

IN THE HIGH COURT OF SOUTH AFRICA

(CAPE OF GOOD HOPE PROVINCIAL DIVISION)

In the matter between:

TREATMENT ACTION CAMPAIGN	First Applicant
SOUTH AFRICAN MEDICAL ASSOCIATION	Second Applicant
and	
MATTHIAS RATH	First Respondent
DR RATH HEALTH FOUNDATION AFRICA	Second Respondent
SAM MHLONGO	Third Respondent
DAVID RASNICK	Fourth Respondent
ALEXANDRA NIEDWIECKI	Fifth Respondent
ANTHONY BRINK	Sixth Respondent
TREATMENT INFORMATION GROUP	Seventh Respondent
GOVERNMENT OF THE RSA	Eighth Respondent
DIRECTOR-GENERAL OF HEALTH	Ninth Respondent
CHAIRPERSON, MEDICINES CONTROL COUNCIL	Tenth Respondent

REGISTRAR OF MEDICINES

Eleventh Respondent

MEC FOR HEALTH WESTERN CAPE

Twelfth Respondent

AFFIDAVIT

I, the undersigned

NIGEL CAMPBELL ROLLINS

hereby make oath and say:

1. I am a Professor of Paediatrics and Child Health, and Head of the Centre for Maternal Child Health Research, at the Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban.
2. The facts deposed to in this affidavit are true and correct and, except where the context indicates otherwise, within my personal knowledge.
3. Since 2004 I have been the chairperson of the World Health Organization Technical Advisory Group on Nutrition and HIV/AIDS. This is an honorary position for which I receive no remuneration.

- 3.1. I participated in the technical meeting held in Geneva, May 2003 that reviewed the nutrient requirements of persons living with HIV. I was a co-author to the report 'Nutrient requirements for people living with HIV/AIDS. Summary Report of a Technical Consultation. Geneva, May 13-15, 2003'. This work is referenced by Dr Rath (**MWR 66**).
- 3.2. I served as a technical adviser to the WHO/UNICEF review team which was established to look at the findings of the Randomized Trial of Multivitamin Supplement and HIV Disease Progression and Mortality published by Fawzi et al. in the NEJM 2004;351:23-32. This study is referenced by Dr Rath on several occasions.
- 3.3. As chairperson of the WHO technical advisory group on Nutrition and HIV, I co-chaired the technical consultation held in Durban 2005 which reviewed all the available evidence at that time on the relationship between nutrition and HIV including the issue of micronutrients and HIV disease prevention, mitigation and cure. I was a co-author of the '*Participants' statement*'.
- 3.4. I served as a technical adviser in the preparation of the secretariat report submitted to the Executive board and the

World Health Assembly, May 2006. The recommendations of the WHA in response to this report are referenced by Dr Rath.

(MWR 64)

4. I also serve as a technical adviser to the WHO on the prevention of mother to child transmission of HIV and also the management of children with severe malnutrition.

5. My qualifications and experience in this area are set out in my curriculum vitae (**NCR1**). The focus of my research and study, over an extended period, has been the impact of nutrition, including vitamins, on disease in infants and children. The research includes the following:
 - 5.1. I completed my doctorate in 1995 following field work in the Morogoro region of central Tanzania. The study was community-based and involved living and working in three remote villages in the Uluguru mountains near Dodoma. This work demonstrated an interaction between vitamin A deficiency (clinical or sub-clinical) and iodine deficiency. The work highlighted the need for concurrent supplementation of both Vitamin A and iodine, otherwise an exacerbation of the other deficiency was likely. Following this I investigated vitamin A absorption in HIV-infected and uninfected children presenting

with either acute or persistent diarrhoea. This study demonstrated that vitamin A was well absorbed in most cases but had no effect on the recovery period of diarrhoea. This highlighted the need for health workers to use any opportunity e.g. during admissions to provide vitamin A supplements to children as a measure to reduce the future incidence of persistent diarrhoea.

5.2. Thereafter I conducted three studies namely:

5.2.1. a jointly funded WHO-Bayer therapeutic trial assessing the efficacy of ciprofloxacin in the management of shigellosis in children, the findings of which changed WHO recommendations on the Prevention and Management of Shigellosis. Although the South Africa site was supported by WHO and Bayer, I did not receive any personal remuneration for this work. The protocol-development was researcher-driven (as opposed to pharmaceutical industry developing a protocol and then identifying willing researchers to perform the research i.e. contract research). I have not undertaken any contract research.

- 5.2.2. the efficacy of nutritional interventions in the management of persistent diarrhoea in HIV-infected children. Funding for this research was obtained through a competitive grant process from the Elizabeth Glazer Pediatric AIDS Foundation. Two nutritional products used for children in the study were received free-of-charge from the manufacturers. The respective nutritional products were issued in tins that were labelled without any reference to the manufacturers. I was responsible for designing, implementing and analysing the results of the project. I did not receive any personal remuneration for the work;
- 5.2.3. gut permeability changes in children born to HIV-infected women with respect to maternal vitamin A supplementation and different infant feeding practices. Funds for the project were obtained through a competitive grant process via the Institute of Child Health, London. I did not receive any personal remuneration for the work.
- 5.3. I was responsible for developing and writing the protocol for a cohort study investigating the relationship between prophylactic

micronutrients and enteric infections in both HIV-infected and uninfected children. Funds were awarded by the National Institutes of Health to implement the study at the Africa Centre for Health and Population Studies in 2003.

- 5.4. I was project leader (1998-2002) of the Vertical Transmission Study, an interventional cohort study of 2,500 HIV-infected and uninfected mothers and children to investigate the impact of exclusive breastfeeding on the postnatal transmission of HIV from mothers to children. In that time it was my responsibility as a co-applicant to develop and write the proposal and budget to Wellcome Trust in conjunction with the PI and other senior scientific members of the Child Health Group, recruit all staff and oversee development of each component of the field operation. To date there have been 14 publications in peer-reviewed journals and the analysis of the main study outcomes will start at the end of this year.

The Wellcome Trust (UK) is one of the largest non-industry funders of medical research and is fully independent of the pharmaceutical industry.

- 5.5. I was part of the writing group for an international collaboration assessing risk factors for infant mortality in relation to maternal health and feeding practices. This individual patient meta-analysis demonstrated the critical relationship between maternal vital status and the survival of children irrespective of the child's HIV status. (*Lancet* 2004)
- 5.6. In early 2004, I secured funds from the Centre for Disease Control (South Africa) and the KZN Department of Health to evaluate the impact of the PMTCT programme on vertical transmission rates and the overall target of reducing infant and child mortality. The study methods were investigated in a pilot study in 1998 (published in *Lancet* 2002) and the data recently published in one of the leading HIV/AIDS journals '*AIDS*'. The project has been extended at the request of the Department of Health and with additional funds from the Department For International Development (UK) to run until 2009.
- 5.7. I have served as a consultant clinical paediatrician based at the King Edward VIII Hospital, Durban since July 1994 having specific responsibility for the ward caring for children with diarrhoeal disease and severe malnutrition.

- 5.8. I have recently written the new WHO 'Guidelines for integrating nutrition into the care of HIV-infected children.' These provide comprehensive guidance to practitioners on how to manage the numerous nutritional complications that children with HIV infection incur, as well as approaches to maintain optimal nutrition in the early years of infection.
6. I was chair of the 6th International Congress on diarrhoea and malnutrition convened by the Commonwealth Association on Paediatric Gastroenterology and Nutrition. As part of the planning of this meeting, I took a principled decision that no funds would be accepted from the infant nutrition industry. This caused much division within the Commonwealth Association as sponsorship from the infant nutrition industry has, in past years, been essential for financing this meeting in different parts of the world.
7. I was co-chair of the WHO Consultation on 'Nutrition and AIDS in Africa: Evidence, lessons, and recommendations for action' (Durban, April 2005). This meeting is referred to by Dr Rath.
8. In recognition of my work, research and experience I have, in the past 2 years alone, given invited talks/plenaries at international meetings and conferences in the UK, the Netherlands, Malawi, Ireland, Austria,

Bangladesh, Kenya, Uganda, Tanzania, Canada and several scientific meetings in South Africa. I was invited to present at the UNICEF Innocenti Research Centre in Florence to a select group of international experts in the field of micronutrients on the subject of micronutrients and HIV.

9. I was commissioned by the South African National Department of Health (Nutrition directorate) to give technical updates to nutritionists and doctors in each of the nine provinces on the subject of Nutrition and HIV during the last quarter of 2006.

10. I have worked extensively on human nutrition and especially the interface between infant nutrition, micronutrients and infectious diseases and severe malnutrition. My research demonstrates that I am committed to the production and interrogation of empiric evidence to inform public policy and individual patient management. My work has largely focussed on the benefits of vitamins and other micronutrients and other 'natural' nutritional interventions particularly breastfeeding rather than pharmaceutical interventions such as drugs or alternative treatments. I respectfully submit that I am qualified as a clinician, an experienced researcher and as a technical adviser to the UN agencies and national and provincial governments to provide expert opinion on the issues and questions outlined below.

11. I have been asked to comment on three main issues: The nature of scientific knowledge with regard to health and specifically micronutrients and HIV disease progression, the evidence provided by Dr Rath and finally the competency and credibility of Dr Rath and the witnesses on whom he relies as experienced researchers and internationally renowned experts in micronutrient research.

The nature of scientific knowledge with regard to health and specifically micronutrients and HIV disease progression

12. I have been asked first to explain the nature of scientific enquiry with regard to health, and the basis on which scientific claims can be made for the efficacy of micronutrients in HIV disease progression.
13. Micronutrient is a general term used to describe a nutrient that is required by the body but in small amounts. This includes vitamins, minerals e.g. calcium and trace elements such as zinc or copper. The other main group of nutrients are called macronutrients namely proteins, carbohydrates and fats.
14. Vitamin interventions may either be a single vitamin such as vitamin A or vitamin C, or a combination of several vitamins at recommended daily intakes, or in multiples of the recommended daily intake.

Multivitamin preparations may be offered in just about any combination of vitamin at any multiple of recommended daily intake. They may also be combined with minerals or trace elements again in different combinations at different doses. These preparations are then called multiple micronutrients.

15. Any single multivitamin preparation can therefore be significantly different in composition and dose from another multivitamin preparation. A multiple micronutrient preparation can also vary immensely in composition and dosages.
16. While vitamins, minerals and trace elements are 'natural', they are also essentially chemicals that have direct effects on cells and functions in the body. Their effect can be significantly different depending on the dose in which they are given, the combination in which they are delivered and the other foods with which they are given. For example zinc given in high doses precipitates copper deficiency. Iron absorption is improved when given with vitamin C while zinc absorption is impaired when consumed with cereal crops that are high in naturally occurring phytates.
17. Furthermore, certain infectious disease can precipitate specific nutritional deficiencies e.g. worm infestations will result in iron

deficiency. Some infectious diseases are made much worse by nutrient interventions e.g. iron given to children with malaria or diarrhoeal disease will lead to deterioration.

18. Measuring micronutrients in the body can be complex to perform and especially to interpret. Simple blood levels may not optimally measure how much of a particular micronutrient is in the body, especially when the individual has a concurrent infection. For example, vitamin A is predominantly stored in the liver and during an infection tends to get 'locked away' in the liver. Blood levels, indicating only the amount of vitamin A circulating around the body in blood itself, will fall even though the total amount of vitamin A in the body may be normal.
19. Many vitamin levels in the blood will fall during periods of fever or infections. Restoring vitamin, mineral or trace element levels in the body through supplements may not however, correct the underlying cause of the low level.
20. The outcome of any single or multiple micronutrient intervention will therefore depend on the background nutritional status of the individual patient, the local diet, the exact combination and dose of micronutrients included. A micronutrient intervention in one setting may have a different outcome in another depending on these factors. These are

very well established principles of human nutrition that have been discovered and described in textbooks over several decades and are not HIV specific.

21. Vitamins and other trace elements are essential for life and have multiple functions in the body, including a central role in maintaining the immune system. However they are not the only determinant of immune competency. While vitamins and other micronutrients such as zinc or iron are essential for normal immune function, high doses of vitamins or other micronutrients are also capable of suppressing the immune system and causing abnormal cellular function. For example, high doses of vitamin A given to pregnant women can cause fetal abnormalities due to its regulatory function in normal cell division. High dose β -carotene, a precursor of vitamin A, when given to adults in a large trial in the US with the aim of reducing coronary heart disease, resulted in increased rates of cancer.
22. For the reasons stated above, findings related to micronutrient interventions need to be replicated to verify that any benefit or disadvantage is true and are able to be extrapolated as a general recommendation to all individuals with a certain condition.

23. There are many examples in history of wrong conclusions having been reached about medical matters as a result of scientifically inadequate study. Science and the determination of truth, or as best we can approximate truth, is a dynamic process. Evidence is produced, examined and then re-examined in the light of new evidence to understand the implications for human health. Evidence produced and reported 10 or 20 years ago may or may not be regarded as accurate today because of more recent evidence produced using better technologies and a broader base of understanding. For example, the energy requirements of adults and children that were regarded as 'normal' in textbooks and publications produced by the Food and Agricultural Organization of the UN (FAO) and WHO in the 1950's and 1990's were revised on the basis of evidence made available through more advanced methods such as stable isotope techniques. The energy requirements were revised to lesser energy values. Clinical recommendations based on old reference ranges included in old textbooks and reference documents need to be updated.
24. Any claim that a substance, including naturally-occurring nutrients, has medical efficacy should be subjected to at least the following scrutiny before it can be considered reliable. The full process should be applied and the evidence examined before any intervention is recommended

and extended as a public health intervention. This process is summarised in a paper authored by Dr I de Zoysa and published in the Bulletin of the World Health Organization. I attach a copy of the publication 'Research steps in the development and evaluation of public health interventions.' **(NR2)**:

- 24.1. There should be biological plausibility that the substance under examination may be able to have an effect based on other knowledge or evidence.
- 24.2. the substance should be tested and found to have an effect using appropriate laboratory tests such as testing on cell lines or non-human animals before moving on to human subject research.
- 24.3. substances with proven in vitro efficacy should thereafter be tested using properly constructed clinical trials which have been designed so as to exclude the results of the effect of any placebo or other confounder of outcome.
- 24.4. the number of subjects included in such trials should be adequate to yield a result that is statistically reliable.

- 24.5. the research should be carried out by researchers who are properly qualified by training and experience with adequate resources to implement, analyse and interpret the results;
- 24.6. the researchers should be independent, in the sense that they are not employed by the producer of the medicine, and they have no personal financial interest in the outcome of the research;
- 24.7. the research should be of a quality which indicates that others can place reliance on the report.
- 24.8. the outcome of the research should be published in peer-reviewed publications so that it can be assessed, and where appropriate challenged or supported, by others who are appropriately qualified and experienced.
- 24.9. the results should be reproducible in other settings by other investigators to exclude any possibility of a chance finding or manipulation of data.
- 25. These principles are the basis of standard research methods and the process should be familiar to any experienced researcher and

competent scientist.

26. I have read the affidavit of Professor George Ellis in this case. I endorse what he says in paragraphs 7 to 13 of his affidavit.

The Cochrane Review of Micronutrient supplementation in children and adults with HIV

27. There is a vast amount of material published on medical and medicine-related research around the world. This is equally true for literature published on HIV and nutrition. It is not possible for individuals to keep track of, and assess, all of the published material which is relevant to their work.
28. The Cochrane Collaboration has been set up to assess evidence with respect to medical issues of major public health concern and promote the concept of evidence-based medicine.. The Cochrane Collaboration is an international not-for-profit organization, providing up-to-date information about the effects of health care. Its vision is that healthcare decision-making around the world will be informed by high-quality, timely research evidence, and that the Collaboration will play a pivotal role in the production and dissemination of this evidence across all areas of health care.

29. The Cochrane Library is a collection of databases that contain high-quality, independent evidence to inform healthcare decision-making. It provides reliable information from systematic review abstracts, technology assessments, economic evaluations and individual clinical trials.
30. The Cochrane Collaboration assesses most areas of health care. To do this, it is divided into Cochrane Groups which include *Cochrane Review Groups*.
31. Each of the Cochrane Review Groups concentrates on a specific healthcare area. They review and assess research reports, and publish a review of the evidence in the area in question. Cochrane Reviews are based on the best available information, both old and recent, about healthcare interventions. They explore the evidence for and against the effectiveness and appropriateness of treatments (medications, surgery, education, etc) in specific circumstances. The review is itself subjected to peer-review in terms of its design (including search strategies, inclusion criteria for literature and analytical approach) as well as its findings and interpretation.
32. It is widely accepted that the Cochrane reviews reflect the highest level of evidence on which to base clinical treatment decisions. Implicit in a

Cochrane review is a process that is acknowledged by scientists worldwide to be of the highest quality in terms of comprehensiveness, rigour, objectivity and interpretation.

The Cochrane Review

33. I am a co-author of a Cochrane Collaboration review titled *Micronutrient supplementation in children and adults with HIV*. I attach a copy of this review (**NR3**). This study examined “[r]andomised controlled trials comparing the effects of micronutrient supplements (vitamins, trace elements, and combinations of these) with placebo or no treatment on mortality and morbidity in HIV-infected individuals.”
34. The Cochrane Review is a definitive analysis of the benefits and risks of micronutrient supplements for people with HIV. The Review used standard search techniques to identify all published peer-reviewed randomized controlled trials examining the effects of micronutrient supplementation on people with HIV.
35. The primary objective of the review was to assess whether micronutrient supplements are effective in reducing morbidity and mortality in adults and children.

36. Objective criteria were used to include or exclude trials based on their quality and suitability for determining the primary objective of the review.
37. The review included the randomised clinical trials referenced by Dr Rath and in particular the studies by Fawzi conducted in Tanzania (**MWR 52**), by Jiamton conducted in Thailand (**MWR 57**) and by Allard conducted in Canada (**MWR 59**).
38. The conclusion of the Cochrane Review states:

“There is no conclusive evidence at present that micronutrient supplementation effectively reduces or increases morbidity and mortality in HIV-infected adults. It is reasonable to support the current WHO recommendations to promote and support adequate dietary intake of micronutrients at RDA [Recommended Daily Allowance] levels wherever possible. There is evidence of benefit of vitamin A supplementation in children. The long-term clinical benefits, adverse effects, and optimal formulation of micronutrient supplements require further investigation.”

The WHO recommendation quoted is taken from the same WHO publication referenced by Dr Rath, namely ‘Nutrient requirements for people living with HIV/AIDS.’ (**MWR 66**)

Micronutrients and AIDS

39. I have been asked to comment on the truth of the claim that “micronutrients alone reverse the course of AIDS”. In order to avoid repetition I refer to this as “the claim”.
40. As I have stated above, the Cochrane Review of which I was a co-author conducted a comprehensive search of all of the published peer-reviewed randomized controlled trials examining the effects of micronutrient supplementation on people with HIV.
41. None of the evidence examined in the Cochrane Review supports the claim that multivitamins, alone or not alone, reverse the course of AIDS, in adults or in children.
42. I have read those parts of the affidavit of Matthias Rath which deal with the validity of this claim. I have also read in full the affidavits of Raxit Jariwalla and Alexandra Niedwiecki. I have seen some of the advertisements that are the subject of this case and that make the claim. I have also been shown the label of VitaCell describing the micronutrient contents of that product.

43. I understand the claim “micronutrients alone reverse the course of AIDS” to mean that micronutrient supplements (which include multivitamin formulations) restore people with advanced HIV-disease (i.e. AIDS) to normal or almost normal health. I understand it to imply that it applies to a large percentage of people with AIDS, and not merely to a few exceptional patients.
44. On the basis of my research and my extensive review of the research of others, it is my considered opinion that there is no evidence that micronutrients reverse the course of AIDS. The scientific evidence, whether that presented by Dr Rath in this case or that presented by others, does not support the claim.
45. It is plausible that micronutrient supplementation offers benefit to people with HIV. However a claim that micronutrient supplements reverse the course of clinical AIDS is not substantiated by the available evidence in published medical literature, is biologically improbable and should be considered false. .
46. The statement remains false if the word “alone” is deleted from it. Even when used with other medicines or interventions, micronutrients have not been shown to reverse the course of AIDS.

47. There is conclusive medical evidence that highly active antiretroviral therapy restores the health of most people with AIDS to the point where they can lead normal or almost normal lives for periods of time that can be measured at least in years, and possibly even decades. Currently, no other medicines or interventions are known to be able to do this for HIV infection. There is no evidence that micronutrients do this.
48. There is consensus among all credible institutions dealing with HIV that malnutrition and undernutrition adversely impact on the health of people with HIV/AIDS. There is also evidence that people with AIDS have micronutrient deficiencies.
49. Several clinical trials have been conducted to determine whether people with HIV benefit from micronutrient supplementation. Some have demonstrated evidence of benefit, and others have not. It is possible that micronutrient deficiencies are better corrected with adequate and appropriate diet, as opposed to micronutrient supplements.
50. The most that micronutrient supplementation can have been demonstrated to achieve in people with HIV is to assist recovery from malnutrition, delay the onset of AIDS, or improve the response to antiretroviral treatment. However, further research is needed to determine conclusively whether or not they achieve this.

51. This is also the view of several review groups that have assessed the relationship between nutrition and HIV including micronutrients, including:

51.1. The joint WHO/UNICEF/UNAIDS/WFP task team that was established to review the nutrient requirement of people living with HIV/AIDS. The full findings and conclusions of this task team and the technical advisory group that assisted in the review are included in the WHO publication 'Nutrient requirements for people living with HIV/AIDS. Summary Report of a Technical Consultation. Geneva, May 13-15, 2003.' This report is also referenced by Dr Rath (**MWR 66**) though the conclusion was omitted.

51.2. The WHO/UNICEF review team established to look at the findings of the Randomized Trial of Multivitamin Supplement and HIV Disease Progression and Mortality published by Fawzi et al. in the NEJM 2004;351:23-32. concluded that '*The results already available need to be carefully studied before drawing definite conclusions with regard to the public health implications of micronutrient supplementation in HIV population at this stage. Results from several studies raise concerns that some micronutrients supplements such as vitamin A, zinc and iron*

may produce adverse outcomes in HIV-infected populations.' A summary of the review team's conclusions is attached **(NR4)**

51.3. The same conclusion was reached at a technical consultation convened by WHO/UNICEF/WFP and UNAIDS in 2005 and summarised in the Participant Statement. This statement reflected the findings of an updated literature review which was conducted by Professor Henrik Friis, and was independent of the Cochrane review which I co-authored. The main points from the statement pertaining to the issue of micronutrients and HIV (also detailed in Dr F Venter's affidavit) were:

51.3.1. Adequate nutrition cannot cure HIV infection but it is essential to maintain the immune system and physical activity and to achieve optimal quality of life

51.3.2. Adequate nutrition is required to optimise the benefits of antiretroviral drugs which are essential to prolong the lives of HIV-infected people and prevent HIV transmission from mother to child

51.3.3. Micronutrient intakes at daily recommended levels need to be assured in HIV-infected adults and children

through consumption of diversified diets, fortified foods and micronutrient supplementation as needed.

51.3.4. Studies have shown that some micronutrient supplements may prevent HIV disease progression and adverse pregnancy outcomes. Additional research is urgently needed.

51.3.5. Micronutrients are not an alternative to comprehensive HIV treatment including ARV therapy

51.4. W Fawzi, the lead scientist and author of the Tanzanian study referenced by Dr Rath in support of the claim, subsequently conducted a review of the published studies of vitamins and minerals and HIV transmission and disease **(NR5)**. In this review, he concludes that *'It is important to underscore that multivitamin supplements should not be considered as an alternative to ART in developing countries but as a complementary intervention that is part of a comprehensive care package.'*

51.5. Dr A Tang, lead scientist and author of the early observational study (1996) that reported on the Effect of micronutrient intake

on survival in human immunodeficiency and also the review article published in 1999 (**MWR 61**), both referenced by Dr Rath (**MWR 58**) in support of the claim, subsequently conducted a further review 'Micronutrients: current issues for HIV care providers' (**NR6**) that was published in the prestigious scientific journal AIDS (2005) and concluded *'Multivitamin supplementation, but not vitamin A, did appear to confer some benefits on HIV-infected women and their offspring. ... To conclude, it appears that a combination of some vitamins may afford some benefits to undernourished HIV-infected populations, particularly those with more advanced disease. ... As HIV becomes a more chronic, manageable disease, and treatment becomes available to more of those infected throughout the world, it may be possible to begin to more precisely define the areas in which micronutrients may help to maximise the clinical status of HIV-infected patients.'*

52. In the paper referenced by Dr Rath as **MWR 61** (Semba and Tang, 1999), the principal authors Richard Semba and Alice Tang highlight the unproven benefit of micronutrients in HIV infection. They conclude *"The advent of highly active antiretroviral therapy has dramatically changed the therapeutics of HIV for the minority of individuals living in industrialised countries (Sepkowitz, 1998). Combination antiretroviral*

therapy alone may have an impact on increasing resistance to gastrointestinal microsporidiosis and cryptosporidiosis infections (Carr et al. 1998). Billions of dollars are spent each year on vitamin and mineral supplements in industrialized countries, and many individuals with HIV infection are taking supplements although there is a lack of clear data which show that such health expenditure is worthwhile.” This statement is at odds with the claim that micronutrients reverse the course of HIV/AIDS.

53. It is my opinion, and I believe the consensus amongst international experts and active experienced researchers in the field of micronutrients and HIV, including those referenced by Dr Rath in support of the claim, that:
 - 53.1. micronutrients are a potentially valuable adjunct to comprehensive treatment including ARVs but there is no evidence that micronutrients reverse the course of AIDS.
 - 53.2. micronutrients can ameliorate some of the symptoms such as diarrhoeal disease or malnutrition that are resultant of the immune deficiency due to HIV infection but do not reverse the course of AIDS

- 53.3. micronutrients confer the same nutritional benefits as in HIV uninfected malnourished adults and children and should certainly be provided in this context
- 53.4. further research is required to fully appreciate the gains that micronutrients might afford to HIV-infected adults and children early and late in their disease course
- 53.5. Public health messages need to be clear, unambiguous and based on the most complete and current evidence regarding the potential benefits of micronutrients in order to avoid confusion, and wasting of resources of individuals and public health systems
54. It is also possible that micronutrient supplementation may be harmful for people with HIV. Studies in both HIV-infected and uninfected adults and children have demonstrated significant adverse outcomes when certain micronutrients are given in high doses and even in normal recommended dosages, especially when given to individuals with concurrent infections or who are severely malnourished. Examples of this include high dose vitamin or its precursor β -carotene causing fetal deformities or cancer in adults, or iron supplements given to children with concurrent malaria or with severe malnutrition resulting in higher

mortality rates. These adverse outcomes are well-established in the medical literature.

55. The mechanism by which any benefit is conferred by micronutrients in patients with HIV infection is unclear. It may be a general effect of restoring or optimising micronutrient status in otherwise undernourished and micronutrient depleted individuals rather than an HIV-specific effect. This is likely given the fact that amongst the studies that have demonstrated clinical benefit of micronutrient interventions to HIV-infected adults or children none, apart from one namely the Fawzi study, showed significant improvement in either CD4 counts or HIV viral load. In that sense, micronutrients improve the health of undernourished infected individuals through the established mechanisms known and described in textbooks and the scientific literature. This is not the same however, as reversing the course of HIV/AIDS.
56. This would be biologically plausible and consistent with the experience of micronutrients in the treatment of other viral infectious diseases as well as severe malnutrition.
 - 56.1. In no other viral infection are micronutrients, in any combination, curative even if they do confer clinical benefit. For example, measles is another viral infection with high mortality rates, in

part due to immune suppression secondary to the virus, and especially in children already undernourished. Vitamin A supplement given during the infection reduces mortality and ameliorates the specific eye complication of the infection. It may also reduce diarrhoeal disease that may follow in the weeks after that complicate the recovery period of the infection. However, it is not curative.

56.2. In severe malnutrition, the immune system of children is compromised. WHO includes micronutrient as part of the interventions that are recommended as standard of care. However, even though micronutrients are essential for recovery, they are not curative when given alone. Severely malnourished children are also routinely treated with antibiotics as well as macronutrients i.e. high protein, high energy diets. Micronutrients are part of a comprehensive care package but cannot reverse the course of severe malnutrition alone.

57. While it is attractive to believe that one intervention will reverse the course of HIV/AIDS, it is not biologically plausible that micronutrients could achieve that, even when the evidence from basic laboratory experiments are considered, and it is not consistent with the results of research studies or clinical experience. The experience of Virodene in

South Africa should be salutary; a group of laboratory scientists claimed to have the cure to HIV/AIDS but without evidence based on clinical trials to prove it. The claim falsely elevated the hopes of those infected with the virus and undermined the tried and tested process of finding effective interventions to life threatening diseases.

The evidence submitted by Dr Rath

Dr Matthias Rath

58. In my opinion, Dr Rath's statements about AIDS and nutrition have to be treated with great reserve, and cannot be relied upon, for the reasons below.

59. First and foremost, not a single scientific report included in Dr Rath's affidavit, even if read uncritically, proves that the claim that micronutrients reverse the course of HIV/AIDS is correct. More critically, isolated, semi-scientific statements are linked together in notices (adverts) presented to the general public that give an impression of evidence but are in fact a set of disconnected assertions from a wide range of sources. Given the catastrophic impact of the HIV epidemic in South Africa and the massive human loss that has already been experienced, any claim of an intervention that reverses the course of

the disease should be backed by evidence of the highest order, collected with the utmost rigour and objectively analysed and interpreted. It is irresponsible to make claims that are not commensurate with the evidence to back those claims. Anything less, falsely elevates the hopes of those who are desperate to live and potentially wastes time and resources.

60. Second, both the affidavit and public notices borrow assertions from the historical body of nutritional literature that are totally HIV unrelated and apply them in an uncritical manner to the HIV disease paradigm. For example:

60.1. In paragraph 86 of his affidavit Dr Rath states that micronutrients are essential and indispensable for blood cell formation. While this is true, he positions this statement immediately after another statement that 'The pathological basis of AIDS is a dysfunctional immune system clinically indicated by low levels of white blood cells.' That statement is also true. The statement about micronutrients is however a non-sequitur, It has no immediate relationship to the immune dysfunction induced by HIV/AIDS. There are many other causes of a dysfunctional immune system other than HIV/AIDS that are clearly not the result of basic micronutrient deficiency. For

example, leukaemia secondary to nuclear radiation or congenital immune disorders such as the Severe Combined Immunodeficiency (SCID) or Nezelof's syndrome.

- 60.2. Dr Rath implies that attributing one cause of immune dysfunction to a virus is de facto a failure to recognise and advocate for the fundamental role of micronutrients in maintaining the immune system. This is clearly not the case.
- 60.3. Dr Rath continues in this argument referring to the role of B vitamins in the formation of blood and what happens when these vitamins are not present. All this is correct and as he states in paragraph 93, this knowledge is firmly established. However, it is entirely different to assert, as in paragraph 94 of his affidavit, that because of the biological activity of micronutrients, micronutrients therefore '[... effectively improve the immune function and well-being of people living with AIDS]'. It cannot be extrapolated, simply by virtue of their activity in the supporting the immune system, that *micronutrients reverse the course of HIV/AIDS*.
- 60.4. Dr Rath uses WHO reports on general nutrition and anaemia (**Para 98, MWR 62, 1961 and MWR 63 1967**) and a UNICEF

report on vitamin and mineral deficiency (**Para 107, MWR 68 2002**) as evidence of the importance of nutrition and thereby on HIV. Apart from the fact that several of the areas covered by these very dated expert reports have been updated (e.g. FAO/WHO report on energy requirements 2001 **NR7**), these reports do not contain any evidence that micronutrients have any bearing on the course of AIDS.

61. Third, Dr Rath's use of scientific literature is selective. He fails to fully represent the findings and conclusions of the papers he references. He refers only to studies which he asserts support his conclusions. He does not make reference to studies which do not support his conclusions. For example:

61.1. Dr Rath relies on **MWR 52** (Fawzi et al., 2004) to support the claim that multivitamins slow down the risk of developing AIDS. This is an important clinical study for determining whether multivitamins reverse the course of AIDS. I therefore I deal with it in some detail.

61.1.1. The study found that daily doses of a particular combination of multivitamins in a particular population slowed down progression to AIDS. In his affidavit, but

not in the public notices, Dr Rath acknowledges the benefit of micronutrients as limited to a specific population.

61.1.2. There were three multivitamin arms tested against placebo. Only one of the arms, which specifically excluded vitamin A, achieved statistically significant results. This unexpected finding demonstrates that even if multivitamins do have benefits for people with HIV, achieving such benefit is not a simple matter of prescribing an arbitrary large combination of high-dose vitamins (such as for instance in VitaCell).

61.1.3. The study was conducted on Tanzanian women. The study subjects who benefited from the multivitamin supplementation likely had poorer nutritional status than many other sub-populations infected with HIV. The Cochrane Review states “[T]he reduced morbidity reported may not strictly be an HIV-specific effect, as HIV-free women in a nutritionally depleted population might also benefit from similar supplementation; an uninfected group would therefore be required to determine this with certainty.”

61.1.4. In the placebo arm 31.1% of women progressed to WHO stage 4 or death. In the multivitamin arm, 24.7% progressed to WHO stage 4 or death. This relative difference is modest, especially considering that it was achieved over a long median follow-up period of 71 months.

61.1.5. Dr Rath is correct that the study was a large one, of good quality, conducted over many years. However, the study in fact undermines rather than supports the claim, because it provides compelling evidence that multivitamins alone do not reverse the course of AIDS. The placebo and the multivitamin arms both progressed to AIDS. In this regard, it is important to note that:

61.1.6. Across all the arms of the study, 343 out of 1078 women died, 243 deemed to be due to AIDS. Over a median follow-up of about six years, this is an extremely high mortality rate. Mortality was high in all arms of the study i.e. the three multivitamin arms and the placebo arm, though to a lesser degree in the multivitamin arm.

61.1.7. Dr Rath refers to this as proof that *micronutrients reverse the course of HIV/AIDS*. A more complete portrayal of the data would highlight that the benefits were modest, were particular to a specific group of study participants, and in an environment with high maternal mortality and malnutrition. Extrapolating this specific finding to assert that micronutrients *reverse the course of AIDS*, is a much greater claim than achieved in the study.

61.1.8. By contrast, clinical trials have demonstrated that antiretrovirals restore the vast majority of patients with AIDS to almost normal health. Their positive effect on health in people with advanced HIV disease is significantly more profound than that of micronutrients.

61.2. Dr Rath similarly overstates and therefore misrepresents the findings of the study annexed as **MWR 57** (Jiamton et al, 2003). Outlining the data as for the Fawzi study would illustrate how the benefits of a very different formulation of micronutrients are over-interpreted by Dr Rath. A few additional points about this study different from the Fawzi, Tanzania study are:

61.2.1. There was not a statistically significant lower mortality in the micronutrient arm taken as a whole.

61.2.2. There was a statistically significant lower mortality only in a sub-group of patients with CD4 counts lower than 100.

61.2.3. Numerous patients in both arms were lost to follow-up, in fact more than died. A slightly higher percentage of patients in the placebo arm were known to have survived at the end of the trial period of 48 weeks. This limits the analytical power of the study.

61.2.4. In contrast to the Fawzi, Tanzania study, patients randomised to the micronutrient intervention did not experience an increase in CD4 counts or any reduction in HIV viral load. Hence, any clinical benefit was not mediated by improvement of the CD4 component of the immune system. It would be expected that any intervention that reverses the course of HIV/AIDS would have a consistent effect on these universally-accepted indicators of HIV-related immunocompetence.

61.2.5. Some of the trial subjects were on antiretroviral treatment. This further restricts any interpretation that the trial provides evidence that micronutrients (either alone or in combination with other medicines) reverse the course of HIV/AIDS.

61.2.6. The authors themselves state that their findings need to be reproduced in other settings. They use cautious phrases, e.g. "micronutrients may enhance the survival of HIV-infected individuals with CD4 counts $< 200 \times 10^6/l$." They do not suggest that micronutrients should be used as alternative to antiretrovirals, but only that they may be of use in settings where access to antiretrovirals remains poor. Dr Rath never makes mention of this conclusion in either his affidavit or public notices.

61.3. Dr Rath fails to refer to many of the studies that do not show HIV-specific benefits of micronutrient supplementation. A failure to address all of the evidence demonstrates scientific incompetence or bias, or both. The Cochrane review included all randomised clinical controlled studies.

61.4. In paragraph 96 d ii Dr Rath refers to an article by Tang et al (**MWR 58**). This was, in fact, an observational study. In the hierarchy of scientific evidence randomised controlled trials are regarded as the most important demonstration of causality. While observational studies can provide useful insights, they cannot be relied upon in the same way. This study at most offers inconclusive evidence that some micronutrients taken in particular doses are of benefit to people with HIV. The lead author herself, in a subsequent review, acknowledges the ill-defined benefit of micronutrients in the comprehensive management of people living with HIV (see para 51.5 above). The study does not support the claim that *micronutrients reverse the course of HIV/AIDS*.

62. Fourth, Dr Rath incorrectly interprets data indicating either an inability to understand research design and medical statistics or an alternative reason for interpreting the data as included in his affidavit and public notices. In paragraphs 82 and 83, Dr Rath makes assertions about the progression from HIV to AIDS, and as to the consequences of treatment with antiretrovirals. He claims antiretrovirals cause higher mortality than HIV itself in people with HIV. In my opinion, these paragraphs contain scientific errors that display either incompetence or dishonesty:

- 62.1. In paragraph 82 Dr Rath refers to **MWR 39**, which is a WHO document (Weekly Epidemiological Record, 7 December 2001). Dr Rath states that “From all people infected with HIV statistically less than 20% develop the immune deficiency condition AIDS, even after 13 years.” Dr Rath does not explain how he derives this claim from MWR 39. He merely asserts it.
- 62.2. In paragraph 83 Dr Rath claims that MWR 40 (Palella et al., 1998) and MWR 41 (Hogg et al., 2001) demonstrate that the death rate from AIDS among HIV-positive patients taking antiretrovirals is statistically at least 7% per year, and that this means 100% of patients taking antiretrovirals would have died after 13 years. Besides the obvious arithmetical error, this is false. Both of these studies provide evidence that contradict Dr Rath's assertions about antiretrovirals.
- 62.3. The Palella et al. paper was in fact a seminal study which demonstrated that antiretroviral treatment in operational settings substantially prolongs and improves the lives of people with HIV.
- 62.4. It compared mortality and morbidity between HIV patients with advanced disease taking (a) no antiretrovirals, (b) one

antiretroviral, (c) combination antiretroviral treatment, and (d) combination antiretroviral treatment plus an antiretroviral from the protease inhibitors class. The study found reduced mortality and morbidity for each additional antiretroviral used.

62.5. The study concludes that the *“recent declines in morbidity and mortality due to AIDS are attributable to the use of more intensive antiretroviral therapies.”* It therefore says the opposite of what Dr Rath asserts it to say.

62.6. There were indeed high mortality rates in this study in all arms. That was because the subjects examined all had at least one CD4 count below 100. This means their HIV infection had already progressed to AIDS. It is therefore fundamentally incorrect to compare the mortality rate of this cohort against the general population of patients with HIV, half of whom take approximately ten years from infection to progress to a similar stage of the disease.

62.7. To treat the cohort of patients in this study as suitable for comparison with the general population with HIV therefore suggests either incompetence or dishonesty.

- 62.8. The article by Hogg et al. (MWR 41) begins with the statement, *“Triple-drug combination antiretroviral therapy has been shown to dramatically decrease morbidity and mortality in symptomatic and asymptomatic human immunodeficiency virus type 1 (HIV infected) individuals.”* This fundamentally contradicts the conclusion which Dr Rath suggests is to be drawn from it.
- 62.9. The purpose of that study was to determine disease progression rates for patients on antiretrovirals, stratified by CD4 and viral load counts.
- 62.10. The paper did not find, as Dr Rath claims, a mortality rate of at least 7% per year in patients taking antiretrovirals. It found an overall crude mortality of 6.7% amongst patients over the entire period of the study, which was considerably longer than a year, as was the median follow-up period. The cumulative mortality rate at 12 months was 2.9% (ranging between 1.1% and 4.4% depending on the patients CD4 count and viral load), less than half of that claimed by Dr Rath. Dr Rath’s statement seriously misrepresents the data.
- 62.11. Even more fundamentally, the patients were studied not from the onset of their HIV infection, but from the point where they

were prescribed antiretroviral treatment. Most of the patients had CD4 counts lower than 200 when they were included in the study. This means their HIV disease had progressed to AIDS. As with the Palello et al. (1998) paper, it is either incompetent or dishonest to compare, as Dr Rath does, the mortality rate of this cohort with the general population of patients with HIV.

63. I attach (**NR8**) the abstract of a study by Morgan et al. published in 2002 in *AIDS*, a highly reputable peer-reviewed journal. It provides evidence of the time from HIV infection to AIDS, and from AIDS to death, in an African setting for patients who did not generally have access to antiretroviral treatment.
 - 63.1. The study began in 1990. It followed a cohort of people who were HIV-prevalent (i.e. known to be HIV-positive at the start of the study), HIV-incident (i.e. who contracted HIV infection during the course of the study), and HIV-negative.
 - 63.2. The study found that the “median time from seroconversion (first infection) to AIDS was 9.4 years and from AIDS to death was 9.2 months.”

- 63.3. It concluded “survival with HIV-1 infection is similar in Africa to industrialized countries before the use of antiretroviral therapy; when they do die, many of those in Africa are severely immunosuppressed and most have clinical features of AIDS.”
64. Other studies in other countries have reached similar conclusions.
65. The finding that half of people infected with HIV progress to AIDS within approximately ten years, contradicts Dr Rath's assertion that less than 20% of people with HIV develop AIDS after 13 years since infection. Dr Rath's assertion is therefore not only unsupported by the report which he claims provides the evidence, it is also false.
66. In paragraph 84 Dr Rath refers to **MWR 42**. The source of **MWR 42** is not stated. It seems that it is either a document prepared for this case, or published by Dr Rath or his colleagues. It does not appear to be a peer-reviewed paper. **MWR 42** is based on Dr Rath's conclusions of **MWR 39, 40 and 41**. As his conclusions from those papers are false, **MWR 42** is itself false.
67. Dr Rath incorrectly represents the findings of the study referenced in the annexures as **MWR 48**. He states that the study “established that vitamin C alone can block the replication of HIV by 99%”. Rather, the

publication reports that, under highly controlled laboratory conditions, vitamin C blocked replication of HIV in some cells by 99%; not that HIV was blocked in 99% of cells infected with HIV.

68. In paragraph 96 d iii Dr Rath refers to **MWR 59** (Allard et al., 1998). The viral load results of this study were not statistically significant. The study was very small (49 subjects), and the number of infections reported by patients in both the micronutrient and the placebo arms was similar. No conclusion can be reached from this study for the benefits of micronutrients for people with HIV.
69. Fifth, Dr Rath equates the findings of all studies as the same. This is not valid. The type of study design imposes limitations on the way that data from the study can be interpreted and the importance that can be attributed to that data. For example:
- 69.1. Dr Rath affords the same value to data obtained from simple observational studies as evidence derived from randomised clinical controlled trials. The latter is of much higher value and thereby importance.
- 69.2. Dr Rath fails to acknowledge the limitations of laboratory experiments. In paragraph 96 a, Dr Rath relies on the study

annexed as **MWR48** (Harakeh et al., 1990). This was conducted *in vitro* (i.e. in a laboratory, not in bodies). No claim of benefit to humans can be made about a product solely on the basis of *in vitro* studies, or for that matter of *in vivo* studies in non-human animals. This is a critical point. Dr Rath also relies on **MWR50** (Roederer et al., 1990) and **MWR51** (Kalebic et al., 1990) to show some value to N-acetylcysteine in the treatment of HIV. Again, both of these studies are *in vitro*, and one can not rely on them to reach any conclusion about their efficacy in human beings. Frequently, successful results obtained under laboratory conditions or in non-human animals do not translate into successful results when tested on humans. Many substances (such as virodene and vitamin C) can destroy HIV in cells *in vitro*. However, such experiments, including that described in **MWR48**, often do not answer the next important questions: Can the same substance be absorbed by the human body and effectively act upon the target cells? How much of the substance must be ingested for it to achieve its objective of destroying a pathogen in sufficient quantities? Would ingesting it in an effective dose be safe? Consequently *in vitro* experiments, although essential to start with, in fact only suggest what might be achieved *in vivo*.

- 69.3. Dr Rath's inclination to place great value on these studies reflects on his own expertise and that of his team. The next logical step for an experienced and competent team of scientists would be to seek proof of clinical benefit in humans by conducting a randomised, placebo-controlled trial.
70. Sixth, Dr Rath claims to have conducted research but seems to have disregarded the standards required by the MCC, international ethics and Good Clinical Practice (GCP)
- 70.1. In paragraphs 294 to 297 Dr Rath summarises what he says are the results of his clinical research in what he terms "a micronutrient program in Khayelitsha".
- 70.2. The paper in question (MWR6) appears to be self-published. To the best of my knowledge it has not been published in any credible peer-reviewed journal. Dr Rath does not assert that it has been so published. As I have pointed out, and as is also stated by Professor Ellis, this is an essential requirement for any scientific claim to be taken seriously.
- 70.3. I have however been shown the purported results of this research in various advertisements. Nothing can be learnt from

such research. In my view it is inappropriate and arguably unethical to publish the claimed results of clinical research conducted on humans, which has not been subjected to peer-review, as newspaper advertisements.

70.4. If, as the applicants allege, no approval was given by any recognised ethical authority for Dr Rath to conduct this research, then he has committed a serious breach of medical ethics.

70.5. It appears from the paper that there was no control group in Dr Rath's study. This is a serious shortcoming. There is simply no way of determining whether the benefits that he ascribes to micronutrient supplements were indeed due to them.

71. In paragraphs 97 to 103 Dr Rath refers to the World Health Organisation and the applicant's reference to the position of the WHO on micronutrients and HIV. I have not been requested to respond to respond to these paragraphs, because they do not support the claim that micronutrients alone reverse the course of AIDS.

72. However I will point out again that I sit on the WHO Technical Advisory Group on Nutrition and HIV/AIDS. The claims of conspiracy made by

Dr Rath are insulting and frankly absurd.

73. As stated above, Dr Rath refers to reports of technical meetings held in 1961 and 1967 to support the assertion that nutrition is important for life. This is patently so and can not be disputed.
74. In paragraphs 104-109 Dr Rath refers to four WHO, UN and UNICEF documents: **MWR64**, **MWR66**, **MWR67** and **MWR68**. I was a technical advisor for, and co-author on **MWR 64** and **MWR 66**
75. Not one of these documents in any way suggests that micronutrients reverse the course of AIDS, whether taken alone or not.
76. In paragraphs 234-242 Dr Rath attempts to cast himself as a leading researcher in the field of micronutrient science (not related to treatment for HIV and AIDS).
77. This positioning is completely inconsistent with his publication and research records. Most (if not all) credible scientists in this field would not recognise him as a serious or significant researcher in the field. Any credibility he might have is undermined by the extravagant claims, apparently linked to the marketing of his multivitamin products.

Raxit J Jariwalla

78. I have read the affidavit of Dr Raxit Jariwalla.
79. I have noted the research that Dr Jariwalla has conducted in the field of micronutrient research and HIV. The work seems to have been predominantly laboratory-based. The peer-reviewed papers included in these court records bearing his name are with few exceptions published in journals with low citation indices. Dr Jariwalla is not recognised as a leading researcher in the field of micronutrient supplementation and HIV.
80. Dr Jariwalla heads virology research at one of Dr Rath's institutions (Rath para 96 v). From this it seems that he is employed by Dr Rath or one of his institutions. In my opinion this undermines his reliability as an independent objective scientist and witness.
81. For the reasons which I set out below, Dr Jariwalla's affidavit contains statements that are frequently misleading.
82. Like Dr Rath, Dr Jariwalla has been highly selective in the studies to which he refers. He refers only to those which he says support his thesis. He does not address or refer to the many studies (described in

the Cochrane Review) that do not show any benefit of micronutrient supplementation. Again, this demonstrates scientific incompetence, bias, or both.

83. In any event, even if one uncritically accepts everything which is said by Dr Jariwalla, his affidavit does not support the claim that micronutrients alone reverse the course of AIDS. At most, he attempts to show that micronutrients are beneficial for people with HIV, sometimes in conjunction with antiretroviral treatment. Although Dr Jariwalla concludes that “it is not true that vitamins or micronutrients do not reverse the course of AIDS” (paragraph 20), he appears to fail to understand the meaning of the statement that micronutrients reverse the course of AIDS. Instead, he re-interprets it to mean that micronutrients in some cases reverse the course of some AIDS symptoms. Even this claim is not substantiated, but it is in any event a far more modest claim.
84. I now deal with the specific evidence on which Dr Jariwalla relies for his more modest claim.
85. In paragraphs 6-7 it is not clear what Dr Jariwalla means by the phrase that HIV is not the sole cause of AIDS. If he means that additional factors such as nutritional deficiency exacerbate progression to AIDS,

then I agree with him. However, HIV is necessary for the clinical condition described as AIDS to occur. Progression to AIDS takes place in the vast majority of people with HIV irrespective of their socio-economic background, nutritional status or lifestyle. The papers that Dr Jariwalla is co-author on, acknowledge that HIV is the cause of AIDS and the need for specific anti-HIV agents to be developed.

86. Dr Jariwalla refers to **J 1**, an article published by RH Gray in 1983. It speculates on the similarities between protein calorie malnutrition and AIDS. This study was published before it became generally known that HIV is the cause of AIDS. As mentioned earlier there are several causes of impaired immunity including severe malnutrition as well as HIV.
87. None of the studies to which Dr Jariwalla refers in paragraphs 6 and 7 either states or implies that micronutrient supplements reverse the course of AIDS.
88. Dr Jariwalla relies on **J 4** (Tang et al.), which is a review of the current state in 2005 of research on micronutrients and HIV. It however has the following features which do not support Dr Rath's case:
 - 88.1. The authors state that since "HAART [i.e. highly active

antiretroviral treatment] has become the standard of care in the treatment of HIV infection in the resource-sufficient world, the incidence of opportunistic infections and death has significantly declined in these regions". The authors thus clearly support the use of antiretroviral treatment.

88.2. The article generally emphasises that more research is needed in order to determine the effects of micronutrient supplementation. Table 4 lists key outstanding research questions about the role of micronutrient supplementation.

88.3. Table 4 also refers to "decreased HIV progression" due to micronutrients. However, nowhere in the article is there any suggestion of micronutrients reversing the course of AIDS.

89. In paragraphs 8 to 12, Dr Jariwalla addresses the side-effects and shortcomings of antiretroviral treatment. Dr Jariwalla does not claim to have undertaken any research on antiretroviral treatment, or to be an expert in that area. I believe he is a laboratory scientist and not a clinical researcher. I therefore do not address this section of his affidavit. Rather, I defer to Dr Venter, who is an acknowledged expert in this field, and whose affidavit is before the court.

90. I would point out that most of the studies to which Dr Jariwalla refers are old, and have been surpassed by more recent research. It appears to me that Dr Jariwalla seeks to exaggerate the side-effects of antiretroviral treatment. His account does is not consistent with my experience as a paediatrician working at King Edward VIII hospital in Durban where we have several hundred children on ARVs. This has been more substantially dealt with in Dr Venter's affidavit.
91. In paragraph 13. Dr Jariwalla comments that the statement that the benefits of antiretrovirals outweigh their risks is not persuasive. This opinion is not based on any apparent track record of research on antiretrovirals or HIV in a clinical setting. In my opinion he is wrong. Nearly all scientists working in the field of HIV and every medical institution proceed on the basis that the benefits of antiretrovirals do indeed outweigh their risks. Following a technical consultation on Nutrition and HIV in Durban 2005, WHO/UNICEF/UNAIDS were joint signatories to the statement saying both ... "Micronutrient supplements are not an alternative to comprehensive HIV treatment including ARV therapy" and ... "The value of ARV therapy far outweighs the risks and the metabolic complications need to be adequately managed." (**NR9-Participants statement**).

92. All of the studies referred to in paragraph 14 were conducted *in vitro*. They therefore can not be used to conclude that micronutrients alone reverse the course of AIDS.
93. I find it remarkable that in paragraph 15 Dr Jariwalla refers to the study annexed as **J 25** (Cathcart, 1984). This was published in the journal *Medical Hypotheses* in 1984, years before the first antiretroviral was registered. This journal specialises in publishing highly speculative articles that do not constitute accepted medical theory. The paper in question does not describe a randomized clinical trial with a control group. It is based entirely on anecdotal experience from 90 patients. The paper is for numerous reasons very poorly written, and was written at a time when AIDS was poorly understood. It would be very unlikely to pass peer-review in a more credible journal. Nevertheless, Cathcart actually states that “the basic AIDS condition was not reversed”, a direct contradiction of the claim in question. Remarkably, Dr Jariwalla does not refer to or address this.
94. The study annexed as **J 26** (Asuncion et al., 1998) is of no assistance because it examines micronutrients when used in conjunction with antiretrovirals. It can therefore not provide any basis for substantiation of the claim.

95. The study annexed as **J27** (Allard et al., 1998) is dealt with in the Cochrane Review. We raised the following issues: “Randomization was by means of a random-number table, but the method of allocation concealment was not clear from the trial report. Placebo was used and outcome assessors were blinded. Nine of 49 participants (18.4%) had baseline and follow-up measurements (one or two months) but were unable to keep their three-month appointments.” Again, in any event the study makes no claim and offers no evidence to support the claim that micronutrients reverse the course of AIDS.

96. The study annexed as **J 28** (Muller et al., 2000) had no control group, and no significant changes in HIV viral load or CD4 counts were noted. Nothing in this study can be used to support the claim.

97. Dr Jariwalla misrepresents the study annexed as **J 29** (Herzenberg et al., 1997):

97.1. The study examined patients with glutathione deficiency. In other words, this was not a general population of people with HIV, but a subset of the population with a known nutritional deficit.

97.2. The use of N-acetylcysteine (NAC) did not reverse the course of

AIDS, although it may have conferred a survival benefit on patients.

97.3. Patients who were on stable antiretroviral treatment were not excluded from the study.

97.4. The study is not a randomized controlled trial to determine the survival benefit of NAC, as implied by Dr Jariwalla. The paper explicitly states that “although the data suggest that NAC ingestion may well contribute to improved survival, we emphasize that no conclusion can be drawn until NAC is administered in a properly controlled prospective clinical trial with survival as the primary endpoint.” Dr Jariwalla simply does not refer to this statement or address it.

98. In paragraph 20 Dr Jariwalla refers to various studies which, he says, show the beneficial effect of micronutrients. This is a different proposition from the claim that micronutrients reverse the course of AIDS in this paragraph.

99. I have pointed out above that annexure **J 4** undermines, rather than supports, Dr Rath’s case.

100. Annexure **J 31** (Tang et al, 1993.) at most supports a claim that appropriate intake of micronutrients in food **and** supplements is associated with slower progression to AIDS. Furthermore, the results between different micronutrients and even the same micronutrients at different doses were inconsistent. Many of the patients in this study would have been taking antiretroviral treatment, which would confound the effects of micronutrient supplementation. This was not a randomised controlled study.

101. Annexure **J 33** (Fawzi et al., 1998) is an earlier publication of the trial that is the subject of MWR52 which I have discussed above. Its conclusions on outcomes for women are superseded by the later publication discussed above. Its conclusions on pregnancy outcomes are promising and are discussed in the Cochrane Review – they may well be benefits for all women and their infants in Tanzania and not an HIV-specific gain. They are however irrelevant to determining whether micronutrients reverse the course of AIDS.

102. Annexure **J 34** is the same as MWR 52 which I have discussed above. Annexure **J 35** is the same as MWR 57 and has also been dealt with above.

103. Annexure **J 36** (Kaiser et al., 2006) is an unhelpful and flawed study for a number of reasons:

103.1. The sample size was small and the data collection procedures for the morbidity outcomes were not appropriate. Hence it is difficult to make any reliable claims on benefit.

103.2. The average baseline CD4 count of the placebo arm was higher than the multivitamin arm, and remained higher at the end of the trial. Little meaning can therefore be attached to the statistically significant increase in CD4 count in the multivitamin arm. Furthermore, the higher the baseline CD4 count of a cohort on antiretroviral treatment, the less it is expected to rise with time. The findings are difficult to explain and therefore to interpret in terms of clinical benefit.

103.3. All the patients in the trial were on antiretroviral treatment. The purpose of the study was to examine micronutrients used as an adjuvant therapy to antiretrovirals, not to demonstrate that micronutrient supplements alone reverse the course of AIDS.

103.4. An undeclared conflict of interest by the authors of this study has since come to light. The first author has acknowledged it

and published an apology in the *Journal of Acquired Immune Deficiency Syndrome* Volume 45, Number 1, May 1, 2007, pages 128-129. Undeclared conflicts of interest severely undermine the credibility of a research paper.

104. There is much in paragraphs 22 to 30 that is inaccurate. However, I have been advised that as they do not deal directly with the issue of whether or not micronutrients reverse the course of AIDS, it is not necessary for me to detail these inaccuracies.
105. Dr Jariwalla appears to assert in paragraphs 31 to 34 that multivitamins might be a useful adjuvant treatment to antiretrovirals. That may or may not be so, depending on the circumstances and the nature of the multivitamin provision. To the extent that it is true, this does not assist in showing the truth of the claim that micronutrients alone reverse the course of AIDS. In fact, in acknowledging that antiretrovirals have a place in the treatment of HIV/AIDS, Dr Jariwalla recognises that HIV is the cause of AIDS and antiretroviral drugs have an important and credible role in managing patients with AIDS.

Alexandra Niedwiecki

106. I have read the affidavit of Alexandra Niedwiecki.

107. Dr Niedwicky does not demonstrate any expertise in the field of HIV and nutrition. Only one of her peer-reviewed articles appears to deal with HIV and nutrition. As with Dr Jariwalla, her peer-reviewed papers are with few exceptions published in minor journals with low citation indices. She is not a recognised researcher in the field of nutrition and HIV.
108. Even if one accepts Dr Niedwicky's statements uncritically, she does not present any evidence that *micronutrients reverse the course of AIDS*.
109. It is however, my opinion that Dr Niedwiecki greatly exaggerates the importance and benefits of the work of Dr Rath and his research institutes.
110. In paragraph 7 Dr Niedwiecki makes several claims that imply that Dr Rath's research institutes have made important breakthroughs in the treatment of various diseases using micronutrients. I am not aware of a single published peer-reviewed paper in credible journals by researchers at Dr Rath's institute that conclusively demonstrate benefit of any micronutrients for any diseases in humans.
111. At paragraph 7c Dr Niedwiecki repeats the claims made by Dr Rath regarding their study in Khayelitsha. I have previously dealt with this and do not repeat what I have said in that regard.

Other evidence as to the scientific competency and credibility of Dr Rath as experienced researcher and internationally renowned expert in micronutrient research

112. Dr Rath asserts that he has the experience and knowledge to be regarded as an expert in the field of micronutrients and HIV. However, I would suggest otherwise on the basis of the following points, many of which have been described in greater detail above as they related to the science of the matter.

112.1. Dr Rath uses the general media to disseminate results of his own work and to pass judgment on the work of others.

112.2. In his affidavit, Dr Rath mixes statements about scientific matters with political statements and opinions, and ad hominem attacks on those with whom he disagrees. It is difficult to analyse precisely which of his statements are claimed to have scientific validity.

112.3. Dr Rath argues that the basis for all evidence supporting the value of ARVs in controlling HIV disease progression, and for a conspiracy to suppress his belief that micronutrients reverse the course of HIV/AIDS, is the work of the pharmaceutical industry.

Dr Rath alleges that the pharmaceutical industry funds many of the protagonists of ARVs and supports the production of evidence in support of ARVs. He argues that this undermines the credibility of the results produced by such research and the integrity of researchers involved with such trials. Ironically, Dr Rath chooses not to mention that the micronutrient supplementation trial in Thailand (Jiamton et al, 2003) that he references in support of his claim (**MWR 57**), was funded by the Nestle Institute, that has major financial interests in infant nutrition (see acknowledgements in the paper).

112.4. The materials on which Dr Rath relies are themselves of inconsistent quality. For example, he relies on the authority of a newspaper article in support of his scientific contentions. Science does not rely on “evidence” of this kind to support major claims that would have massive implications for public health policy and practice.

112.5. Prince Charles, on whom Dr Rath relies in paragraph 103, is not a known expert in any medical field. This is another example of Dr Rath’s reliance on non-scientific material in an attempt to support a scientific claim of immense public health importance. In any event, Prince Charles’s statement does not support the

claim that micronutrients alone reverse the course of AIDS.

113. The above approaches bring into question Dr Rath's competency as a scientist, researcher and clinician. In paragraphs 234-242 of his affidavit and in notices presented to the general public, Dr Rath describes himself as an internationally renowned scientist with extensive research experience. Personal representation in this way may influence members of the public who are not qualified or skilled to discern otherwise. I personally query the competency and expertise for the reasons detailed above. In addition, it would be expected that any senior scientist and researcher, proficient and expert in a scientific field such as micronutrients and HIV would have a significant peer-reviewed publication record, would present findings of original work at internationally accredited meetings and would be prominent as an invited speaker or participant at the same international nutrition or HIV meeting. With these expectations in mind, I would comment:

113.1. Dr Rath's publication record in high quality peer-reviewed medical journals, either nutrition or HIV-focussed, is scant and inconsistent with an expert in the field of either nutrition or HIV. None of the work cited in the notices presented by Dr Rath's foundation to the general public was identified or included in the major reviews on micronutrients and HIV infection published

over the past 5 years. In none of the scientific literature reviews conducted and published by Fawzi, Tang, Drain, Friis or the Cochrane review was any original work conducted by Dr Rath or his foundation identified or considered of value for inclusion. These reviews did comment on all evidence including those reporting effects as well as those reporting no effects. In contrast, Dr Rath's list of publications (**MWR 107**) does not list any peer-reviewed paper that deals with nutrition with respect to HIV infection. The papers Dr Rath has published on general nutrition are in scientific journals with low citation indices. Citation indices are an indication of the value placed by other scientists on the scientific merit of papers published in a journal. Low ratings indicate articles and journals of lesser significance.

113.2. Dr Rath has not presented any of the findings reported in the notices presented to the general public at any major international, South African national or provincial nutrition or HIV meeting. Examples of such meetings held in South Africa in the past few years would include the International Nutrition Society 2006 (first time the conference was ever held in Africa), the South African Nutrition Society annual conferences, the South African AIDS Conference held every two years, the International AIDS Conference held every two years and hosted

in Durban in 2000. There are several smaller meetings such as those convened by the South African Paediatric Association and the South African HIV Physician Association. However Dr Rath has chosen not to present findings for peer review at any of these meetings.

113.3. It would be expected that an experienced and renowned scientist and researcher would be invited to give plenary presentations at national and international meetings. As a scientist who attends many of the meetings directly concerned with nutrition and HIV, I have never been present at a meeting where Dr Rath gave a plenary presentation nor have I heard of any major national or international meeting that I did not attend at which he was an invited speaker.

114. My conclusion is that the evidence detailed above in relation to the science and clinical evidence base with respect to micronutrient and HIV/AIDS reflects a lack of truthfulness and integrity on the part of Dr Rath. These are fundamental and absolute necessities for scientific pursuit. The consistent pattern of misrepresentation and failure to consider or address contrary evidence makes it unsafe to rely on Dr Rath's evidence in this regard. His evidence in this regard is, in my opinion, unreliable.

NIGEL ROLLINS

THUS SIGNED AND SWORN TO BEFORE ME AT
_____ ON THIS ____ DAY OF JULY 2007 THE
DEPONENT HAVING ACKNOWLEDGED THAT HE KNOWS AND
UNDERSTANDS THE CONTENTS OF THIS AFFIDAVIT, HAS NO OBJECTION
TO TAKING THE PRESCRIBED OATH AND CONSIDERS THE OATH TO BE
BINDING ON HIS CONSCIENCE.

COMMISSIONER OF OATHS