they called it. And swore by it. And then conceded that it wasn't so hot after all. Currently rated the most toxic substance known to man, having regard to risk of exposure, by the US Department of Health and Human Services's Agency for Toxic Substances and Disease Registry.

I've really made an enormous fool of myself. I feel sick with shame. I'm terribly sorry. I'm actually considering resigning over the role I've played in landing our country in this dreadful mess.

You must be dreaming. I'm a judge of the Supreme Court of Appeal. I don't have to apologise when I screw up. The 'Constitution says I can't be sacked, except for very rare conditions'. Excluding getting involved in big drug scandals. I'm not accountable to anyone. Certainly not to murderous denialists such as the President and the Minister of Health, who've been withholding life-saving medicines from Africans. Until forced in the courts by my much-admired friend and 'man of principle', Zackie Achmat. Obviously, as 'a white, gay man in an epidemic that overwhelmingly affects black heterosexuals but ... claimed as an African who spoke out on the fact that I had AIDS', I care much more about their own people than they do. And as you can see, they clearly lack my 'natural intellectual gifts'.

After all, a concession from me about nevirapine – about AZT too – would be a mortal blow to my public reputation.

And I'm much too proud to admit that they were right and I was wrong. As Zackie put it in May 2004, explaining why before the April elections he'd dishonestly concealed the fact that a couple of months of antiretroviral drug treatment had crippled him mentally and physically to the extent that he could no longer walk, conduct interviews as before, even answer his own cell phone: 'I can't let Manto win, I can't let Mbeki win.' At least when I die before my time, everyone will be talking about me as a heroic martyr in the great war against the deadly scourge. Stories about how I bravely battled with AIDS until my tragic death will be filling the newspapers for months. About how courageously outspoken I was. About how my medicine just wasn't strong enough.

And I agree with NIAID director Anthony Fauci and his deputy Clifford Lane, writing in their opinion piece in *Nature Medicine* on 5 March, that Associated Press's revelations about HIVNET 012 have been 'widely misconstrued to the potential detriment of public health' and might 'lead to the decreased use in developing countries of a proven intervention [where] no other options are available'. I go with guys like these. I look up to them. I respect medical authority. I don't question it. I like taking advice from doctors; they feel to me like the father I never knew. And when they advise me to go on pharmaceutical drugs, the deadlier they are the better. (There are some complex psychological reasons for this, but that's for another book.)

And that's all I've got to say.

Ahead of the release of the IOM's report, AP's John Solomon probed the financial conflict of interest of the IOM panels' nine members – appointed to evaluate and possibly condemn the conduct of some of the NIH's top officials in DAIDS. He reported what he found on 14 March 2005: six of the nine of panel members were being funded by the NIH to the tune of between \$125,000 and \$2 million dollars a year. An acquittal was guaranteed. It would be big business as usual. The all-American way.

Two weeks later, on the 30th, the Kampala *Monitor* quoted Professor Geoffrey Miiro disclosing that

Seventy-three children and about thirty mothers died during the [HIVNET 012] study, but they were not dying because of the drug. They were dying of the disease.

What disease? Isn't it elementary that AIDS is not a disease, but a syndrome of unrelated, diverse diseases? Anyway, wasn't nevirapine supposed to stop 'the disease'? And again, what disease? Only clinically healthy women had been inducted into the trial. In fact, how many died on the drug trial we'll never know; thanks to Fishbein it's become public knowledge that proper clinical records weren't kept.

The IOM announced its findings on 8 April. Skipping past Fishbein's charges concerning the defective conduct of HIVNET 012 and the cover-up that followed, it turned out a pail of whitewash – pronouncing the trial 'both scientifically sound and ethically implemented'. As just mentioned, six of the nine guys saying so were pulling massive research grants from very same NIAID Division of AIDS whose scientific misconduct they'd been asked to investigate. And some of them, I subsequently found out, are members of research networks competing for DAIDS funding amounting to hundreds of millions of dollars.

In a letter to the IOM on 30 March, Senate Finance Committee chairman Charles Grassley fumed over having been lied to about this gross financial conflict of interest, and underscored the patent credibility problem that arose from it:

I am ... troubled by the fact that at a meeting with the IOM on January 5, 2005, your staff assured my staff repeatedly that the current members of this IOM committee did not have any financial or professional conflicts of interest. ... IOM's failure during that staff briefing to openly acknowledge the financial ties of its committee members to the NIH casts doubt on the objectivity and integrity of the committee's review.

Not only did the NIH crookedly contrive to define the IOM's enquiry brief narrowly in order to keep the necks of its rogue staffers such as Fauci and Tramont out of the noose, it also fundamentally misled the IOM about the purpose of HIVNET 012, in order to divert attention from the fatal lapses in the manner in which the study was conducted, by claiming that it was 'not

originally intended to provide data for later submission to the FDA' and therefore 'not required to comply with specific procedural rules outlined in the voluntary "Good Clinical Practices" guidelines'. But a letter from Boehringer Ingelheim on 22 October 1997 to a quality control contractor directly contradicted this:

The Division of AIDS has documented that this study will be conducted according to GCP and in a manner that meets the regulatory requirements for a registrational study. Thus, Boehringer believes that HIVNET 012 could be used to support an application for a prevention of perinatal transmission.

And again on 4 January 2001 in a letter to DAIDS:

We hope to submit our package to the FDA by the end of first quarter this year. As per our previous discussions, the data from HIVNET 012 will serve as the centerpiece of our submission.

This deception by the NIH vitiated the IOM's findings completely: had the IOM been properly briefed, it would have found that elementary Good Clinical Practices had not been observed in the conduct of HIVNET 012 – just as Fishbein had pointed out in page after page of testimony – thus disqualifying the trial as a 'registrational study ... that meets the regulatory requirements' of the FDA. In other words useless, and unfit to rely on for any purpose.

One of the six IOM panel members enjoying a fat undisclosed NIH grant was Mark Kline. Cooing over his panel's report at a press conference on the day it was released, he revealed the bias with which he and his mates had approached the job:

Nevirapine really is the cornerstone of efforts to reduce mother-to-child transmission of HIV in poor countries around the world, particularly in Africa, so the concerns that have been raised about the study really have had a chilling effect on the use of this drug. So we're happy to report that the drug is efficacious and is safe because we would obviously like to do anything we possibly can do to help to provide tools for the

prevention of mother-to-child transmission of HIV in poor settings around the world.

We Americans really like to help people in other countries, particularly over in Africa. It's unimaginable to us that we're harming their children, when we mean so well.

Another panel member corruptly enjoying big NIH funding while sitting in judgement of the NIH-sponsored trial, Steven Lagakos, was asked by a brown-nosing journalist from *USA Today*: 'Would you rank this as a halcyon example of a trial given the challenges that the researchers faced?' Lagakos responded: 'For a trial of HIV, this was an A. In my personal opinion, this was a very well done trial.' Sure, Steve, top of the pops.

As they were giving HIVNET 012 their thumbs-up, however, the IOM's panel members made clear that they thought nevirapine fit for giving African mothers and babies only: although

The committee finds that there is no reason based in ethical concerns about the design or implementation of the study that would justify excluding its findings from use in scientific and policy deliberations

the under-reporting of severe adverse reactions 'may limit the generalizability' of the study's conclusions. To American babies, they meant. Where different ethical concerns are applicable. In 'scientific and policy deliberations'. About whether we should give this stuff to our own blue-eyed kids.

Responding to the announcement of the IOM's findings in regard to the conduct of HIVNET 012, Fishbein persisted in telling it like it is: 'This study is garbage' and the IOM report 'lies, distortions and a cover-up of the truth'. In doing so, though, he emphasized the focus of his own particular concerns, deliberately skirting the fundamental scientific questions:

The effectiveness of the drug is an issue I can't comment on. My issue is the conduct of this one study. ... It's a scientific-integrity question for me, not a nevirapine safety and effectiveness issue.

Not supposed to talk out of line like that, the NIH gave Fishbein the final shove on 1 July. Senators Grassley and Baucus protested

in a letter to director Zerhouni: ‘Retaliation against an employee for reporting misconduct or voicing concerns is unacceptable, illegal and violates the Whistleblower Protection Act.’ Senators Mikulski and Hoyer and Representative Cardin agreed, and wrote to Zerhouni as well, demanding the rescission of Fishbein’s dismissal.

‘I am out for the restoration of my career and the restoration of my reputation,’ said Fishbein. ‘That’s what I want and I will not stop until it’s done. And along the way I will do everything I can to press the NIH until they are accountable for what they’ve done.’ His persistence paid off with a Christmas present: the NIH folded and reinstated him a week before the year ended in a new post as special assistant to the deputy director of NIAID.

Back in South Africa, thanks to the useless, anonymous, secretive and wholly unaccountable pharmaceutical industry sweethearts on our Medicines Control Council, nevirapine remains registered for administration to HIV-positive pregnant women and their newborn babies – despite the absence of any supporting clinical trial evidence for this considered acceptable by it, by the US FDA or by the drug regulatory board of any other Western country. Consequently, newborn African babies are needlessly being poisoned in their tens of thousands. With the blessing of the learned justices of the Constitutional Court, full of human rights. Crying over them.

Celia Farber traced the moral of HIVNET 012 in a round-up of the saga for the *New York Press* on 28 December 2004. Mentioning also the case of Joyce Ann Hafford, a healthy eight-months-pregnant black American woman killed by a couple of weeks of experimental nevirapine treatment given to her because she was HIV-positive (the doctors initially tried pretending she died of ‘AIDS’), she concluded observing that

the AIDS establishment has shown itself to be lost, with a broken compass, on the map of medical ethics. Once it becomes acceptable to kill patients in experimental clinical trials and cover it up, without consequence, you might argue that all is lost.

We agree with you, Celia, we do, we do. The trouble is that over here in South Africa we’re lumped with all these fervent doctors

and lawyers, judges and journalists, and drug company pimps who don't.

Part Nine

Sooner or later, Mr Fowler, one has to take sides, if one is to remain human.

Hinh in *The Quiet American*
Graeme Greene

Like the Americans' Ed Tramont, South Africa has its own 'man of integrity and common sense'. The same sort of guy with the same professional and corporate loyalties. The same kind of medical ethics. And the same attitudes towards Africans.

An editorial in the March 2003 issue of the *South African Medical Journal* written by deputy editor and de facto boss JP de V van Niekerk, his grinning mug alongside his piece, announced that as far as his journal was concerned all enquiry about AIDS medicine was now closed. As a cameo study in stultified medical thinking, 'Politics must move mainstream on AIDS' was richer than tipsy tart:

Medical journals have a responsibility to put all sides of important questions to readers. However, there comes a time when continuing to pander to tangential viewpoints serves no useful purpose and indeed may be harmful. ... The SAMJ therefore does not accept such material.

The grinning doctor meant business. His first act of censorship was to bounce a whistle-blowing report by two Austrian gynaecologists working in the maternity ward at Zomba Central Hospital in Malawi, concerning an AZT and nevirapine experiment conducted there and at other Malawian hospitals by American researchers from Johns Hopkins Medical School. Even by the debased norms of AIDS research, the study was a scandal. The plan was to give nevirapine to pregnant African women and a combination of nevirapine and AZT to their newborn babies, a course of seven days worth of the latter – violating the age-limit and special provisos in the 'INDICATIONS' section of GlaxoSmithKline's 'RETROVIR PRODUCT INFORMATION':

Pediatrics: Retrovir is indicated for HIV-infected children over 3 months of age who have HIV-related symptoms or who are

asymptomatic with abnormal laboratory values indicating significant HIV-related immunosuppression.

Pregnant women pitching up at the hospital in groaning labour to give birth to their babies were administered a single rapid result probe for what doctors call HIV antibodies, Abbott Laboratories's Determine HIV-1/2 antibody test. If they lit up, the researchers deemed the mothers HIV-infected – not bothering to comply with the two peremptory stipulations of the test-kit manual:

Positive specimens should be retested using another method and the results should be evaluated in light of the overall clinical evaluation before a diagnosis is made.

The reason for these requirements is that the test is not specific. In other words, it cannot be relied upon to make a diagnosis. According to the report of the study later published in *Lancet* on 11 October 2003 under the title, 'Short postexposure prophylaxis in newborn babies to reduce mother-to-child transmission of HIV-1: NVAZ randomised clinical trial', 'All HIV-positive results were retested with Wellcozyme HIV test ... and the results were available either before discharge or at the first follow-up visit.' But by this time, of course, the follow-up test results were perfectly irrelevant, since the African women had already been enrolled in the study and their babies fed the toxic drugs on the basis of an insupportable diagnosis, based on a rapid result test, that they (the mothers) were infected with the sex germ.

It was in any event completely incompetent for the researchers to have 'retested' the 'HIV-positive' mothers with a 'Wellcozyme HIV test' to confirm the results of the rapid test. The Wellcozyme test is a simple ELISA antibody test, and even the dullest AIDS doctor knows that you can't hang a diagnosis of HIV infection on the result of a single ELISA. And that purporting to confirm a rapid result test with a single ELISA is perfectly ridiculous. Except maybe in Africa where AIDS doctors apply different standards for Africans. Since they've all got it, so what does it matter?

And although, as just mentioned, the rapid result test manual required that

Positive specimens should be retested using another method and the results should be evaluated in light of the overall clinical evaluation before a diagnosis is made

no such ‘clinical evaluation’ was performed. No matter how clinically healthy they appeared, the women were considered infected and enrolled in the study if they lit up a rapid result test.

In a crowded delivery room without any privacy, the sweating, heaving women – more than half of whom were illiterate – were terrorized by being told that they had the killer virus in them that could slay their babies, and were inducted into the drug experiment on the basis of what was read to them from an ‘Informed Consent’ form. It could have been drawn by the dustman.

The women might have consented, but they certainly weren’t informed. About the fact that the test drugs were exceptionally toxic. Under ‘Dangers’, the form (translated from the vernacular) reads:

There is no specific danger that we expect, other than a little pain on taking the blood and occasional inflammation at the site of the injection. AZT can also reduce the amount of blood in your baby’s body.

Nothing else. About AZT. And zero about nevirapine. Especially not the manufacturer’s cautionary notes about the latter drug’s acute liver toxicity: ‘Severe, life-threatening, and in some cases fatal’. Or that: ‘Severe, life-threatening skin reactions, including fatal cases have occurred in patients treated with VIRAMUNE. ... Some events occurred after short-term exposure to VIRAMUNE.’ Nor that according to the first report of the famous Ugandan study HIVNET 012,

The rates of maternal serious adverse events were similar in the two groups (4.4% in the zidovudine group, 4.7% in the nevirapine group). ... The occurrence of clinical or laboratory abnormalities in mothers was similar in the two groups (82.2% in the zidovudine group and 80.7% in the nevirapine group had at least one such event). ... The rate of serious adverse events in the two groups [*of babies*] was similar up to the 18-month visit (19.8% in the zidovudine group. 20.5% in the nevirapine group), with the median age at last visit being 183 days ... The

most frequent cause of serious adverse events within 56 days of birth were sepsis [*bacterial infestation of decaying tissue*], pneumonia, fever, congenital anomaly [*birth defect*], asphyxia [*defective oxygenation of blood*], and dyspnoea [*breathing difficulty*]. [*The report also noted that eighteen babies suffered maculopapular (erupted skin) rash, and twenty-two anaemia.*] The frequency and severity of laboratory-detected toxic effects, including neutropenia [*depleted immune cells*], thrombocytopenia [*depleted clotting platelets*], and abnormalities in creatinine [*energy metabolism*] or bilirubin [*breakdown product of oxygen-carrying haemoglobin*], were similar in the two groups. ... 38 babies (6.8%) died (22 (7.9%) in the zidovudine group, 16 (5.7%) in the nevirapine group). The most frequent causes of death were pneumonia, followed by gastroenteritis, diarrhoea, dehydration and sepsis.

All of which numbers, shockingly high as they were, were way below the real incidence of adverse events, severe adverse events and deaths, as emerged from audits of HIVNET 012 by Boehringer Ingelheim and by Westat, the independent auditors hired by the NIH. Which the American principal investigators Jackson and Guay both admitted. And which the director of DAIDS suppressed.

The ‘Advantages’ of joining the study, as sold in the ‘Informed Consent’ form, were:

You and your child will get NVP for free. Also you get AZT for free. It can prevent MTCT of HIV. It can help you to have a healthy life. And when the results of this study are published, they will help other Malawians and other people in the Third World.

As for ‘Costs’, ‘You don’t need to pay anything. Participation is voluntary. Each time you come to the hospital, you get a refund for transport.’ That was all the Americans were prepared to squeeze out: the bus-fare. And if the women or their babies succumbed to drug poisoning, ‘there is no compensation in the case of side-effects’. Making Africa just brilliant for American drug trials.

The researchers refused to identify who was on the trial drugs, with the result that doctors and nurses were unable to determine whether clinical events among the women and babies in their ward

were the manifestations of drug intoxication and then administer appropriate emergency palliation. One woman died. When ward staff enquired as to whether she'd been on nevirapine, the researchers wouldn't say. A hospital staff meeting was called on 4 February 2002 to discuss this outrageous state of affairs. The matron, Mrs Banda, wondered out loud how the study could ever have been approved by the ethical review committee, commenting: 'Studies which could not be conducted in the Western World should also not have a place in Malawi, misusing the poverty and the low educational status of a part of the patients.' Her country ought not to be a 'dumping ground' for drug research of this sort, she said.

With the help of the Health Ministry, the chief gynaecologist in the maternity ward at Zomba Hospital, Dr Peter Safar, demanded information about every patient in his ward on the trial and the experimental drug they were being put on. Unwilling to cooperate, the Americans called off the trial there shortly thereafter.

Safar and fellow gynaecologist Christian Fiala reported the abuses they'd witnessed in an article they submitted to the *SAMJ*, entitled 'AIDS research in Africa – as if we're still in colonial times'. On 6 January 2003, after all queries had been settled, and having received the American researchers' response to the indictment set out in the gynaecologists' paper, as well as the latter's reply in which they persisted with their charges, *SAMJ* assistant editor Emma Thompson wrote: 'Proofs received – thanks so much. I hope to publish the article in the February or March *SAMJ*', together with the drug researchers' answer. On 17 March, when it hadn't yet appeared, the authors queried why. 'Owing to extreme pressure on space I have been unable to place your article yet, but it will definitely appear in the May *SAMJ*,' Thompson replied. But it wasn't to be. When the grinning guy got to see it, he spiked it – writing on 23 April:

It is with regret that we inform you that the editorial advisory group has again reviewed your manuscript and has decided not to publish it in the *SAMJ*. The principal investigators for the Johns Hopkins Project have responded in detail to your various statements and allegations. These are refuted including that this study has been stopped prematurely. We do not believe

that a polemic based on unsubstantiated facts will advance research and science in our region and be of benefit to the management of the HIV/AIDS pandemic.

The authors of the canned paper asked for particulars of these ‘unsubstantiated facts’. None came. Chances are that what really got Van Niekerk’s goat was the annoying appellation behind Fiala’s name on the paper: ‘Member of the Presidential AIDS Advisory Panel’. Sort of like a Wiccan coven.

In his editorial embargoing all future critical writing about AIDS medicine in his journal, Van Niekerk referred, with a grin, to the ‘apartheid era treatment of doctors such as Wendy Orr, who incurred the wrath of the authorities for reporting injuries of prisoners as a result of police detention’, implicitly claiming her singularly rare company. But in suppressing Safar and Fiala’s exposé, he chose to sup instead with the likes of those other famous doctors of the apartheid era, Benjamin Tucker and Ivor Lang. Who, seeing Steve Biko lying naked in chains on the floor of his cell, frothing at the mouth from brain damage after having had his head kicked in by the security police and murmuring desperately under a blanket sodden with his own piss, noted, for their report, that he was ‘shamming’. Being powerful, comfortable. Not paid to cause trouble. And grinning to themselves on their drive home to scotch and roast: What the hell, he’s only a kaffir.

Part Ten

‘Who will guard the guards?’

Juvenal, 160 AD

Until the publication of John le Carré’s bestseller *The Constant Gardener* in January 2001, hardly anyone had ever heard of *BUKO Pharma-Kampagne*. Certainly not outside Germany – mainly because, it says on its website, this

campaign group committed to Rational Drug Therapy ... monitors the marketing practices of the German pharmaceutical industry in Third World countries. It tries to stop unethical practices of the companies such as the sale of dangerous, useless and irrational drugs, the distribution of misleading information and unethical promotion. ...

Multinational companies based in the rich countries are selling harmful, useless and far too expensive drugs to the world’s poorest nations. They are corrupting medical practice and earn huge profits from people who have to struggle for their everyday survival.

BUKO (Bundeskoordination Internationalismus) is the German acronym for Federal Congress of Development Action Groups, about two hundred of which banded together in 1977, back in the heyday of keenly analytical militant political radicalism in Germany. *Pharma-Kampagne* began three years later as a ‘public awareness raising campaign group’ advised by ‘a number of experts (medical doctors, clinical pharmacologists, pharmacists, sociologists)’ who select ‘issues to be taken up’, since ‘there are a lot of irrational drugs on the market, and some of them can do more harm than good’. Looking at ‘the quality of German drugs in developing countries’, it

tries to answer important questions: Do German drugs meet important basic criteria for rational drugs? Is there a sufficient and reliable clinical and empirical data basis on efficacy and safety for each drug?

In a note at the end of his novel – about a drug corporation killing Africans in clinical trials with wrong doses of a new TB medicine, and then murdering activists publicising it – le Carré commends *BUKO Pharma-Kampagne* for keeping the pharmaceutical industry on its toes, and even appeals to readers to support it. Setting an example, he donated it his fee for a frothy article he wrote in *New Statesman* in April 2001, entitled ‘Their Sacred Duty: Multinational drug corporations put profits ahead of lives’. The moral of the piece was that they cook up wonderful life-saving chemicals that you need to swallow to stay alive if you’re sick – just as their marketing propaganda claims – but then they charge too much for them, leaving the poor to die. Especially AIDS drugs: a major theme of his article was that ‘Big Pharma’ was preventing poor countries from

making their own cheap forms of the patented lifesaving drugs that could ease the agony of 35 million men, women and children in the Third World who are HIV-positive, 80 percent of them in sub-Saharan Africa.

Such generic drugs would ‘save the same lives that Big Pharma could save, but at a fraction of the cost’. Their ‘lifesaving drugs’ are overpriced; and ‘for want of ... generic AIDS drugs ... people were dying by the millions’. And again: ‘The price [of the drug industry’s patents] is the lives of millions of the Third World’s citizens.’

BUKO Pharma-Kampagne was thrilled to be mentioned in *The Constant Gardener*, both in the endnote by name, as well as obliquely in the story itself: the novel features ‘HIPPO’ with the same mission and operating out of the same city, Bielefeld. You can see a photograph of its leaders Jörg Schaaber and Claudia Jenkes on the group’s website, posing happily with copies of le Carré’s book and basking in the moral glow.

No sooner had Boehringer Ingelheim begun dumping nevirapine in developing countries in 2000 than *BUKO Pharma-Kampagne* crossed swords with it. Being brave and determined defenders of human rights in *die Dritte Welt*, they were upset when they heard that the German government had just concluded a ‘Public Private Partnership’ with the company to buy nevirapine for giving to Kenya, Uganda and Tanzania to save their babies from being

infected with their mothers' supposed sex-virus. Great news to the activists you would have thought, but no. *BUKO Pharma-Kampagne* objected to the deal on two scores: Boehringer Ingelheim would only be in for 'a meagre 1.2%' of the estimated 6 million German Marks per year cost of the drug; and, more mysteriously, on a matter of general principle,

Drug donations are very likely to create expensive vertical interventions which are not integrated into health systems and take away money from a comprehensive health care approach.

The group therefore 'started a letter campaign to Boehringer Ingelheim and the German Ministry to stop this unhealthy donation'.

In view of the subject of his book, and his criticism of the pharmaceutical industry in the press, I wrote to le Carré in July 2001 and sent him a copy of my exposé *Debating AZT: Mbeki and the AIDS drug controversy*. Until then, what had evidently never entered his crackling imagination was the possibility that the merchandise which he'd been extolling as the best thing since Holy Water was itself rotten, and not just the commerce around it. In a two-page hand-written reply, signed off under his real name David Cornwall, le Carré responded warmly, complimenting me on the book and wishing me luck with it. He'd evidently been appalled by its disclosures and embarrassed to discover that he'd been taken for a ride, along with just about everyone else, swept along by the raging moral fervour behind the drug. The nub of his letter went:

I agree with (the alas late) Donald Woods: [AZT] needs much more serious debate than Big Pharma and the usual club of fringe beneficiaries are permitting. There is simply too big a case to answer, and it's not being answered. Having said that, I suppose I look a bit of a fool because I'm one of the numberless well-intentioned people who have been championing cheap antiretrovirals for the Third World's afflicted etc. But the book worries me deeply, and, until the debate has been properly joined and fought, will continue to do so.

Le Carré's remark that the drug 'needs much more serious debate', his suggestion that 'the debate' hadn't yet been 'properly joined

and fought', and that the damning 'case' I'd presented from the medical literature against it was 'too big ... to answer, and it's not being answered' spoke, I think, more to his difficulty in reconciling himself with the horror of what he'd got himself into, rather than the facts, because 'the debate' had indeed 'been joined' in *Debating AZT*, and by no less eminent an authority than South Africa's leading AIDS treatment expert, Dr Desmond Martin, president of the Southern African HIV-AIDS Clinicians Society. Martin had 'answered' my critique of the drug in detail, giving it his best shot, only to come off sounding like a cross between a parson, a used car salesman, and the village idiot.

In late 2005 I sent the manuscript of *The trouble with nevirapine* for comment to several prominent white public commentators in South Africa, all of whom had been bashing the government for worrying about the toxicity of ARVs. I also sent a copy to *BUKO Pharma-Kampagne's* Schaaber and Jenkes. No one responded. Among approving reviews of *Debating AZT* by several notables on the back cover, I included le Carré's thumbs-up for *Debating AZT* at his suggestion, although quoting him more extensively than he'd had in mind (as a suggested pull-quote he'd underlined his last sentence cited above, starting with 'But'). Expecting that le Carré would appreciate *The trouble with nevirapine* as much as he had *Debating AZT*, I sent him a copy too. But this time he exploded:

When I wrote to you four years ago, I congratulated you on contributing to the difficult arguments that at that time raged around the HIV/AIDS crisis. I was not then aware of the extremity of your views, and I did not in any case support them. Now I learn that you have made a convenient extrapolation from my letter which conveys the totally false impression that I am on your side of the argument. I am not. I stand fair and square in the opposing camp and I am humiliated and angered that you have traduced my letter in this way.

Gone was his wincing sheepishness for obviously looking 'a bit of a fool because I'm one of the numberless well-intentioned people who have been championing cheap antiretrovirals for the Third World's afflicted'. He was now firmly back in the 'opposing camp ... of numberless well-intentioned people' still 'championing

cheap antiretrovirals for the Third World's afflicted'. He was going to issue a press release, and blow me out the sky, he said. I'll admit I was rocked; had I anticipated his reaction, I'd hardly have quoted his approving comments on the back cover of the book and sent him a copy. I offered a resolution: I'd strip all mention of him from my work, and in turn he'd let things be. We'd call it a day. But it wasn't to be.

On 5 February 2006, without approaching me first for comment, the *Sunday Times* quoted le Carré's letter against me, making me out to be a liar and a general scumbag. But by now the reason for le Carré's position had become clear to me.

When *The Constant Gardener* movie came out the year before, I went to check it out. Imagine how sick I was to see nevirapine punted by way of a product placement not once but twice. Now in the ordinary course of the movie business, you pay a lot of money to get your products showcased in big commercial films, and it seems most unlikely that Boehringer Ingelheim got its proprietary drug advertised free. Aside from the fictitious TB one in the story, no other drug was mentioned in the film, let alone twice. The look of it was that the producer had taken a sizeable kickback from Boehringer Ingelheim for the favour – handy for paying production costs such as for the film rights from the author of the novel on which the film was based.

In his *New Statesman* article five years before, le Carré had fairly complained that

Big Pharma is also engaged in the deliberate seduction of the medical profession, country by country, worldwide. It is spending a fortune on influencing, hiring and purchasing academic judgment to a point where, in a few years' time, if Big Pharma continues unchecked on its present happy path, unbought medical opinion will be hard to find.

Not only medical opinion, apparently.

When movie was released in Germany in January 2006, *BUKO Pharma-Kampagne* capitalized on the glorious public profile that le Carré had raised for it. Together with Medico International – another German organization committed to pushing its country's toxic drugs on Africans – it used the occasion to issue a press release.

By this time *BUKO Pharma-Kampagne* had long forgotten its original undertaking to ensure that only ‘rational’ drugs for which there was a ‘sufficient and reliable clinical and empirical data basis on efficacy and safety’ were being sold in the Developing World, and not the sort disallowed in the North as ‘dangerous, useless and irrational’. Or licensed in the North for one indication, but pushed in the South for another one not approved as safe and effective in the North – such as nevirapine in maternity wards. Having once campaigned against bad drugs, it had now turned to campaigning for them. Its mission had switched to getting as many of the drug industry’s AIDS drugs to Africa as possible – in this project marching in lock-step with George W Bush and the gangsters around him; other foolish retired presidents; no end of aggressively determined American corporate philanthropies; scores of European NGOs; all the corporate media; and drug industry financed treatment action campaigners everywhere, such as the Treatment Action Group, Project Inform, ACT UP, Positive Action, and so on. Our TAC too, with whom *BUKO Pharma-Kampagne* had established warm ties early on.

In its press release about the film on 11 January, ‘Unfortunately Not a Fiction’, *BUKO Pharma-Kampagne* confirmed that indeed

pharmaceutical companies test their new developments in many countries – as portrayed in the movie – without considering the otherwise commonly accepted ethical measures or the well-being of the patients. The tests are carried out without the consensus [*sic: informed consent*] of the test persons. There is an insufficient clarification about the risks involved and there is an inadequate therapeutic control.

They could have been talking about HIVNET 012 as a shocking illustration of the problem in recent times, but of course they weren’t; Fishbein’s revelations about it, aired by Associated Press and elaborated in this book, had gone right over their heads. The rest of the statement beat the familiar drill of patents and prices and unaffordability and lack of access to essential medicines and too few drugs for the poor. Under ‘The Organisations’ listed at the end of the press release, it told us that ‘*BUKO Pharma-Kampagne* was the paradigm for the initiative HIPPO, a critique [*sic: critic*] of the pharmaceutical industry, which has been portrayed both in a book

and in a movie.’ This was tremendously important to know. That they’d made it in Hollywood. *Super!*

In its December 2006 ‘Pharma-Brief’ *BUKO Pharma-Kampagne* announced, in as many words, that getting nevirapine to the poor little African children had moved up to become its first order of business. The front-page headline blared (I translate): ‘Boehringer hinders access to AIDS syrup for children’. Declaring the granite premise of the piece in the very first line, ‘Nevirapine syrup is essential for the treatment of HIV-infected children,’ the rest of the report fuffed about patents and generics and ‘profits over lives’ and the usual stuck gramophone, all completely missing the point.

It must be said in *BUKO Pharma-Kampagne*’s defence that its claim that nevirapine syrup ‘is essential’ for African children is made on the highest medical authority (and AIDS activists like kneeling before the medical authorities). The WHO includes nevirapine ‘Oral Liquid’ in its list of ‘Essential Medicines’; and in terms of its original definition of such drugs in 1977 what the WHO means by this is that nevirapine for children is ‘of utmost importance, basic, indispensable, and necessary’. Absolutely.

On 27 March 2007 *BUKO Pharma-Kampagne* and Medico International issued another joint press release, announcing the launch of a *Protestaktion* against Boehringer Ingelheim to place it under *Druck* by way of an online petition (I translate):

Access to life-saving medicine must be accessible to all. We demand that Boehringer withdraws its patent claim against generic nevirapine syrup in India.

So that it can continue to be inexpensively produced there and shipped across the Indian Ocean to save the lives of ‘two million HIV-positive children in Southern Africa’.

BUKO Pharma-Kampagne’s next move, again collaborating with Medico International, was to convene an international ‘Patents, Patients and Profits’ symposium in Berlin on 10 May, which they got the German Protestant charity *Brot fuer die Welt* (Bread for the World) and its Catholic counterpart *Miserior* to pay for – funded in turn, under a curious historical quirk of German law, by the German taxpayer. The conference was honoured by the presence of special guest Jonathan Berger, TAC Treatment Project committee member and AIDS Law Project attorney, who opened

the first session under the title 'Patients Come First: The Debate on the Access to Life-saving Medicines', by talking about 'Politics and Patents: Campaign for Patient Rights'. They must have all been dabbling their eyes.

A week later, under the combined moral pressure of the activists and Germany's Christians across the Reformation divide, Boehringer Ingelheim finally caved in. Six years earlier, in a press release on 26 January 2001, 'Boehringer Ingelheim rejects MSF's claims', the company had dismissed a demand by *Médecins Sans Frontières* that

the price of VIRAMUNE® should be reduced by 95 per cent for developing countries or that voluntary licenses be granted to developing countries where Boehringer Ingelheim holds patent rights for this drug.

Now it was throwing in the towel. A press release on 17 May 2007 entitled 'Boehringer Ingelheim further intensifies fight against AIDS' announced that 'patents on nevirapine will not be enforced by Boehringer Ingelheim in developing countries', and in addition, it would be cutting its already reduced 'preferential price' by half 'in all African countries and all other low-income countries' amounting to 'a more than 90 percent discount on the price for the treatment in highly industrialized countries'. This was

to be seen in addition to the well-established Boehringer Ingelheim Viramune® Donation Program for pregnant HIV-positive patients in developing countries ... 59 countries in Africa, Asia, Latin America and Eastern Europe.

It was important that we saw this. And tapping into the characteristically stupid sentimentality of the Age of AIDS, the statement concluded: 'In all HIV research activities of Boehringer Ingelheim special care is given to paediatric indications. Viramune® is registered in most countries for use in children.' We're a very caring company.

But Boehringer Ingelheim could well afford to abandon its patents on nevirapine in the Developing World, as all the AIDS activists had been demanding, so that they could all fight AIDS together, shaking their fists from behind the same barricade. On 6 April 2006 the company had convened a symposium in Rome,

calling it ‘HIV: From Yesterday to Tomorrow’, and flew out the world’s most powerful AIDS treatment activist to address it. No, not Zackie Achmat: Mark Harrington, executive director of the Treatment Action Group (TAG) in New York. Qualified with a Bachelor of Arts degree in Photographs and Films, and with applied experience gained from storming the FDA’s headquarters in 1988, and the NIH’s in 1990, shouting and screaming, Harrington is co-author of the latter’s ‘Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, October 10, 2006’ – septic with financial conflict of interest, its authors swimming in drug corporation grants, openly declared at the end by everyone, everyone except Harrington, whose salary is paid by the TAG’s principal corporate sponsors, Boehringer Ingelheim and AZT manufacturer GlaxoSmithKline, but which he didn’t think to mention.

Harrington also co-authored the WHO’s recommendations in 2003 that his patrons’ drugs be flooded into the Developing World: ‘Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Treatment Guidelines for a Public Health Approach’. So with experts like these setting the standards in AIDS medicine, it shouldn’t have come as any surprise when in early May 2007 Oxman and others published a ‘seismic’ shocker of a report in *Lancet* online, as the journal’s editor Richard Horton described it, that the WHO’s ‘evidence-based’ guidelines were pervasively troubled by a total lack of it. Summing up bluntly, Horton noted that ‘there is a systemic problem within the organization [in] that it refuses to put science first’. Chew on that the next time the activists refer you to their top AIDS experts when promoting Boehringer Ingelheim’s nevirapine for African mothers and babies.

Although his talk in Rome bore the rather fruity and petulant title ‘AIDS Activism, Boehringer Ingelheim, and the Broken Social Contract’, it was all perfectly tame, as might be expected from an embedded drug activist playing loyal opposition to his sponsor. He mentioned along the way how swell it was doing:

According to figures from the market analysts IMS, which all pharmaceutical companies use, Boehringer Ingelheim was last year the fastest growing company. Boehringer Ingelheim grew by 23% ... while the pharmaceutical market average could

only add 6%. This growth dynamic was particularly marked in the USA, where Boehringer Ingelheim's 33% growth clearly outstripped the US market (5%) ... BI's 2005 global sales ... were \$10 billion.

Harrington provided a second reason for Boehringer Ingelheim's newfound generosity:

Ultimately, despite the development of generic forms of nevirapine by many companies around the world, its price as the lowest of any generic NNRTI either as a single drug or in fixed-dose combinations [but despite] seven years of promises by BI, UNAIDS, UNICEF, and others, and massive increases in resources for HIV/AIDS prevention and care programs through GFATM, PEPFAR, and others, uptake of nevirapine for PTMCT remains pathetic. According to the 28 March 2006 WHO 3x5 update, 'In most low- and middle-income countries ... less than 10% of pregnant women living with HIV/AIDS [are] estimated to be receiving antiretroviral prophylaxis.' ... It is not Boehringer Ingelheim's fault, or that of GFATM, PEPFAR, UNAIDS, UNICEF, or WHO that uptake of PMTCT is so pathetic – it is all of their responsibility, and that of governments that do not take care of their people.

Which is to say that relative to what Boehringer Ingelheim and the experts and activists in its pocket had wished for – namely millions of mothers and babies in the Developing World dosed with nevirapine – there was 'pathetic' interest in the drug, even though the company was dumping it at no charge for a while to try to establish its market. Indeed, according to a report on Boehringer Ingelheim's patent surrender by the Indian business paper *Mint*, of sales of \$371 million in 2006, 'Some \$300 million of Nevirapine is sold in the US and Europe with the remaining revenue coming from all other countries.' So the company's concession on its patents over the drug in the Developing World was close to painless.

I sought a meeting with *BUKO Pharma-Kampagne* while working in Berlin between April and July, but had no joy. A colleague who rang for me was told, 'We know his name. He's one of those AIDS denialists.'

All of which leaves one wondering about *BUKO Pharma-Kampagne*'s seduction by the kind of drug marketing propaganda that it had previously been so astute to see through. And its bristling hostility to any reminder of this. Perhaps the collapse of its critical intelligence concerning nevirapine is explained by the common phenomenon of fatigue among the Left, especially in changing times. Look, we've been at this more than twenty-five years. It's hard working alone against something horrible year after year, hated and attacked for what you say, and always made to feel like a misfit and treated like an outcast; it's so much nicer working for something positive and feeling the joy of belonging, of being accepted and respected by everyone, and the fabulous moral bloom you experience when rallying with masses of other good people fighting together for a good cause. This is why we've turned into AIDS activists campaigning to get the pharmaceutical industry's AIDS drugs across to the poor people of Africa, the kids especially. Plus, times have changed; this is the MTV era now. What counts these days is what's popular and what's trendy. What counts is the appearance of resistance and opposition, like wearing Che Guevara tee-shirts and joining *Die Grünen*. What matters is to pose against the system – like in Rostock in early June, where we mingled with the real G8 protesters and complained some more about patent and price restrictions on the supply of nevirapine to Africans, sounding cool and feeling hip and part of the exciting anti-G8 action. It gives us the same rush we used to get when we were still seriously involved, addressing hardcore political issues both in Germany and in the Developing World. Before we gave up and joined the middle class, fighting AIDS in Africa with pop stars like Bono, Bob Geldorf and Herbert Grönemeyer, little red ribbons on our tits.

Perhaps it was just as well that *BUKO Pharma-Kampagne* and I didn't meet. For what do you actually say to the sort of *Gutmenschen* with God on their side who offer a glass of water to a man who's drowning?

Appendix 1: An unanswered submission to the MCC on 6 August 2002 regarding perinatal nevirapine treatment

1. The US Food and Drug Administration (FDA) licensed nevirapine on 21 June 1996 in terms of an accelerated 'fast-track' licensing procedure, without a conventional full assessment of its safety and efficacy.
2. Boehringer Ingelheim's licence application to the FDA was based upon an indication that in combination with the nucleoside analogue drugs, AZT and ddI, nevirapine might possibly have some therapeutic value.
3. This indication derived solely from the effect of a triple combination of the said drugs on a single surrogate marker for antiretroviral activity, CD4 cell counts.
4. Nevirapine alone had no effect on CD4 cell counts, and combined only with AZT, the effect was negative.
5. The FDA's licence granted to Boehringer Ingelheim (BI) was provisional only.
6. Confirmation of the provisional licence was dependent upon BI conducting further clinical studies and demonstrating that the drug has clinical benefits i.e. improves quality of life and or extends life.
7. The provisional licence for nevirapine was furthermore subject to restrictive conditions concerning marketing and prescription, inasmuch as the FDA approved the supply of the drug in combination with nucleoside analogue drugs only, and not for prescription solo.
8. Nevirapine was approved only for use in adults demonstrating clinical and/or immunological deterioration.
9. BI was granted provisional licences subject to similar conditions by the European Medicines Agency (EMA) on 5 February 1998 and by the Therapeutic Products Programme (TPP) of Health Canada on 17 September 1998.
10. Before the grant of a provisional, conditional licence in Canada, nevirapine had twice been rejected by the TPP due to

‘an absence of scientific evidence of efficacy and ... concerns about safety’.

11. The TPP continues to have ‘outstanding concerns about efficacy associated with this drug’.
12. To date, BI has yet to demonstrate to the FDA, the EMEA or the TPP that the administration of nevirapine has any clinical benefits.
13. Accordingly, the licences granted in all these jurisdictions remain provisional and have still to be confirmed.
14. High rates of severe hepatic and dermatological toxicities, all life threatening and some fatal, led the EMEA and the FDA to issue special safety alerts about nevirapine in April and November 2000 respectively.
15. On account of its severe toxicity, nevirapine is categorised by the EMEA in its register of approved drugs for prescription only to persons with ‘pronounced immunological and/or clinical deterioration’ – in other words, as a drug of last resort.
16. On 5 January 2001 the US Centers for Disease Control (CDC) contraindicated the administration of nevirapine even for short term administration as an anti-HIV prophylactic to medical workers suffering needlestick injuries, in view of reports fielded by MedWatch (the FDA’s drug toxicity reporting system) of the drug’s life-threatening acute hepatic toxicity, in at least one case requiring liver transplant, after an average of just two weeks of nevirapine treatment.
17. Nevirapine is a chemotherapeutic drug, and is categorised as such by its manufacturer Boehringer Ingelheim (BI).
18. All chemotherapeutic drugs have significant cytotoxic activities.
19. It is not conventional to administer chemotherapeutic agents to pregnant women or neonates in view of their known hazards.
20. Because neonates are incomparably more susceptible to drug toxicity than adults, reducing an adult dose of a dangerous drug per body weight for a neonate does not result in a correlative reduction of risk level for drug-injury or fatality. In

Clinical Management of Poisoning and Drug Overdose, Haddad et al. sum up: ‘The physiology of the newborn is unique [in the manner in which ‘drugs are absorbed, distributed, metabolized and excreted’], and organs that have an important role in susceptibility to and the moderation of toxic reactions, such as the liver and kidney, are immature in their function. As a result, the manner in which the neonate handles a toxic exposure is frequently quite different from the response of an older child or adult.’

21. BI claims that ‘nevirapine binds to reverse transcriptase’ and that ‘eukaryotic DNA polymerases (such as human DNA polymerases α , β , γ , or δ) are not inhibited by nevirapine’.
22. The implication of these claims is that nevirapine specifically inhibits the retrotranscription of HIV RNA, does not inhibit cellular DNA formation, and is harmless to human cells.
23. BI’s implicit claims about the specific antagonism of nevirapine for HIV are indefensible, given that (i) reverse transcriptase is not unique to retroviruses, and is a component of uninfected human cells; (ii) the extreme cellular toxicity of nevirapine has manifested in numerous ‘severe and life-threatening’ ill effects, ‘including fatal cases’.
24. In other words, whatever its notional, potential antiviral activity in vivo, nevirapine has known profound general human systemic toxicity, presenting in a broad range of dangerous ill effects, as set out in extensively detailed warnings in the nevirapine package insert approved by the South African Medicines Control Council (MCC) on 14 April 2000. These severe toxicity warnings are summarised and emphasized in special hazard notices set in boxed, bold typeface against conspicuous highlighted grey backgrounds.
25. BI has yet to show that nevirapine has any antiviral activity in vivo: ‘The relationship between in vitro susceptibility of HIV-1 to nevirapine and the inhibition of HIV-replication in humans has not been established’ and ‘At present there are no results from controlled clinical trials evaluating the effect of VIRAMUNE in combination with other antiretroviral agents

on the clinical progression of HIV-1 infection, such as the incidence of opportunistic infections or survival.’

26. The MCC granted a provisional licence to BI to supply nevirapine for administration to HIV-positive pregnant women in January 2001.
27. The basis of BI’s application to the MCC for a licence to supply nevirapine for this particular indication was a single study reported in *Lancet* on 4 September 1999, ‘Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial’.
28. BI, represented by Kevin Dransfield BS, participated directly in the conduct of HIVNET 012.
29. Following publication of the HIVNET 012 report, BI successfully relied upon it to win licences in numerous developing countries for the supply of nevirapine as a perinatal anti-HIV prophylactic.
30. BI is currently promoting nevirapine by way of ‘donations’ in these countries to establish its future market.
31. Nevirapine is not licensed for perinatal administration in the US, Europe or Canada, or in any other First World country.
32. Relying solely on the results of HIVNET 012, BI applied to the FDA for an extended licence to market nevirapine as a perinatal anti-HIV prophylactic.
33. When the FDA called for the production of the original 645 medical case files in HIVNET 012 for examination and auditing, in order to process BI’s licence application based on the study, the trial overseers were unable to produce them.
34. On 3 April 2002 the *Kampala Monitor* reported Professor Geoffrey Miiro of Mulago Hospital in Kampala, one of the Ugandan overseers of HIVNET 012, stating that he had only been able to locate 100 of the files that the FDA had called for.
35. The unavailability of the files and the consequent inability of the FDA to review the conduct of HIVNET 012, and the integrity of its reported data, stymied the processing of the

extended licence application, and on 22 March 2002 BI withdrew it accordingly.

36. The ‘potentially quite serious’ problems with HIVNET 012, as FDA spokesman Jason Brodsky described them in the press, went beyond the missing original case files and the consequent unverifiability of the researchers’ efficacy claims, in that John La Montagne, Deputy Director of the National Institute of Allergy and Infectious Diseases (NIAID), a branch of the National Institutes of Health (NIH) of the US Department of Health and Human Services, revealed further in a press statement that there were often ‘differences of professional opinion’ between the American and Ugandan researchers, concerning the incidence of serious toxic reactions among mothers and babies given a single dose of nevirapine.
37. The researchers’ claim in the report of the study that nevirapine apparently ‘seemed safe’ is rendered insecure by these frequent ‘differences of professional opinion’ about the incidence and gravity of toxic reactions, revealed by La Montagne, but not mentioned in the trial report.
38. The data reported by the HIVNET 012 researchers founding their conclusions about the safety of perinatal nevirapine administration is accordingly compromised and cannot be relied upon for drawing any conclusion at all, other than that the safety of perinatal nevirapine remains moot.
39. The missing medical case files renders the ‘differences of professional opinion’ in the critical matter of the safety of nevirapine for pregnant women and their babies impossible to resolve.
40. Unless and until all the original case files are produced for auditing, the FDA will not accept the trial overseers’ reported claims about either the safety or the efficacy of nevirapine in perinatal situations.
41. The original records appear no longer to exist, given that La Montagne claimed in press statements that ‘[There are] differences in the way hospitals in Uganda keep records and the requirements of the FDA’, which, ‘quite rightly has a

rigorous standard' and that the records will need to be 'reconstructed'. This contradicts Miiro's allegation that the missing files are 'stacked up in a container due to the ongoing rehabilitation at the hospital'. La Montagne also made the claim, contradicting both Miiro and himself, that the files are scattered over three different sites – Seattle, Baltimore and Uganda, i.e. by implication, still exist.

42. NIAID's interest in defending HIVNET 012 derives from the fact that NIAID researchers (Fowler, Miotti) participated in the conduct of the trial, and NIAID sponsored its cost. Other US federal health officials from the NIH (Mofenson) and the HIVNET Statistical Center (Fleming, Deseyve, Emel) also participated. To the extent that the American government was directly involved in the study and paid for it, considerable prestige is at stake, thus accounting for La Montagne's less than forthright statements concerning the fatal trouble with the study.
43. On the basis of HIVNET 012, and its endorsement by NIAID, the World Health Organisation (WHO) recommends the perinatal administration of nevirapine in the Third World.
44. The negative ramifications of the missing source data for the integrity of the study, on the basis of which the WHO supports perinatal nevirapine treatment, are obviously very far-reaching.
45. Although only clinically healthy pregnant women were accepted into the trial, approximately seven per cent of the drug-exposed babies reportedly died.
46. The strikingly high mortality rate among treated babies does not support the conclusion that nevirapine administered perinatally 'seemed safe' for them.
47. Since there was no placebo wing to the study, it was not possible to make a relative mortality comparison, and the tentative conclusion that nevirapine 'seemed safe' for babies has no proper foundation accordingly.
48. No controlled, blinded epidemiological study has ever been performed anywhere in the world to establish the mortality rate among children born to HIV-positive mothers versus HIV-

negative mothers, and consequently, fatal nevirapine toxicity is an equal contender with any other speculative cause for the seven per cent death rate noted among treated babies.

49. The conclusion that the drug 'seemed safe' is also irreconcilable with the fact that eighty per cent of clinically healthy mothers exposed to a single dose of nevirapine suffered 'clinical or laboratory abnormalities' (not specified in the report), twenty per cent developed viral or bacterial infections, fifteen per cent parasitic infections, thirteen per cent anaemia and about five per cent severe adverse events. Given the well-established acute toxicity of nevirapine, the aforementioned data support a conclusion contrary to the one reported, namely, 'No adverse event was definitely or probably related to the study drugs.' It is trite that patients exposed to chemotherapeutic agents risk greatly increased susceptibility to infections. The absence of placebo and untreated cohorts in the study for comparative purposes renders the reported conclusion invalid, or at minimum merely unsupported opinion.
50. On 19 April 2002 the *Mail&Guardian* reported a case of a pregnant South African black woman killed by a single dose of nevirapine. [*Erratum: she was killed by combination of ARV drugs; see article: 'Death of an activist'.*]
51. Nevirapine was officially identified as the likely cause of death in at least two of the several fatalities that occurred in 2000/2001 among women on the FTC 302 trial conducted, inter alia, at Kalafong Hospital, Pretoria.
52. La Montagne's press statement that nevirapine is 'a very, very safe drug' is inconsistent with its widely and officially recognised serious toxicity profile, and is insupportable.
53. Based upon La Montagne's press statements, the assertions of the WHO and other bodies that there is no cause to question the safety and efficacy of nevirapine for perinatal administration, notwithstanding BI's withdrawal of its extended licence application to the FDA, are equally vacant and indefensible.

54. The short- and mid-term safety of nevirapine for babies remains unascertained.
55. The HIVNET 012 researchers themselves recommended that the long-term effect of exposing a baby to nevirapine should be researched, and to date it remains unknown.
56. La Montagne's press statement that 'There is no question that the drug works' is inconsistent with the fact that the majority of the original HIVNET 012 case files are missing, *ipso facto* placing the trial overseers' efficacy claims for perinatal nevirapine administration in question in the view of the FDA.
57. The HIVNET 012 researchers failed to observe a single one of the essential prerequisites for a valid clinical drug trial, as reflected in the original protocol drawn for the conduct of the trial.
58. It was not blinded.
59. It was not placebo-controlled.
60. It contained no untreated cohort (neither on test drug, nor placebo, the importance of which has been stressed by the CDC).
61. It comprised a little over a third of the originally intended number of trial subjects, thus greatly reducing the statistical cogency of its results.
62. It was not properly randomised, inasmuch as two distinct testing protocols for determining HIV infection among pregnant women were reported. On one hand, subjects for the study were drawn from pregnant 'women attending antenatal clinics at Mulago Hospital in Kampala, Uganda ... screened for HIV-1 infection by EIA [ELISA] for HIV-1 antibody. If a woman tested positive, she received post-test counselling about her infection status and was informed about the opportunity to enrol in HIVNET 012.' In other words, women reactive to a single ELISA HIV antibody test were diagnosed HIV-infected, told so, and invited to enrol in the trial. However the next sentence of the report states: 'Women were eligible

for the study if: they ... were positive on EIA and western blot for HIV-1 antibody.'

63. AIDS experts in the First World universally agree that a single reactive ELISA HIV antibody test result is an inadequate basis upon which to make a diagnosis of HIV infection, and require confirmation by follow-up testing.
64. Subsequent negative or indeterminate Western blot test results exclude a significant number of reactive ELISAs.
65. '13 839 [women were] tested for HIV-1. 2144 [were noted as] with positive HIV-1 test. 1499 [were] excluded [i.e. about seventy per cent]. 645 mothers randomised.' In other words, about seventy per cent of women 'told of their infection status' on the basis of a 'positive HIV-1 test' were excluded, among whom were an unreported number with negative or indeterminate Western blot test results.
66. The necessary conclusion is that an unknown number of women who were 'told of their infection status', and were 'counselled' accordingly because they had a 'positive HIV-1 test', were not infected.
67. It is impossible to establish from the report how many women 'with positive HIV-1 test' and 'told of their infection status', who participated in the study, were enrolled without a Western blot test performed on them.
68. It is similarly impossible to tell how many would have been negative or indeterminate upon subsequent Western blot testing.
69. In any event, a positive Western blot for 'HIV antibodies' itself does not in fact establish or confirm HIV infection: The specificity of HIV antibody tests, be they ELISA or Western blot, has never been established by reference to the gold standard of HIV isolated from patient blood plasma by purification and electron photomicrograph verification; the positive predictive value of such tests is impossible to compute without knowledge of the prior probability of infection, based on the infection rate of the 'risk group' to which the patient belongs (determined by some other testing method); antibodies

are inherently polyclonal and frequently exhibit as much if not a higher affinity for antigens other than those that putatively generated their production; and all the proteins employed in antibody tests, assumed by AIDS experts to be uniquely constituent of HIV, are demonstrably cellular, not retroviral – the necessary corollary being that high levels of ‘HIV antibodies’ detected by ELISA and Western blot tests are actually auto-antibodies to endogenous human proteins, or antibodies to common mycobacterial and fungal organisms.

70. The possibility that uninfected women entered the trial corrupted it completely and vitiated its conclusions.
71. The HIVNET 012 researchers employed RNA-based qualitative and quantitative assays manufactured by Roche Diagnostics to diagnose and confirm HIV infection in babies, in contravention of the manufacturer’s express prohibitions against such uses in view of their unknown specificity, thereby rendering meaningless the transmission rate data reported in the study.
72. The only RNA-based HIV assay approved by the FDA for use in clinical settings in the US is Roche Diagnostics’s quantitative RNA assay, licensed for determining ‘viral load’ only – after HIV infection has been established by way of antibody testing.
73. In terms of its current AIDS surveillance definition, the CDC inexplicably permits the use of RNA assays for determining mother-to-child HIV transmission in babies (but not infection via contaminated blood transfusion or any other source).
74. The CDC has stated that it supports such use of the assay for ‘surveillance purposes’ only, and not for making a ‘clinical diagnosis’.
75. The CDC has been unable to explain how and why RNA-based assays, too non-specific even for anonymous blood screening, and consequently prohibited for diagnosing and confirming HIV infection in adults and children, could and would be accurate and reliable for neonates infected by their mothers at birth or by breast feeding (but not by other means); nor has it

been able to explain why an RNA-based assay should be good for determining mother-to-child HIV infection for surveillance purposes, but not clinical purposes, and why there should be any difference (since a baby is either infected or it isn't, and if the test is unreliable for one purpose, it can't be reliable for another).

76. Neither Roche Diagnostics nor the FDA permit the exception allowed by the CDC.
77. The HIVNET 012 researchers' other basis for confirming HIV infection, namely the simple fact of neonate death without regard to the actual cause, be it pneumonia, gastroenteritis, diarrhoea, dehydration, sepsis (as reported), or toxic drug reaction (acute, or leading to the development of these conditions) was manifestly incompetent.
78. The extent to which the trial results were further corrupted by illegitimately treating neonate death per se as confirmation of HIV infection, as suggested by an experimental qualitative RNA test, cannot be determined because the report does not provide the figures.
79. Although the HIVNET 012 researchers stipulated that absolute prerequisites for the efficacy of perinatal nevirapine administration were reduction of maternal viral load, alternatively attaining virustatic concentrations in neonates, nevirapine failed on both scores in the trial: it neither reduced maternal viral load, nor did the doses given attain in vivo inhibition concentrations (IC₅₀) in any child. (Apparently ignorant of the IC₅₀ of nevirapine in vivo as determined by Havlir et al. in 1995, the HIVNET 012 researchers arbitrarily picked a notional in vivo value for their clinical trial ten times the in vitro value originally determined by BI – but orders of magnitude below the in vivo value determined by Havlir et al.)
80. The HIVNET 012 researchers' positive claims for perinatal nevirapine efficacy are irreconcilable with the fact that neither prerequisite for perinatal efficacy of nevirapine was met in the trial.

81. The foundational assumption made by the HIVNET 012 researchers in proposing the experimental administration of nevirapine at the onset of labour was that ‘Most vertical transmission occurs during active labour because of maternal blood transfusions to neonates and direct exposure to virus during passage through the birth canal.’ However the two studies cited in the report in support of the hypothesis do not prove it and are only tentative.
82. The organising hypothesis of the HIVNET 012 experiment was therefore merely speculative. That the hypothesis is bad is borne out by the fact that throughout their pregnancies mothers and foetuses share the same fluids. Any virus with which the mother is infected would therefore have nine months to reach and infect the child, not just a few hours of labour via the speculative vectors proposed by the HIVNET 012 researchers. In the premises, administering nevirapine at the onset of labour to prevent HIV transmission must invariably be too late.
83. The HIVNET 012 researchers failed to take account of the fact that it takes an average of 4.6 hours for an oral dose of 200 mg of nevirapine to reach its maximum concentration in the blood. Since women generally deliver at between 0.9 and 10.5 hours after dosing, and nevirapine takes between 1-8 hours to reach maximum plasma concentration, an unascertained number must give birth before the target concentration can be reached. Accordingly, a single dose of nevirapine administered to women going into labour will, on average, always be too late to prevent transmission for about half of them.
84. The fundamental flaws in the design and execution of the HIVNET 012 study, evident from the report of the trial itself, even without regard to the contents of the missing case files, are inconsistent with La Montagne’s loose statements that: ‘There is absolutely no evidence that I know of that the effectiveness of nevirapine ... has been compromised ... There is no question that the drug works. ... We believe the studies were done to extremely high standards and that they were done properly and ethically. ... I don’t think that anyone is alleging that anything was improperly done.’ On a considered analysis,

the HIVNET 012 clinical drug trial was so radically flawed in its design, conduct and interpretation that no drug licensing authority acting reasonably can accord it any weight.

85. The implications for the South African public of the unverifiability of the reported data in HIVNET 012, and their worthlessness on their face in any event, are that in terms of a wide-scale court-mandated programme South African women and their babies are to be treated with a profoundly poisonous chemical compound having no proven clinical benefits.
86. The hearings of both the High Court application for a mandamus to enforce this programme, and the Constitutional Court appeal against it, proceeded from the premise that HIVNET 012 established the safety and efficacy of nevirapine.
87. The failure of the State's legal representatives to argue the root flaws of HIVNET 012, rendering its positive conclusions for perinatal nevirapine treatment completely invalid, resulted in the High and Constitutional Courts proceeding from a foundation of agreed facts that were fallacious, and both Courts were fundamentally misdirected on the facts accordingly.
88. The perinatal administration of nevirapine to pregnant HIV-positive women and their babies in South Africa will result in an unacceptable and pointless hazard to them.
89. No effective machinery exists in South Africa, akin to MedWatch established by the FDA in the US, for monitoring the predictable harm caused by the perinatal administration of nevirapine to mothers going into labour and then their babies after birth.
90. The victims of this programme will almost exclusively be poor black women and their children, whose special vulnerability to the well established profound toxicity of nevirapine is likely to be exacerbated by their poverty-weakened health.
91. Since the benefits, if any, and the full extent of the harmfulness of nevirapine to this especially vulnerable class of people have yet to be defined, a programme of nevirapine administration to

poor black women and their babies across the country amounts to an open-ended, dangerous experiment upon them.

92. In the gamble, nevirapine manufacturer BI stands to make a certain financial gain, whereas poor black South African women and their babies stand to lose their lives and their health by way of acute toxic insult or the consequent onset of life-threatening opportunistic infections, inter alia, that are the well-known concomitants of exposure to chemotherapeutic agents.
93. In the situation, the perinatal administration of nevirapine in Such Africa is a violation of the Hippocratic Oath, and of international medical conventions concerning medical experiments on humans.
94. It is unreasonable and indefensible that a toxic drug not approved anywhere in the First World for perinatal administration, should be supplied to poor black women and their babies in South Africa on the false premise that it has been shown to be both effective and safe.
95. None of the 53 countries named by BI in a list it supplied to the MCC on 22 April 2002, in which nevirapine is licensed for perinatal administration, are modern First World industrial countries falling within the North of the North/South development divide. In plain terms and in practical effect, nevirapine is not considered fit for perinatal administration to whites.
96. The pharmaceutical industry's persistent promotion of dangerous drugs in the South for indications prohibited in the North is a well-documented, unconscionable abuse of vulnerable markets.
97. If nevirapine is not accepted by the drug licensing authorities of any First World countries as safe and effective for perinatal use, there can be no reasonable justification for the MCC applying a lower standard when assessing its safety and efficacy.
98. Nevirapine is omitted from the CDC's latest revised recommendations for preventing perinatal HIV transmission,

issued on 17 May 2002. This implies that in the view of the CDC, HIVNET 012 does not establish the efficacy and safety of nevirapine for pregnant women and their babies in America.

99. Having regard to the foregoing, a failure by the MCC to intervene by withdrawing BI's provisional licence to supply nevirapine for perinatal administration in South Africa, alternatively, suspending it *pro tem*, will constitute an unreasonable breach of its statutory duties to the South African public to protect it from the sale of useless and harmful medicines, alternatively, medicines that have not been shown to be both effective and reasonably safe. I am advised that such dereliction would be unlawful and would consequently be subject to judicial review and compulsion.
100. I am further advised that any 'Informed Consent' to nevirapine treatment and its risks granted by any pregnant woman treated at a public hospital, who has not been fully informed of all the facts detailed herein, will be idle, and any harm suffered through nevirapine exposure will consequently be actionable, i.e. unless patients are so informed, the state will face massive exposure to civil liability for damages in a potentially limitless and uncontainable run of toxic tort actions, brought by women and children injured by perinatal nevirapine treatment, whether the injuries be fatal or slight, immediate or long-term.

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Appendix 2: A letter to the MCC on 22 June 2004 concerning its review of its provisional registration of nevirapine for perinatal use

THE REGISTRAR: MS PRECIOUS MATSOSO
MEDICINES CONTROL COUNCIL
2nd Floor, Hallmark Building
Cnr Andries and Vermeulen Streets
Pretoria

Dear Ms Matsoso

**MCC REVIEW OF SPECIAL REGISTRATION OF
NEVIRAPINE FOR PERINATAL ADMINISTRATION**

We would like to pose several questions to Council concerning the status of its pending review of its special registration of nevirapine as an anti-HIV perinatal prophylactic drug. Before we do, it might assist if we recapitulate the history of the review to date:

1. On the basis of findings reported from HIVNET 012, a clinical trial in which the efficacy of perinatally administered nevirapine to prevent mother to child transmission of HIV was investigated, Council provisionally approved the drug for this novel indication in March 2001 – taking the lead as the first developing country in the world to do so. (Nevirapine has never been licensed for perinatal use in any First World nation.)
2. On 16 March 2002, in view of what the US Food and Drug Administration described in a press statement as ‘potentially quite serious’ data integrity problems that it had discovered with HIVNET 012, Council notified National Minister of Health Dr Tshabalala-Msimang by letter that ‘We are to review nevirapine in the light of these developments and will inform you of the decision as soon as information is available.’
3. On 22 March 2002, Boehringer Ingelheim withdrew its application to the FDA for a licence to market nevirapine as a perinatal anti-HIV prophylactic in the US.
4. On 4 May 2002, Council made a public announcement confirming that its special registration of nevirapine as a perinatal anti-HIV prophylactic drug was under review.

5. In April 2003, the US National Institutes of Health, which had sponsored and participated in HIVNET 012, delivered a final report to Council, in which it identified several basic problems with the study – concluding nonetheless:

In summary, the re-monitoring of the study determined that nevirapine, 200mg orally given to the mother at delivery and 2mg/kg given to the neonate within 72 hours, is safe and effective. However the conduct of the study lacked the necessary documentation to support a request to the FDA to consider this study as a stand alone pivotal trial.

6. In short, notwithstanding the fatal deficiencies of HIVNET 012 as a pivotal licensing trial by US drug licensing standards, the NIH contended that the study proved the safety and efficacy of perinatally administered nevirapine for ‘a developing country’ (per final NIH report).

7. Council naturally disagreed with the NIH’s implication that a double standard should apply in its assessment of the drug’s efficacy and safety for South African babies, and on 25 July 2003 resolved to ‘reject the study HIVNET-012 as a pivotal study for the approval of the use of Nevirapine for the reduction of risk of intrapartum transmission of HIV-1 infection’, and to put nevirapine manufacturer Boehringer Ingelheim on terms

to submit in 90 days any new evidence (other than previously submitted evidence on HIVNET-012 and SAINT information) to convince the MCC of retention of this indication.

8. Council based its reasons for rejecting HIVNET 012 on findings recorded in the NIH’s final report on it, namely that patient records did not support the published results; there were problems with the manner in which the study was conducted; records did not account for how the drug was stored, handled and distributed; records indicating which treatments were allocated to trial participants were missing; and the obtaining of voluntary informed consent for the trial participants could not be confirmed in all cases.

9. In other words, Council found HIVNET 012 to have been irredeemably compromised by radical data integrity defects and by fundamental problems with the manner in which the trial was conducted, which vitiated any conclusions drawn from it.

10. It bears emphasizing that it was the preliminary findings of HIVNET 012 that gave rise to the Treatment Action Campaign's complaint against the state 'for not providing nevirapine to every HIV positive pregnant woman and babies born to HIV positive mothers' and that founded its successful case in the High and Constitutional Courts for a mandamus directing it to do so. The effect of this order was that the state was compelled to abandon its UNAIDS-sanctioned pilot studies of perinatal nevirapine (UNAIDS director Peter Piot had recommended in the *New York Times* on 11 July 1999 that it was 'unrealistic to introduce it on a large scale in developing countries without first using pilot programs') and was ordered to provide nevirapine to women in labour and their new-born babies 'on a large scale' without further preliminary testing for safety and efficacy. (HIVNET 012 itself had been an unconvincingly small study, with only about a third of the originally intended number (1 500) of mother-child pairs enrolled in it (645), just under half of whom were assigned to the nevirapine wing – an unconvincingly small cohort for a clinical drug trial intended to serve as the basis of a licensing application.)

11. In giving its reasons for rejecting HIVNET 012, however, Council took no account of a numerous even more fundamental flaws in the design, execution and interpretation of the study, discussed in *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine* by Papadopoulos-Eleopoulos et al., a 170 000-word monograph submitted to the Department of Health in November 2001, amplified by *A Critical Analysis of the Evidence Considered Proof that Nevirapine Prevents Mother-To-Child Transmission of HIV*, a PowerPoint slide presentation prepared by the same authors (both accessible at www.theperthgroup.com), and further canvassed in Professor Sam Mhlongo's 100-point submission, *Issues Concerning Perinatal Nevirapine Treatment* (copy annexed), a formal synopsis (as at August 2002) of the writer's polemic *The trouble with nevirapine* (posted at www.tig.org.za), delivered to Council on 6 August 2002, and acknowledged by Council's Director of Clinical Evaluation and Trials, Dr Rajen Misra, by telephone two days later. Nor was any account taken of the neonatal toxicity considerations canvassed in Dr Roberto Giraldo's paper, *Scientific Data Against*

the Use of Nevirapine in Pregnant Women, Infants, Children, and Anybody Else, submitted to the Department of Health via Ministerial advisor Dr Ray Mabope in October 2001 (posted at www.robertogiraldo.com).

12. On 5 September 2003, purporting ‘to clarify the intention of this resolution’ (to reject HIVNET 012 and require extrinsic evidence to ‘convince the MCC of retention of this indication’), Council recalled it, and substituted it with a second one, in which it reiterated its rejection of ‘HIVNET 012 as a pivotal study’ and required Boehringer Ingelheim ‘within six months of this resolution’ to present ‘data that you have in your possession, or which you are in a position to obtain ... demonstrating the efficacy of Nevirapine’, alone or in combination with other antiretroviral drugs, as a perinatal anti-HIV prophylactic.

13. The following day, on 6 September 2003, the HIVNET 012 research team published a second report on the study in *Lancet* – heralded by an extraordinary and unprecedented simultaneous press release by the US State Department, puffing the second report under the headline, *Findings could help prevent 800,000 annual infections*.

14. A week after putting Boehringer Ingelheim on terms to demonstrate the efficacy of perinatally administered nevirapine, Council issued a press statement on 12 September 2003, in which it stated that

Nevirapine has been shown to be effective in reduction of the risk of intrapartum transmission of HIV-1 infection from mother to child. Scientific evidence was provided to the MCC to support this.

15. However, Council’s categorical statement concerning the allegedly freshly demonstrated perinatal efficacy of the drug was contradicted by a tentative statement in the same press release concerning the origin of the ‘scientific evidence’ in question – identified as comprising ‘additional data from South African researchers ... that *may* support the continued use of Nevirapine for this indication’ (my emphasis).

16. Council further referred to ‘additional information regarding the original study [that] has also now been published’. (In fact, the

second HIVNET 012 report was only published in *Lancet* the following day, but presumably Council was given sight of the paper in proof.)

17. Council concluded in its statement:

Recognizing the importance of the new information, the MCC, on 5 September 2003, adopted a new resolution, which extends the time period for Boehringer Ingelheim (the supplier of nevirapine) to review existing evidence, and to submit additional data for expert assessment by the MCC.

18. According to a report in the Health Systems Trust bulletin *Healthlink* on 19 September 2003, the ‘additional data from South African researchers’ comprised findings in studies conducted at Chris Hani-Baragwanath and Coronation Hospitals.

19. The six-month period commencing on 5 September 2003 that Council afforded Boehringer Ingelheim to prove the efficacy of nevirapine as a perinatal anti-HIV prophylactic expired on 5 March 2004.

20. In ‘The pathologist who struck gold’, published in the Spring/Summer 2001 issue of *Hopkins Medical News*, lead author of the second HIVNET 012 report, Professor J Brooks Jackson, restated one of the trite, elementary requirements of a valid clinical drug trial:

No researcher can assess a drug’s effectiveness with scientific certainty without testing it against a placebo. That’s the only way we can know for sure if a short course of AZT or nevirapine is better than nothing.

QUESTION ONE: Are we correct in assuming that by ‘data ... demonstrating the efficacy of Nevirapine’ (to quote the language of its second resolution), Council envisaged that such ‘data’ would be clinical trial findings of sufficient cogency as to support the special registration in question – in other words (to quote the language of its first resolution), that the ‘data’ would amount to a ‘pivotal study for the approval of the use of Nevirapine for the reduction of risk of intrapartum transmission of HIV-1 infection’, that is, the kind of study that would meet the criteria and standards

for efficacy and safety for this special indication set by First World drug regulatory authorities such as the US FDA, the European Medicines Agency (EMA) and the Therapeutic Products Programme of Health Canada?

QUESTION TWO: Have any of these ‘additional data from South African researchers’, to which Council referred in its press statement of 12 September 2003, been published in a peer-reviewed journal, and if so when and where?

QUESTION THREE: Were the clinical trials conducted at Chris Hani-Baragwanath and Coronation Hospitals that gave rise to ‘additional data from South African researchers’ placebo-controlled?

QUESTION FOUR: Have the findings in these local studies been deemed sufficiently cogent to serve as pivotal support for the special registration of nevirapine as a perinatal anti-HIV prophylactic in any other country of either the First or Developing World?

QUESTION FIVE: Has Council determined whether these new ‘additional data from South African researchers’ do indeed ‘support the continued use of Nevirapine for this indication’ and that, to quote Professor Jackson, they do so ‘with scientific certainty’?

QUESTION SIX: Having regard to Council’s unequivocal rejection of the HIVNET 012 researchers’ preliminary findings reported in *Lancet* on 4 September 1999, does Council share the US Administration’s conclusion asserted in the headline of its press statement that the second report on the study, published on 6 September 2003 in the same journal, establishes that nevirapine administered perinatally prevents mother to child transmission of HIV?

QUESTION SEVEN: Indeed, having rejected HIVNET 012 on the grounds that it was radically flawed, rendering all data produced from it insecure, does Council accord any significance to the second HIVNET 012 report whatsoever, and if so, on what basis?

QUESTION EIGHT: Precisely what ‘additional data’ did Boehringer Ingelheim ‘submit ... for expert assessment by the

MCC' in the six-month period that Council allowed it on 5 September 2003 to support the 'retention' of its special licence to market nevirapine for administration to HIV-positive women in labour and their new-born babies?

QUESTION NINE: If in reviewing its special registration of nevirapine as a perinatal anti-HIV prophylactic, Council (a) abides by its resolution to reject HIVNET 012 *in toto*, and (b) considers that none of the 'additional data from South African researchers' constitutes a 'pivotal study for the approval of the use of Nevirapine for the reduction of risk of intrapartum transmission of HIV-1 infection', for the reason that the studies at the South African hospitals in question were not placebo-controlled (and/or for any other reason), and so do not establish the 'drug's effectiveness with scientific certainty' (to quote Professor Jackson), what is delaying Council's immediate deregistration of nevirapine for this special indication?

QUESTION TEN: In the situation, does Council accord itself with the estimation expressed by Supreme Court of Appeal Judge Edwin Cameron in an interview on the MNet programme Carte Blanche on 4 November 2001 that 'nevirapine is a very good drug ... to give to mothers who are about to have babies' and to the babies themselves shortly after their birth, and that the state's concern that the safety and efficacy of the drug for babies first be established in local pilot trials 'is a tragedy I think' – and if not, why, almost four months since the expiry of the time allowed Boehringer Ingelheim to 'submit additional data for expert assessment by the MCC', are South African babies, overwhelmingly African, still being exposed to this extremely poisonous chemical without any justification for it in the medical research literature?

We suggest that there is some urgency to the determination of Council's pending review of its registration of nevirapine for perinatal administration for the following reasons:

(a) Nevirapine is a dipyrindiazepinone compound characterised by Boehringer Ingelheim in its package insert as a chemotherapeutic agent. It is an exceptionally dangerous drug, having what the company describes in detailed warnings in the

insert as ‘severe, life-threatening’ toxicities, notably to the liver and epidermal tissue – summarised and emphasized in special hazard notices set in boxed, bold typeface against conspicuous highlighted grey backgrounds, as required and approved by Council on 14 April 2000 when the drug was approved for adult ingestion. On information supplied by Boehringer Ingelheim, the *Physicians’ Desk Reference* similarly emphasizes the toxicity of nevirapine in a lengthy paragraph, whose text is set in upper case throughout.

(b) In view of the caveat in the *Physicians’ Desk Reference* that ‘Severe or life-threatening hepatotoxicity, including fatal fulminant hepatitis ... has occurred in patients treated with Viramune’ (nevirapine), the company advises that ‘Clinical chemistry tests, which include liver function tests, should be performed prior to initiating Viramune’. (Due to the failure of Council to issue guidelines in this regard, such tests, even though mandated by the manufacturer to avoid toxic tort liability, are not routinely conducted before the administration of nevirapine to South African women in labour and to their babies.)

(c) Notwithstanding the prominent toxicity warnings in the inserts packaged with nevirapine in Europe and the US, continuing reports of serious adverse reactions to nevirapine in the form of ‘SEVERE AND LIFE-THREATENING CUTANEOUS AND HEPATIC REACTIONS’ (to quote the EMEA), some fatal, moved the EMEA and US FDA to issue special urgent alerts about this in April and November 2000 respectively.

(d) For the reason mentioned in a report in the *New York Times* on 5 January 2001 – ‘nevirapine can produce liver damage severe enough to require liver transplants, and has caused death in such use, the Centers for Disease Control and Prevention said in its weekly report’ – the US CDC proscribed nevirapine on 5 January 2001 for even short-term administration to medical professionals suffering needle-stick injuries on the advice of the US FDA, following numerous reports of acute toxic reactions fielded by its monitoring arm, MedWatch.

(e) All chemotherapeutic drugs have potent cytotoxic activities and are particularly hazardous for neonates, for the reasons noted by

Haddad et al. in their text, *Clinical Management of Poisoning and Drug Overdose* (WB Saunders, 1998):

The physiology of the newborn is unique [in the manner in which ‘drugs are absorbed, distributed, metabolized and excreted’], and organs that have an important role in susceptibility to and the moderation of toxic reactions, such as the liver and kidney, are immature in their function. As a result, the manner in which the neonate handles a toxic exposure is frequently quite different from the response of an older child or adult.

(f) Babies are consequently incomparably much more susceptible to the effects of toxic drugs than adults, so reducing an adult dose of a dangerous drug per body weight for a baby – as is the practice with neonatal nevirapine treatment – does not result in a correlative risk of drug-injury or fatality.

(g) It is universally recognised current medical policy to avoid or minimise foetal and neonatal exposure to harmful or potentially harmful chemicals, because it has become notorious that early exposure to such agents can have severe long-term health-damaging consequences, often only presenting clinically in later life.

(h) Nevirapine was pointedly omitted from the US CDC’s latest revised guidelines for interventions to prevent mother to child transmission of HIV, published on 17 March 2002, which is to say American AIDS experts do not consider the drug safe and effective for administration to American women in labour and their newborn babies.

(i) A recent query to the US FDA’s Division of Drug Information in March 2004 by Dr Valendar Turner of the Department of Health, Western Australia, concerning whether nevirapine is approved for the treatment of mothers and their newborn babies to prevent mother to child transmission of HIV in the US, drew a categorically negative reply:

Viramune is not FDA approved for the prevention of HIV in mother-to-child transmission, by itself or in combination with other drugs. If used in this fashion, it would be an off-label use. Viramune is FDA approved for HIV infected, pediatric

patients 2 years and above. It is not approved for use in the newborn at their time of birth to prevent whatever HIV is transmitted from the mother establishing itself as infection in the newborn.

(j) The first report of HIVNET 012 in *Lancet* recorded that

The rate of serious adverse events in the two groups [of babies] was similar up to the 18-month visit (19.8% in the zidovudine group, 20.5% in the nevirapine group), with the median age at last visit being 183 days ... The most frequent cause of serious adverse events within 56 days of birth were sepsis, pneumonia, fever, congenital anomaly, asphyxia, and dyspnoea. [Eighteen babies suffered maculopapular rash, and twenty-two anaemia.] The frequency and severity of laboratory-detected toxic effects, including neutropenia, thrombocytopenia, and abnormalities in creatinine or bilirubin, were similar in the two groups. ... 38 babies (6.8%) died (22 (7.9%) in the zidovudine group, 16 (5.7%) in the nevirapine group). The most frequent causes of death were pneumonia, followed by gastroenteritis, diarrhoea, dehydration and sepsis.

(k) Although only clinically healthy mothers were accepted into HIVNET 012, almost six per cent of their babies treated with nevirapine died.

(l) Even the strikingly high one-in-five incidence of serious adverse events among babies following nevirapine administration appears to have been under-reported: a press statement by the NIH on 22 March 2002 revealed that there had been 'professional differences of opinion' between the American researchers and the Ugandan hospital staff concerning what constituted a 'serious adverse event'.

(m) The HIVNET 012 researchers cautioned in their first report that 'long term follow up of the babies remains a high priority to find out about possible long-term toxic effects'. In other words, without having first conducted conventional animal studies to determine the safety of nevirapine administration to neonates, the researchers were unperturbed by the ethical implications of conducting an open-ended medical experiment on African children

to ‘find out’ whether they might be seriously and permanently injured by nevirapine’s ‘possible long-term toxic effects’.

(n) It is apparent from their second report that whether the children treated with nevirapine suffered ‘possible long-term toxic effects’, perhaps sub-clinical in some cases, was not a matter given any close attention.

(o) The likelihood that a dose of nevirapine will have significant toxicity for human neonates is predicted by the *Physicians’ Desk Reference*’s note that prenatal exposure in rodent studies resulted in ‘significant decrease in fetal body weight’.

(p) One of the serious possible ‘long-term toxic effects’ of dosing neonates with nevirapine that the HIVNET 012 researchers did not entertain was its effect on neonatal brain development, particularly having regard to the note in the *Physicians’ Desk Reference* that ‘Animal studies have shown that nevirapine is widely distributed to nearly all tissues and readily crosses the blood-brain barrier.’

(q) The neurotoxicity of nevirapine was noted in the *British Medical Journal* on 13 April 2002: Wise et al. reported ‘Neuropsychiatric Complications Of Nevirapine Treatment’ in three cases in which adults attempted suicide following the development of ‘delirium, an organic affective state, and an organic psychosis’ evidenced by

low mood ... cognitive impairment and clouding of
consciousness ... impaired consciousness ... visual
hallucinations ... persecutory delusions and depressive thoughts.

The psychologists found that the ‘nevirapine treatment was clearly related to the evidence of symptoms’.

(r) The particular vulnerability of neonates to neurotoxic chemicals is illustrated by the hexachlorophene debacle in the middle decades of the 20th century, in which an antiseptic in the dioxin class that was considered safe for inclusion in soap and talc for decades, with which babies used to be routinely washed and powdered after birth, was banned in the US in 1976 for inclusion in such products when it was finally identified as the cause of epileptic seizures and death among new-born babies – thirty-four at a Parisian Hospital in 1972. Subsequent infant autopsies and animal experiments

confirmed the chemical's activity as a nerve poison. (A six-year investigation published in 1978 found that nurses who routinely washed their hands with hexachlorophene solutions had borne an extraordinarily high number of deformed children.)

(s) The risk that South African babies, born to mostly poor Black mothers, might suffer 'possible long-term toxic effects' from even a single dose of a drug as extremely poisonous as nevirapine administered shortly after birth cannot be underestimated – even if the percentage harmed might be low. Thalidomide, the most notorious pharmaceutical drug catastrophe in the modern era provides an object-lesson in this regard, albeit that the toxic drug exposure in question occurred earlier in the child's development. Goth recounts in *Medical Pharmacology* (Mosby, 1984, 9th ed.):

The piperidinedione hypnotic thalidomide was responsible for thousands of children with disastrous defects such as absence of limbs. ... Pregnant women ingesting a single hypnotic dose of the drug between the twenty-fourth and thirty-sixth day of their pregnancy have delivered severely deformed babies.

Having regard to how many thalidomide doses were ingested (taken alone or combined with aspirin and other drugs it was briefly a best-seller) it is noteworthy that the incidence of physical deformity was relatively rare: only about twenty thousand babies born deformed in the West. (No tally exists of babies killed in the womb – or of children crippled in developing countries.) As President Mbeki correctly pointed out in his letter to Judge Cameron on 15 March 2000: 'Undoubtedly, such "consensus" and "available evidence" [*citing Cameron's language*] also existed on the use of thalidomide'. Between 1958 and 1962, relying on the manufacturer's assurance that thalidomide

can be given with complete safety to pregnant women and nursing mothers without adverse effect on mother or child. ... a harmless, safe and effective sedative with no side effects. ... Harmless even over a long period of use ... completely harmless even for infants ... Outstandingly safe

doctors in turn effusively extolled the drug to pregnant women as both safe and effective. It is noteworthy that it was public and political pressure, and not medical reaction to the sudden spate of

physical deformities, that led Chemie Grünenthal and British Distillers (Biochemicals) to withdraw the drug.

(t) Not only newborn babies are at dire risk from exposure to nevirapine; according to a report in the *Mail & Guardian* in April 2002, a single dose administered to a woman in labour proved fatal. [*Erratum: see note to point 50 of Appendix 1.*]

(u) Since the *Physicians' Desk Reference* pertinently warns that 'the safety profile of Viramune in neonates has not been established', whether South African children suffer liver and other organ damage, and or brain damage and/or impairment – perhaps initially sub-clinical and only apparent in later years – on account of their exposure to nevirapine as babies will be only be evident in time, that is when Boehringer Ingelheim's experiment upon them is complete. Another drug calamity serves as a precedent for the baleful potential in this regard:

(v) Hundreds of thousands of women were medically advised to take the synthetic hormone diethylstilbestrol (DES) in the nineteen-fifties and sixties, advertised by its manufacturer

for routine prophylaxis in ALL pregnancies ... 96 per cent live delivery with desPLEX in one series of 1200 patients – bigger and stronger babies, too. No gastric or other side effects with desPLEX – in either high or low dosage.

Thousands of women exposed to diethylstilbestrol in utero developed ordinarily very rare clear-cell adenocarcinoma of their vaginas and cervixes in adulthood, and suffered structural changes in their reproductive organs (virilization), causing infertility, ectopic pregnancies, miscarriages, and preterm labour and deliveries. The damage caused by the drug only became evident decades after administration.

(w) It is indeed so that expert medical opinion in South Africa strongly supports the continued use of nevirapine in maternity wards. In a striking departure from the basic principles of evidence-based medicine, local experts unanimously condemned Council's decision to reject the corrupt HIVNET 012 data. For instance, Professor 'Jerry' Coovadia, Professor of HIV/AIDS Research at the Nelson R Mandela School of Medicine, University of KwaZulu-Natal called it 'unscientific and downright perverse. ...

I think this is just such a dreadful mistake.’ Eighteen members of the executive committee of the Health Sciences faculty at the University of Cape Town issued a public protest:

Deregistering nevirapine on unscientific grounds will be a devastating blow to our evolving Aids prevention programme and will be morally and ethically indefensible. If the council has any evidence to suggest that nevirapine is indeed toxic or not effective, then they should make such information available immediately. If not, they should refrain from creating the belief in the minds of the public that this proven and effective treatment is useless or even harmful.

Dr Keith Bolton, chairman of the South African Paediatric Association opined equally frantically:

I am convinced that millions of lives would be lost if this bungle is allowed to happen. ... The executive committee of Sapa believes the efficacy and safety of Nevirapine usage, as part of a strategy for the prevention of transmission of HIV from mother to child, has been adequately established beyond reasonable doubt. We believe that failure to continue to administer Nevirapine at this time would constitute a dereliction of the ethical duties of individual health care professionals as well as an unconstitutional abdication of responsibilities of our health authorities. ... We urge our members in the field to follow their conscience by utilising the accepted practice of providing Nevirapine as part of the PMTCT programme. In doing so they will dramatically and significantly lower the risk of transmission of HIV from mother to child and thus prevent most cases of childhood Aids.

Yet another drug disaster, undoubtedly the worst in the history of medicine, is instructive here:

(x) As late as 1939, the 24th edition of *Hale-White's Materia Medica: Pharmacy, Pharmacology and Therapeutics* was still expressing the expert medical consensus that mercury is ‘one of the most valuable medicines we have. ... Children take mercury very well.’ Any doctor today prescribing mercury – ranked by the University of Tennessee’s renowned Toxicology Center near plutonium as one of the most poisonous substances known to man

– in even the smallest amount to anyone for whatever reason, would be struck from the medical roll for dangerous professional incompetence. As a guide to deciding good drugs from bad ones – both useless and extremely dangerous – the prevailing expert medical consensus has consistently failed us.

(y) It will be recalled that the HIVNET 012 researchers ascribed all the deaths of drug-treated babies in their study to HIV infection. No doubt similar conclusions are being drawn by South African doctors administering nevirapine under the country's judicially ordered perinatal treatment programme when nevirapine-exposed babies fail to thrive, fall ill or die. Certainly this was the experience reported by people gravely harmed by nevirapine combined with other AIDS drugs in the local FTC 302 trial, aborted by order of Council in April 2000 after several fatalities; approached by injured trial-subjects, doctors conducting the study discounted the extreme toxicity symptoms they were suffering to the onset of AIDS.

(z) In 1554, in his textbook *Universa Medica*, French physician Jean Francois Fernel had already observed that nearly all the symptoms of tertiary syphilis (distal gangrene, paralysis and dementia before death) were really due to mercury poisoning. Yet four centuries later, the 13th edition of *Black's Medical Dictionary* published in 1936 was still recommending: 'In syphilis, mercurial preparations are very extensively used, and must be taken by the subjects of this disease over many months in order to render a cure likely.' The tendency of medical practitioners to ascribe the toxic ill effects of their treatments to microbes, especially those to which their imaginations are in thrall in their particular era, is evidently an enduring one.

Might we expect your replies within the next fourteen days? Please confirm by return.

Yours faithfully

ADV ANTHONY BRINK
CONVENOR AND NATIONAL CHAIRMAN:
TREATMENT INFORMATION GROUP

Postscript: This enquiry takes no account of manifestly spurious claims by provincial health officials published on the front-page of the *Star* on the 8th instant under the headline, ‘Nevirapine has in three years saved nearly 58,000 newborn babies in Gauteng from contracting HIV and Aids’.

Annexure ‘A’: Unanswered 100-point submission to the MCC on 6 August 2002 regarding perinatal nevirapine treatment.

Appendix 3: the MCC's eventual non-response

As mentioned in Part Nine, it emerged in December 2004 that the serious problems with HIVNET 012 were even worse than they appeared to be from the limited information available to me when the 100-point submission and letter were sent to the MCC in mid-2002 and mid-2004 respectively: hard evidence had come to light of the actual toxicity of nevirapine for newborn babies – as opposed to the neonatal toxicity that I'd predicted.

MCC Chairperson Professor Peter Eagles informed me on 22 November 2004 that an 'independent expert' had been engaged to consider my letter.

On 28 October 2005, well over a year after it (and several more concerning the foetal toxicity of AZT), Eagles wrote:

your documentation has not shown that the potential risks of adverse effects of the antiretroviral agents in question are greater, more serious, or on a larger scale than the risks of complications from HIV-infection and its adverse effect on the lives of babies and children. Information which has become available subsequent to the Medicines Control Council (MCC) resolution of 02 July 2004 has also not changed the overall assessment of the risk of HIV-1 infection compared to the adverse effects of antiretroviral agents in PMTCT. (For example, we refer you to the frequently updated guidelines on the 'Aidsinfo' website: www.aidsinfo.nih.gov.)

Nowhere in his cursory letter did Eagles deal with any of the issues raised in my enquiry. Nowhere did he even attempt to explain the continued registration of nevirapine for perinatal use in South Africa in the absence of any clinical trial data acceptable to the MCC showing it to be effective and safe. And nowhere did he address the evidence that nevirapine is dangerously toxic for babies appearing in:

- the minute of the special meeting of DAIDS officials in early January 2002 to discuss the unreported deaths and other serious adverse events discovered during HIVNET 012;
- Boehringer Ingelheim's damning report on the 27th of that month, containing such 'Sensitive information' about

unreported and late reported ‘fatal and life-threatening’ adverse events experienced by babies on the drug trial that the company ‘Asked for it to be destroyed when audit [by the FDA] is upon us’ (as noted by DAIDS head of Regulatory Affairs Mary Anne Luzar);

- the independent clinical trial auditor Westat’s findings regarding ‘deaths not reported to the FDA’ and unreported serious adverse events during the study (‘thousands’, in the language of principal investigator Laura Guay); and,
- Paediatric drug safety expert Elizabeth Smith and her colleagues’s gravely negative ‘Safety Review’ report, the one DAIDS director Edmund Tramont corruptly suppressed, but which the world got to hear about in December 2004 when Associated Press exposed his attempted fraud in coolly rewriting the report himself in positive terms and then furnishing it to our MCC as part of his Division’s so-called ‘Remonitoring Report’ on HIVNET 012 in a bid to deceive it about the known dangers of giving nevirapine to newborn babies in South Africa.

According to a Department of Health press release on 12 March 2007,

3 382 out of 3 663 primary health care facilities (clinics) [are] offering Prevention of Mother to Child Transmission of HIV. This represents 83% of public health clinics ... it is expected that all clinics rendering antenatal care services should be providing PMTCT services by December 2007. At least 580 880 pregnant women accessed the PMTCT services during the calendar year 2006. Of these, 74 052 antenatal clients received Nevirapine prophylaxis.

Nearly all these 74 052 ‘clients’ in 2006 will have been African women – with many thousands more in the preceding years since the Constitutional Court’s order in mid-2002 that the government make nevirapine available to them in public hospitals. Returning to their peri-urban shacks many would be wondering why their babies, like those in Uganda treated with nevirapine or AZT during the HIVNET 012 trial, are so sickly and sometimes die.

Notes, sources and acknowledgments

Parts One to Four were substantially complete by April 2002, and, apart from updates with some citations from subsequently published medical literature and official toxicity alerts, are largely a record and analysis of information publicly available at the time – press reports, press statements and the like. Subsequent chapters were written as events unfolded.

My thanks: to David Crowe in Calgary for procuring a wad of internal Canadian government memoranda and for telefaxing them to me to equip me to write Part Two; to Vivienne Vermaak in Johannesburg for information from her investigation notes, which I've used in Part Three, and to Professor 'Sas' Strauss and Johan Viljoen for vetting the facts within their knowledge in this chapter; to John Crossley, formerly of e.tv, for providing me with his video recording of Judge Albie Sachs's performance at the National Arts Festival in Grahamstown in July 2003, which I transcribed for Part Five; to Dr Jonathan Fishbein, formerly Director of the Office for Policy in Clinical Research Operations in the Division of AIDS, NIAID, for sharing information about the HIVNET 012 scandal with me, written up in Part Eight; to Dr Christian Fiala in Vienna for briefing me to write Part Nine; to Dr David Rasnick in California for alerting me to some key research reports about nevirapine as they reached print; to bio-physicist Eleni Papadopulos-Eleopulos at Royal Perth Hospital and consultant emergency physician Dr Val Turner of the Western Australian Department of Health for checking the manuscript for scientific accuracy; to Robert Payne in Cape Town for formatting it for publication; and to Celia Farber in New York for her kind foreword.

On the scientific aspects, Part Four draws heavily, but not exclusively, from *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence*, a monograph by Papadopulos-Eleopulos et al. submitted to the South African government and to the Medicines Control Council in November 2001 – amplified by their PowerPoint slide show, *A Critical Analysis Of The Evidence Considered Proof That Nevirapine Prevents Mother-To-Child Transmission Of HIV*, presented by the late Professor Sam Mhlongo at a meeting of the

South African Association of Professionals in Health Care on 7 February 2002. My gratitude to Eleni Papadopulos-Eleopulos for the honour of a co-authorship credit for the monograph and slide presentation. Both are online at www.theperthgroup.com and www.tig.org.za.

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