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COMMENTARY ON UNAIDS 18 GUIDANCE POINTS

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BACKGROUND

Beginning in 1997 and continuing for two years, UNAIDS held regional and international deliberations and consultations concerning the issue of HIV/AIDS and vaccine research in particular. According to the organisers the purpose of such international consultations was 1) to further define important ethical issues and 2) to formulate guidance that might facilitate ethical design and conduct of HIV vaccine trials in the international context.[1] Although consensus was reached among the 85 participants[2] on some issues, a solution to the question of treatment for those infected with HIV during the course of trials was not attained. UNAIDS then decided to publish its own position paper and policy statement.

THE DEBATES: A SENSE OF URGENCY

The multi-national participants who took part in developing the document *Ethical Considerations in HIV Preventive Vaccine Research* were, among others, scientists, researchers, ethicists, lawyers, and members of activist groups. Implied on the part of those coming from developing worlds, is that their ability to act – the power to intervene in a sequence of events and so change their direction – and the power to act in pursuit of positive goals was to some extent compromised. This is because they came to the table with a sense of urgency based on real and practical experience of what it means to live with the dying and without, for a myriad of reasons, adequate health-care resources. The developed world

[1] D. Guenter, J. Esparza and R. Macklin. Ethical considerations in international HIV vaccine trials: summary of a consultative process conducted by the Joint United Nations Programme on HIV/AIDS. *J Medical Ethics* 2000; 26: 37–43.

[2] J. Cohen. No Consensus on rules for AIDS vaccine trials. *Science* 1998: 281.

participants, on the other hand, with even the consideration of good will granted, came in a power position with functioning medical care systems, funds and scientific expertise, negotiating for whatever they thought would result in the best overall arrangement for them. That consensus was not reached on all the issues is not surprising. The reasons for this may be identified at least in part by looking at the participant groups. They included those from 'North' and 'South' essentially politically mobilised into categories of 'difference'[3] such as economy, nationality, ethnicity, 'race', gender and sexuality. Yet, diverse as these factors are, it appears that the disparity in their particular 'differences' (and this is to be celebrated) did not override meaningful dialogue: they were moral agents face to face under conditions of physical and moral proximity bound by an over-arching moral issue. According to Guenter et al., all rising disagreements (and thus no consensus) sourced from one implicit factor – that of economic disparity. The participants, in other words, differed in their perceptions of what justice requires: specifically, what rich nations owe to poor ones, what sponsors owe to poor countries in which they carry out their research and what researchers owe to their trial participants.

The recent movement (although not totally inclusive) to take bioethical and research issues into international debates is a new and welcome process in the history of medical research. One may hope that the reason for this is the realisation that the best interests of developed countries are always the interests of some community or another[4] including developing countries. I suggest that the playing field was more level than commonly perceived. In the face of HIV/AIDS, even in the industrialised West, where it is now generally treated as a chronic condition, the role of pharmaceutical companies in vaccine development was hindered by research that initially went in the wrong direction,[5] as well as by the interest in financial gain.

Nonetheless, looking back on the debates from a moral perspective, they took place in the social space of 'being with', the beginning of what Vetlesen[6] refers to as the 'we-experience', conceived as the responsibility for others, which represents, in addition, a capacity. The challenge will be for all players,

[3] N. Fraser. 1997. *Justice Interruptus.* New York and London. Routledge: 11.

[4] H.F. Haber. 1994. *Beyond Postmodern Politics.* New York. Routledge: 5.

[5] B. Schoub. 1994. *AIDS and HIV in Perspective: A guide to understanding the virus and its consequences.* Cambridge. Cambridge University Press: 65.

[6] A. J. Vetlesen. Why does Proximity Make a Moral Difference? *Praxis International* 1993; 12: 371–386.

including institutions such as UNAIDS, to move to the next position, the moral act of 'being for'. [7]

THE 18 GUIDANCE POINTS

Without going into the details of every guidance point, it could be said that, overall, the UNAIDS document appears flexible enough to accommodate the specifics of a given research project in a given setting. While the title addresses specifically 'HIV preventive vaccine research', the guidance points are loose enough that almost any research topic, for example 'childhood leukaemia vaccine research' could be substituted. A major hurdle, however, is that without the knowledge of the specifics of a particular HIV preventive vaccine research (e.g. the relative risk of contracting the disease from the vaccine) it is difficult to assess in depth the ethics of such research projects. Certainly, politically correct words are in abundance although their impact is diluted with phrases such as 'where relevant'. As an example, Guidance Point 7 states, 'Where relevant, the research protocol should describe the social contexts of a proposed research population (country or community) that create conditions for possible exploitation or increased vulnerability among potential research participants...' Applying to all research projects I would consider the 'social context of any research population ... possible exploitation and their increased vulnerability' to be relevant across the board and in all countries.

Let me conclude with Guidance Point 18, the inclusion of children[8] in clinical trials. As the topic develops, however, other common problems, such as Guidance Point 16 (to, as an ideal, 'provide for the best proven therapy and the minimum to provide the highest level of attainable care in the host country') and Guidance Point 13 ('Special measures to protect persons who are, or may be, limited in their ability to provide informed consent') will be briefly discussed. Before this topic is developed, and because it is inter-related, we are obliged to detour and overview phase III vaccine testing.

[7] Z. Bauman. 1993. *Postmodern Ethics*. Oxford. Blackwell Publishers: 185.

[8] Guidance Point 18, in its vagueness, does not specify the age group included in the broad category of 'children'. Do we follow the WHO classification of a 'child' defined in Article 1 of the WHO Convention on the Rights of the Child as all 'human beings under the age of eighteen years unless the law applicable to the child, majority is attained earlier' or perhaps follow the US National Institute of Health's (NIH) classification of a child as a human being 0 to 12 years, or leave it to local determination?

PHASE III VACCINE TESTING

HIV/AIDS vaccine development in phases I and II have moved to a stage where candidate vaccines (efficacy trials, phase III), may be implemented. Such trials are by design randomised, controlled, long-term and implemented on a large-scale. With developing worlds demonstrating the highest rates of HIV/AIDS infections, currently estimated at 95% of the total number of cases reported world wide,[9] it is only natural that developing countries be the playing field for this phase of vaccine research. This is because in order to measure the success or failure of phase III clinical trials there are certain prerequisites: (1) populations are needed where new infections are common and (2) where, despite intervention, the incidence of acquisition remains consistently high. To determine vaccine efficacy, the incidence of new HIV cases in both the vaccinated group and the control group are then evaluated. This is a moot point, for the need to acquire HIV may be conceived to place bias on the researcher who must prove the vaccine's efficacy. Simply stated, the vaccinated group must practice or be subjected to unsafe behaviour such as unsafe sex /unsafe needle-sharing in order to acquire HIV, to identify if that particular HIV vaccine works. Yet, at the same time, the researcher is morally bound to promote conditions of safety for trial participants such as 'risk-reduction counselling and access to prevention methods' (Guidance Point 13). To ensure the success of the vaccine trial, the choice of research participants becomes critical. What better group to include than the young?

INTO THE FRAY

The ethical position concerning inclusion of children as research participants was clearly defined by the Nuremberg Code in terms of consent.[10] Because (informed) consent is morally required for research, all participants must have the ability to give their (informed) consent. Children cannot give free informed consent therefore children are excluded from research. The Declaration

[9] WHO Current HIV Epidemiological Statistics at http://www.who.int

[10] US Government. Trials of War Criminals before the Nuremberg Military Tribunals Under Control Council Law. Nuremberg, October 1946-April 1949. Number 10, Volume 2. Washington DC. US Government Printing Office: 181–182.

of Helsinki (revised 2000)[11] disallows non-therapeutic research on non-consenting subjects.

It would seem obvious that protection of children should be a moral imperative, but history has proven otherwise. No animal other than Homo sapiens knowingly places its young alone in perilous positions. No animal other than Homo sapiens so disvalues a blood member of their species that they are considered expendable. We have all read the stories: children killed or tortured by police, targets, refugees, perpetrators of violence, receivers of oppression – and to this litany do we now add children – prime candidates for HIV phase III vaccine trials?

With an HIV preventive vaccine, where the procedure is of no direct benefit to the child, the risk to the child should be so minimal as to be little more than the risks run in everyday life. Risks of research in this milieu include the threat of causing physical disturbance, discomfort, anxiety, pain or psychological disturbance to the child or his/ her parents rather than the risk of serious harm, which would be unacceptable.[12] Yet there is an innate tension present in balancing the welfare and rights of children against the good that may result from research that has the potential to benefit future children and society, and not necessarily the present child. The prerequisite of informed consent without coercion has reduced the amount of research conducted with institutionalised or incarcerated persons but certainly in the case of children the notion of informed consent remains fragile. The consent of guardians, parents or by proxy may not correspond to what the child might choose if s/he had the ability to do so. To further complicate the problem, the very social circumstances and environment of decision-makers for children to consent to vaccine trials may be compromised by factors as simple as the historically based notion that all vaccinations are good (e.g. measles, polio) therefore this 'vaccination' is also good. The selection of children as participants in vaccine trials raises questions concerning distributive justice and asks if this is not simply exploitation of an assessable group that will carry, in the end, a disproportionate share of risk. How disproportionate the

[11] Declaration of Helsinki. Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects, adopted by 18th World Medical Association Assembly (WMA), Helsinki Finland, 1964; amended 29th WMA, Tokyo, Japan; 35th WMA, Venice, Italy; amended 41st WMA, Hong Kong, 1989; amended 48th WMA, Somerset West, Republic of South Africa, 1996; amended WMA, Edinburgh, Scotland, October 2000.

[12] Council of the Australian College of Paediatrics. Report on the Ethics of Research in Children. *Australian Paediatric J* 1981; 17: 162.

share of risk may be is made more explicit in Guidance Point 16: '…the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country…' Thus it is conceivable that children, an extremely assessable group, will be used as research participants and left to the wiles of an unknown 'highest level of care available in the host country' which might equal a minimum of care and treatment for HIV/AIDS and its associated complications.

CONCLUSION

> 'Every game has rules: it is not cynical but vital for them to be revealed. Only after that can we all debate and agree to change them'. (Roger Higgs)[13]

This is a superficial overview of the UNAIDS 18 Guidance Points for HIV preventative vaccine research. 'Superficial' because there is no single other ethical issue in biomedicine that can equal the complexity and pain of the HIV/AIDS epidemic which would take books upon books to begin to unravel. The UNAIDS guidance points, akin to general ethical guidelines, are meant to provide direction but are not necessarily explicit rules. They should be regarded only as a step to further debates. Since it was agreed that no consensus could be reached in the broad category of justice and therefore UNAIDS decided to publish its own guidelines, why did they not 'err' on the side of trial participants and state that the best-proven therapy should be provided for all? This is a major flaw, in my opinion. As I have suggested, the need for further medical research into HIV/AIDS and the development of a vaccine is a moral imperative for both developed and developing worlds. Viruses are not stable – the playing fields should be regarded as equal.

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[13] R. Higgs. Guest Editorial (2) (Guest editors: A.J. Pinching, R. Higgs, K.M. Boyd). The impact of AIDS on medical ethics. *Journal of Medical Ethics* 2000; 26: 3–8.