

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

LESLIE LONDON

hereby make oath and state as follows:

1. I am a Senior Specialist and Professor in Public Health at the University of Cape Town (UCT) in the School of Public Health and Family Medicine.
2. I am the Associate Director of the Occupational and Environmental Health Research Unit in the School and Head of the Health and Human Rights Division. I serve on the School Executive Committee and hold the position of Portfolio Manager for Transformation and Equity in the Faculty. I have been a medical doctor for 22 years, an Associate Professor for 10 years, and a full Professor since 2004.
3. The facts contained herein are true and correct, are within my personal knowledge.
4. The contents of this affidavit have the support of the Executive Committee of the UCT School of Public Health and Family Medicine.
5. I have served on the research ethics committee of the University of Cape Town, am a member of the Interim National Health Research Ethics Council, and teach courses in Health and Human Rights to post-graduate students and train undergraduates in research ethics.
6. I am a member of the Advisory Committee on Human Rights, Ethics and Professional Practice for the Health Professions Council of South Africa,

and co-convene the Ethics and the Law Committee of the South African Society for Occupational Medicine.

7. I have published in national and international peer reviewed journals on the ethical and human rights issues in biomedical research. I have been invited to address national and international meetings on these topics. In this regard I refer to my Curriculum Vitae (**LL1**).

Research

8. The purpose of biomedical research is to use scientific methods to identify new methods and technologies to promote health and limit disease, disability and death.
9. In conducting biomedical research, researchers are obliged to protect their research subjects and to ensure that their research is conducted in a manner which meets ethical standards.
10. Provisions to protect research participants were first codified internationally after it was revealed that German doctors had conducted unethical research studies on vulnerable prisoners in the Nazi concentration camps during the Second World War. This led to the adoption of the Nuremberg Code, which sought to regulate the conduct of biomedical research to protect research participants.
11. The Nuremberg Code has laid the basis for an extensive literature on the ethical conduct of research involving human subjects. The World Medical Association Declaration of Helsinki: Recommendations guiding physicians

in biomedical research involving human subjects is of great importance in this regard. It was adopted at the WMA Assembly in 1964 and revised in 1975 (Tokyo), 1983 (Venice), 1989 (Hong Kong), 1996 (Somerset West) and 2000 (Edinburgh) with Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002 (attached as **LL2**). Another international document of great importance is the Council for International Organizations of Medical Sciences International Ethical Guidelines for Biomedical Research Involving Human Subjects, updated in 2002. This document is in the public domain and can be made available to the court upon request.

12. In South Africa, the Department of Health has published *Guidelines for Good Clinical Practice in the Conduct of Trials in Human Participants in South Africa: Clinical Trial Guidelines* (July 2000); *Ethics in Health Research: Principles, Structures and Processes* (2004); and a pamphlet for prospective research participants, *What you should know when deciding to take part in a clinical trial as a research participant* (2002) (**LL3**). In addition, the South African Medical Research Council has published *Guidelines on Ethics for Medical Research*, which have recently been updated. These documents are in the public domain and can be made available to the court on request. They are accepted South African guidelines for ethical standards in the conduct of health research involving human subjects. They were based upon the International standards to which I have referred above.

13. Common to all these guidelines is the following
 - 13.1. Any clinical trials should be conducted in ways that meet ethical standards.
 - 13.2. In particular, clinical trials should ensure that there is no exploitation of research subjects and that study procedures do not cause harm to participants or to related groups.
 - 13.3. All research participants should be able to make an informed decision as to their participation in the study. To do so, they must be provided with sufficient information to do so without coercion or undue incentives.
14. Where existing treatments are available and in use for a particular condition (termed the 'standard of care'), new methods for the treatment of this condition may be tested on human subjects only if there is sufficient evidence from animal studies or other data sources that the new treatment is likely to be as efficacious or more efficacious than the existing treatment. This condition is termed clinical equipoise. The presence of clinical equipoise is the *sine qua non* for any trials of new therapy, which are usually conducted as trials in which one experimental group of participants receives the standard treatment while the second group of participants receive the new treatment. In the absence of evidence for clinical equipoise, conducting a study in which some research participants may be deprived of the standard of care is considered unethical and is not permitted in terms of ethical oversight unless the researchers are able to

meet stringent conditions for permissible exceptions, to the satisfaction of an Ethics Committee. The permissible exceptions would be where

- 14.1. Use of the new treatment that may be less efficacious than the standard of care causes minimal adverse effects that are entirely reversible; or
 - 14.2. Use of the new treatment that may be less efficacious than the standard of care is the only scientifically justifiable option for the control group in the study AND the anticipated benefits of the study substantially outweigh the risks to participants.
15. It is expected that all biomedical research involving human subjects will be subject to institutional ethical oversight, which will involve, at the very least, approval of the study protocol prior to initiation of any field studies, and monitoring of the conduct of the study.
 16. Typically, such institutional ethical oversight is provided by Research Ethics Committees (sometimes called Institutional Review Boards) of Universities, Nursing Colleges or Health Facilities where the researchers are based. In the private sector, Research Ethics Committees have been set up by the Medical Association and private groupings to perform this ethical oversight function for studies outside University or Health Service settings.
 17. All such Ethics Committees in South Africa operate in terms of the provisions of the National Health Act (sec 72 and 73), which prescribes how these Committees should consider, approve and monitor the conduct of

biomedical research in South Africa so that it complies with ethical standards.

18. In terms of the National Health Act, the National Health Research Ethics Committee has set norms and standards for the conduct of clinical trials, and the oversight required of ethics committees. These have been issued in the form of the Guidelines referred to above and represent the minimum standards to which all Ethics Committees in South Africa should adhere.
19. In my understanding, no distinction is ever made between the collection of pilot data in a pilot study and any other form of clinical trial, with regard to the obligation to obtain ethical clearance before commencing a trial. In all my research activities, I have never proceeded with pilot data collection without first obtaining approval to proceed from an appropriate ethical review authority.
20. In my view any graduate in the health professions, whether from South Africa or any other country, should be aware that biomedical research involving human subjects must receive ethical approval prior to conducting the study. Failure to know or to act upon such knowledge will reflect
 - 20.1. professional incompetence,
 - 20.2. willful misconduct, or
 - 20.3. severe impairment of the judgment of the practitioner

Professional advertising and claims to efficacy

21. In the biomedical sciences, it is well recognized that new treatments for various conditions may supersede existing treatments because of evidence of improved safety and/or efficacy emerging from new scientific discoveries.
22. The process by which new evidence translates into acceptance of new approaches to treatment throughout the profession involves processes of peer review, such as peer review of findings presented at conferences and in publications in scientific journals.
23. Diffusion of research findings may occur quickly in the case of public health emergencies or rapidly escalating and serious public health findings. However, no matter how rapidly such diffusion of research findings takes place, the hallmark of acceptance of findings in the public domain is the process of subjecting claims to efficacy to some form of independent peer review, which validates the findings, through publishing the findings in the peer-reviewed environment.
24. From my service on the Advisory Committee of Human Rights, Ethics and Professional Practice, first for the Medical and Dental Board of the Health Professions Council of South Africa (HPCSA) and currently for the HPCSA itself, I am aware that misleading claims made by practitioners with regard to therapeutic efficacy of a particular modality of treatment may constitute unprofessional conduct, particularly where the practitioner holds a vested interest in the marketing, sale or uptake of that particular modality of treatment.

25. Misleading claims to therapeutic efficacy of a particular modality of treatment or technology will violate the rights of patients to make informed decisions, and are an abuse of the professional's relationship with his or her patients. In my professional opinion the HPCSA would consider that misleading claims to therapeutic efficacy constitute grounds for a charge of professional misconduct.

Evidence that there was a clinical trial

26. I have been asked to review the publications which are attached as **LL4** and **LL5**. In my professional opinion these describe a clinical study on human subjects, and fall into the definition of a clinical trial as defined in sec 72(7) of the National Health Act. Two parts of the pamphlets explicitly describe the conduct of a study that uses systematic methods to answer specific questions about the efficacy of vitamins and other essential nutrients in treating patients with HIV:

- 26.1. "This new scientific approach has now been confirmed in a clinical pilot study. We present here for the first time the results of this clinical study in HIV infected patients who had developed advanced stages of AIDS. They received a combination of vitamins and other essential nutrients for a period of four weeks. None of the patients had received any ARV drugs prior to or during this nutritional program. The clinical condition of all patients significantly improved, including weight gain, decreased

lymph node swellings, healing of ulcers and other signs of recovery. These clinical improvements were paralleled by dramatic improvements in the production of immune system-related white blood cells. The blood test results conducted before and after four weeks of this nutrient synergy program showed significant increase in the body's defense cells, including lymphocytes, monocytes and other immune function cells." (LL4)

- 26.2. "We conducted a clinical pilot study in HIV-positive patients with advanced AIDS. The goal of the study was to show that vitamins and other micronutrients alone reverse the course of AIDS, even in its advanced stage. Thus, it was essential that none of the patients had received any ARV drugs before or during this nutritional programme. The nutrient programme consisted of vitamins, minerals, amino acids and certain other essential nutrients. Blood tests and clinical evaluations were performed at the start and after 4 weeks on the nutrient programme. The results of this pilot study were so profound after only one month that we decided to publish the data of the first 15 patients without delay. After the completion of the study a comprehensive report will follow." (LL5)

27. There is no way to characterize what is described above as anything other than a clinical trial.

28. I have read the affidavits of Ms Vellem, Ms Ngubo, Ms Ntsholo and Mr Ngqase which are attached to the affidavit of Nathan Geffen. In my opinion the experiences they describe are consistent with an attempt to conduct a clinical trial. The fact that respondents were asked to sign forms and that pictures were taken of respondents, explained by Ms Ntsholo as intended to demonstrate the efficacy of the treatment, are consistent with a clinical trial intended “to show that vitamins and other micronutrients alone reverse the course of AIDS ...” (LL5)

Ethical conduct of the trial

29. The affidavit by Ms Xoliswa Vellem indicates that she was asked to sign consent in a manner consistent with a clinical trial. However, her affidavit discloses a number of violations of the principle of informed consent:
- 29.1. She appears to have been asked for consent after information had been collected from her about her clinical condition.
- 29.2. She was not given information on which to make an informed decision. In particular, it does not appear that she was told that she was to be on a trial.
- 29.3. She was not given a copy of the consent form which she had signed. This is standard practice for any biomedical research.
- 29.4. None of the personnel involved in the research introduced themselves to Ms Vellem nor identified themselves in any written

documentation provided to her as a research participant. Again, this is standard practice for any biomedical research.

30. The affidavit by Ms Thembeka Ngubo indicates that she was asked to sign consent in a manner consistent with a clinical trial. Her affidavit discloses a number of violations of the principle of informed consent.

30.1. She appears to have been asked for consent after information had been collected from her about her clinical condition, a medical examination had been conducted and blood had been taken.

30.2. She was not given information on which to make an informed decision. In particular, she indicates that she was not told the purpose of the medicines she was given.

30.3. Ms Ngubo does not mention being given any written documentation on the study or a copy of the consent form.

30.4. None of the personnel appear to have introduced themselves to Ms Ngubo.

31. In addition, Ms Ngubo reports two violations of privacy which are unacceptable from an ethical point of view:

31.1. Being asked questions in the presence of a group is a violation of confidentiality required of any study.

- 31.2. Being asked to undress and having photographs taken is an extremely intrusive form of data gathering. It would be normal practice to indicate to a patient that this will happen, as part of the consent procedure before entering a study, so that they may decide whether they wish to participate.
32. The affidavits by Ms Ntsholo and Mr Ngqase are consistent with those submitted by Ms Vellem and Ms Ngubo in highlighting serious breaches of the ethical conduct of research related to informed consent and confidentiality. None of the respondents report being given current scientific information indicating that ARV medication is indicated in the treatment of patients with advanced AIDS and may have been able to improve their health. Indeed, it appears that at least some of the respondents were given information to the contrary – that ARV medication would harm their health. In addition, the affidavit of Mr Ngqase indicates that financial incentives appear to have been offered to secure participation and follow up of research subjects. The size of the incentive mentioned (R770) is substantial and would raise concerns about undue influence on participants' decision regarding informed consent.
33. There is also some evidence that the scientific validity of the study may be questionable.
- 33.1. The claim in the Dr Rath Foundation pamphlet that “none of the patients had received any ARV drugs before or during this nutritional programme” appears to be contradicted by Ms Vellem,

who indicated that she was recruited to a study having been on ARVs. There is no evidence that the researchers sought to verify participants' ARV status, or even were concerned as to whether they were or were not taking ARVs. A recent Cape Times report of 13 October 2005 (**LL6**) stated that at least two of the patients presented to the media by Dr Rath as being healthy on vitamins and micronutrients were actually on ARVs. If this were true of the patients included in the clinical study, it would completely undermine the scientific basis of the findings claimed from the study.

33.2. The manner in which data appears to have been collected, based on the affidavits of Ms Vellem, Ms Ngubo, Ms Ntsholo and Mr Ngqase, appears to be non-standardised and haphazard.

34. The relevance of weak scientific validity in a study is that no study that is so poorly designed as to be unable to provide meaningfully interpretable results should be considered ethical. Issues of scientific validity are considered by ethics committees inasmuch as they may compromise the ethical acceptability of a study and be grounds for disapproving a study.

Claims to therapeutic efficacy – professional conduct

35. In my professional opinion **LL4** and **LL5** describe a claim to therapeutic efficacy of vitamins and micronutrient supplements, as illustrated:

- 35.1. “Clinical Proof: Micronutrients Reverse the Course of AIDS!”
(LL4)
- 35.2. “World’s first scientific and clinical evidence that micronutrients alone dramatically improve clinical conditions and immune function of HIV/AIDS patients, increasing white blood cells, lymphocytes, monocytes, T-cells and CD4 counts*” (LL4)
- 35.3. “THE CLINICAL PROOF: THE HIV/AIDS EPIDEMIC CAN BE CONTROLLED NATURALLY” (LL4)
- 35.4. “No previously tested vitamins or ARV drugs have been able to show the reversal of clinical symptoms of AIDS as documented here. Moreover, all known immune system markers - not only CD4 counts – significantly improved within the short period of only four weeks!” (LL5)
36. No evidence is produced that such claims to therapeutic efficacy have been subjected to any independent peer review.

Ethical oversight

37. I have read the communication from the chair of the Research Ethics Committee of the University of Limpopo (formerly MEDUNSA), Professor du Plooy, who states that the study in question was submitted to his committee for approval, and that approval was not granted because various

concerns expressed by the Committee had not been addressed by the researchers (LL7).

38. It is fairly typical for the process of ethical approval of a clinical trial to involve iterative interactions between the committee and the researcher to clarify ethical concerns identified by the committee prior to granting approval. Researchers are aware that they should not proceed with the study until these concerns have been settled to the Committee's satisfaction and official notification confirms ethical approval of the study.
39. Prof. du Plooy indicates that there are many outstanding issues with regard to the protocol "and a myriad of technical questions" (LL7). Based upon the nature and context of the study, and the current standard of care for people living with HIV and AIDS, I expect that a number of the guiding principles for human subjects research that an ethics committee would consider may have been grounds for concern in the research referred to above.
40. In particular, I expect that one of the concerns of the Committee may have been whether the condition for clinical equipoise with regard to the equivalence of ARV treatment and vitamin/micronutrients had been adequately demonstrated. Had I been on an Ethics Committee considering such a proposal, this would have been a key concern for me, given my understanding of the current literature on HIV and its management. In the absence of evidence for equipoise, such a study would fail to meet ethical

standards since it would risk exposing study participants to harms that cannot be justified.

41. As indicated above, I would also have serious concerns about the use of financial incentives and how that would undermine the principle of informed consent.
42. It is standard practice for Ethics Committees to consider potential conflicts of interest on the part of the researcher. While such conflict of interest is not automatically grounds for disqualifying a researcher, such conflicts must be declared and considered by the Committee as integral to the ethics of the study. Dr Rath and the doctors associated with the Foundation appear to stand in an obvious conflict of interest with regard to any study seeking to evaluate the efficacy of vitamins and/or micronutrients in the treatment of persons with HIV/AIDS.
43. Whatever the basis of the ethical concerns that may have been expressed by the Committee, it appears that the study conducted under the auspices of the Dr Rath foundation did not have the approval of a recognized Ethics Committee.
44. It is illegal and unprofessional to conduct biomedical research with human subjects in South Africa without approval of a recognized Research Ethics Committee.
45. On the evidence I have seen, it is my professional opinion that the basic procedures of ethical approval of clinical research have been ignored, and

that the research is therefore in contravention of the guidelines for such research.

46. Regulation 34 under the Medicines and Related Substances Control Act 101 of 1963 requires that all clinical trials of unregistered medicines be registered with the Medicines Control Council.
47. According to Professor du Plooy (**LL7**), no evidence of such registration has been furnished to his committee.
48. Irrespective of whether the vitamins and micronutrients used in the clinical trials described in **LL4** and **LL5** meet the definition of a medicine under the Act, it is apparent from the way these vitamins and micronutrients are described by the Foundation, that they are intended to be used as therapeutic agents and are being marketed as such in the promotional material. I base this on evidence such as:
 - 48.1. “...the finding that the amino acid lysine in combination with certain other micronutrients can block the spread of viruses through the connective tissue of our body paves the way for the control of this disease...” (**LL4**)
 - 48.2. A research subject (“Marieta”) who claims “There is an alternative to ARV drugs and its working, I am the living proof that nutrients work ...” (**LL4**)
 - 48.3. “micronutrients alone dramatically improve clinical conditions and immune function of HIV/AIDS patients” (**LL5**)

49. These claims imply that micronutrients alone or in combination with lysine play a treatment role that is an alternative to existing drugs such as ARVs. The authors go further to provide a mechanistic explanation related to blocking the spread of viruses through the connective tissue. There is no way to interpret these claims other than as an agent for therapy. Most health professionals and the non-professional public would therefore understand these agents to be medicines.
50. It is illegal and unprofessional to conduct a clinical trial with human subjects involving medicines in South Africa without approval of the Medicines Control Council (MCC).
51. I am aware that the HPCSA has lodged a complaint with the SAPS against Dr Rath Foundation for running unregistered practices in Khayelitsha.
52. In my opinion the absence of any peer-reviewed evidence, the self-advertising of these claims to efficacy, and the apparent vested interest of the Dr Rath Foundation in the efficacy of these treatments, would be grounds for the HPCSA to consider a case of professional misconduct against any medical practitioners involved with these claims who are registered with the HPCSA.

