Joint Advocacy on HIV/AIDS Treatments, Microbicides and Vaccines

Background Paper

CANADIAN HIV•AIDS LEGAL NETWORK
RÉSEAU JURIDIQUE CANADIEN VIH•SIDA

Joint Advocacy on HIV/AIDS Treatments, Microbicides and Vaccines:
Developing an Agenda for Action

Background paper

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PREFACE

In July 2002 the Canadian HIV/AIDS Legal Network, the AIDS Law Project (South Africa), and the Lawyers Collective (India) hosted a satellite meeting (with UNAIDS support) prior to the 14th International AIDS Conference in Barcelona. The meeting focused on access to treatments and HIV vaccines for developing countries. The meeting voiced agreement that vaccine advocates, treatment advocates, and microbicide advocates should work together in appropriate areas to advance a common agenda, and that their respective efforts would be strengthened by collaboration in areas such as information sharing, joint advocacy to improve health services and research infrastructure, use of human rights laws and enhancement of funding. To take this idea forward, the Canadian HIV/AIDS Legal Network initiated a project to explore these issues further and to foster greater coordination between vaccine, treatment and microbicide advocates.

This paper proposes discussion points relevant to the development of a plan of action to support collaborative advocacy. It was informed by a meeting of community advocates and global experts from the three fields held in Montreal from 17-19 November 2003. The Montreal meeting reviewed a draft version of the paper and made suggestions for improvement. The assistance of the numerous advocates working in the fields of HIV treatments, vaccines and microbicides who provided input to the drafting of this paper is gratefully acknowledged.

Based on the recommendations of the Montreal meeting, the Network has produced the following related documents (also in French and Spanish), available on the Network's web site:

- **Issues Paper**: a shorter, more accessible version of the Background Paper for advocacy organizations and individuals involved in HIV vaccine, microbicide and treatment activism.
- **Statement of Commitment:** a joint commitment to advocate for a comprehensive response to the HIV/AIDS epidemic, based on principles such as the prevention-care-treatment continuum and the human rights-based approach.
- **Plan of Action for Advocacy on Treatments, Microbicides and Vaccines against HIV/AIDS:** sets out twelve objectives and strategies for treatment, microbicides and vaccine advocacy, and identifies opportunities for advocacy at global, regional and national levels.

These documents will be launched at the 15th International AIDS Conference, Bangkok, 2004.

EXECUTIVE SUMMARY

HIV treatments, microbicides and vaccines are not in competition. Rather they are complementary components of a comprehensive approach to combating HIV/AIDS.

Advocates share the common goal of the promotion of the human right to the highest attainable standard of health of people living with HIV/AIDS and HIV/AIDS affected communities.

Added value is likely to be gained by advocates from the three fields joining forces particularly in the following areas:

- Action on strategic policy initiatives at the global and regional level:
    - Enhanced support by donor governments for product development initiatives that address the priority health needs of the global South
    - Equity pricing for HIV/AIDS treatments and other essential health products
    - Bulk procurement mechanisms for HIV/AIDS treatments for low and middle-income countries that can be adapted for procuring vaccines and microbicides when required
    - Enhanced funding to support purchases of global public health goods and scale up of delivery systems in the South.

- Action on law and policy at the national level:
    - Development of comprehensive national plans that support R&D and access to treatments and new prevention technologies
    - Implementation of price control measures and support for generic competition so as to ensure affordability of essential treatment and prevention products
    - Scrutiny of trade and investment agreements to ensure that public health is not compromised by 'TRIPS-plus' intellectual property provisions
    - Initiatives to build the capacity of regulatory authorities in low and middle-income countries
    - Coordination between sponsors of vaccine, microbicide and treatment trials to address issues relating to trial planning, community preparedness and competition for trial site capacity.

- Action on operational aspects at the local level:
    - Integrated community education programs in countries hosting large or multiple prevention trials, focused on vulnerable communities and people living with HIV
    - Adopting approaches that ensure prevention trials support treatment scale up at trial sites
    - Developing ethical review capacity at trial sites and supporting community involvement in development, application and review of ethical standards.

- Development of new models for collaborative advocacy so as to secure maximum benefits from strategic opportunities for progressing common agendas including:
    - Building World Health Assembly support for a new pro-South deal for global health R&D
    - Submissions to the WHO Commission on Intellectual Property Rights, Innovation and Public Health
    - Targeting WTO delegates and WIPO to influence the evolving global IP regime
    - Proposals on key global R&D and access issues to submit to the G8 summits
    - Input to the UN Millennium Project
    - Input to the work of the UN Special Rapporteur on the Right to Health
    - Work with UNAIDS to ensure that monitoring of compliance with the Declaration of Commitment on HIV/AIDS supports R&D and access agendas
    - A program of work with HIV organizations & people living with HIV groups to support their role in community education on access and R&D issues.

Part I The advocacy environment

Chapter 1 Premises of this paper

1.1 The primary audience for this paper is community advocates

This report will focus primarily on exploring the common agendas of treatment, microbicide and microbicide advocates who are working through organised NGO, not-for-profit and community based agencies.

It is hoped that this report will also inform the work of those who are active in the three fields in the public and private sectors, and the work of key multilateral agencies. It is acknowledged that there are passionate advocates within the scientific community and in the private sector, within national Governments, and within international bodies such as UNAIDS, the World Bank and WHO. Public research agencies such as the US NIH, the UK MRC, and the French ANRS have a history of leadership in research and development (R&D) efforts. Many people working within the framework of government responses to HIV/AIDS in countries in the global South, such as Brazil, Thailand, and Uganda, are also significant advocacy players.

The primary focus on NGO and community advocates recognizes:

- the unique role that this segment of civil society can play in adopting a vanguard role in shaping agendas;
- their capacity to be responsive to community needs and to ensure a 'bottom up' approach to issues that might otherwise be defined in 'top down' terms;
- the relative freedom of community advocates from the constraints of working within large public and private institutions, and hence their willingness to take greater risks in pressing for social, cultural and political change.

Agencies with an advocacy remit that are currently playing significant roles at the global level in the three fields include:

Vaccines: AIDS Vaccine Advocacy Coalition (AVAC), International AIDS Vaccine Initiative (IAVI).

Microbicides: Alliance for Microbicide Development (AMD), Global Campaign for Microbicides (GCM), International Partnership for Microbicides (IPM), International Working Group on Microbicides, International Family Health.

Treatments: Consumer Project on Technology, Health Action International, Health GAP, International HIV Treatment Access Coalition (ITAC), Médecins Sans Frontières (MSF), Global AIDS Alliance, and Oxfam. There are many other NGOs involved in global treatments advocacy including people living with HIV/AIDS groups such as the Global

Network of People Living with HIV/AIDS (GNP+), and regional groups such as the European AIDS Treatment Group (EATG), and the Pan African HIV/AIDS Treatment Access Movement (PHATAM).

This is not an exhaustive list. A short description of some of the major global advocacy organizations can be found in Appendix 1. Beyond these organizations, there are many other HIV agencies with an interest in advocacy on treatments and prevention technologies, including global groups such as the International Council of AIDS Services Organizations (ICASO) and the International HIV/AIDS Alliance, medical associations such as the International AIDS Society (IAS) and International Association of Physicians in AIDS Care (IAPAC), and national NGOs such as Treatment Action Campaign (TAC)(South Africa), Grupo Pela Vidda (Brazil), AIDS Access Foundation (Thailand) and Thai AIDS Treatment Action Group.

1.2 We need new tools and approaches

Globally there are very few, if any, social environments within which currently deployed treatment and prevention strategies are keeping HIV/AIDS in check. Difficulties are being confronted, even in wealthy low prevalence settings, as education and behaviour change efforts confront a complex range of behavioural challenges. Treatment side effects, drug resistance and treatment failure are a reminder that we need new and better ways to manage HIV disease. Cheaper, simpler treatment regimens, monitoring tools and diagnostics are urgently required to facilitate treatment scale up in resource poor settings.

Certainly part of the solution is to scale up those interventions we know already to work well.[1] Vaccines, microbicides and treatments all exist within the broader spectrum of HIV interventions such as behavioural and harm reduction interventions, and measures to address stigma. But new approaches and a broader range of options to fight HIV/AIDS are required and R&D efforts in the fields of vaccines, treatments and microbicides hold great promise to deliver powerful new tools for fighting the epidemic. Breakthroughs in immunology, genomics and other disciplines are transforming the possibilities for developing new biotechnological interventions against HIV/AIDS. New approaches are being conceptualized utilising both as yet unlicensed products and licensed products, such as antiretroviral therapies (ARVs) in new dosages or simplified combinations to increase adherence, reduce resistance and facilitate supply.

This Paper explores how, by working together, vaccine, microbicide and treatment advocates can:

- accelerate progress in developing new products and approaches; and
- ensure that interventions that are safe and effective against HIV/AIDS are made available and accessible without undue delay to those in greatest need.

[1] See eg J Stover et al. Can we reverse the HIV/AIDS pandemic with an expanded response? *The Lancet* 2002; 360:73-7.

This is not to suggest that any or all technological solutions will provide a magic bullet solution. Biotechnologies exist in and are shaped by social, political, cultural and economic contexts. Advocates need to be aware of the critique of over-medicalized HIV responses. For example, it has been suggested that "better understanding of 'the parts' including cellular and molecular mechanisms that cause disease, has brought with it the potential to marginalize broader discussions about the whole."[2] Structural interventions addressing social determinants of HIV vulnerability need to be pursued in parallel with scaling up R&D into biotechnologies. Purely technological solutions to social problems will not succeed without complementary measures to address profound factors that drive the epidemic, such as HIV related poverty, conflict and pervasive gender inequalities, and we need scaled up responses and new approaches to tackle these factors as well. Advocates from all three fields need to engage with broader political agendas regarding the social and economic contexts of the epidemic at the same time as pursuing their R&D and access advocacy goals.

1.3 Advocates face common, rapidly developing political contexts

Features of the political context that are currently shaping advocacy opportunities particularly in the North include biodefense policy responses to perceived anthrax and smallpox threats, and strategies to combat the emergence of SARS and other potential new communicable diseases. The rapidity with which the scientific and political communities responded to SARS provides us with lessons for HIV. There is growing realization in Northern constituencies that it is in the interests of people in rich and poor countries alike to be protected from and have access to treatments for diseases that are spread through increased global mobility.

The unprecedented attention drawn by HIV to the impact of diseases of poverty more generally in the South is in itself changing the context within which HIV advocacy operates. Increasingly HIV responses are grouped with tuberculosis (TB), malaria and other diseases of poverty (particularly since the advent of the Global Fund to Fight AIDS, Tuberculosis and Malaria)[3], and advocates are exploring the opportunities presented through building stronger alliances outside of HIV.

Political leadership plays a critical role in the success of current prevention and treatment responses, and will also shape how and when new treatments and prevention technologies are made available. Failures in leadership in the South are demonstrated by the denial of some governments, as reflected in delays in committing to and implementing a national treatment and prevention plans. Lack of leadership from Northern governments is evidenced by the continued prioritization of private interests in profit over public interest in health in bilateral and multilateral trade and investment agreements, and by the

[2] P Pronyk. *Social Capital and the HIV/AIDS Epidemic in Rural South Africa The New Magic Bullet?* London School of Hygiene and Tropical Medicine, Department of Infectious and Tropical Diseases 2002.
[3] See eg, *NIAID Global Health Research Plan for HIV/AIDS, Malaria and Tuberculosis,* National Institutes of Health, May 2001; *Programme for Action: Accelerated Action on HIV/AIDS, Malaria and Tuberculosis* Brussels: European Commission, 2001.

collective failure of donor governments to mobilize sufficient resources to address the global epidemic.

Discussion point

- *Advantages could be gained by advocates sharing intelligence about, analysis of, and planning for responses to critical external social and political developments, both between themselves and, collectively, with key external allies. For example, it may be useful to share information about strategies and priorities, and to plan collaboratively, in preparation for annual G8 meetings, World Health Assembly meetings, World Bank meetings and meetings of the UN General Assembly where HIV is on the agenda.*

1.4 Prevention and treatment are inseparable goals

The 2002 Barcelona AIDS Conference delivered two headline messages:

- That rapid scale up of ARV provision in resource poor settings is an achievable global priority
- That delivery of prevention and treatment are recognised as inseparable goals.[4]

The treatment-care-prevention continuum is now a widely accepted concept, but we are at an early stage in understanding the full range of preventive impacts of treatments. Aspects of the interrelationship include:

- Where treatment and care are available, the stigma attached to HIV may be reduced, meaning that people are more likely to come forward for testing, counselling and to access prevention services. There is evidence from pilot sites for the provision of ARVs in South Africa that reduction in stigma is associated with expanded treatment access.[5] Reduction in stigma provides a more supportive environment for prevention work in general and in particular it makes it easier to involve people with HIV in prevention strategies.

- Testing, treatment and care services can incorporate a range of prevention services.

- ARVs are used for prevention strategies, particularly in mother to child transmission and post-exposure prophylaxis (for rape survivors, health care workers and others). Studies have commenced to assess the preventive impact of providing uninfected people with a single daily dose of Tenofovir in an attempt to

[4] As articulated by Joep Lang, President International AIDS Society, in the Closing Plenary, 14th International AIDS Conference, 12 July 2002.

[5] "(At the Khayelitsha site) the synergy between treatment and prevention has been striking, with the availability of treatment providing a powerful incentive to learn one's status…. a recent survey of 9 sites around South Africa found that Khayelitsha had the highest rates of HIV testing, and desire to be tested among those who had yet to be tested, as well as the highest levels of condom use.": T Kasper et al, Demystifying antiretroviral therapy in resource poor settings *Essential Drugs Monitor* 2003;32:20-21 at 21.

block infection.[6] Clinical trials based on this approach are planned with HIV negative sex workers in Asia, gay men in the USA, and other high-risk communities in Africa.

- The lowering of viral load in individuals is predicted to make the transmission of HIV on average less likely per risk incident.[7] Hence, where ARVs (which suppress viral load) are readily available across a population there may be a public health benefit in terms of reduction of HIV incidence.[8]

The treatment-care-prevention continuum concept has been developed in the context of current prevention efforts such as voluntary counselling and testing, condom promotion and behavioural programs, rather than with the trialling, delivery or use of vaccines or microbicides specifically in mind. However, advocates point out that the relationship is similarly mutually reinforcing.[9]

- Investing in health infrastructure and training to bring expanded access to ARV treatments in developing countries can enhance capacity to trial (and eventually deliver) vaccine and microbicide products. This has been the experience in Brazil, where a long process of building laboratory, health care and community infrastructure to enable access to ARV treatments is providing a basis upon which vaccine and microbicide trials are able to proceed.[10]

- Treatment access programs strengthen the health sector, as health care workers gain skills, community confidence in services is generated, and there are reduced losses of health care professionals to HIV illness and deaths. A strong health sector that is accessible to and supported by local communities is important for delivery of an HIV vaccine.

- The conduct of large scale vaccine and microbicide clinical trials in low and middle-income countries presents opportunities to build health care infrastructure, train staff, and improve and expand treatment and care services for communities that are hosting trials.

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[6] K Kresge. *Tenofovir as Pre-Exposure Prophylaxis*. American Foundation for AIDS Research, May 2003; Weaknesses of ARVs as a pre-exposure prophylactic include sustainability, cost, deliverability and side effects, but these barriers may not be insurmountable. There are also concerns about the behavioural impact of use ARVs as a prophylactic.

[7] T Quinn et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *New England Journal of Medicine* 2000; 342(13): 921-29.

[8] M Musicco et al Antiretroviral treatment of men infected with HIV type 1 reduces the incidence of heterosexual transmission *Archives of Internal Medicine* 1994: 154: 1971-1976; Ethically controversial randomised control trials to evaluate impact of ARVs on risk of transmission between sero-discordant couples are planned by NIH: see HPTN 052 study at www.hptn.org/research_studies/study_details.asp

[9] See eg. P Weidle et al. HIV/AIDS treatment and HIV vaccines for Africa. *Lancet* 2002; 359:2261-67.

[10] P Teixera. Brazil: a New Paradigm for Vaccine Development and Access to Treatment, in *Vaccines for the World: Working Together to Accelerate Development and Delivery* IAVI, October 2002, at 4.

- HIV vaccine research is likely to lead to the development of both therapeutic and preventive products.[11] Vaccine research focusing on cellular immunity may lead to development of therapeutic vaccines for people living with HIV that reduce progression of HIV illness, as well as reducing onward transmission of HIV.

Treatment and prevention are not always depicted as complementary. Some argue that improved treatment prospects will lead people to become less fearful of infection and therefore more likely to engage in high risk behaviour. There are a number of studies that show HIV treatments optimism is associated with unprotected anal intercourse among gay men.[12] Although an association can be demonstrated, there is insufficient evidence to conclude that treatments optimism is a significant factor driving increases in the rate of episodes of unprotected intercourse recently seen in gay communities in the US, Europe and Australia. Further, the optimism thesis presupposes control over one's own risk behaviour. The thesis does not apply, for example, to the risk behaviour of a monogamous woman who lacks the power to refuse unprotected sex with her partner.

Economic arguments have been advanced as to the benefits of prioritizing prevention over treatment in high prevalence settings, given that prevention is almost always, in the short term, cheaper than treatment.[13] These have been rebutted on a range of grounds. French economist Jean Paul Moatti persuasively argues that it is more expensive *not* to treat HIV/AIDS in poor countries than to treat it, pointing out that in Brazil the cost effectiveness of treatments has been amply demonstrated through savings to hospital budgets. Moatti argues that the macroeconomic impacts of HIV have been systematically underestimated, as depletion of the workforce and erosion of social infrastructure due to HIV illness and deaths can be economically devastating.[14]

It is clear that prevention alone will not address the immediate consequences of the epidemic in terms of illness, deaths and orphans. There is a clear moral imperative to provide treatment wherever possible. It is not an 'either/or' situation when the global community has the know-how and resources to do both at vastly enhanced levels.

The consensus reflected by the UN *Declaration of Commitment on HIV/AIDS,*[15] the work of the Global HIV Prevention Working Group[16] and a range of other global authorities is

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[11] Note however that vaccines are discussed in this paper chiefly as a prevention technology.
[12] International collaboration on HIV optimism. HIV treatments optimism among gay men: An international perspective *Journal of Acquired Immune Deficiency Syndrome* 2003;32(5): 545-550.
[13] A Creese et al. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence *Lancet* 2002; 359:1635-42; E Marseille et al., HIV prevention before HAART in sub-Saharan Africa. *Lancet* 2002; 359:1851-56; M. Potts, J Walsh. Tackling India's HIV epidemic: lessons from Africa *British Medical Journal* 2003; 326:1389-1392.
[14] J Moatti. *Expanding access to antiretrovirals in the developing world: the economic rationale.* Slide presentation at IAS Conference on HIV Pathogenesis and Treatment, Paris: July 2003 (www.kaisernetwork.org/health_cast/uploaded_files/slides_moatti_paris_071303.pdf)
[15] UN General Assembly Special Session on HIV/AIDS. *Declaration of Commitment on HIV/AIDS Global Crisis-Global Action.* New York: June 2001.
[16] H Gayle, Curbing the global AIDS epidemic *New England Journal of Medicine* 2003; 348:1802-1805; Global HIV Prevention Working Group *Global Mobilization for HIV Prevention: A Blueprint for Action*, July 2002 (www.kff.org/content/2003/200207/HIV_prev_report.pdf).

that a comprehensive HIV/AIDS treatment, care and prevention package needs to be delivered,[17] the elements of which are mutually supporting.[18]R&D into new prevention and treatment technologies, and preparatory efforts for future access to new products, need to be situated within this package.

1.5 A human rights approach is a common reference point for advocacy

The human rights approach to health and development provides a conceptual framework for linking advocacy in the three fields, and underscores the notion that access to prevention, care and treatment are rights to be positioned in a continuum rather than in opposition. A rights framework implies a unified vision of treatment and prevention goals, which is inclusive of vaccines, microbicides and treatments, and recognises the importance of continued support for education, behavioural interventions, harm reduction and other measures. It also reminds us that success or failure of R&D and scale up efforts must be measured from a pro-poor, community oriented perspective. Important aspects of a human rights based approach include:

- An emphasis on participation of individuals and communities in decisions affecting their rights
- The universality of rights, in that they are intended to be enjoyed by everyone without discrimination
- The responsibility of States to transfer the benefits of scientific progress and its applications[19]
- The concept of progressive realization of the right to health
- The centrality of the role of States in assuring the public health and addressing epidemic diseases.[20]

The imperative to scale up equitable treatment access derives not only from pragmatic and utilitarian considerations, such as the cost savings to the acute care sector and the economic imperative to preserve the workforce, but also from fundamental moral obligations (derived from theories of needs, rights and social justice[21]) and from the legal obligations of states to respect, protect, promote and fulfil human rights including the right to health. These obligations derive from international law (principally the *Universal Declaration of Human Rights* 1948[22] and the *International Covenant on Economic,*

[17] Essential elements of which are access to treatments, voluntary testing and counselling, services to test and treat STIs and TB, mother to child transmission interventions, education to support behaviour change, clean needles and syringes, male and female condoms, home and community care and support, measures to prevent transmission through medical procedures and blood products, and anti-discrimination measures.
[18] See also P Wilson et al. *Background Paper of the Task Force on Major Diseases and Access to Medicines Subgroup on HIV/AIDS.* NewYork: UN Millennium Project, April 2003.
[19] *International Covenant on Economic, Social and Cultural Rights* Article 15(b).
[20] D Patterson. *Resolving Legal, Ethical and Human Rights Challenges in HIV Vaccine Research.* Canadian HIV/AIDS Legal Network, 2000 at 7 (www.aidslaw.ca/durban2000/vaccinefinal.pdf).
[21] See eg, P Harris, P Siplon. *International Ethics, Environmental Change, and the Global AIDS Crisis: Precedents and Arguments for Action.* Oxford UK: Oxford Centre for the Environment, Ethics & Society, 2001.
[22] Articles 25(1) & 27(1).

Social and Cultural Rights 1966[23]), regional human rights agreements[24] and some national laws.[25]

The right to access HIV medicines is already acknowledged in international human rights norms.

International commitments to the full realization of human rights related to HIV/AIDS, including improved access to health services for people living with HIV/AIDS, are articulated in the UN General Assembly's *Declaration of Commitment on HIV/AIDS*[26], General Comments of the UN Committee on Economic, Social and Cultural Rights[27] and in resolutions of the UN Commission on Human Rights on the right to the highest attainable standard of health and access to medication.[28] The UN's *International Guidelines on HIV/AIDS and Human Rights* require States to assure access to affordable medications including ARVs and preventive technologies.[29] These obligations are shared between nations, and there is an obligation on wealthy nations to assist less wealthy nations in realizing the right to health.

In the context of patents, the statement in the WTO's *Declaration on the TRIPS Agreement and Public Health* (the Doha Declaration) that the TRIPS Agreement "can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all" is a further acknowledgment of the evolving importance of the right to health.

There is a significant growing jurisprudence on the right to health as a justiciable right, much of which relates to battles to win access to ARVs in Latin America and South Africa, such as the Treatment Action Campaign's victory in the *Nevirapine Case* in South Africa's Constitutional Court.[30]

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[23] Article 12. The right to health can also be derived from a range of other international treaties and covenants eg Convention on the Rights of the Child Article 24; Convention on the Elimination of All Forms of Discrimination Against Women Articles 11 and 12.

[24] Article 16 *African Charter on Human and Peoples Rights*; Article 10 *American Convention on Human Rights in the area of Economic Social & Cultural Rights*; Article 11 *European Social Charter.*

[25] Over 60 nations include health rights in their Constitutions: P Hunt *Report of the Special Rapporteur on the Right to Health, Report to the 59th Session of the Commission on Human Rights*, February 2003,at 7.

[26] Supra, note 15 at Article 55.

[27] *General Comment 14: The Right to the Highest Attainable Standard of Health* 2000; Doc.E/C, 12/2000/4

[28] 2001/33, 2002/32, 2003/29

[29] See *HIV/AIDS and Human Rights International Guidelines, Third International Consultation on HIV/AIDS and Human Rights* New York & Geneva: OHCHR & UNAIDS, 2002. Revised Guideline 6 is reproduced below at Appendix B. States have been requested to report periodically on compliance with guidelines: UN Commission on Human Rights resolution E/CN.4/2003/29 (medications); E/CN.4/RES/47 (human rights generally).

[30] G Annas. The Right to Health and the Nevirapine Case in South Africa. *New England Journal of Medicine* (2003) 348:750-754; and for an overview of efforts to litigate the right to health see R Elliott. *Access to Treatment and the Human Right to Health: Recent Developments and Future Strategies* Montreal: Canadian HIV/AIDS Legal Network, June 2002.

The right to health implies that health goods and services should be available, accessible, acceptable and of good quality.[31] Hence a State's obligations to ensure access requires not only the development and implementation of an appropriate regulatory framework, but also public provision of essential products and services to people who cannot afford to purchase them.

A limitation of the rights approach is that obligations derived from international law rest principally, although not exclusively, with nation States, rather than corporations or individuals. States have a legal obligation to regulate the behaviour of non-state actors to ensure that human rights are not violated. To enforce health rights, citizens generally need to claim against States for failing to ensure access to essential health services through regulation, rather than by claiming against private corporations directly. This can be problematic given the global dominance of pharmaceutical companies in provision of treatments and medical technologies. Some non-State actors are working within human rights frameworks voluntarily (eg, corporations responding to pressure from consumer groups have adopted industry codes of conduct), but this is less satisfactory from a consumer perspective than imposition of international human rights obligations directly on corporations. The law is still evolving in this area and there is a gradual trend towards imposing obligations directly on non-state actors in other areas of international law such as humanitarian and criminal laws.

A further limitation of the rights approach is that the right to health is subject to progressive realization. This is a weakness in that states may seek to excuse limited progress by reference to budgetary concerns or other governmental priorities. This aspect of the right is currently being explored by the UN's Special Rapporteur on the Right to Health, and was an issue in the South African nevirapine litigation where the Government's obligation was described as to take reasonable legislative and other measures "within its available resources" to achieve the progressive realization of the right to access to health care services: the outcome would probably have been different had nevirapine not been available at low cost.[32] Immediate obligations derived from the right to health include the requirement to "take deliberate, concrete and targeted steps towards the full realization of the right, such as the preparation of a national public health strategy and plan of action".[33]

The Commentary on Revised Guideline 6 of the *International Guidelines on HIV/AIDS and Human Rights* states:

> "Universal access will be achieved progressively over time. However, States have an immediate obligation to take steps, and to move as quickly and effectively as possible, towards realizing access for all to HIV/AIDS prevention, treatment, care

[31] Supra, note 27,at para 12.
[32] G Annas, supra, note 30, at 352: The Court found that all branches of the government have the obligation to "respect, protect, promote and fulfil" the socioeconomic rights spelled out in the SA Constitution. The legislative branch is obligated to pass "reasonable legislative" measures, and the executive branch is obligated to develop and implement "appropriate, well-directed policies and programs."
[33] P Hunt, supra, note 25, at 9.

and support at both the domestic and global levels. This requires, among other things, setting benchmarks and targets for measuring progress." [34]

Advocates might benefit from developing detailed indicator sets to measure progress towards R&D and access objectives. UNAIDS has developed indicators for measuring follow-up of the *Declaration of Commitment on HIV/AIDS*. The UNAIDS indicator for R&D measures only public sector funding available for R&D on vaccines and microbicides[35], and there is no indicator for R&D on new diagnostics and treatments (see appendix B). More comprehensive indicators should be developed that measure private and public R&D investments in treatment, diagnostic and prevention technologies. There is no indicator to measure policy actions taken to support ethical conduct of trials or to prepare for access to and delivery of vaccines and microbicides.

It should also be noted that the human rights approach is far from universally accepted as the most appropriate approach to public health policy. In the US, the tendency of human rights discourse is to privilege civil and political rights over economic and social rights, particularly given that the US has not yet ratified the *International Covenant on Economic, Social and Cultural Rights*, and there is political hostility towards the concept of a right to health. In the African context, some commentators have argued that a pragmatic public health approach is required which sets aside Western sensibilities about human rights.[36] The dominant paradigm determining the development policies of many countries in both the North and South is neo-liberal economics rather than (and often in conflict with) a human rights approach, as reflected for example in the contents of bilateral and multilateral trade and investment agreements. This underscores the importance of advocates clearly stating their commitment to a human rights approach, and the rationale and implications for making that commitment.[37]

Discussion Points

- *A human rights perspective provides a powerful advocacy tool for progressing joint agendas through a globally recognised framework of laws and norms, and should be explicitly adopted as a common rallying point for advocacy.*

- *Advocates should develop a set of detailed indicators for measuring progress in R&D on treatments and new prevention technologies and measures to prepare for delivery and access to new technologies. This could be advocated as an evaluation tool against which progressive realization of the right to health is assessed. These indicators could be proposed for integration into the*

[34] Recommendation (b), at 15.
[35] See *Progress Report on the Global Response to the HIV/AIDS Epidemic2003.* Geneva: UNAIDS, 2003.
[36] Controversially it has been argued that "the emphasis on human rights…has reduced the importance of public health and social justice, which offer a framework for prevention efforts in Africa that might be more relevant to people's daily lives": K De Cock, D Mbori-Ngacha & E Marum. Shadow on the continent: public health and HIV/AIDS in Africa in the 21st Century *Lancet* 2002; 360: 67-72.
[37] See R Elliott *TRIPS and Rights International Human Rights Law, Access to Medicines, and the Interpretation of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights* Montreal: Canadian HIV/AIDS Legal Network, 2001 (www.aidslaw.ca/Maincontent/issues/cts/TRIPS-brief.htm)

monitoring and evaluation frameworks for the Declaration of Commitment and the Millennium Development Goals (see appendix B), and submitted to the UN's Special Rapporteur on the Right to Health (see 13.6).

- *Indicators could address progress towards:*
  - *Transfer of skills and technology to support growth of R&D capacity in the global South*
  - *Establishment of comprehensive local ethical standards and review processes especially with a view to support treatment access for trial participants*
  - *Investment in regulatory infrastructure sufficient to ensure timely approval and monitoring of clinical trials and rapid approval of new products demonstrated to be safe and effective*
  - *Trade and investment agreements and national patent laws that maximize developing countries' capacities to pursue autonomous public health objectives.*

Chapter 2 Characteristics of the fields

2.1 The advocacy movements

The separate vaccines, microbicides and treatments advocacy movements each have their own histories, agenda setting processes and political subcultures.

With a few notable exceptions, competition rather than collaboration has characterised relationships between the fields: competition for funds, political support, media attention, and for the high moral ground when presenting the respective merits of each cause. To an extent competition and stress between and within the fields has arisen as a by-product of the environment of chronic under-funding. There is growing awareness however that competition is unproductive, particularly given that many of the strategic policy barriers faced, such as regulatory pathways, patents and financing, are the same. In the US, for example, legislative lobbying has occurred involving a joint approach from vaccine, microbicide and treatment advocates.[38]

Core messages emanating from the three fields might be stated as follows:

Vaccines: A safe and effective vaccine is our best long term hope, as demonstrated by the dramatic public health benefits of previous immunisation programs; we need to maintain a long term view if we are ever going to succeed in turning the tide on the epidemic.

[38] *Promoting Development and Delivery of Preventive Medical Technology To Fight AIDS, Malaria and TB: Legislative Proposals for Consideration*. AVAC, IAVI, GCM, IPM, Alliance for Microbicide Development, Gay Men's Health Crisis, Malaria Vaccine Initiative, Alan Guttmacher Institute, Sequella Global Tuberculosis Foundation, March 2003 (available at www.avac.org/action.htm)

Microbicides: The HIV epidemic is largely driven by gender inequalities. Today's prevention options - condoms, mutual monogamy, and STI treatment - are not feasible for many people at risk, especially women. Many women do not have the social or economic power necessary to insist on condom use and fidelity or to abandon partnerships that put them at risk. Because microbicides would not necessarily require a partner's cooperation, they would put the power to protect into women's hands.

Treatments: We now have effective and affordable treatments for HIV/AIDS that could save millions of lives over the next few years. The international community must respond urgently on the necessary scale to avert a disaster unprecedented in human history.

These basic positions are by no means irreconcilable and advocates have increasingly recognized the need to value a comprehensive approach and have adopted more inclusive language. Nonetheless, by their nature the 'single issue' advocacy organizations can be expected, for the most part, to continue to give priority to their own agendas.

A treatment advocate's perspective (stated recently to the author) is: "Vaccine advocates have pitted themselves against treatment advocates, at least in the years 1996-2000. Arguments like 'a vaccine is the only solution' were very damaging to the cause of joint advocacy. Vaccine advocates have moved away from this, but the shift has not been wholesale, most still believe that a vaccine is more important than treatment access, and working together on treatment access is still very uncommon."[39]

Some treatment activists are dismissive of both microbicides (particularly after the Nonoxynol-9 trial results) and vaccines (after the poor results of the AIDSVAX efficacy trials).[40] Investing advocacy efforts in unproven technologies is perceived as carrying an opportunity cost. Time arguably could be better spent advocating for access to the treatments which we know work for most people most of the time. It is not encouraging for collaboration that early vaccine and microbicide products are likely to be only partially efficacious. This raises concerns that preventive technologies may lead to greater risk taking and more HIV transmissions rather than less.

To appreciate the factors that contribute to creating attitudinal barriers to collaboration, it is important to consider the histories of the movements and their constituencies of support.

Microbicides are predominantly being developed for women. The field originated from a body of scientific inquiry in the late 1980s regarding the potential efficacy of spermicides against HIV. Organised microbicide advocacy grew out of the sexual and reproductive health rights movement, particularly in the US and global South, and more recently the UK and Europe. It is no coincidence that most leading microbicide advocates are women,

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[39] Anon. informant.

[40] In the 1990s, four randomized controlled trials to evaluate different Nonoxynol-9 products in different settings failed to demonstrate a protective effect against HIV (see www.global-campaign.org/historyN9.htm); in 2003 results of the first phase III preventive HIV vaccine trial failed to demonstrate efficacy (www.avac.org/pdf/UnderstandingAIDSVAX.pdf).

who generally come to the movement with a strong background in feminist analysis. Unlike the treatment and vaccine fields, microbicides advocacy requires frank discussion about sex, which has ramifications in relation to political acceptability and campaigning style.

Microbicides are often depicted as the 'poor relation' of the other two fields and, as a largely untested product category, do not enjoy the same conferred validity as vaccines or treatments. Microbicide science is rarely accorded the status of other aspects of HIV medicine by the scientific community, and microbicides are given little prominence within major Conference scientific programs. Microbicides have not had the political champions that vaccines and treatments have had (such as Clinton for vaccines in 1997, Mandela for treatments in 2000). Sexism may well play a role in these factors. The microbicides movement has only very recently gained a level of political and financial support at the global level. Developments such as financial support from the Bill and Melinda Gates Foundation announced in 2003,[41] the establishment of the International Partnership for Microbicides, and the growth in US federal funding for microbicides from $27 million in 1997 to $88 million in 2003. These developments are products of consistent advocacy efforts over the preceding 5 years.

By contrast, vaccine advocacy has a long history of support from within the academic scientific establishment in countries such as the US, UK, and France, and maintains extensive direct links to medical research and mainstream public health communities. Public sector support has also been a feature of the field for the last decade in key Southern countries, particularly Brazil, Thailand, Uganda and more recently South Africa. The field tends to be more male dominated. To date, vaccine advocacy has lacked the natural relationship to community-based constituencies that microbicide and treatment advocates enjoy. Whereas microbicides advocacy has tended to link HIV prevention with sexual and reproductive health rights and women's empowerment,[42] HIV vaccine efforts are more closely allied with developments in HIV treatments, TB and malaria control efforts.

Vaccine advocates have faced a degree of hostility from the more established prevention community. This has arisen as a result of scepticism regarding whether development of an efficacious preventive vaccine is achievable, concern regarding the potential for adverse behavioural impacts of a partially efficacious vaccine, and the worry that many of the broader social and political benefits that have been associated with community mobilisation in support of behavioural interventions may be discarded if a vaccination strategy is adopted.

Vaccine and microbicide advocates confront barriers in generating support for the conduct of clinical trials. Both decision makers in the North and poor communities at trial

[41] *Bill Gates Giving $60M for HIV Research.* Associated Press, 31 March 2003. (www.aegis.org/news/ap/2003/AP030329.html)

[42] However, the current political realities in the USA are pushing the microbicide conversation away from reproductive health rights and the focus is increasingly on infection prevention: Polly Harrison, Alliance for Microbicide Development, personal communication, July 2003.

sites in the South have concerns about the potential for exploitative trial practices in what is perceived as a race to find a magic bullet prevention solution. There is a degree of mistrust and scepticism particularly towards vaccine and microbicide trials, which can be perceived as being highly experimental and are often not well understood by host countries. On the other hand, treatment trials are more often associated with a sense of hope and optimism, particularly where people have already seen the positive impacts of ARVs and improved treatments for opportunistic infections (OIs).

Treatments advocacy is heavily influenced by mainstream international development debates, and the politics of trade, globalisation and human rights advocacy. There is a strong culture of PLWHA participation in treatments advocacy, and the field is informed by almost two decades of radical activism. Many Northern activists can trace their roots to gay community responses to AIDS in the late 1980s. Over the last five years, mobilization of community based treatments advocacy in low and middle-income countries has gained momentum and the most groundbreaking treatment activism is now coming from the global South (eg, South Africa, Brazil and Thailand). There is an acceptance among treatment advocates of the need to at times adopt confrontational tactics such as civil disobedience, and the field has a history of strategic use of litigation to achieve policy objectives.

These different histories mean that the movements tend to use different advocacy language and have different external reference points to inform their decision making about priorities. It is important that advocates are conscious of and value these differences when seeking to engage in joint work, as recognition of the reasons for differing perspectives may make it easier to understand disagreements and to pinpoint areas where common interests are best served through working together.

2.2 Characteristics of the products[43]

Characteristics of the technologies also inform the nature of the agendas held by their advocates. The technical characteristics of the treatment, vaccine and microbicide products are quite different. This has important policy implications, for example in terms of regulatory burdens, financial requirements for R&D, private sector involvement, patentability, manufacturing requirements and delivery issues.

Fundamentally, the efficacy of HIV vaccines and effectiveness of microbicides are yet to be proved, and are unlikely to be for at least another 5 to 10 years. There is an obvious difference between vaccine and microbicide advocates, who seek support for untested products, whereas treatment advocates foremost concern is to secure greater access to existing approved products whilst simultaneously promoting R&D into new treatment options. To some extent this difference has reduced since the vaccine field had taken on board the need to promote expanded access to existing non-HIV vaccines as part of the

[43] M Gross, M Johnston HIV vaccines and topical microbicides: a complementary combination *Microbicide Quarterly* 2003; 1(1):5-9; and see R Gorna *Wishing on a Star: The Vaccines and Microbicides Race* Microbicides 2002 Conference, Antwerp, May 2002 (hdnet.org correspondent report).

agenda for preparing for delivery of HIV vaccines. However the distinction is fundamental to an understanding of the dynamics of, and between, the fields.

Emerging aspects of the technologies suggests a trend towards convergence in some areas of both applicable science and practical applications.[44] All three products will likely provide benefits for people living with HIV, as well as for prevention of new infections. Vaccines based on inducing T cell responses may reduce progression of HIV infection as well as prevent onward transmission; ARVs may prove to be effective as a preventive technology not just in the context of mother to child transmission but also as prophylaxis for high risk populations such as sex workers and for people in sero-discordant relationships; and ARVs may play a role in microbicide preparations.

Microbicides have the technical advantages of generally not being influenced by genetic factors or clades. Microbicides prevent viral entry, integration or the establishment of infection. By contrast, vaccines seek to stimulate immune function to either prevent primary infection or to control disease and reduce the likelihood of onward transmission.

Unlike microbicides, vaccines are disconnected from sex. Vaccines do not necessarily require sustained behaviour change to be effective. Unlike vaccines, microbicides and most treatments can be self-administered but require adherence to behaviour that supports effective use.

At the operational level, concurrent trials will increasingly be occurring (see Chapter 4 below).

Participation in microbicide trials entails regular use of the trial product over many months, the provision of detailed information about sexual practices, and use of a product that may be noticed by male partners. This suggests ongoing participant issues associated with microbicide trials of a qualitatively different nature to vaccine and treatment trials.

It is possible that vaccines and microbicides will eventually be rolled out in parallel. It can be anticipated that populations will be encouraged to use both vaccines and microbicides, with microbicides acting as the first barrier to HIV and protecting against other STIs. Microbicides may be available over the counter, whereas vaccines and treatments require access to a health care professional.

It is highly likely that the first preventive vaccine and microbicide products to be licensed will be only partially efficacious or effective in preventing HIV transmission, and condom use will of course continue to need to be promoted. If this scenario eventuates, there may be advantages gained by pursuing complementary product promotion and social marketing programs, and joint planning of behavioural education, social and epidemiological research and monitoring strategies.

[44] See M Gross , M Johnston, ibid.

Discussion points

Advocacy organizations should agree a Statement of Commitment to a comprehensive HIV response that is guided by a human rights approach. The function of such a Statement would be:

- *to educate internal and external stakeholders, including the media and general public, about the interrelationship of treatment and prevention advocacy*
- *to encourage use of inclusive language and non-competitive organizational cultures*
- *to refute arguments that prioritize prevention over treatment in high prevalence countries*
- *to acknowledge the specific role of biotechnological responses within the broader spectrum of behavioural and structural interventions and the status of products to prevent and treat HIV as global public goods*
- *to recognise the legitimacy of, and need for, a diversity of approaches, including recognising the importance of microbicides and vaccines in broadening the spectrum of choices available for prevention*
- *to highlight the importance of a human rights approach to advocacy on biotechnologies (as distinct from approaches based only on economic or utilitarian grounds).*

Part II Constructing the advocacy agenda

Chapter 3 Funding

3.1 Funding for global HIV/AIDS programs

It is common ground amongst advocates that funds available generally for HIV/AIDS programs in low and middle-income countries need to increase dramatically to support scale up of prevention and treatment. There have been recent advances on a number of fronts, notably the US Emergency Plan for AIDS Relief in Africa and the Caribbean,[45] the World Bank's Multi-country AIDS Program (MAP), and the EU's *Programme for Action on HIV/AIDS, Tuberculosis and Malaria*.[46] However, overall funding for HIV/AIDS programs in low and middle-income countries remains at less than half of the amounts estimated by UNAIDS as necessary to mount an adequate global response. Resource requirements are estimated by UNAIDS at $10.7 billion by 2005 and $14.9 billion by 2007, taking into account absorptive capacity. [47] Extra funds are required to fund expansion of capacity through investing in health infrastructure and personnel.

Despite additional commitments to the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) from the EU and US in 2003, total pledges to the Global Fund total only around $5 billion to be spread over the entire period 2002-2008, and an additional $3.5 billion needs to be raised to meet the Fund's expected disbursements in 2005 alone.[48]

More broadly, inadequate attention is being paid to the funding needs of communities facing rapidly escalating HIV and TB epidemics in South Asia, China, and the Commonwealth of Independent States of the former Soviet Union. Estimates of the Global HIV Prevention Working Group are that HIV prevention spending in developing countries needs to increase fourfold to reach adequate levels.[49]

It is particularly problematic that US international aid remains well below historical standards and far below other major donor countries as a percent of GNP, and US appropriations for international HIV programs for 2004 of $2.4 billion fall well short of the $3 billion per annum target set by the 2003 US legislation because of competing budgetary demands such as the cost of the Iraqi war and mounting US deficits.

In the light of these shortfalls, the significance of the UK proposal for a new International Finance Facility (IFF) to fund the UN's Millennium Development Goals (see Appendix

[45] The $15 billion five year US Plan was published in February 2004 and was authorised by the *US Leadership Against HIV/AIDS, Tuberculosis and Malaria Act* of 2003.
[46] *European Parliament and Council Regulation on Aid for Poverty Diseases (HIV/AIDS, Malaria and Tuberculosis) in Developing Countries* 2003.
[47] *Report on the State of HIV/AIDS Financing* Geneva: UNAIDS, June 2003.
[48] *Global Fund Observer Newsletter* Issue 10, 12 June 2003(www.aidspan.org/gfo/archives/newsletter); and see estimates of resource needs for 2005 on the Global Fund website (www.theglobalfund.org).
[49] H Gayle, supra, note 16; J Stover, supra, note 1.

B) merits closer attention. By raising funds through issuing bonds backed by donor commitments, the proposed IFF has the capacity to double the total amount of development assistance available globally from current levels of around $50 billion per annum to $100 billion per annum, and to ensure predictability of these enhanced aid flows for the next decade. The additional aid funds generated would be linked directly to achievement of the Millennium Development Goals, which suggests that a portion of the additional aid generated would be required to be invested in HIV, TB and malaria programs and measures to enhance access to essential medicines.

The IFF proposal received support at the Evian G8 meeting from France and is being further developed for consideration by the IMF and World Bank in 2004.[50] Concerns raised about the IFF include the choice of disbursement channels that would be used by donors, whether civil society in developing countries would have a role in deciding how aid will be distributed, and the sustainability of the arrangement past 2015. The UK proposal is that donors would nominate existing disbursement channels for the extra funds raised, such as the Global Fund or bilateral mechanisms.

The way in which conditionality is expressed and monitored in new development financing mechanisms such as an IFF may be crucial in terms of whether the funds are likely to be invested in health sector strengthening or HIV related programs by beneficiary states.

The IFF may provide an opportunity to fund a credible multilateral financing mechanism for the purchase and delivery of global public health goods such as vaccines, microbicides and treatments (eg, through the Global Fund or WHO).

In terms of debt relief, the Commission on Macroeconomics and Health[51] noted the success of the Heavily Indebted Poor Countries Initiative in allocating gains from debt relief directly to the health sector, and recommended increasing the number of countries included in the Initiative, and deepening the amount of debt reduction on offer. Similarly, the recommendations for implementing Revised Guideline 6 of the *International Guidelines on HIV/AIDS and Human Rights* call for debt relief to be implemented more quickly and extensively, and recommend that developing countries use a proportion of resources freed up by debt relief for HIV programs.[52]

HIV advocates may benefit by working more closely with civil society groups in advocacy regarding appropriate models for financing development assistance (eg, Jubilee and development NGOs). There may be advantages in HIV advocates pursuing these relationships as a bloc. This may enable HIV advocates to engage more fully in debates about new proposals such as the IFF and discussions regarding the increasingly

[50] See *Statement by Gordon Brown (UK) to International Monetary and Financial Committee.* Dubai, 21 Sept 2003 (www.imf.org/external/am/2003/imfc/index.htm).
[51] *Report of the Commission on Macroeconomics and Health: Investing in Health for Economic Development* Geneva: WHO, 2001 at 61.
[52] Recommendation (v), supra, note 29, at 20.

significant role of the World Bank as a major source of grants and loans for HIV programs in the developing world.

Governments in low and middle income countries should be held to account for national budgetary allocations for HIV/AIDS. Advocates in the South have a long history of challenging their governments for not giving HIV sufficient priority in national budgets as compared to items such as defence. HIV advocates could develop common minimum standards by which they hold Southern governments to account for increasing allocations to HIV scale up and health sector strengthening. This might be based on a benchmark approach similar to that adopted by the Commission on Macroeconomics and Health, which recommended that for low and middle-income countries an additional 1 percent of Gross National Product be directed to health by 2007 and 2 percent by 2015.[53]
A perceived barrier to joint work on advocating funding needs is the assumption that vaccine, microbicide and treatment advocates will not agree over an appropriate balance between treatment and prevention investments. There is little consensus amongst policy makers on how best to strike the balance and the terrain remains highly political. In the *US Leadership Against HIV/AIDS, Tuberculosis and Malaria Act* of 2003 for example, language was included to recommend that 55 percent of direct aid go to treatment programs, 20 percent to prevention, 15 percent to palliative care and 10 percent to orphan care. Potts and Walsh from the University of California assert that "money spent on antiretroviral drugs (in India) is money removed from prevention, and vice versa….. 21 of 28 countries receiving grants (from the Global Fund) will use this money to purchase antiretroviral drugs. These drugs are difficult to use (except to prevent mother to child transmission) and, even at the greatly reduced prices, are very expensive, especially when the necessary testing, monitoring, and counselling costs are included."[54]

A human rights approach would suggest that this is a false dichotomy and that 'either/or' approaches are seriously flawed. The emphasis should be less on the precise split of funds and more on funding processes ie, that they are transparent, accountable and facilitate disbursement without undue delay, and that richer countries make contributions to poorer countries proportionate to their respective capacities and in compliance with their international obligations to provide development assistance. In any event, advocates are likely to agree that precise apportionment of program funds will vary depending on the state of the epidemic in-country and that communities affected, including people living with HIV/AIDS, need to be actively involved in these decisions.[55]

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[53] Supra, note 51, at 6.
[54] M Potts, J Walsh. Tackling India's HIV epidemic lessons from Africa. *British Medical Journal.*2003; 326:1389-1392, at 1390.
[55] See eg, interview with D Zewdie, Director, Global HIV/AIDS Program for the World Bank, 29 April 2003 for International AIDS Economics Network (available at www.iaen.org): : "if you take, for example, the Sub-Saharan region… it will become very difficult to put more money on prevention and less money on treatment. Whereas if you take other countries where the epidemic is still very young, then the best option for that country might be to put more allocation on prevention."

3.2 R&D funding that prioritizes the health needs of the South

Far more money goes into R&D on treatments than prevention technologies. However most of this is private sector investment directed towards Northern markets and is not directed at specific needs for treating HIV and opportunistic infections (OIs) in resource poor settings. Microbicide funding remains at far lower levels than vaccine funding, and there is minimal private sector involvement in microbicide R&D. Vaccine, microbicide and treatment advocates have a common interest in advocating for a better global deal for R&D which is responsive to the public health needs of poor communities rather than market driven. Governments have a responsibility to invest in research and development of products that address the health needs of the poor. Strategies to support this may be to establish a specific R&D Fund, and to define R&D funding benchmarks required for compliance with the *Declaration of Commitment on HIV/AIDS* and the Millennium Development Goals.

The Global Fund to Fight AIDS, Tuberculosis and Malaria does not fund R&D as such. The strengthening of primary health sectors through Global Fund supported projects will potentially result in significant benefits for vaccine and microbicide developers, both in terms of trial and delivery issues. To supplement the work of the Global Fund, the Commission on Macroeconomics and Health recommended that a new health research fund be established, funded at a level of about $1.5 billion a year, to finance basic scientific research on diseases of the poor:

> "This fund would support basic and applied biomedical and health sciences research on the health problems affecting the world's poor and on the health systems and policies and policies needed to address them. A key goal … would be to build long-term research capacity in developing countries themselves, by providing vital funding for research groups in low-income countries."[56]

As there have been considerable difficulties experienced in raising funds for the Global Fund, it may be unwise to try to create another distinct fund in the current climate of donor fatigue. It may be more useful to focus on fundraising for existing research and product development initiatives.

Given the centrality of the Millennium Development Goals in informing donor priorities, reference should be made to the importance of extra R&D fund for vaccines, treatments and microbicides if the Goals regarding HIV, TB and malaria and access to medicines are to be met by 2015 (see appendix B).

In its role in monitoring implementation of the *Declaration of Commitment on HIV/AIDS*, UNAIDS conducts a periodic survey of financial resource flows through questionnaires distributed to countries with governments that provide funding to research institutions for R&D of vaccines and microbicides. This is intended to provide a proxy measure of the commitment of governments to HIV related R&D. Public funding from governments is

[56] Supra, note 51, at 192; Oxfam have also called for a global R&D fund as an element of their Cut the Cost campaign.

only a small fraction of the total expenditure on R&D. Public funding for HIV drugs is (by comparison to private funding) minimal and therefore not included in the indicator.

In recognition of the human right to share in scientific advancement and its benefits, the commentary on Revised Guideline 6 of the *International Guidelines on HIV/AIDS and Human Rights* recommends that States increase HIV related R&D funding to the public sector and encourage the private sector to undertake more R&D, paying special attention to the health needs of developing countries.[57]

It may be useful for advocacy purposes to provide a cost estimate for global HIV R&D needs for the next three to five years, coupled with related scaling up costs, premised on the need to bring multiple products into phase III trials at the same time as scaling up treatment provision in trial communities.[58] Estimates could be informed by the Commission on Macroeconomics and Health's analysis of R&D needs, which resulted in its call for:

- $1.5 billion in annual R&D funding through a new Global Health Research Fund for basic biomedical and health research; plus
- $1.5 billion in annual funding for existing vaccine and drug development institutions and public-private partnerships; plus
- increased outlays for operational research at the country level in conjunction with the scaling up of essential interventions, equal to at least 5 percent of country program funding (the investigation of interventions in practice, including issues of acceptability of treatment regimens, adherence, toxicity, dosing, and modes and costs of delivery).[59]

The Commission's analysis did not include estimates for microbicides R&D. The Microbicide Initiative estimated in 2002 that, if all candidate microbicide leads were owned by one company, at least US$775m would need to be invested over five years in product development costs to ensure a high likelihood of developing a safe and effective product.[60] This calculation does not include the discovery and exploitation of new leads, work on access and advocacy.

Discussion points

Treatment, microbicide and vaccine advocates should:

- *present a common agenda to donors regarding enhancement of funding to the Global Fund to sustainable levels, including advocating for national contributions to the Global Fund at a scale appropriate to meet the growth in demand for resources and in amounts proportionate to the relative size of each country's Gross Domestic Product.*

[57] Recommendations (o), (p), supra, note 29 at 18.
[58] The Alliance for Microbicide Development and IAVI are developing estimates for their fields.
[59] Supra, note 51, at 83.
[60] Pharmacoeconomics Working Group of the Microbicide Initiative, *The Economics of Microbicides: A Case for Investment*, New York: Rockefeller Foundation, 2002.

- *promote debt relief targeted at building health systems in low income countries*
- *develop common minimum standards by which to hold Southern governments to account for increasing budgetary allocations to prevention and treatment scale up and health sector strengthening efforts*
- *develop cost estimates for meeting global HIV R&D needs (eg, for the next five years) premised on the need to enhance basic research and to bring multiple products into phase III trials, and cost estimates for treatment and prevention scale up*
- *map resource flows relating to treatment and prevention provision so that resources can be better directed to ensure existing capacity can be better utilized and to rapidly expand capacity where need is greatest*
- *lobby for enhanced financing by donor governments of product development initiatives that address the priority health needs of the global South.*

Chapter 4 R&D and clinical trials

4.1 Basic research and preclinical studies

Advocates have a common interest in arguing for enhanced programs of publicly funded basic research in virology and immunology. Significant breakthroughs in immune based therapies or vaccines stand to benefit treatment and prevention fields alike.

There is a strong case for public support for basic research on therapeutic and preventive products to tackle the clades of HIV prevalent in developing countries. Public funds can be used to leverage additional private funds to be invested in basic research, or the public sector can fund and undertake basic research, handing emerging candidates over to the private sector for development, with conditions imposed regarding accessibility and affordability.

In addition to building on existing expertise in the North, long-term strategies need to be developed to address the 'brain drain' of research expertise from the South to the North. An important element of this is encouraging development of independent basic research capacities in centres of research excellence in the South, such as South Africa, Uganda, Brazil, Argentina, India, Malaysia and Thailand. Gaps in expertise in developing countries are generally most acute in the areas of pre-clinical development and animal toxicity studies.[61]

The Drugs for Neglected Diseases Initiative (DNDi) (see discussion of PPPs at 5.1 below) could make an important contribution to developing research capacity in the South by attracting funds to develop regional centres of research excellence.

[61] Y Yuthavong *Development and production of drugs for neglected diseases in endemic countries: A key to solving the medicines crises* MSF/DND Working Group, 2001 (www.neglecteddiseases.org/2-1.pdf)

4.2 Development of clinical trial infrastructure

Building the capacity of low and middle-income countries to conduct large scale clinical trials is a high priority for vaccine and microbicide researchers given the large cohorts required to demonstrate efficacy of preventive technologies. The issue of building clinical infrastructure is becoming of more central importance as more products move into phase III trials. Product developers are being confronted with difficult decisions on how to make best use of the limited trial infrastructure available.

Building trial site capacity will also facilitate trials of treatment strategies designed specifically for resource poor settings including simplified treatment regimens and simplified diagnostic and monitoring tools. By improving the local skills base and resourcing clinical services, development of local trial infrastructure will improve health care services. Opportunities exist to improve treatment, care and prevention provision for HIV, STIs, TB and malaria through development of clinical trial sites.

Gaps in expertise and infrastructure in developing countries need to be assessed in terms of the ability to conduct research at the level required to meet international minimum regulatory standards. There is a need for GLP (Good Laboratory Practice) and GMP (Good Manufacturing Practice) compliant facilities, and clinical centres need to be supported to perform studies to GCP standards (Good Clinical Practice). The capacity of institutions to provide effective oversight to trials is being stretched by the demands that rapidly widening research agendas place on Review Boards and Ethics Committees. Issues requiring systematic assessment include:

- pre-clinical capacities
- capacity to engage in community preparedness work, develop recruitment strategies and establish cohorts
- capacity to support participation of community representatives and people living with HIV/AIDS in trials through:
  - Community Advisory Boards or other participatory advisory structures
  - direct involvement in trial management
  - involvement in ethical oversight.
- capacity to conduct epidemiological, behavioural and social research
- increasing the number of scientists, clinicians, and health care workers trained in:
  - basic, clinical and behavioural research methods
  - data management and dossier preparation skills
  - assessing and acting upon ethical, human rights and community participation issues.
- Institutional Review Board/Ethics Committee capacities.

The challenge is not only to ensure that products developed initially by Northern sponsors can be trialled in Southern hosts, but also to build capacity for Southern countries to be able to exercise greater independence in conducting all aspects of R&D within their own countries. The longer term goal needs to be comprehensive transfer of skills and technology to regional centres of excellence in the South. This imperative arises not only

from pragmatic considerations, but also from international human rights norms derived from the right to share in scientific advancement and its benefits. This right is expressed in various international declarations including Article 27 of the *Universal Declaration of Human Rights*, the UN *Declaration on the Use of Scientific and Technological Progress*,[62] the *Declaration of Commitment on HIV/AIDS*, and Paragraph 7 of the *Doha Declaration,* which affirms "the commitment of developed-country Members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country Members".

Technical cooperation amongst developing countries is an essential component of capacity building. The development of South-South trial networks is important to encourage long-term sustainability of research capacities. Brazil, South Africa, India and Thailand currently have the expertise, good manufacturing practices and facilities required to manufacture drugs and vaccines that have been trialled elsewhere, as well as rapidly developing clinical trial expertise and infrastructures. They can act as a source of expertise for other countries in the South. Increased North-South collaboration will facilitate the introduction of best practice procedures and new clinical technologies.

Technology transfer from developed countries to developing countries does takes place but is often ad hoc rather than sustainable. The establishment of clinical trial centres and networks in developing countries (eg HVTN, HPTN), as well major new programs to build clinical trial capacity in poor and middle-income countries through the European and Developing Countries Clinical Trials Partnership (EDCTP) and investments by the US NIH in the Comprehensive International Program of Research on AIDS (CIPRA) are significant steps forward. The US Military HIV Program (Walter Reed Army Research Institute), which has a presence in East Africa and Thailand, is also committed to technology transfer. The Wellcome Trust, the Bill and Melinda Gates Foundation and other foundations are playing a role in bioethics and R&D capacity building in developing countries. Advocates from all fields need to assess the impact of these various capacity building initiatives, with a view to recommending how they may be better coordinated, targeted or expanded.

The EDCTP, launched in 2003, provides support for trials relating to HIV/AIDS, tuberculosis and malaria. The EDCTP's five year planning includes provision to establish a coordinating centre in sub-Saharan Africa, a capacity strengthening program, a €15m South-South network and a global advocacy element. Services to be supported by the Partnership within the EU include: joint planning and design of trials to improve their complementarity and comparability; stimulation of multi-centre trials; networking of laboratories and sharing of specialised facilities; facilitating access to Good Manufacturing Practice; and shared data management structures.[63] To promote coordination, EDCTP is developing a strategic clinical trials Action Plan that identifies the pipeline of interventions in development, the probable numbers per year, and the capacities of trial sites.

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[62] UN General Assembly resolution 3384 (XXX) of 10 November 1975.
[63] *EDCTP Strategic Plan Concept Document,* Vienna: EDCTP Steering Committee, June 2002 (edctp.cineca.org/edctp_concept_document.pdf).

EDCTP priorities for the South include development of research infrastructure, professional training, population censuses and mapping exercises, epidemiological studies, population awareness and cohort recruitment, support to local ethical review systems and support to long-term follow up of study subjects.

NIH's CIPRA program supports R&D in countries with an annual per capita income of less than $5000.[64] Major grant recipients are China's Integrated Research Program for Research on AIDS (Beijing and Tianjin), and the Collaborative AIDS Programme of Research in South Africa (Durban) and the 'Safeguard the Household' program (Soweto and Capetown). The Chinese project has both treatment and vaccine components, whereas the South African projects are oriented towards ARV treatments.

4.3 Opportunities and barriers to joint clinical trial efforts

Advocates have a common role in encouraging community involvement and transparency of trial programs such as those funded by EDCTP and CIPRA. Advocates might usefully focus on critiquing mechanisms for community participation in trial processes, such as developing locally owned Participants' Bills of Rights,[65] community advisory or management input mechanisms and identifying education and training requirements which will support community participation (including of people living with HIV/AIDS).

Prevention and treatment trials face common community engagement, preparedness and recruitment challenges. To date, community preparedness efforts have tended to be ad hoc and product specific. Cooperative approaches could rectify this.

Trials in the three fields also face common epidemiological, social and behavioural research needs, and there are similar challenges faced by long term follow up of subjects. Social and behavioural research needs include:

- Collecting contextual information, such as social risk factors and population vulnerability
- Attitudinal studies investigating belief systems and cultural values
- Social implications of trial participation and factors influencing willingness to participate
- Compliance of participants with trial requirements
- Behaviour change during trials
- Community mobilization and support for trials.

Consideration could be given to setting up long term trial sites that can host both vaccine and microbicide trials, which could also incorporate treatment and care components for the local population. The UK Medical Research Council's *AIDS Vaccine Research Strategy* notes the value of coordinating vaccine and microbicide trials, and flags the

[64] See www.niaid.nih.gov/daids/cipra/
[65] Eg, *South African HIV Vaccine Trial Participant Bill of Rights* (www.saavi.org.za/bill_of_rights.htm).

possibility of complementary trials.[66] This could lead to economies of scale in cohort recruitment and clinical facilities, and would present new challenges for trial design and management (integrated trials, parallel trials or trials linked by common behavioural research, epidemiological and governance components).

A significant concern for those conducting trials is how to address and negotiate competition for site capacity and the challenges of strengthening capacity in a systematic, collaborative way. Competition is likely to occur in finding enough recruits for phase II and III trials, as has been reported from sites in Uganda. Competition will also be faced over laboratory capacity, Institutional Review Board and Data Management & Safety Board (DMSB) needs, and regulatory requirements. The human and technical resources adequate to respond to the diverse demands that are placed on trial sites are likely to be in short supply. Capacity building efforts will reduce pressures for limited resources, but are unlikely to be able to keep pace with the demand generated by large-scale vaccine and microbicide trials.

All of these factors make joint advocacy efforts potentially difficult. Competition in the field is likely to have repercussions for collaborative advocacy. There may be discomfort in working together at the policy level if there are tensions between product developers on the ground.

To address the negative impact of competition in the field, dialogue between the main players in the conduct of clinical trials (eg NIH, MRC, IAVI, host country governments etc), on a rational system for according priority access to trial sites may be required. Multilateral agencies, WHO in particular, could take a role in facilitating discussions about how to resolve these dilemmas. At a more fundamental level this may require the willingness of funders and leading R&D agencies to agree to promote a culture of collaboration rather than competition in addressing global public health needs (as exemplified in the treatments arena by the DNDi). Funders are in strong position to leverage rational collaboration among competitors. The negative impacts of competition may be countered if the rationale for according priority to trialling a particular intervention is known, understood, and agreed by broader constituencies.

In the vaccines field, a Global HIV Vaccine Enterprise has been proposed that would bring the major global players in vaccine R&D together to prioritize the scientific challenges to be addressed, product development efforts and implementation planning.[67] This proposal draws from the approach of the Human Genome Project which involved many funders agreeing on a scientific road map, voluntarily dividing the work, and agreeing to an evolving set of production standards. Frequent sharing of progress and problems allowed coordination, cooperation, and internal competition.

Mapping out upcoming interventions in the R&D pipeline may need to occur regionally, with a view to forging consensus on the priority to be accorded to trials of products

[66] *AIDS Vaccine Research Strategy* London: Medical Research Council 2000, para 2.6.6; and see M Gross and M Johnston, supra, note 43.
[67] R Klausner The need for a Global HIV Vaccine Enterprise *Science* 2003; 300 (5628); 2036-2039.

showing greatest promise for addressing needs of poor countries. There is a case for formalising approaches to clinical trial investments at the international level to give greater priority to diseases of poverty and neglected diseases, for example, through new treaty initiatives relating to health or investment agreements. To some extent, the EDCTP is aiming to achieve this through coordination of trials in Africa funded by EU members. Although it is useful to maintain some degree of competition, greater coordination between US and European sponsored trial programs would be desirable to focus efforts toward common goals, reduce duplication and enhance opportunities for sharing facilities and expertise.

4.4 Ethical review capacity

Much work has been done in the last few years to define ethical issues involved in conducting research in developing countries, notably the UNAIDS vaccine ethics guidance document,[68] the UK Nuffield Council Report, the US National Bioethics Commission report and the Guidelines produced by CIOMS.[69] Efforts are now required to equip countries in the South to apply these frameworks and to engage in consultative processes with communities to develop guidelines that take into account local cultural and legal contexts.[70]

A threshold issue is the existence of a formal regulatory structure to support ethical conduct of trials, comprising a human research ethics committee for approval of the study protocol and a Data and Safety Monitoring Board (DSMB) to monitor study data for adverse events. Other structures that may input to decisions on trial ethical issues include Community Advisory Boards and community representatives involved in trial management and funding bodies. Lack of capacity to review trial protocols and grant trial approval is already causing delays to vaccine trials.[71]

Local communities need to have confidence that issues are appropriately addressed within these structures. Prominent issues to be considered relate to informed consent, confidentiality, compensation, guarantees of future local access to products which prove safe and effective, and the standard of care for prevention trial participants who seroconvert ('breakthrough' or 'intercurrent' infections). Advocates could benefit by agreeing a 'gold standard' to strive towards on these issues.

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[68] *Ethical Considerations in HIV Preventive Vaccine Research: UNAIDS Guidance Document*, Geneva: UNAIDS, 2000.

[69] *The Ethics of Research Related to Healthcare in Developing Countries*, London: Nuffield Council on Bioethics, 2002. (available at www.nuffieldbioethics.org/publications) *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries* Bethesda, Md.: National Bioethics Advisory Commission, 2001 (available at www.georgetown.edu/research/nrcbl/nbac/pubs.html); *International Ethical Guidelines for Biomedical Research Involving Human Subjects* Geneva: Council for International Organizations of Medical Sciences (CIOMS) 2002; see also European Group on Ethics in Science and New Technologies *Ethical Aspects of Clinical Research in Developing Countries* Brussels: European Commission 2003.

[70] For example, South Africa's Medical Research Council is developing HIV Vaccine Ethics Guidelines.

[71] Saul Walker, IAVI Policy Advisor, personal communication 12 August 2003.

Participation of people living with HIV in advisory, formal ethical review and management structures is as important for prevention trials as for treatment trials to ensure adequate resolution of ethical issues. Human rights and ethics training is a common requirement. Educational efforts should target vulnerable communities involved in trials such as sex workers and drug users so that they can better engage in discussion, debates and decisions on ethical issues. This will involve basic education about trial processes and product candidates as well as ethical standards and human rights principles, so that community members can engage meaningfully in review processes.

Mutual benefits would be gained from sharing practical approaches adopted by prevention and treatment trials to issues such as ensuring continuing informed consent throughout trial processes, 'community consent' issues such as involvement of community leaders in decision making, issues arising in use of placebo in control arms (rather than another product or intervention), and ethical responsibilities to sexual partners of trial participants. South-South information sharing on ethical issues should be facilitated.

4.5 Treatment scale up at trial sites

A human rights approach would suggest the need to link treatment scale-up with microbicide and vaccine trials, to ensure that the maximum health benefits flow to host communities. Research organizations can contribute to ARV scale-up efforts as part of a comprehensive response.

In 2002, the Pan African HIV/AIDS Treatment Access Movement called for pharmaceutical companies to provide free treatment for life for all participants in clinical trials and for WHO to develop international ethical standards to that effect.

There is an emerging consensus on the part of vaccine trial sponsors (including IAVI, NIH, HVTN and the Walter Reed Army Institute) that participants who become infected during a trial should be provided with access to ARVs, reflected at a consultation that IAVI and GCM convened on treatment in the context of prevention trials in February 2003. The consultation revealed substantial need for ongoing collaborative discussion of trial related ethical issues, and participants said that researchers and advocates from microbicides and other prevention fields should be involved in the UNAIDS revision of its ethical Guidelines for Vaccine Trials. [72]

Issues involved in treatment provision for trial participants include the mechanisms for provision over extended periods, how to link in with broader efforts to treat local communities, and determining who bears the cost and administrative burden of organising treatment and care. Concerns arise that ARV provision to trial participants could exacerbate inequities in local communities, and it is therefore crucial that local communities are involved in decisions regarding treatment provision. ARVs are usually not required for several years after infection and in many instances will not be required

[72] E Bass *Meeting Report: Consultation on HIV Treatment in the Context of Prevention Trials February 28, 2003,* Global Campaign for Microbicides & International AIDS Vaccine Initiative, 2003.

until long after the prevention trial has ended. Sustainable solutions to treatment and care provision at research sites are therefore required.[73]

Funding ARV treatment and monitoring will require funds to be provided by the trial sponsor, government, donor agencies or through novel arrangements such as consortia of pharmaceutical manufacturers, trial sponsors and local governments. It is also possible that an insurance provider could develop a liability policy to cover costs. Alternatively, a fund could be established in each participating country to provide treatment and monitoring.[74] These approaches could help resolve some of the difficulties facing developing countries that currently receive little benefit from research grants and that lack private health insurance or uniform healthcare.

UNAIDS hosted a meeting in July 2003 to establish consensus between organizations involved in prevention trials on care and treatment for trial subjects infected with HIV in the course of a prevention trial (including vaccine, microbicide or behavioural trials), as well as to build stronger links between treatment scale-up efforts and vaccine research. The meeting emphasised the need for shared responsibilities between trial sponsors, donors and governments to support R&D and to maximize the benefit of trial investments. Brazilian representatives at the meeting expressed the view that it is important that governments take up some responsibilities in providing treatment and care for people who become infected in prevention trials, or for continuation of treatment relating to ARV trials. [75]

4.6 Post-marketing surveillance

There is a need for large, randomized, long-term post-market studies to ascertain effects of new products over time on different populations. Post-market studies are required to ascertain the clinical risks and benefits of different treatment management strategies. Phase IV trials are particularly important in evaluating HIV treatments that have been given accelerated approval with small amounts of clinical data about the drugs' effectiveness.

Post-marketing surveillance will also be an issue for assessing the long term safety and efficacy of microbicides and vaccines. For public health and safety reasons, communities will want to track adverse events and continued adherence and acceptability. For-profit companies will also want to do so for market reasons. Studies could also track patterns of use and availability, and delivery through health and social infrastructures.

Advocates have a common interest in ensuring that both public R&D agencies such as the US NIH and UK MRC as well as private sector product developers are required by regulators to invest more in phase IV studies. Regulators rely almost entirely on data provided by product developers when determining safety and efficacy, and, despite

[73] See E Bass Ethics, Antiretrovirals and Prevention Trials *IAVI Report* 2003-2004; 7(3):3.
[74] A Ammann *HIV Vaccine Breakthroughs: Who Pays?* The Scientist 2003;17(2):16 (www.the-scientist.com/yr2003/jan/opinion_030127.html)
[75] Personal communications from David Patterson, August 2003.

ethical safeguards, profit motive can play a role in selection of favourable data for submission to regulators. Government and industry should support rigorous post-marketing surveillance studies by independent researchers and trial networks

Discussion Points

Advocates should work together on the following issues:

- *Encouraging transparency and collaboration in trial planning by trial sponsors.*
- *Developing new models for running concurrent, complementary vaccine, microbicide and treatment trials so as to achieve economies of scale.*
- *Scrutiny of community involvement aspects of major trial capacity building initiatives such as EDCTP and CIPRA.*
- *Advocating for greater investment in capacity to conduct social, behavioural and epidemiological research programs in the South that support concurrent vaccine, microbicide and treatment trials.*
- *Defining best practice approaches for ensuring access to treatment and care for breakthrough infections in prevention trials in resource poor settings. A key component of this will be ensuring that both trial participants and the communities within which trials take place benefit from enhanced treatment and care. A comprehensive model for provision of enhanced prevention, treatment and care at vaccine and/or microbicide trial sites should be developed.*
- *Advocating for support to Southern NGOs and community groups at trial sites to provide community education about new prevention and treatment products being trialled in their communities, paying particular attention to the rights of vulnerable communities such as sex workers and drug users to engage in discussion, debates and decisions.*
- *Support for establishment of community participation infrastructures applicable to both prevention and treatment trials, such as community advisory boards and other locally appropriate community involvement mechanisms.*
- *Initiatives to increase ethical review capacity, including human rights training, technical support and facilitation of South-South learning on issues such as informed consent, confidentiality, compensation and standard of care .*
- *Inclusion of people living with HIV/AIDS in trial management and advisory structures.*
- *Persuading regulators of the importance of post marketing studies, arguing for product developers to fund such studies, and educating communities about the importance of post marketing surveillance from consumer perspectives.*

Chapter 5 Strategies for stimulating strategic R&D

5.1 Public private partnerships (PPPs)

Much of the R&D expertise for treatment, vaccine and microbicide products is located within the private sector. Public-private partnership models are at an early stage of development and there is scope for sharing experiences and developing principles to inform effective partnerships and best practice models.

In the vaccine field, IAVI's model of social venture capital is providing a template for PPPs. IAVI funds and sponsors fast-tracked product development and clinical testing. Funding is provided to private partners in exchange for which IAVI obtains a degree of control over patent rights so as to ensure distribution of the product in developing countries at low cost (see 6.3).

In the microbicide field there are a growing number of PPP models. The IPM promotes PPPs for promising products. The CONRAD Program's Global Microbicide Project (GMP) provides funds for projects that usually involve a cost sharing arrangement with an industrial partner. GMP funding comes from a Bill and Melinda Gates Foundation $25 million grant. In the UK, the Medical Research Council Clinical Trials Unit and Imperial College London administer a Microbicide Development Project, which is seeking to trial microbicides in the UK and Africa manufactured by biotechnology companies.

In the treatment field, PPPs relating to HIV have been focused on discounts, donations and distribution programs rather than product development and clinical trials. For example, the Accelerated Access Initiative is a partnership between the UN (WHO, UNICEF, UNFPA, and UNAIDS) and six pharmaceutical companies (Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, Roche, GlaxoSmithKline and Merck) and negotiates discounted drug prices. The AAI has been criticised for being ad hoc, lacking long term sustainability and excluding participation of generic suppliers.

The Geneva-based Initiative on Public Private Partnerships for Health (IPPH) is developing models of best practice and may help inform the development of commonly supported principles. The Bill and Melinda Gates Foundation has also conducted considerable work on PPPs. Roy Widdus of the IPPH has observed:

> "True partnership is really about combining different skills, expertise and other resources- ideally in a framework of defined responsibilities, roles, accountability and transparency - to achieve a common goal that is unattainable by independent action. The health benefits of these social experiments must be maximized and potential risks minimized. The current crop of PPPs can in time yield a body of experience on which to construct evidence-based 'best practices'. Agreement on these may seem far-off but we can help build consensus now by rejecting

ideological suspicions, and pragmatically analysing the many existing and emerging efforts." [76]

Issues that arise in PPPs that vaccine and microbicide advocates could collectively develop principles for include:

- input from Southern communities and people living with HIV/AIDS into partnership arrangements
- governance models
- conflict of interest issues, particularly where not-for-profit NGOs partner with private corporations
- accountability and transparency
- measuring effectiveness of different models
- intellectual property arrangements which maximize developing country access.

5.2 Public R&D initiatives

An alternative model to PPPs is the development of capacity for innovation largely independent of the private sector. This model is particularly relevant for the most neglected diseases which have little or no market in developed countries. MSF, Oxfam and others argue that a new paradigm based on public sector leadership is required. The Drugs for Neglected Diseases Initiative (DNDi)[77] formed in 2003 is pursuing this model with the aim of establishing a publicly (and private foundation) funded research network for medicines for neglected diseases in the developing world.

Public bodies such as the US NIH, French ANRS and the UK MRC play very significant roles in basic research fields such as HIV pathogenesis, microbiology, immunology, virology, and animal model development. They can also develop product development facilities (such as the NIH's Vaccine Research Center) with capacity to engage in preclinical development and clinical trials. Public agencies provide a range of support to product developers including provision of access to animal models, funding clinical trial networks and assistance with product manufacturing.

5.3 Tax relief [78]

Tax relief as a strategy to promote R&D has been promoted particularly by vaccine advocates, but has potential benefits for the microbicide and treatment fields as well. However it can be argued that a more useful approach than tax relief is to invest funds

[76] R Widdus. Public–private partnerships for health require thoughtful evaluation. *Bulletin of the World Health Organization* 2003; 81(4): 235.
[77] Partners in the DNDi include MSF, WHO Special Programme for Research and Training in Tropical Diseases ,The Oswaldo Cruz Foundation (Brazil), Indian Council for Medical Research , Malaysian Ministry of Health, and the Pasteur Institute (www.dndi.org)
[78] See: C Collins S Morin *The Policy of AIDS Vaccines: Exploring Legislative Options for Advancing AIDS Vaccine Research and Delivery*, San Francisco: AIDS Policy Research Center & Center for AIDS Prevention Studies, 2001 at 11-14.

directly in public funded research programs rather than subsidizing private industry through the tax system. Some treatment advocates observe that tax incentives are unlikely to alter the dominant dynamic of the pharmaceutical industry, which is to secure profits to be gained from sales of treatments in Northern markets.

Two approaches to tax relief have been proposed to promote R&D on HIV technologies. One approach focuses on tax relief for expenditure on R&D during the product development phase (targeted R&D tax credits). The other approach only provides relief when and if the product is approved for marketing, and sales of the product occur (sales tax credits).

Both the US and the UK provide tax credits for general R&D on pharmaceuticals, and tax credits have been a feature of orphan drug legislation in the US and Europe. Credits have been deployed to foster investment and increase the competitiveness of pharmaceutical industries in the US, Japan and the UK, and are popular with industry. Tax credits increase the projected profitability of R&D and hence make it easier for bio-technology companies to attract venture capital. Recently attention has been focused on the benefits of specific additional targeted credits for R&D on HIV products.

There are UK precedents for use of tax credits to reward HIV R&D. In its 2002 budget, the UK introduced tax credits of 50 percent on expenditure on pharmaceutical research into medicines and vaccines for HIV, TB and malaria.[79]Qualifying R&D activity is defined to include R&D relating to 'vaccines for the prevention of infection by human immunodeficiency virus, or vaccines or medicines for the prevention of the onset, or for the treatment, of AIDS resulting from infection by HIV in prescribed clades only'. "Prescribed clade" means clade A, C, D or E or such other clades as the Treasury may prescribe.

The current wording of the UK tax credit is ambiguous, and one interpretation is that the credit targets R&D relating to therapeutic vaccines and HIV treatments for clades specific to the developing world, whereas qualifying R&D for preventive vaccines is not restricted to specified clades. It is unclear whether microbicides would fall within the scope of this provision as to do so they would have to be considered a 'medicine'. Extending targeted tax credits to microbicides could help in overcoming industry's current extreme reluctance to invest in the area.

The UK targeted tax credit is in addition to an existing 25 percent tax credit for qualifying R&D generally applicable in the UK. This model advantages R&D in that credits are received whether or not the product is marketed. The HIV, TB and malaria vaccine credit is estimated to provide benefits to around 50 companies in the UK, and the annual cost of vaccines research relief to the UK Government has been estimated at £10m in 2002-03, £10m in 2003-04 and £20m in 2004-2005.[80]

[79] Section 54 *Finance Act 2002* (UK) (www.hmso.gov.uk/acts/acts2002/20020023.htm#aofs)
[80] *Regulatory impact assessment for research and development tax credit for large companies/ vaccines research relief* London: Inland Revenue, 2002.

UK targeted tax relief will extend to expenditure sub-contracted overseas by UK companies, recognising that R&D carried out in developing countries is important for capacity building, and for R&D partnerships between industry, universities and bio-technology companies.

The US has been considering proposals for tax credits contained in the proposed *Vaccines for the New Millennium Act* of 2001. The bill did not pass into law but contained several provisions designed to accelerate R&D for microbicides and vaccines. The bill included a 30% targeted tax credit on HIV vaccine and microbicide R&D expenditures. The tax credit would be refundable for companies that have no income tax liability for both the current and previous two tax years.

Advocates in the US are backing away from targeted tax credits as a strategy in the light of biodefense initiatives. Instead, advocates are arguing for more direct incentives such as direct government contracting with the private sector and public assistance with vaccine manufacturing. However, advocates are continuing to argue for tax incentives to encourage larger pharmaceutical companies to contract with biotechnology companies for vaccine and microbicide research. The 2001 bill proposed that the existing tax credit on a broad range of contracts between companies would be increased from 65% to 100% for research on microbicides, HIV vaccines and other targeted vaccines. A joint legislative memo adopted by US vaccine and microbicide advocacy organizations in March 2003 recommends that this measure be enacted.[81]

The US bill also proposed sales tax credit for vaccines. Sales tax credits only provide a tax advantage to industry if the product is sold. The fact that the credit costs nothing unless and until a product is developed and sold makes the sales tax model politically attractive.[82] Sales tax credits provide a useful incentive for large pharmaceutical companies to become involved in marketing products that they might otherwise view too risky to invest in, such as microbicides.

Kremer argues that sales tax credits enjoy advantages over enhanced R&D credits. Tax credits for sales create incentives for biotechnology firms anticipating future profits from sales of new products. Most biotechnology firms license their inventions to larger firms, and a sales tax credit is likely to raise the price biotechnology firms receive for licensing their inventions.[83]

The US sales tax credit proposal included the following features:

- A maximum amount of sales eligible for a credit of $100 million per year for 2002 through 2006 and $125 million per year for 2007 through 2010, with a cap for the entire period of $1 billion.

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[81] AVAC et al, supra, note 38.
[82] A Attaran, et al *A Tax Credit for Sales of HIV, Tuberculosis, and Malaria Vaccines* Boston: Center for International Development, Harvard University, 2001.
[83] M Kremer. Appendix 8: Stimulating R&D on Neglected Diseases: Problems with an Enhanced Research and Development Tax Credit, in Performance and Innovation Unit *Tackling the Diseases of Poverty*, London: Cabinet Office, 2001.

- Unallocated credits for any year would be carried over and available for allocation until 2020.
- To qualify, vaccines would have to be sold to approved non-profit organizations or foreign government for distribution in developing countries.

Tax relief can also provide incentives for treatment R&D oriented to developing country needs. Sales tax credit models could provide benefits for treatment access, for example by rewarding sales or donations of new diagnostics and treatments to specified non profit bulk purchasers, or which meet specifications which indicate that they are designed for use in developing country contexts.

Tax relief for corporate donations of HIV treatments to developing countries is provided by section 55 *Finance Act 2002* (UK) which provides that costs of transportation, delivery or distribution incurred by a company in making a gift of medical supplies or equipment for humanitarian purposes is deductible.

Advocacy relating to tax credits should target major R&D players such as the US, UK, France, Switzerland, Germany and Japan, and support should be sought from industry associations as well as bodies such as the European Commission, the G8 and the OECD for promoting legislative action. Tax credits should be tied to preferential pricing for the public sector.

Discussion points

Advocates should develop best practice relating to Public Private Partnerships that support accelerated product development for global health goods in areas such as input by communities from the global South in partnership arrangements, and accountability and transparency mechanisms.

Advocates should promote greater public sector involvement in R&D relating to neglected diseases including HIV/AIDS, including collaborative research networks such as DNDi.

In choosing strategies to address market failure, advocates should consider whether tax relief to the private sector is an appropriate remedy rather than promoting direct public investment in research programs.

Advocates should assess the effectiveness of R&D tax credits for stimulating R&D on HIV medicines and vaccines, and further investigate sales tax credit models.

5.4 Purchase commitments, bulk procurement and financing mechanisms

Prior commitments from Governments or multilateral agencies to purchase new products have been considered by vaccine advocates in particular as a potentially important incentive to stimulate private sector investment. Pre-commitments to purchase bulk quantities of new vaccines, and also microbicides or drugs, may provide a powerful

incentive for new investment in R&D. Purchase guarantees could also facilitate rapid delivery of new products after licensure, by ensuring immediate product acquisition and because product developers would be encouraged to build manufacturing facilities at a scale required to meet developing world demand.

Use of purchase commitments and procurement schemes could help achieve a balanced approach to promoting treatments and prevention technologies. It can be argued that the mobilization of funds for treatment access, whilst essential, may result in the lowering of market incentives for R&D into prevention technologies. Production of treatments that are required to be taken for life may be perceived by pharmaceutical companies to be more lucrative than development of a two or three dose vaccine or a low cost microbicide. Purchase commitments for prevention technologies could help rectify this effect by creating market incentives. On the other hand, a policy focus on establishing pre-commitments for prevention technologies could be argued to detract from efforts to mobilize funds for current treatment purchases. Governments and multilateral agencies should work to achieve an appropriate balance of incentives for investments in treatments and prevention technologies.

The UK Government's Cabinet Office has supported the establishment of a system of advance purchase commitments, stating "an advance purchase commitment is the most cost-effective means of encouraging the development of new health products. Crucially, funds committed to the advance purchase commitment would not be spent until more effective health products are developed."[84]

The US Government is committed to purchasing millions of doses of anthrax and smallpox vaccines through the *Public Health Security and Bioterrorism Preparedness and Response Act* of 2002, which authorised $640 million for a Strategic National Stockpile of drugs and vaccines. AVAC and IAVI point to this legislation in making the argument that purchase commitments are required for vaccines and other products required to address HIV and other diseases prevalent in the developing world. US proposals for a vaccine fund have previously been outlined in the *Vaccines for the New Millennium Act* of 2000, which sought to authorise the US Treasury to spend up to $100 million per year for purchases of vaccines for HIV, malaria, and TB for distribution in developing countries. The legislation, which failed to pass into law, would have also directed the US President to enter into negotiations for creation of a multilateral vaccine purchase fund with other governments.

To insulate purchase commitments from domestic policy influences, it may be preferable for purchase programs to be managed through multilateral agencies such as the Global Fund, WHO, or a new Fund rather than a single US or EU fund.

The design of an advance purchase program will be critical to its success. It must be credible: product developers must have confidence that the sponsors of the program will fulfil their obligations once a product has been developed. Setting substantial funds aside represents a significant opportunity cost but may be necessary to demonstrate credibility.

[84] Performance and Innovation Unit *Tackling the Diseases of Poverty* London, Cabinet Office 2001.

Industry will expect commitments to have legislative backing. Credibility could be enhanced by "clearly specifying eligibility and pricing rules [and] insulating decision makers from political pressure."[85] The rules governing a procurement fund should specify that procurement priorities will reflect the need to give priority to new, more cost-effective products as they become available. Purchase commitments could lead to new R&D efforts but would not necessarily result in countries actually wanting to use products that result from this research unless there is some certainty that the products are the most appropriate and effective available. Countries will want to avoid a system that encourages the dumping of products in the developing world that have been superseded in wealthier markets by more effective products.

Michael Kremer[86] has proposed a system of purchase pre-commitments for vaccines whereby governments and international organisations commit to purchase products meeting certain specifications. One option is for a commission with members from industry and the public sector to be established that is charged with determining requirements for vaccines, such as efficacy level. A base price for particular vaccines would be set in advance and bonus prices would be paid for vaccines meeting higher standards. Developing countries could be given separate country accounts to use in partial payment for vaccines to allow them to evaluate the usefulness of vaccines for their own populations. Elements of this model could be extended to microbicides.

In addition to pre-commitments, structures need to be put in place to enable countries with similar needs and buying power to negotiate good prices when procuring global health goods. A range of mechanisms exist for bulk procurement of existing products, such as the Pan American Health Organization's Regional Revolving Fund for Strategic Public Health Supplies which is empowered to procure ARVs in bulk. Establishing bulk procurement mechanisms for ARVs is an important strategy to keep prices down, and may provide a structure that can be used for vaccines and microbicides as they become available. WHO is currently investigating bulk procurement mechanisms to help achieve its target of providing ARVs to 3 million people by 2005. Some countries have sought to establish pooled procurement arrangements with the support of the Global Fund. Collaborative negotiations on prices can drive prices down dramatically, as demonstrated by the success of nine Andean nations and Mexico working together to lower the purchase price for ARVs in 2003 through joint negotiations. The Clinton Foundation has demonstrated the price reductions achievable through successful bulk procurement negotiations for generic antiretrovirals on behalf of African and Caribbean countries in 2003. UNICEF could also play an important role in procurement, as it has a proven track record in bulk procurement and distribution of medicines and vaccines at the global level.

[85] M Kremer. *Public Policies to Stimulate the Development of Vaccines and Drugs for the Neglected Diseases.* Commission on Macroeconomics and Health: Working Group 2 Paper 8, WHO 2001.
[86] M Kremer, Creating markets for new vaccines: Part 2 Design issues, in A Jaffe, J Lerner, and S Stern (eds), *Innovation Policy and the Economy*, Cambridge MA: MIT Press, 2001.

The Microbicide Initiative has suggested that a coordinated, donor funded commodity bank for new products be established.[87]

The Vaccine Fund, which supports the work of the Global Alliance on Vaccines and Immunization (GAVI), is funding vaccine procurement and delivery infrastructure for some of the poorest countries. Consolidated procurement for traditional vaccines has also occurred through UNICEF. The Global Fund also has an emerging role in establishing approaches to procuring ARV drugs and other health products relating to HIV, TB and Malaria.

The UN Millennium Project has set out the following conditions for the success of pooled regional procurement schemes[88]:

- Homogeneity of member states
- Harmonized national regulatory and tax requirements
- Financial stability
- Common approach to quality
- Accurate predictions of need
- Competent and stable central staff
- Reliable data on patents
- Loyalty of member states so that national procurement agencies do not compete with the pool
- Monitoring of performance at pool and national level.

Even with regional and public sector procurement structures in place to keep prices down, to ensure that poor countries will be able to afford both to pay for large supplies of HIV medicines, vaccines and microbicides and to build domestic delivery systems requires new targeted financing mechanisms. The World Bank has proposed that a $1 billion revolving fund be established using International Development Association loans to provide interest-free financing for the purchase of vaccines against HIV and malaria, and vaccines and treatments for TB.[89] The financing of ARV purchases and treatment scale up is a pressing global need, and may become even more critical once TRIPS becomes fully operational in 2005 should access to generic medicines become more difficult.

IAVI has proposed a model whereby a financing mechanism for both vaccine purchases and delivery costs is established well in advance of product availability. A pre-

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[87] Access Working Group of the Microbicide Initiative. *Preparing for Microbicide Access and Use.* Microbicide Initiative of the Rockefeller Foundation, 2002, at 27.
[88] G Dukes *Interim report of task force 5: Working group on access to essential medicines*, Millennium Project, New York 2004, at 73.
[89] *Discovering Medicines for the Poor* Financial Times, 2 February 2000, at 7.

commitment to finance vaccines when they become available would provide a powerful incentive for industry and facilitate countries to plan delivery in advance. A financing facility could be managed by the Global Fund or GAVI and be linked to other financing to allow countries to select their preferred option (direct grants from the Fund, leveraged grants, or combined loans and grants).[90] This model could be extended to financing microbicide purchase and delivery. Debrework Zewdie of the World Bank announced at the Microbicides 2000 Conference that the Bank would ensure "the availability of funds to purchase and distribute microbicides to developing countries once they become available." Realising this commitment through establishing a functional purchase program may be one way to go forward multilaterally.

Proposals for new global financing mechanisms may be more likely to succeed if presented as part of a general package applying to existing and future global health goods (eg, treatments and prevention technologies for HIV, TB and malaria), rather than as being for a specific purpose such as future HIV vaccines.

One option may be to extend the role of the Global Fund to managing a finance scheme that provides a combination of loans and grants to low and middle-income countries in conjunction with the World Bank and/or regional development banks. If the Global Fund proves successful in guaranteeing better commodity security with existing products it could play an important role in building the confidence of product developers that future products would be purchased.

Discussion points

Treatment, microbicide and vaccine advocates should support:

- *Regional bulk procurement mechanisms for HIV medicines that can be adapted for procurement of vaccines, microbicides or other new technologies as and when they become available.*

- *multilateral financing initiatives to support procurement and delivery of global public health goods, which can be used to support rapid treatment scale up within the context of the 3 by 5 Initiative and to support purchase and delivery of vaccines, microbicides and other new essential health products as and when they become available.*

Vaccine and microbicide advocates have a common interest in investigating advance purchase commitment models.

[90] *A New Access Paradigm: Public Sector Actions to Assure Swift, Global Access to AIDS Vaccines, IAVI Access Project White Paper* New York: IAVI, 2001, at Chapter 2.

5.5 Orphan drug legislation

Orphan drug legislation provides a package of financial and practical incentives for R&D into rare diseases. Models exists in the US, Europe, Japan and Australia.[91] The focus of the legislation has been domestic needs, rather than R&D to address developing world needs. Elements of orphan drug legislation could be adapted to provide incentives for HIV related private sector R&D.

European orphan drug legislation, which commenced in 2000,[92] established a Committee for Orphan Medicinal Products within the European Medicines Evaluation Agency (EMEA). Benefits of the status include fast track approval, fee waiver and guaranteed market exclusivity for ten years.

The US *Orphan Drug Act* of 1983 established an Office of Orphan Products Development and incentives including a 50% deduction tax credit for clinical trial expenses, market exclusivity of seven years and flexibility in registration requirements designed to accelerate the approval process.

Grants and protocol assistance are especially useful to biotech companies with few resources and little experience of the system. Market exclusivity provisions are very attractive to sponsors of products that are not patentable (eg, natural substances) or for which the patents have already expired. Market exclusivity is also important for R&D conducted by biotechs and funded by venture capitalists, who typically require some assurance of intellectual property protection once the product resulting from their investment reaches the marketplace. However market exclusivity can only be guaranteed within the jurisdiction of the legislation so would be unhelpful for products unless they have a likely northern market as well.

Orphan drug legislation has succeeded where companies can recoup costs by charging high prices during the period of exclusivity in addition to gaining the benefits of tax incentives and grants. To make this model work in the case of HIV products for use in the developing world, an equity pricing system will need to be in place, and measures to ensure that regulatory approval will rapidly flow for use of the products in the developing world (eg, a WHO pre-qualification system). This may not be a viable model for microbicides because they would have to be cheap even in Northern markets to be a viable prevention tool.

A review of applications made under US and European orphan drug legislation concluded that it seems not to have been effective at stimulating R&D for preventive vaccines.[93] One option for consideration is the establishment of a global office of Orphan New

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[91] See eg *Biotechnology and Sustainability: The Fight Against Infectious Disease* Paris: OECD, 2003 at 29; *The Orphan Drug Program and Improving Community Access to Effective Drugs for Rare Diseases* Canberra: Therapeutic Goods Administration 2002.

[92] Commission Regulations (EC) No 847/200 of 27 April 2000 and (EC) No 141/2000 of 16 December 2000.

[93] J Milstein, R Widdus *Facilitating Access to Vaccines: an Overview of Legal Issues* 2003 (pre-publication manuscript at 25).

Prevention Technologies Development to coordinate assistance to orphan prevention products.

Discussion point

- *Vaccine and microbicide advocates should agree on a package of legislative incentives to promote private sector R&D on products relating to HIV, TB and malaria, including R&D financial assistance, fast-track approval, fee waiver, tax credits and market exclusivity provisions.*

Chapter 6 Patents

6.1 Patents as an access barrier: TRIPS and access to generics

Debates about the role of patents in limiting access to HIV innovations have focused on the impact of patent laws on poor countries' access to generic medicines. This issue remains high on global agendas as indicated by ongoing debates about the WTO TRIPS Council decision on the capacity of countries to import generic medicines (due to be considered again at the WTO's 2004 meeting).[94] It is crucial that the right of low and middle-income countries impacted by HIV to import generics is fully supported by patent laws, WTO rules and trade agreements before the WTO Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) comes fully into force in 2005.[95] Countries such as India and Brazil will have to ensure patent protection for new drugs from 2005, causing competition from generic suppliers to diminish. New options beyond those already incorporated in the TRIPS Agreement are required to ensure the continued production and dissemination of low cost generic medicines, particularly fixed dose combination antiretrovirals, after 2005.

Although clearly a priority issue for treatment advocates, obtaining a satisfactory resolution to the generic medicines issue should also be viewed as a matter of common concern for vaccine and microbicide advocates. Flexible intellectual property rules that encourage generic competition and which are responsive to the health and development needs of poor countries should be perceived as a common goal.

Debates on resolving the right to import generic medicines have become a testing ground for the principle that the right to health of citizens of poor countries should take priority over private interests in profits from intellectual property. Entrenching this principle stands to benefit poor countries in terms of their future enjoyment of access not only to drugs, but also vaccines, diagnostics, microbicides and other products. Failure to obtain a satisfactory resolution to the generic imports issue could lead to the creation of an increasingly hostile trade environment for developing countries seeking affordable access to new therapeutic and preventive products.

It is important to note that, in addition to WTO rules, bilateral arrangements restrict countries' access to generics. In particular, trade and investment agreements with the US that require compliance with 'TRIPS-plus' provisions can result in exclusion of generic competition in developing country markets for extended periods. These provisions effectively extend the life of patents and impose obligations in relation to data protection and data exclusivity which denies generic manufacturers access to information about products. This has been a significant issue in negotiations on the Free Trade Area of the

[94] The August 2003 agreement is a temporary waiver; a permanent amendment to the TRIPS is scheduled for consideration in 2004: Council for TRIPS, Decision of 30 August 2003 *Implementation of paragraph 6 of the Doha Declaration on the TRIPS Agreement and public health* WT/L/540 (available at www.wto.int)

[95] Middle-income countries such as South Africa are unlikely to qualify to import generics under the 2003 agreement where they have some domestic generic manufacturing capacity.

Americas (FTAA) and is anticipated as an issue in the US-Thailand Free Trade Agreement. Proposed FTAA provisos include a five year delay for small generic companies using test results completed by brand-name competitors, and restrictions on compulsory licensing. Such agreements undermine the *Doha Declaration on TRIPS*, which explicitly prioritized public health over profit. Trade and investment agreements should focus on appropriate burden sharing for funding R&D, rather than exclusively promoting intellectual property rights regimes.[96]

One commentator has argued that "in terms of international human rights law (in the context of HIV/AIDS understood in the light of Revised Guideline 6 of the International HIV/AIDS Guidelines), resource-poor countries not only may wish to avoid 'TRIPS-Plus' standards, but are indeed obliged to do so to increase access to medicines. Rather than merely permitting countries (to abandon TRIPS-plus standards), they should be encouraged and obliged to do so." [97]

The 2002 *Report of the Commission on Intellectual Property Rights* (UK) provides a useful tool for advocates. It asserts a human rights framework: "The IP (intellectual property) right is best viewed as one of the means by which nations and societies can help to promote the fulfilment of human economic and social rights. In particular, there are no circumstances in which the most fundamental human rights should be subordinated to the requirements of IP protection. IP rights are granted by states for limited times …whereas human rights are inalienable and universal."[98]

The Commission recommended that developing countries adopt intellectual property rules to facilitate generic competition, particularly compulsory licensing provisions, and provisions for "government use" which allow governments to make use of patented products without infringing a patent under a wide range of circumstances. The Commission noted that the Doha Declaration allows Least Developed Countries to exempt pharmaceutical products from patent protection until at least 2016, but that most Least Developed Countries have already provided patent protection to pharmaceuticals and will need to amend their legislation accordingly.

Developing countries should have the freedom to choose an intellectual property system that best meets their development objectives. For example, it may be in the interests of many developing countries to encourage competition by restricting the scope of patent protections provided and limiting the scope of subject matter that can be patented. There is strong pressure to harmonise the international patent system, and this is viewed as likely to reduce delays in getting new products to market. However the danger for developing countries is that harmonization will enforce developed country standards of

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[96] J Love, T Hubbard *An Agenda for Research and Development* Meeting on The Role of Generics and Local Industry in Attaining the Millennium Development Goals in Pharmaceuticals and Vaccines, The World Bank, Washington DC, 24-25 June 2003, at 7. (www.cptech.org/ip/health/rndtf/lovehubbard06242003.doc).

[97] Barbara Klugman, University of Witwatersrand quoted in A Irwin, E Ombaka *Background Paper of the Task Force on Major Diseases and Access to Medicine, Subgroup on Access to Essential Medicines*, New York: UN Millennium Project, 2003, at 38, fn 152.

[98] *Report of the Commission on Intellectual Property Rights: Executive Summary* London: September 2002.

patent protection, which may not be suitable for them. In this context the proposal of the World Intellectual Property Organization for a *Substantive Patent Law Treaty* is concerning, as it will likely apply patent standards used in wealthy countries worldwide.[99] This may lead to a system where any new medicine put on the market is patented worldwide.

HIV/AIDS treatment advocates have been leading international advocacy on IP and medicines policy and are likely to continue to play this role. It would however be in the interests of vaccine and microbicide advocates for their voices to be included in lobbying exercises on the nature of the global IP system, so that the breadth of concern in the public health advocacy community about the negative consequences of imposing inflexible patent standards on developing countries is understood by politicians in both the North and South.

The 2003 World Health Assembly directed WHO to establish a Commission to review intellectual property issues affecting innovation and public health. The Commission's review is occurring throughout 2004. A common agenda for HIV advocates to present to the WHO Commission on Intellectual Property, Innovation and Public Health could include:

- Action to ensure that developing countries are able to develop intellectual property systems which are responsive to domestic public health need and which maximize TRIPS flexibilities to promote public health
- Extending the deadline for TRIPS compliance from 2005 to allow a phased approach based on a country's public health needs
- Safeguards to ensure that harmonization of IP requirements does not disadvantage developing countries
- Simplifying the TRIPS procedure for approving exports of generic medicines to countries without the capacity for local production.

6.2 Patents as an R&D incentive: patent pools and patent extensions

The creation of patent pools has been proposed as a strategy for facilitating R&D in relation to both vaccines and fixed dose combinations of ARVs.

A patent pool is an agreement between patent holders to license their patents to one another or a third party. The freedom to share intellectual property between members of the pool removes a major cause of delay in progressing product development, reduces licensing transaction costs and litigation, distributes risk and provides an incentive for innovation.

James Love of the Consumer Project on Technology (CPTECH) has suggested the creation of an R&D patent pool that all recipients of NIH funds could be required to

[99] C Correa, S Musungu, *What are WIPO up to? What does it mean for developing countries?* South Centre, 2002 (available at www.eldis.org)

join.[100] He has also proposed that "South Africa, Kenya, Zimbabwe and other countries should require that any patents that are useful to treat AIDS be placed in a pool, and be freely available to anyone who wants to provide a product to treat AIDS, subject to the patent owners being compensated by a reasonable royalty, not to exceed some maximum percent of the product price."[101]

The US Department of Justice has developed *Guidelines for Forming Intellectual Property Pools* that require consideration of "whether the proposed program is likely to integrate complementary patent rights and, if so, whether the resulting competitive benefits are likely to be outweighed by competitive harm posed by other aspects of the program." [102]

Richard Laing argues that patent pooling for antiretrovirals could benefit pharmaceutical companies by prolonging the life of products: "By pooling products the company may prevent resistance and increase the duration of their income from the product."[103]

A system whereby Governments grant patent extensions on products meeting prescribed criteria could operate as an incentive by making HIV R&D more profitable. However extensions would only act as an effective incentive provided that demand for these products exists. For products with markets that have a low ability to pay, a patent extension is not a valuable reward. Kremer has criticized patent extensions on the grounds that "absent other interventions, this method of encouraging investment would worsen the ability of the poor to access new health technologies. The patent extension lengthens the period in which prices will be above marginal cost."[104]

A more complex form of patent extension is known as 'international roaming exclusivity' or 'patent exchange'. This rewards manufacturers that produce a useful but non-profitable product by extending patents on other, profitable products. A possible precedent was provided in the US by the paediatric studies provision, added to the *FDA Modernization Act* of 1997, under which drug sponsors are awarded a six-month extension of market exclusivity for all products they own which have the same active ingredient as the product for which a paediatric study is conducted.[105]

These patent extension arrangements can be facilitated by orphan drug legislation (see 5.5 above). Patent extensions could vary in duration depending on how quickly a pre-set level of additional revenue will be earned from the extension.[106] The sponsor of the product would need to assess the extension of market exclusivity as sufficiently profitable to warrant investment in the orphan product. Patent extensions can be enforceable in

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[100] *Patent pools*, Ip-health listserv 16 March 2002 (available via http://lists.essential.org/pipermail/ip-health/)
[101] *Richard Laing on patent pools and FDC ARVs*, Ip-health listserv, 20 March 2002.
[102] *Patent pools*, Ip-health supra, note 100.
[103] R Laing, supra, note 101.
[104] M Kremer. Paper prepared for UK Government Performance and Innovation Unit, May 2001, at 22, available via www.pm.gov.uk/files/pdf/Appendix202_072701.pdf
[105] OECD, supra, note 91, at 30.
[106] C Collins, S Morin, supra, note 78, at 34.

multiple countries through existing international treaties. A period of market exclusivity can be provided by the regulatory agency of the country granting the approval, enforceable only in that country or in countries with mutual recognition agreements.

5.2 Contractual approaches to managing patent issues

IAVI has integrated patent provisions into its product development agreements. IAVI's intellectual property strategy ensures that IAVI owns, or has a transferable license for, all developing country applications of the technology developed under any grants or contracts. Contracts either specify a non–exclusive, royalty–free license to produce a vaccine for developing countries, or an exclusive license with some restrictions, or receipt of 25 percent of the net royalties from any patents. This allows commercial partners to recover R&D costs through sales in the developed world while being prevented from pricing the vaccine out of reach of developing countries.

Other vaccine developers, and treatment and microbicide developers, could benefit from IAVI's experience with these patent mechanisms. IAVI's intellectual property agreements are tailored for each partner. IAVI's requirement for reasonable pricing applies to the public sector in developing countries, which includes governments and non-profit organizations. Should a company funded by IAVI decline to produce the candidate vaccine for developing countries in reasonable quantities at reasonable prices, IAVI retains rights to licenses to contract with other manufacturers.

A similar approach is adopted by the Medicine for Malaria Venture (MMV), whereby private partners receive patents in non-endemic countries and for applications other than malaria, whereas MMV receives the patents in disease-endemic countries and for treatment of malaria.

The London-based Centre for the Management of Intellectual Property in Health Research and Development has been established to act as an international focal point for public sector intellectual property management issues for health R&D. Its aims include codifying effective licensing practices for public sector management of intellectual property so that new products can more readily become available to the poor in developing countries. Advocates should investigate engaging the Centre to explore the issues specific to HIV products in more detail.

6.4 Open collaborative models

Advocates may wish to consider investigating more radical models to circumvent patents such as 'public patent' proposals (drawing for example from the experience of SARS research, the Human Genome project, the Global Positioning System, and open source software).[107] Providing funding to research efforts for public health priorities on the condition that patents would be held by the government and non-exclusive licenses would be attached to them allows companies to be free to compete to manufacture products.

[107] D Kucinich. The Case for Public Patents. *The Nation* 19 June 2003 (available via www.denniskucinich.us/)

WIPO is considering convening a meeting in 2004 to discuss open collaborative product development models, and NIH is increasingly supportive of open drug development models.[108]

Discussion Points

Treatment, microbicide and vaccine advocates can work together to:

- *Promote a more flexible approach to implementing the TRIPS Agreement that enables developing countries to maximize public health objectives using compulsory and voluntary licensing, and government use options*
- *Oppose the inclusion of 'TRIPS-plus' provisions in trade agreements that result in restricting the capacity of generic providers to compete with brand name pharmaceutical manufacturers by requiring high levels of data protection, data exclusivity and patent protections*
- *Ensure that trade and investment agreements maximize countries' capacities to pursue public health objectives*
- *Oppose bilateral and regional trade agreements that impose 'TRIPS plus' provisions on countries*
- *Monitor and evaluate the impact of the 2005 deadline for TRIPS compliance for some low and middle income countries*
- *Assess whether the TRIPS Council procedure for permitting countries without manufacturing capacity to import generics is workable and equitable from the perspective of low and middle-income countries and advocate for the WTO to adopt streamlined procedures*
- *Advocate for countries with the capacity to export generic medicines to legislate to allow TRIPS compliant compulsory licensing, without providing a right of first refusal to the patent holder*
- *Scrutinize the impact of initiatives aimed at international harmonization of patent laws on affordability of medicines and preventive technologies*
- *Advocate for governments to support innovative use of open collaborative intellectual property models for stimulating HIV product development*
- *Coordinate efforts in providing input to WHO's Commission on Intellectual Property, Innovation and Public Health in 2004-2005 on the above listed issues.*

[108] See discussion of models at www.cptech.org/ip/health/rndtf/

Chapter 7 Pricing

7.1 Equity pricing

Establishing a robust global framework for equity pricing of pharmaceutical products will support expanded access to treatments, and has the potential to also support expanded access to HIV vaccines and microbicides.

A distinction needs to be drawn between differential pricing and equity pricing. 'Differential pricing' may be defined as the adaptation of prices to the purchasing power of consumers in different countries. This is consistent with the commercial practice of charging for each market the highest prices that buyers will tolerate. In a developing country this may mean that prices are set so as to maximise returns from affluent urban groups.

'Equity pricing' involves the use of strongly differentiated pricing policies that reduce prices to as low as possible so as to maximise affordability for poor communities. An equity pricing approach is already adopted for vaccines and oral contraceptives distributed in developing countries by UNICEF, GAVI and the Vaccine Fund.

Desirable features of an equity pricing approach that systematically expands access to pharmaceutical products for the world's poorest include:

- a structure that ensures sustainability (ie, rather than being based on ad hoc donations)
- a regional or global approach with legal backing
- a system that aims to achieve the lowest possible prices for the poorest markets based on marginal cost of production
- transparency of prices.

Industry concerns about equity pricing include backflow of discounted medicines to rich markets, and the risk that political demands will be generated for drug prices in rich countries to be reduced to match levels in the developing world. Industry also point out that beyond the marginal costs of manufacturing drugs, the costs of freight, insurance, in-country distribution and post-marketing surveillance need to be met. Developing countries have a role in providing a supportive policy environment for equity pricing eg, by eliminating tariffs on differentially priced medical products. Ideally prices should be set as close as possible to direct costs of production.

It has been argued that mandatory equity pricing schemes may be politically unworkable because of: "intractable political problems regarding how countries would be grouped as to eligibility for lower prices. ... No government would want to be open to the accusation that it had 'over paid'. If global price setting is politically unworkable, then reliance on

voluntary frameworks is necessary and these leave the final decisions in the hands of pharmaceutical suppliers."[109]

There may be merit in models that would make listing of products for equity pricing compulsory. However recent policy developments indicate that voluntary approaches to pricing remain the preferred option of G8 governments.

The EU's *Programme for Action on HIV/AIDS, Malaria and TB* includes a commitment to introducing reductions in pricing as the norm for key pharmaceuticals for poor countries. In May 2003 EU governments approved a measure to encourage pharmaceutical companies to implement differential pricing for HIV, malaria and tuberculosis drugs.[110] The program applies to 76 countries, mostly in sub-Saharan Africa, but also China and India. Countries not listed include Argentina, Brazil, Thailand, Russia and Ukraine. Companies that agree to sell their products at a 75 percent discount from European prices, or a 15 percent mark up over the cost of production - whichever is cheaper - will qualify for a special logo to use on packaging to prevent backflow to the EU. Manufacturers are encouraged to formulate their drugs so that the version sold within the European Union is easily distinguished from that sold at a discount outside it. The regulation applies equally to generic and proprietary medicines and has no impact on intellectual property rights. Industry participation in the scheme is voluntary.

The G8 Evian Summit *Health Action Plan* refers to the G8's support for "pharmaceutical companies' voluntary long term commitments to provide essential medicines at substantially discounted prices" and states that the G8 takes "an integrated approach that will facilitate availability and take up for the poorest in a manner that is fair efficient and sustainable". The Declaration commits members to take the steps necessary to prevent the diversion of discounted medicines to rich country markets, and undertakes to provide technical assistance to developing countries so that they can take similar measures. The Declaration also states the intention to not use preferential prices as a benchmark for prices of products in G8 domestic markets.[111]

The UK Government Working Group on Access to Medicines has developed a proposal for a voluntary system of equity pricing for which the UK Government is seeking international support through the G8, EU and Commonwealth.[112] The UK Department for International Development has published a framework[113] which proposes that pharmaceutical companies provide medicines for HIV/AIDS, TB and malaria at close to the cost of manufacture in all least developed countries and across sub-Saharan Africa

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[109] J Milstein, R Widdus, supra, note 93, at 7.
[110] *EU Seeks to Encourage Drug Companies to Sell Drugs Cheaper to Poor Countries by Combating Illegal Reimports*, Associated Press, 26 May 2003. (www.thebody.com/cdc/news_updates_archive/2003/may27_03/eu_drug_prices.html)
[111] *Health: A G8 Action Plan* Evian, June 2003.
[112] See Clare Short, Secretary Of State For International Development: *Report to The Prime Minister UK Working Group On Increasing Access To Essential Medicines In The Developing World: Policy Recommendations And Strategy*, 28 November 2002.
[113] *Increasing Access to Medicines in the Developing World: the Context* London: Department for International Development, January 2003.

(whilst preserving viable private markets in sub-Saharan middle-income countries). Steps to prevent re-importation would be adopted and developed country governments would assure industry that lower prices for poor countries would not be used as a benchmark for prices in their own markets. Under the UK proposal, developing countries receiving products under the scheme would be required to remove tariffs.[114]

Oxfam criticized the UK proposal for omitting over 70 low and middle-income countries, such as Thailand and China, and for distinguishing between Least Developed Countries in Africa such that in other African countries (including Nigeria) reduced-price drugs will only be sold to public health services.

The US has been slow to support differential pricing systems for essential medicines. The inclusion of language supportive of differential pricing in the Evian G8 *Health Action Plan* and the agreement of the US in 2002 to the use of differential pricing as a principle informing procurement by the Global Fund suggest that US Government may play a more active role regarding future proposals. However it is unclear as yet how the US Emergency Plan for AIDS Relief will approach pricing issues, or in particular whether the Plan will support procurement of generic medicines so as to encourage generic competition.

The Global Fund has agreed principles relating to its role in purchasing medicines that are intended to establish a transparent way of purchasing drugs of assured quality at the lowest price through international competitive tendering. When grants from the Fund are used to purchase drugs, they must be purchased at the lowest available cost, be of assured quality, the purchases must be in conformity with national and international legal agreements and the Fund requires public disclosure of prices paid for drugs.[115]

7.2 Price transparency

The issue of transparency of pharmaceutical prices is a fundamental concern in efforts to promote more equitable pricing regimes. Treatment advocates have argued for the establishment of a workable system for the monitoring and reporting of global drug prices. WHO and Health Action International have conducted work in this area by preparing a manual for surveying essential medicine prices to support countries to conduct price surveys,[116] and MSF is also active in tracking and publicising prices of essential medicines. There is scope for Governments to be playing a more active role in requiring price transparency through regulation, and it should be noted that the commentary on Revised Guideline 6 of the *International Guidelines on HIV/AIDS and Human Rights* recommends that State's collaborate with NGOs, UN agencies and intergovernmental

[114] This is consistent with Recommendation (c) of Revised Guideline 6 *International Guidelines on HIV/AIDS and Human Rights*, States should adopt laws and policies to realize universal and equal access to medicines including by reviewing duties, customs and taxes that hinder access: supra, note 29, at 15.
[115] *Global Fund Board Meeting Minutes* October 2002 (available via www.aidspan.org/gfo-archives/newsletter/issue1.htm).
[116] See: www.haiweb.org/campaign/access/wha56/ WHA_2003_briefing_EN_final.pdf

organizations in maintaining accessible sources of information on the sources, quality and worldwide prices of pharmaceuticals.[117]

Researchers at the UN Millennium Project have made the following observation about price transparency:

> The case is sometimes made that the ability to conduct price negotiations without public disclosure enables producers and purchasers to come to mutually beneficial solutions. However, on balance, …allowing the dynamics of open, transparent market competition to operate will improve results. The availability of price information and comparisons is a key feature of such an open marketplace… Optimally, price transparency initiatives should enable the examination and comparison not only of manufacturers' prices, but also of the final cost of medicines to consumers in different settings and locations.[118]

7.3 Domestic price controls

At the national level there are a variety of policy and legislative tools that can be used to achieve price reductions. The promotion of competition, particularly through allowing generics to be marketed, can be an important strategy to ensure that prices are fair. Inappropriate tariffs and other taxes should be eliminated, and charges linked to supply or dispensing abolished. Domestic price control options include price fixing and use of reference pricing approaches. To support public sector provision, national legislation should be adapted so as to take full advantage of the flexibility provided for by the TRIPS Agreement in relation to compulsory licensing and government use provisions, and streamlined procedures put in place for importing generic medicines.

Discussion points

Treatment, microbicide and vaccine advocates should work together to advocate for:

- *Rapid implementation of equity pricing for essential medicines as a global norm, to support treatment scale up as well as to provide a framework for future HIV vaccines and microbicides to be made available at low cost*
- *Pricing arrangements that are transparent and sustainable, and offer the lowest possible price (eg, marginal cost of production for least developed countries)*
- *A mandatory system for the monitoring and reporting of global prices of therapeutics, diagnostics and preventive technologies for HIV/AIDS, TB and malaria*
- *Promotion of use of the full range of options available to governments for controlling prices of medicines and preventive technologies, including equity pricing, generic competition, legislated price controls, and pooled procurement.*

Advocates should oppose bilateral and regional trade and investment agreements that restrict the capacity of governments to control prices so as to ensure affordability of essential health products for poor communities.

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[117] Recommendation (u), supra, note 29, at 22.
[118] A Irwin, E Ombaka ,supra, note 97, at 40.

Chapter 8 Regulatory issues

8.1 Regulatory capacity building

The expansion of regulatory capacity in low and middle-income countries will facilitate local decision making about hosting clinical trials and expand each country's ability to assure safety in the conduct of trials.

Most developing countries have only limited regulatory infrastructure. Functions of an independent national regulatory authority include:

- Evaluation of clinical performance for safety and efficacy
- A published set of requirements for licensing
- Establishing requirements for Data Safety and Monitoring Board and Institutional Review Board/ethics committee structures
- A system to ensure compliance with good manufacturing practice
- Systems to monitor adverse events, including post marketing surveillance.

Efforts to strengthen national regulatory infrastructure should be prioritized in countries where clinical trials are being conducted, and countries that are well placed to play a regional leadership role (eg, Thailand, South Africa). These countries could potentially provide regional leadership for other countries including for monitoring product quality and post-marketing surveillance. Countries need to enhance funding for infrastructure, coordination, and technical expertise to support improved regulatory review standards, and adopt formal mechanisms whereby new clinical trials are required to be designed in the context of overall community health and HIV treatment and prevention efforts.[119]

The public sector may need to play a more direct role in identifying and supporting submissions for regulatory approval of promising new products, by supporting companies to file applications for approval in multiple countries.

UNAIDS, WHO and the US FDA need to be supported in expanding their roles in provision of financial assistance and technical advice to low and middle-income countries to ensure informed national regulatory decision making.

8.1 Regulatory pathways

Developing and streamlining regulatory requirements is important to reduce delays in approving clinical trials and licensing new products for distribution in low and middle-income countries.

[119] C Collins, S Avrett HIV Vaccines: Current challenges and future directions. *Canadian HIV/AIDS Policy & Law Review* 2002; 7(1):1, 20-25 at 23. (www.aidslaw.ca/Maincontent/otherdocs/Newsletter/vol7no12002/vaccines_challenges.htm)

Lack of regulatory capacity in the global South means that approval of products for marketing is often heavily influenced by the decisions of the US Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medical Products (EMEA). However, regulatory agencies in the North impose standards appropriate to their domestic markets as required by their mandates, and the trend has been towards tighter rather than more flexible regulatory standards.

To reduce regulatory risks, regulatory pathways should be defined that will: "(1) ensure that (products) developed, produced and licensed for global use are evaluated for their safety and efficacy for all potential target populations; (2) assure maintenance of a license for a pre-existing product when there is no longer a product market in the original country of licensure; and (3) find a pathway to licensure for a product when the market is only in the developing world."[120] This agenda is consistent with the recommendation of the commentary to Revised Guideline 6 of the *International Guidelines on HIV/AIDS and Human Rights* that States should ensure the quality assurance and control of HIV/AIDS-related products through legislative and other measures (eg, functional systems for pre-marketing approval and post-marketing surveillance).[121]

Gross and Johnston have recently reviewed the common and divergent regulatory issues facing vaccine and microbicide development.[122] They point out that there is a need to clarify preclinical requirements to accelerate entry of candidates into initial human trials while minimizing risks to volunteers. They argue that vaccine and microbicide developers have a common interest in streamlining approval of combination products, such as vaccines combining different immunogens and microbicide products combining two or more different microbicide strategies. Currently each constituent of the combination product needs to be separately considered by the regulator, as well as the combination product. Development could be accelerated by requiring only the proposed combination product to be approved, especially if the separate constituents are unlikely to be used other than in combination.

Vaccine and microbicide advocates have pointed out that a partially effective HIV vaccine or microbicide that might not be approved by regulators in the US or Europe, because the efficacy levels is considered too low to provide domestic public health benefits, could nonetheless be highly appropriate for use in countries with rapidly emerging epidemics. Some products may be designed specifically for use in the South. These scenarios indicate the need to provide a new regulatory framework to extend the mandate of northern regulators so that they can make decisions based on the needs of developing countries, rather than just northern domestic markets. Care need to be exercised regarding how such an extended role is framed, as there is a need to avoid creating a situation where safety and public health safeguards for consumers in poor countries are set at low standards that would be unacceptable in the North.

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[120] J Milstein, R Widdus, supra, note 93, at 18.
[121] Commentary (j), Revised Guideline 6, supra note 29, at 19.
[122] M Gross, M Johnston, HIV vaccines and topical microbicides: a complementary combination Part 2: shared regulatory considerations *Microbicide Quarterly* 2003;1(2),8; and see Part 3 *Microbicide Quarterly* 2003; 1(3).

Gross and Johnston have recommended (i) adding a parallel mandate to the FDA to support review of dossiers for specific purposes such as assessing the quality of pre-clinical data and clinical trial conduct that are not being submitted for US licensure; and (ii) expanding the mandate of the EMEA to license products even though the principal populations amongst which a product is likely to be disseminated reside outside Europe.[123] The European Council has recently agreed a Regulation that empowers the EMEA to give a scientific opinion, in the context of cooperation with WHO, for the evaluation of products intended exclusively for markets outside Europe.[124]It may also be desirable to extend the mandate of regulatory authorities in those countries in the South with regulatory infrastructure, so that they could provide approvals that are recognised in similarly placed low and middle-income countries.

8.3 Harmonization of standards

Clarity on international standards of quality, safety, efficacy, manufacture, and the minimum data required for licensing are recognised by vaccine and microbicide advocates as necessary to reduce delays in getting products approved for marketing. In the vaccine field, which carries a heavy regulatory burden, harmonization of administration schedules and manufacturing regulations have been noted as a priority.[125] Gross and Johnston argue for harmonizing and possibly regionalizing approval criteria and procedures for both vaccines and microbicides, in that this may result in:

- Early establishment of relatively large markets for a new product, (potential economies of scale in production, warehousing and distribution);
- Perhaps more comprehensive, equitable distribution systems among similar high-risk populations across national borders.[126]

Harmonization involves generating consensus between regulators from a range of countries on the desirable elements of study design for determining safety, efficacy, and quality, and formats for submitting data, and mutual recognition of approvals complying with common standards. Common standards for fast-tracking approval processes are also important eg, no longer than six months for life-saving products. Countries with similar epidemiological and population characteristics could benefit by pooling their regulatory expertise and linking approval processes. These measures may reduce the need for trials to be repeated in multiple countries.

WHO and UNAIDS convened meetings for vaccine and microbicides advocates in 2002-2003 to discuss these issues, which are particularly pertinent to microbicides as a new product category with no clear regulatory pathway and without an international consensus

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[123] Ibid at 11.
[124] *Amended proposal for a Regulation laying down Community procedures for an authorisation and supervision of medicinal products for human and veterinary use*, Brussels: Council of the European Union 12 June 2003 (10449/03).
[125] J Milstein, R Widdus, supra, note 93, at 10.
[126] M Gross, M Johnston, supra, note 122, at 9.

on safety, effectiveness, and quality assessment. Although it may be too early in the development of microbicides to attempt to define precise guidelines for regulatory authorities, opening up a dialogue on standardized approaches is useful.

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a process dominated by pharmaceutical associations and the EU, Japan and the US. The ICH agenda is determined by the desire of the pharmaceutical industry to bring new products to wider markets more rapidly and with reduced compliance costs. In addition to ICH, some countries work through mutual recognition agreements or through the *Pharmaceutical Inspection Convention* to promote harmonization in manufacturing inspection practices. The ICH has mostly addressed issues applicable to therapeutic pharmaceuticals, but more recently aspects applicable to prevention technologies, such as safety issues for biotechnological products. ICH has also addressed ethical aspects of trials, such as ethics committee responsibilities and informed consent requirements, through Good Clinical Practice guidelines adopted by the EU, Japan and the US.[127]

The ICH process has been criticised for being inappropriate to the needs of developing countries. Trouellier et al argue that "instead of wasting energy on discussing the appropriateness of a possibly too sophisticated set of rules… one should rather concentrate on the training of regulatory personnel in low and middle-income countries and on creating regional centres for the quality of pharmaceutical products…. This can take place through upstream arrangements (e.g., WHO pre-qualification of suppliers of essential drugs for priority communicable diseases) and/or downstream operations (e.g., regional pharmaceutical inspectorates established on a mutual recognition basis)."[128] Dr. Weerasuriya[129] argues that there should not be a globally uniform rules-based technical approach to product quality, safety, and efficacy. Rather, these issues should be tied to country-specific public health needs. To achieve this, support will be needed for drug regulatory authorities in the developing world and regional regulatory networks.

An alternative to ICH is for WHO to take a more proactive role, given that a WHO process is more likely to be more inclusive than the ICH process. WHO has supported the work of the Southern African Development Community and the Association of South East Asian Nations on drug regulatory harmonization, and has conducted training and produced resources on pharmacovigilance and GMP inspections and standards. In the case of childhood vaccines, WHO develops guidelines and recommendations on production and quality control, and by managing the pre-qualification process for manufacturers selling to UN agencies.

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[127] See www.ich.org/ich5e.html

[128] P Trouiller et al. *The Globalisation of Regulatory Requirements and the Development and Availability of Medicinal Products in Developing Countries: Quality, Efficacy and Safety Issues.* MSF/DND Working Group, 2002 (www.neglecteddiseases.org/3-2.doc)

[129] WHO Essential Drugs and Medicines Acting Regional Advisor , at The Crisis of Neglected Diseases: Developing Treatments and Ensuring Access Workshop and Conference, New York City , March 2002 (www.neglecteddiseases.org/summary.pdf)

WHO pre-qualification of therapeutics and vaccines is providing developing countries without strong regulatory capacity with a reliable process to assess vaccines acquired through UN procurement processes, as well as generic ARVs since the publication of a list of pre-qualified suppliers in 2002. WHO prequalification processes should be expanded both to support treatment scale up and because it may prove a useful process for future HIV vaccines and microbicides.

Discussion points

Treatment, vaccine and microbicide advocates should advocate for:

- *investment in strengthening the capacity of Southern regulatory authorities*
- *action by regulators in the global North and South to increase transparency of procedures and accountability in decision making to communities.*
- *the expansion of the role of WHO and Northern regulatory authorities in building the capacity of Southern regulators in relation to safety, efficacy and quality issues relating to trials and licensing of products in developing countries.*
- *the creation of regional regulatory advisory bodies for countries with similar public health needs*
- *the WHO to:*
    - *expand its pre-qualification system to support access to quality assured treatment and prevention technologies*
    - *expand its technical assistance on regulatory issues*
    - *develop and promote guidelines for regulatory requirements on safety, efficacy and quality for HIV product*
    - *work with regulatory authorities in the South to develop regional advisory roles*
- *national plans that considers funding, coordination, and technical training for regulatory review.*

Chapter 9 Liability

9.1 No fault compensation schemes

The risk of product liability lawsuits is a disincentive to pharmaceutical companies and biotechnology companies investing in new preventive products in wealthy nations, particularly the US, due to the potential exposure to expensive and protracted litigation and costs associated with liability insurance. [130]

As preventive products such as vaccines are administered to otherwise healthy persons, they may be an easy target for claims if a recipient suffers an otherwise inexplicable medical problem. There is a long history of litigation associated with vaccines, for example (in the US and UK) claiming that the diphtheria-tetanus-pertussis (DTP) and measles, mumps, and rubella (MMR) vaccines cause autism and brain damage, or (in France) claiming hepatitis B vaccine is linked to multiple sclerosis.

Investment in microbicide product development may also be deterred by the risk of product liability claims, particularly in countries with strong consumer protection laws such as the US. Such claims may originate not only from injuries claimed by the person using the product but potentially their sexual partners as well.

Legislation has been enacted in Europe and the US to establish compensation schemes that define entitlements to compensation for vaccine injuries. Such schemes provide benefits to both consumers and manufacturers and promote the public interest in the continued manufacture of vaccines. There are a number of models that could be applied to HIV vaccines and arguably also to microbicides. Making the case for a compensation scheme for microbicide products would be difficult however. There is lack of precedent outside vaccines for such schemes for health product-related compensation. Further, the possibility of user non-compliance or misuse of a microbicide introduces an extra layer of difficulty in establishing liability that may mean that the government is reluctant to legislate to provide no fault compensation.

Generally, compensation is payable from a public fund under the vaccine schemes regardless of evidence of negligence. Should a case arise where negligence is a factor, the authorities that administer schemes can sue the manufacturer to recover amounts of compensation paid out. This is a better position for manufacturers than that of being exposed to strict liability to compensate consumers directly for injuries regardless of evidence of negligence under general product liability laws.

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[130] The high number of product liability suits in the US as compared to other jurisdictions is largely due to the US contingency fees system, under which plaintiff's lawyers keep 33 to 45 percent of awards, which provides an incentive to pursue speculative cases; the capacity of juries to make high awards of punitive damages and the lack of meaningful caps on awards; and the fact that unsuccessful plaintiffs are generally not penalised by being required to pay the respondent's legal costs. See D Bernstein, *Legal Reform: Learning from the Commonwealth*, Center for Legal Policy Manhattan Institute, Civil Justice Memo No 25 May 1996 (www.manhattan-institute.org/html/cjm_25.htm)

The US has a federal no fault compensation scheme for childhood vaccination, the US National Vaccine Injury Compensation Program.[131] Under this scheme, a causal connection must be established between the vaccination and the injury suffered. This is a no fault scheme and claims may be made according to a table of compensable conditions. Compensation is funded by a tax on each dose of vaccine. Remedies from civil court proceedings can only be pursued after a remedy is sought through the federal no-fault process. By providing an easy to access scheme, claimants are deterred from electing to pursue compensation against manufacturers through the civil courts.

The US federal scheme does not yet apply to HIV vaccines. However, in California, an AIDS Vaccine Victims Compensation Fund was established by legislation passed in 1986. The legislation protects vaccine manufacturers from strict liability if a product is deemed unavoidably dangerous, and provides for a compensation fund to be supported by a surcharge on the vaccine. Congress passed a compensation scheme for health care workers vaccinated against smallpox in 2003.[132]

A range of other compensation models exists in industrialized countries,[133] but they have not been extended to HIV vaccines. The German and Swiss systems provide compensation for injuries flowing from all mandatory vaccines and those recommended by a competent authority.[134] The French Public Health Code provides for compensation for injuries arising from all mandatory paediatric or adult vaccines. Quebec (Canada) also has a no fault scheme for licensed vaccines.

The UK scheme, which was established by the *Vaccine Damage Payments Act* 1979[135] provides a lump sum of £100,000 where a person suffers a serious disability (a 60 percent disablement). The UK scheme does not require claimants to access the scheme as a precondition to pursuing a civil remedy against the vaccine manufacturer.

From the perspective of health consumer groups these schemes have been criticized on the grounds that they do not cover vaccines in human testing (such as HIV), the list of compensable injuries is arbitrarily limited (eg may not extend to neurological injuries), the quantum of compensation is unreasonably low (a particular problem for the UK) and they impose restrictive limitation periods within which claims must be lodged. In addressing liability issues, it is important to ensure that consumer rights to compensation through the civil courts are not unduly eroded, particularly where consumers are relatively powerless such as in poor communities.

From the perspective of manufacturers the schemes are criticized for failing to abolish consumer rights to take civil action through the courts. For so long as a right to pursue product liability tort claims exists alongside the right to obtain no-fault compensation,

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[131] Created by the *National Childhood Vaccine Injury Act* of 1986.
[132] *Smallpox Emergency Personnel Protection Act* of 2003.
[133] Institute of Medicine. *Vaccine Supply and Innovation*. Washington: National Academy Press 1985, at appendix e.
[134] *Law on the Prevention and Control of Communicable Diseases in Man* (Germany) *Federal Law on the Control of Diseases in Man* 1970 818.101 (Switzerland)
[135] See *Regulatory Reform (Vaccine Damage Payments Act 1979) Order* 2002 (UK)

there remains a risk that a rush of successful civil claims could give rise to a crisis in the industry wherein liability insurance becomes unavailable, as happened in the 1970s in the US vaccine industry. The industry also argues that it already needs to comply with strict safety guidelines in the conduct of trials and manufacturing (eg GMP inspections) and this ought to be sufficient to safeguard consumer interests.

Little information is available about vaccine injury compensation in developing countries.[136]

In formulating proposals for extending compensation models to HIV products, it will be important to consider why people who have adverse reactions to a vaccine or microbicide should receive special no fault compensation rights when people who have adverse reactions to ARVs do not. "Special compensation for HIV-negative people may give the appearance of social indifference to the needs of people living with HIV infection. A public debate about the justification for compensating specific injuries may offer a valuable opportunity to reconsider the ways in which responsibility for injuries and illnesses of all kinds should be allocated."[137]

In the US, AVAC has called for the addition of HIV vaccines to the childhood program, indemnification for contractors to HIV vaccines, and Government guarantees of liability insurance - or the creation of an entire new system for all child and adult vaccines.[138] In Canada, the Canadian HIV/AIDS Legal Network has called for the establishment of a no-fault insurance program for all experimental and licensed vaccines to which pharmaceutical companies should contribute.[139]

9.2 Immunity and indemnity provisions

The US state of Connecticut has enacted legislation that provides that when a drug is developed and tested to determine its success as a vaccine against HIV/AIDS, a manufacturer, research institution, or researcher will not be held liable for civil damages resulting from clinical trials where the drug is administered to research subjects. This immunity from liability must be presented to the research subject in writing and that person (or his or her parent or guardian in the case of a minor) must provide informed written consent to act as a research subject.[140] This model reduces insurance burdens for product developers, but is not desirable from a consumer rights perspective and may breach GCP ethical standards unless an alternative source of compensation is provided.[141]

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[136] J Milstein, R Widdus , supra, note 93.
[137] US Congress Office of Technology Assessment *Adverse Reactions to HIV Vaccines: Medical, Ethical, and Legal Issues* Washington DC: US Govt Orinting Office, 1995.
[138] *How Do You Fight a Disease of Mass Destruction?* AVAC, April 2003, at 16 (www.avac.org/pdf/reports/DiseaseofMassDestruction.pdf)
[139] D Garmaise *HIV Vaccines in Canada: Legal and Ethical Issues*, Canadian HIV/AIDS Legal Network 2002 at 31.
[140] CGSA §19a-591 (www.glad.org/Your_Rights/connecticut_hiv.shtml)
[141] See eg, Article 3 European Union *Good Clinical Practice Clinical Trials Directive* 2001/20/EC; the Association of British Pharmaceutical Industry Compensation Guidelines 1994 established the no fault

Clinical trials are generally only conducted with comprehensive liability insurance in place, and pharmaceutical industry guidelines require payment of compensation for adverse event injuries on a no-fault basis.

The US Government has indemnified contractors against lawsuits arising from vaccines against anthrax and other bioterror agents.

Arguably, a special case could be made to provide incentives for manufacturers to invest in microbicide products by governments providing indemnity from future liability arising from microbicides marketed in the US and Europe. This case would rest in part on the potential public health benefits of the products use in other markets ie, developing countries. However such an argument would likely face resistance because of fears that the floodgates would be opened for a wide range of preventive health products to receive special indemnity or insurance protections. The Population Council and IFH have recommended that microbicide advocates consider additional strategies for reducing the risk of litigation, including consumer education and counselling, clear and accurate labelling information, and post marketing surveillance.[142]

A joint approach between vaccine and microbicide advocates may be more powerful in making out the public health case for special liability provisions for new HIV prevention technologies. Advocates could argue jointly for product developers and manufacturers to be indemnified against liability unless they are negligent or engage in intentional conduct causing harm, using the indemnity protection afforded to bioterror vaccine contractors in the US as a precedent. However, microbicide advocates have shied away from proposals to indemnify developers because they are politically contentious and are not considered to be sufficient to entice large pharmaceutical companies to invest in microbicide R&D.

9.3 Reform of product liability laws

An additional or alternative approach is to address liability concerns through reforming generic consumer protection legislation or tort laws. Options include stronger 'development risk' defences, removing strict liability provisions for manufacturers of certain product categories, and limiting the amounts and types of damages awardable in claims against manufacturers.

UK and European laws include a development risk defence that is available to manufacturers facing product liability claims.[143] It is open to a manufacturer to defend a claim for damages arising from an allegedly defective product by showing the defect was not discoverable because the scientific and technical knowledge required to identify the

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principle for compensation for injuries resulting from adverse events, and has been adopted in national ethical guidelines of South Africa and Australia.

[142] *The Case for Microbicides: A Global Priority(2nd ed)* New York, London: Population Council, IFH 2001, at 22.

[143] Article 7(e) of the European *Product Liability Directive* 85/374/EEC; section 4(1)(e) *Consumer Protection Act* 1987 UK

defect was not available at the time. In the US a 'state of the art defence' is available, which is similar to the development risk defence.

An option for microbicide and vaccine advocates is for stronger development risk defences to be introduced for products of significant public health benefit such as HIV prevention technologies, so that manufacturers are not liable for harms caused due to defects in their products about which they had no knowledge or which was not discoverable given the state of scientific knowledge at the time. However this may not be helpful in the case of vaccines if the manufacturers know them to be inherently dangerous for a very small percentage of consumers.

Discussion points

Advocates should work together to:

- *Increase the capacity of governments and communities to assess the acceptable risks and benefits associated with use of therapeutic and preventive technologies, and support community education to improve understanding of risks and benefits of products*
- *Ensure that exposure to the risks of expensive lawsuits in wealthy countries does not unnecessarily deter investment in developing vaccines, microbicides or other new prevention technologies*
- *Promote law reform that reduces the exposure of manufacturers and product developers to the risk of liability arising from use of HIV prevention products, provided that:*
    - *high safety requirements are maintained by regulatory authorities that oversee clinical trials and that license products, and*
    - *people who use products are able to access reasonable compensation should they suffer harm through 'no fault' compensation schemes that permit people who suffer injury to access compensation from a fund without having to establish that a manufacturer's negligence caused their injury.*

- *Investigate the public interest case for governments to indemnify HIV vaccine and microbicide manufacturers in wealthy countries from liability arising from use of HIV prevention technologies based on the unique potential of vaccines and microbicides to stem the global epidemic.*

Chapter 10 Manufacturing

10.1 Capacity building

Lack of manufacturing capacity is a major factor responsible for lengthy delays in getting approved pharmaceutical products to market in low and middle-income countries.

The importance of manufacturing infrastructure has become more acute as the focus of product development has shifted to small biotechnology companies, or non-profit or academic organizations, which have little manufacturing capacity. Lack of manufacturing capacity and uniformity in production facilities has accounted for repeated delays in HIV vaccine clinical trial programs.[144]

In the treatments field, Indian generic manufacturers are seeking to rapidly expand manufacturing capacity in African countries such as Nigeria to supply local markets. Technology transfer in the treatments field is providing an important precedent for prevention technologies.

The challenge for the vaccines field is to ensure that adequate production capacity exists to meet demand in low and middle-income countries early, rather than after ten to fifteen years delay as has occurred with other vaccines. Meeting the global demand for vaccines and microbicides will require substantial private and public sector investments in manufacturing. The public sector needs to demonstrate a willingness to assist the private sector in managing the risks involved in creating sufficient capacity to meet projected global demand for future new products.

Vaccines and microbicides face common challenges to ensure that there is sufficient and timely investment in manufacturing capacity, including developing new facilities in key developing countries. Building manufacturing capacity in the South for treatments is likely to result in future benefit to vaccine and microbicide developers. Countries such as Brazil, India and Thailand currently have the expertise, good manufacturing practices and facilities required to manufacture drugs and vaccines. Investing further in these countries' manufacturing capacities would support them in meeting demand for affordable medicines from the global South. These countries are then well placed to transfer technology where appropriate to assist other countries in the South to develop manufacturing expertise and infrastructure.

Locating production in developing countries could reduce costs (of production and shipping) facilitate technology transfer, and provide opportunities for investment and employment. Local production also has a number of potential drawbacks: "Plant design, development, and ensuring that the plant meets international standards of Good Manufacturing Practices all take time."[145] Technology transfer benefiting the South is important in the long term but it cannot be assumed that this would necessarily be the best, most reliable and quickest option for the production of new products utilising novel technologies. Building manufacturing capacity in the South needs to be accompanied by efforts to ensure that national regulatory authorities have the capacity and expertise to validate facilities and provide ongoing oversight for GMP.

[144] R Klausner et al, supra note 67, at 2037.
[145] Access Working Group of the Microbicide Initiative, supra, note 87, at 22.

10.2 Public sector roles

To support scaling up of treatment provision and to prepare for new vaccines and microbicides, financial assistance from the public sector is required, through loans, grants, subsidies, tax credits or novel financing arrangements, to ensure timely development of manufacturing capacity. Alternatively, public manufacturing facilities may need to be developed, which could be contracted to private manufacturers if required.

Advocates need to define a broad range of innovative and flexible financial incentives to support investment in manufacturing. This task would be assisted by assembling an overview of the manufacturing processes and associated costs for the vaccines, treatment and microbicide fields, and mapping and analysing existing manufacturing capacity and resource flows against these needs.

Support for research on demand estimates is critical to guide these investment decisions. Scaling up manufacturing capacity will necessitate a better understanding of potential demand for products, which in turn needs to be based on a better understanding of the potential impact of different products in different epidemiological contexts.

Discussion points

Advocates should work together to:

- *Define a broad range of innovative and flexible financial incentives and options to support investment in manufacturing capacity including targeted loans, government grants and contracts.*
- *Advocate for increased public sector investments in manufacturing facilities in the South*
- *Create incentives for North-South and South-South technology transfer to support development of sustainable manufacturing capacities.*

Chapter 11 Delivery

11.1 Expanding capacity to deliver existing products

Improving delivery systems for existing treatments and vaccines (eg, through supporting the WHO's 3 by 5 Initiative and the work of the Global Alliance for Vaccines and Immunization) is key to preparing for delivery of new products.

The WHO 3 by 5 Initiative is currently mapping treatment delivery capacity in the worst affected countries to support rapid expansion of capacity where need is greatest and better use of under-utilized capacity. The Initiative is also systematically defining delivery

issues, including service design, human resource and training needs. The Initiative has identified the following principles to inform delivery:[146]

- Antiretroviral therapy should be delivered equitably to everyone who needs it, including children, women, men and all vulnerable populations, including sex workers, injecting drug users, men who have sex with men, displaced persons, prisoners and migrant workers.
- Antiretroviral therapy programmes must strengthen overall health systems and primary health care.
- People living with HIV/AIDS and communities are leaders in the movement to provide universal access to antiretroviral therapy, in designing and implementing programmes, as volunteers and as a vital part of the paid work force of service providers. The most successful pilot programmes for antiretroviral therapy in resource-limited settings have made community involvement a central element of planning and implementation. Unless the treatment and care provided are relevant to and respectful of community needs, people will not use the services.
- A rights-based approach to antiretroviral therapy programming should be used in designing and delivering antiretroviral therapy. A rights-based approach to health care is grounded in the empowerment of individuals and their communities by placing them at the centre of health services.

Each of these principles has application to vaccine and microbicide delivery as well, and valuable lessons can be learnt from the experience of treatment roll out in the context of the 3 by 5 Initiative to inform delivery of prevention products.

11.2 Preparing for delivery of new products

All three fields face the common challenge of ensuring that new products are available as soon as possible in poor countries. The logic of global markets has meant that the usual pattern has been for rich countries to enjoy access to new health technologies years in advance of developing countries. This is not an acceptable model for HIV treatments, vaccines or microbicides. Policy makers need to be preparing well in advance for the introduction of vaccines and microbicides, clarifying issues such as public sector involvement in distribution, guidelines for approval of partially effective products and promotion of products to communities at greatest risk, health professionals and community leaders.

Delivery issues for vaccines and treatments will likely overlap given the involvement of medical staff in prescribing, dispensing and administering products. Microbicides are more likely to be available over the counter and at a broad range of community sites including potentially local shops as well as from family planning and sexual and reproductive health services.[147] In the first instance microbicide distribution might piggyback on existing distribution systems for treatments and/or vaccines, such as

[146] *Emergency Scale-up of Antiretroviral Therapy in Resource-limited Settings: Technical and Operational Recommendations to Achieve 3 by 5: Report from the WHO/UNAIDS Zambia Consultation November 18-21 2003*, Lusaka, Zambia, Geneva: WHO 2003.
[147] Ibid, at 19.

community clinics, but the eventual pattern of delivery is more likely to reflect contraceptive distribution systems than drugs and vaccines. The key issue for microbicides will be promotion at the community level as an integral part of the HIV/STI prevention package.

There are intersecting issues regarding the need for health promotion messages that educate communities about the health benefits of each product. Women with HIV may be needing adherence support both in relation to consistent use of treatments and microbicides. The first vaccines are likely to require a series of vaccinations to be effective. Communities will need to be educated about the importance of receiving the full course of vaccinations, and the length of time that protection will last. Communities will need to understand the implications of partially effective vaccine and microbicide products, and the need to sustain other prevention strategies particularly condom use. There may be benefits in developing integrated community education approaches. These could be piloted in settings where products are anticipated to be trialled concurrently. Education could address the mutually supporting relationship of treatments, vaccines and microbicides, and issues specific to partially effective products.

Microbicide delivery will require education addressing complex issues regarding negotiation of sexual relationships and gender empowerment. Microbicides confront a range of distinctive cultural factors that are intertwined with gender roles and sexual practices (eg, use of a variety of intra-vaginal products across cultures). While some of these factors, such as male dominance and female lack of autonomy, may complicate the introduction of microbicides, others offer the opportunity to develop culturally appropriate microbicide introduction strategies that could increase acceptability. In most cultures, for example, women use intra-vaginal products in some form for hygiene, cosmetic, contraceptive or health enhancing purposes. Understanding the functions and meanings assigned to such products in any given culture is key to understanding how microbicides could most effectively be introduced in that culture.

Microbicides also imply the need for education of both partners in a sexual relationship in order to maximise likely use and acceptability. Product use by women will need to be 'sold' as a concept to men. Microbicides may also face resistance from some religious groups not likely to be encountered by vaccines and treatments (particularly if delivery is accompanied by sex positive or contraceptive messages perceived as promoting promiscuity). Microbicides, as a new form of intervention, may face more significant barriers in terms of acceptance of the legitimacy of the product. On the other hand, by offering a very direct form of empowerment to women, microbicides offer a tool for combating the systematic marginalization of women's rights.

Acceptability of vaccines, microbicides, and the potential use of ARVs as prophylactics will be shaped by cultural factors. Prevention products face the barrier that people may resist access due to concerns about the association between product use and stigmatized groups such as sex workers, or concerns about being perceived as promiscuous. Product 'positioning' is complex for microbicides given the product's immediate connection with sexual behaviour and gender issues.

Ultimately the aim is to promote a comprehensive package whereby a range of affordable prevention and treatment services and products are available at accessible locations. NGOs have a special role in providing support to the roll out of new health technologies. Treatment activists in the South have helped to provide the social and political environment in which access to new therapies is seen as a consumer right, and the continued vibrancy of this movement may be critical to generating local support for the for rapid roll out of vaccine and microbicide products as they become available.

Depending on the likely timing of availability of new products, there may be benefits from combined social research efforts to prepare for delivery. Research will be required to assess consumer attitudes to products (ie, their acceptability, and the influence of gender dynamics on health protection choices), the likely demand for both vaccine and microbicide uptake (individually and in combination), and consumer responses to partially effective prevention products. Epidemiological analyses and social research identifying characteristics of communities at increased risk of HIV are required to forecast need for both vaccines and microbicides. This research must address both those populations traditionally recognized as high-risk (such as sex workers, drug users and migrant populations) and less visible populations (such as monogamous women infected by non-monogamous partners).

The Microbicides Initiative recommended the establishment of pilot initiatives in three to five countries, particularly those with current or future clinical trials, to establish a framework for 'microbicides preparedness'.[148] Given that these could be the same countries where vaccines are being trialled in some of the same at risk communities, consideration could be given to joint approaches to vaccine and microbicide preparedness (although the priority of targeting microbicides for women, women's differential risk factors and preparing women's health services to support delivery may argue against this).

Discussion points

Advocates should work together to:

- *Support the rapid establishment of sustainable health systems to support delivery of ARVs and to prepare for delivery of new therapeutic, diagnostic and preventive technologies, including through investments in laboratory and clinical infrastructure*
- *Promote sustainable strategies for staff training and development*
- *Develop strategies to mobilize communities and providers through integrated community education programs that address the mutually supporting relationship of treatments, vaccines and microbicides*
- *Ensure issues regarding appropriate use of partially effective prevention products are addressed in community education*

[148] Access Working Group of the Microbicide Initiative, supra, note 87, at 6.

- *Ensure that education addresses issues regarding the use of products in the global South that are rejected by Northern regulators or have not been reviewed by regulators for use in the North*
- *Promote the need for social, economic and epidemiological research to assess need and demand for treatments, vaccines and microbicides in different settings, and which explores the social and cultural contexts of delivery and behavioural responses to partially effective prevention products.*

Chapter 12 National plans

12.1 Planning imperatives

National planning is a key strategy for ensuring public and political support for vaccines, microbicides and treatments. National Plans are also an important accountability mechanism and can be used to hold governments to account for national budgetary allocations to HIV treatment and prevention, research efforts and the strengthening of health delivery systems.

National planning as a policy measure to support universal access to treatment and prevention is highlighted as important to a human rights approach by the *International Guidelines on HIV/AIDS and Human Rights.*[149] Advocates need to consider how R&D needs and access measures should be represented in national plans. National planning should support investment in delivery systems, trial capacity and regulatory infrastructure.

National Plans should set out a comprehensive approach to HIV needs. Plans should define an integrated package of measures, including treatments, voluntary counselling and testing, education, harm reduction, condom distribution, care and support, research issues (including new therapies, diagnostics, microbicides and vaccines), and efforts to address stigma, discrimination, gender inequalities and other social and cultural factors that drive the epidemic

There is an immediate need to ensure national planning to support treatment scale up in developing countries. Countries also need to start contingency planning now to enable vaccine and microbicide delivery systems to be operational for priority populations as soon as possible after new products are licensed.

There are different considerations for planning in developing countries as compared to rich countries. The timing and content of planning by developing countries is often heavily influenced by donor requirements rather than as a result of domestic needs. Most low-income countries are currently developing Poverty Reduction Strategy Papers (PRSPs) to comply with World Bank loan requirements. As PRSPs are required to

[149] See Revised Guideline 6, Recommendation (a), supra, note 29 at 15.

address the UN Millennium Development Goals, HIV/AIDS and access to medicines are issues which ought to be addressed in these plans. GAVI has worked with some low-income countries to include vaccine coverage in their PRSPs. Countries seeking to receive HIV/AIDS funding under the World Bank's MAP program are required to develop a national HIV/AIDS strategy.

National planing in rich countries needs to distinguish between efforts to address domestic needs and efforts targeted at developing country needs. Consideration of the contribution of treatment, microbicide and vaccine developments to addressing the global epidemic should include not just R&D priorities, but also the country's role in supporting the development of global mechanisms to support access such as equity pricing and bulk procurement, provision of aid targeted at building the health infrastructure of developing countries, and consideration of whether trade policy (eg, free trade and investment agreements) support or hinder access to medicines and new technologies by developing countries.

UNAIDS has been supporting HIV specific national planning efforts. Most sub-Saharan countries now have national HIV/AIDS plans. Brazil is unique globally in having conducted national planing relating to treatments, vaccines and microbicides (see appendix C below). The African AIDS Vaccine Programme is conducting a review of the position of vaccines within national HIV/AIDS plans. The Canadian HIV/AIDS Legal Network's report on *HIV Vaccines for Developing Countries* stressed the importance of national planning to ensuring commitment to vaccines, and recommended that plans should cover strategies and timelines for:

- Preclinical and clinical research
- Vaccine development and manufacture
- Regulatory review and approval of new clinical research and new vaccines
- Field safety and effectiveness research
- Public health use and accessibility of vaccines. [150]

The Canadian Government agreed in 2002 to develop a National HIV/AIDS Vaccine Plan. In the UK, the MRC has both an HIV/AIDS Vaccine Strategy and a Microbicide Development Program but planning efforts to date have been focused on technical aspects of the clinical development pipeline, rather than on longer term funding needs and the broader access and delivery agendas. The US outlined its commitment to HIV vaccine R&D in NIAID's *Global Health Plan* 2001 but does not as yet have a microbicide plan.

WHO has assisted Brazil, Rwanda, Thailand, and Uganda in the development of National HIV/AIDS Vaccine Plans. These Plans describe national policies, mechanisms for review and approval of research proposals, and priority vaccine-related research. Vaccine plans

[150] S Avrett *HIV Vaccines for Developing Countries: Advancing Research and Access: Summary report* Montreal: Canadian HIV/AIDS Legal Network 2003 at 20.

need to consider how a future HIV vaccine will fit within existing national immunisation strategies.

During 2002 and 2003, TAC advocated for a national prevention and treatment plan for South Africa through the National Economic Development and Labour Council. The Draft South African Treatment and Prevention Plan produced by the Council (see Appendix C) is instructive as a product of partnership between labour, industry and community that includes both public and private initiatives, and in its explicit adoption of a human rights framework which links prevention and treatment. As the emphasis is on access to services, the Plan does not refer to R&D, and vaccines and microbicides are omitted from most recent drafts. The South African Government did not adopt the Council's Draft plan, but developed instead its own plan for public sector ARV provision to be implemented from 2004.

12.2 World Bank role in national planning in developing countries

The World Bank's Multicountry HIV/AIDS Program (MAP) for Africa and the Caribbean are long term (12 to 15 year) programs to support national planning and implementation of national HIV/AIDS strategies and action plans.[151]

MAP guidelines encourage countries to establish a National HIV/AIDS Council, develop a National HIV/AIDS strategic plan that reflects a multi-sectoral approach, and establish a Strategy secretariat to oversee contracting, monitoring and evaluation. Eligibility criteria for MAP encourage broad representation of key stakeholders from all sectors, including people living with HIV/AIDS, in national councils, and Government commitment to quick implementation arrangements, including channelling grant funds for HIV/AIDS activities directly to communities. Governments have a great degree of flexibility in applying MAP funds, including support for clinical trials and provision of treatments.

MAP is structured in three phases. The first phase received US$1B in 2001-2003. Phase 1, which will extend to around 2005, will build capacity and scale up existing programs in prevention, care, support, and mitigation. Later phases will mainstream effective programs, attain nationwide coverage, and expand care, support and treatment interventions. The program is likely to emerge as a major source of support for strengthening health sector capacity in least developed countries. An important element of the MAP approach is support to civil society groups including organizations of people living with HIV/AIDS.

MAP is a possible new source of support for national plans that incorporate capacity building for community and advocacy efforts linked to clinical trials and delivery of new treatment and prevention interventions. Given the program's long term vision, MAP may be more amenable than other sources to providing support for vaccine and microbicide

[151] See www.worldbank.org/afr/aids/map_manuals.htm

related community and infrastructure capacity building and nationally coordinated efforts to prepare delivery systems.

12.3 Key elements of national planning

Countries should be working towards comprehensive national plans that integrate treatment and prevention strategies. Whether as stand alone Vaccine, Treatment or Microbicide Plans, or as parts of National HIV/AIDS Strategies or national poverty reduction or development plans, key elements to be incorporated into the national planning of low and middle-income countries include:

Principles

- A human rights framework, which acknowledges international, regional and national legal obligations regarding the right to health
- Equity in access to treatment and prevention services on a non-discriminatory basis
- Commitment to participation of community representatives including people living with HIV/AIDS, in developing, monitoring and implementing national plans
- Recognition of the mutually reinforcing link between prevention and treatment, and the implications of this for investments in health infrastructure.

Priorities

- Delivery plans for existing and future treatments, vaccines, and microbicides
- A process for involvement of people living with HIV/AIDS and affected communities in decision making about access to and delivery of products, and the conduct of research including clinical trials
- Consideration of the strategic role which the nation may play in hosting or initiating vaccine, microbicide and treatment R&D efforts
- A process for determining locally applicable standards of treatment and care, including for trial participants
- Support for social and behavioural research, including relating to the impact of trials and new technologies on behaviour
- A program of community capacity building to ensure meaningful involvement of people living with HIV in development, monitoring and evaluation of national plan elements
- Ethical review arrangements, including ethical review bodies and the development and review of national ethical guidelines for HIV treatment, vaccine and prevention trials that specifically address the ethical implications of hosting international trials
- Addressing the desired outcomes from public private relationships, particularly the role of the pharmaceutical sector in supporting expanded access
- Initiatives to build capacity of regulatory authorities, to harmonize regulations at a regional level and to enhance community input to regulatory processes
- Demand and need estimates for national vaccine and microbicide uptake

- Consideration of national roles in regional initiatives, such as links to or establishment of centres of excellence in regulatory and intellectual property issues
- Consideration of the impact of trade and investment agreements on national HIV related public health priorities and clinical trial needs
- Review of tax, tariff and trade restrictions with a view to minimising costs for all HIV and OI treatments and prevention products.

Ideally national planning should dovetail with regional planning initiatives. Within Europe, it is intended that the EDCTP facilitate such a strategy. National plans should also allow greater complementarity of initiatives between major national funders of R&D, particularly as between the US and Europe, to avoid unnecessary duplication of efforts.

For reference, Appendix C includes extracts from key low and middle-income country national planning documents.

Discussion points

Advocates should work together to support:

- *Development of National HIV/AIDS Plans or Strategies that adopt a human rights framework promote the prevention–care–treatment continuum and include a comprehensive approach to HIV encompassing treatments, microbicides and vaccines as well as voluntary counselling and testing, education, harm reduction, condom distribution, care and support, and efforts to address stigma, discrimination and gender vulnerability*

- *Development of minimum standards against which advocates can hold Southern governments to account for national budgetary allocations to HIV treatment and prevention, research efforts and the strengthening of health delivery systems.*

- *Promotion of the involvement of people living with HIV/AIDS and civil society groups in the development, content, implementation and monitoring of national plans.*

- *Development of checklists of essential items relating to R&D and access as an evaluation and accountability tool for assessing National Plans (eg, community involvement, ethical review, regulatory issues).*

Part III Advocating the agenda

Chapter 13 Advocacy opportunities 2004-2006

13.1 International Convention or trade framework on health R&D

Some treatment advocates have been investigating the need for an International Convention, Treaty, or multilateral trade framework for health R&D.[152]

A proposal for a Convention was discussed at an international meeting held in Geneva in April 2003 organised by MSF, Consumer Project on Technology (CPTECH), Health Action International, Oxfam and the Third World Network. The meeting involved both HIV treatment advocates (Gay Men's Health Crisis - GMHC) and vaccine advocates (IAVI). A proposal from the meeting was put to World Health Assembly delegates recommending that WHO begin discussions on an international convention aimed at stimulating essential health research and development. The proposal argued for a Convention which could:

- Define a needs-driven international R&D agenda;
- Commit all countries to contribute to R&D for health;
- Outline an agreement and clear rationale for sharing the cost burden of R&D;
- Define appropriate funding and incentive mechanisms so that governments can fulfil their commitments to public sector involvement in R&D;
- Establish and strengthen international mechanisms for exchanging and transferring research results, knowledge and technology.

Precedent for this exists in the *Treaty of Europe,* which includes provisions for public sector funding of R&D, and there are measures to ensure that the least developed countries in Europe receive a relatively greater share of R&D investments in order to promote a more equal level of development. James Love of CPTECH has called for a global treaty or trade agreement on health care, features of which might include:

- Transparency of investment flows,
- Identification of areas of the greatest public health R&D needs,
- Mechanisms to ensure that there is access to new inventions,
- Technology transfer and capacity building in lesser developed countries,
- Greater efficiency in terms of the costs of acquiring R&D, and
- Avoidance of anti-competitive or unfair trade practices.[153]

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[152] See eg, J Love. *From TRIPS to RIPS: A Better Trade Framework to Support Innovation in Medical Technologies*. Presentation at the Workshop on economic issues related to access to HIV/AIDS care in developing countries, Agence Nationale de Recherches sur le Sida, Marseille, 27 May 2003.

[153] Ibid at 5; and see J Love, *Basis for a Treaty on R&D*, presentation at Meeting on global framework for supporting health research and development (R&D) in areas of market and public policy failure, Geneva, 29 April 2003 (available via www.cptech.org/ip/health/rndtf/)

There are a number of areas where it may be useful to have global agreements that would expand access to publicly funded R&D. It may be appropriate for global institutions like the WHO, World Bank or UNAIDS to be granted licenses to use government funded patents in poor countries, or to grant non-exclusive licenses to use such inventions in all developing countries. Public health goods might benefit from agreements similar to that entered into by United States, France, Japan, Germany and the UK to put the human genome research into the public domain.[154]

Advocates seeking to pursue new multilateral initiatives in this area should focus on building support for proposals to put to the annual World Health Assemblies held each May. The willingness of the WHA to agree a Tobacco Control Treaty in 2003 suggests that it is more receptive to taking proactive public health measures through global agreements. The world summit on health R&D scheduled for November 2004 in Mexico City may also be an appropriate focus for advocacy.

13.2 WHO Commission on Intellectual Property, Innovation and Public Health

At the 2003 World Health Assembly, it was agreed that WHO would establish by January 2004 a "time-limited body to collect data and proposals from the different actors involved and produce an analysis of intellectual property rights, innovation, and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries", and to submit a progress report to the 2004 World Health Assembly and a final report to the WHO Executive Board in January 2005. This proposal drew from the experience of the UK's Commission on Intellectual Property Rights, which reported in 2002. Membership of the commission to conduct the review was announced in February 2004. Advocates could benefit by agreeing common points to be proposed to the WHO commission either independently or through joint proposals.

13.3 Globalisation of intellectual property regimes: WTO and WIPO

The neo-liberal policy bias of WTO and WIPO, in putting trade liberalisation and intellectual property interests above public health, needs to be monitored and challenged on a number of fronts. An option would be to advance a joint position to WTO delegates and to WIPO in relation to: (1) ensuring appropriate technical assistance is provided to developing countries to maximize benefits from the Doha Declaration's flexibilities regarding compulsory licensing and to maximize access to generic ARVs; (2) ensuring that provisions of Patent Treaties reflect the need for public health factors to take precedence over intellectual property rights where necessary; and (3) exclusion and roll back of 'TRIPS-plus' provisions in bilateral and regional trade agreements. Advocates might enlist backing of UN agencies in these areas including WHO and the Office of the

[154] J Love, T Hubbard, Medicines without barriers, *New Scientist* 14 June 2003 (http://lists.essential.org/pipermail/ip-health/2003-June/004878.html)

High Commissioner on Human Rights, and pursue issues through UN human rights mechanisms.

After pressure from a coalition of activists, academics and researchers in mid 2003, WIPO made a commitment to convene a conference in 2004 to discuss open and collaborative R&D models.[155] If the conference does occur, it may provide an opportunity for HIV advocates to present the case for WIPO to be actively supporting and promoting new models of collaborative HIV research, such as the Global HIV Vaccine Enterprise proposal.

13.4 G8 summits

In preparation for the 2003 G8 summit, a proposal was submitted by some NGOs to establish a G8 Task Force on New Health Technologies. The 2003 G8 resulted in a disappointing *Plan of Action on Health*. Advocates should coordinate their efforts to ensure that 2004 and 2005 summits result in more concrete outcomes. Joint proposals targeting host US and UK Governments for these summits should be prepared well in advance and with broad cross sectoral support eg, seeking in principle support for proposals from UN agencies. The UK Government has announced its intention to address HIV/AIDS issues at the 2005 G8 summit, which it will be hosting.

13.5 UN Millennium Development Goals (MDGs) and the UN Millennium Project

The MDGs are highly significant in informing the priorities of global donors (see Appendix B and *World Development Report 2004*).The UN's recommended strategies for achieving the Goals will influence the major global bilateral and multilateral agencies such as the World Bank, UNDP, DfID and the EU. The MDGs are the central point of reference for discussions around financing development.

An opportunity to shape UN action on the MDGs is by way of influencing the UN's Millennium Project. The Project's director Jeffrey Sachs of Columbia University serves as Special Advisor to the UN Secretary-General on the MDGs. Over a period of three years the Millennium Project is defining a Global Framework for Action for achievement of the MDGs by 2015. The Project's research focuses on identifying the operational priorities and financing structures necessary to achieve the MDGs. The Project has established separate Task Forces on HIV/AIDS and Access to Medicines, which advocates could target so as to influence priorities. In mid 2004 the Millennium Project will provide an Interim Report, followed by a Final Report due to be delivered to the UN Secretary-General by 30 June 2005.

[155] *Hopes revive for talks on alternatives to patents* Financial Times; 1 Oct 2003; and see: www.cptech.org/ip/wipo/openwipo.html

13.6 UN Special Rapporteur on the Right to Health[156]

The UN Special Rapporteur on Health, Paul Hunt, is conducting a three year investigation from 2002-2005. Focus areas of his work include neglected diseases, poverty reduction strategies and WTO agreements. Under the topic of neglected diseases, the Rapporteur is examining the 10/90 disequilibrium (only 10% of R&D spending is directed at the health problems of 90% of the global population) and the role of funding mechanisms such as the Global Fund. It may be beneficial for advocates to present a joint plan of action to the Rapporteur on priority measures which the UN system should undertake to promote rights to access new health technologies. The Special Rapporteur can also be used to highlight any particularly poor conduct by recalcitrant national governments that is preventing access to affordable medicines.

13.7 UN Declaration of Commitment on HIV/AIDS compliance reporting

Performance indicators were developed by UNAIDS in 2002 for use in monitoring national and global progress towards achieving UNGASS targets. Countries are required to report progress periodically to UNAIDS using the indicators, and UNAIDS presents a summary report for annual consideration by the UN General Assembly.[157] It may be useful to develop more precise indicator sets to monitor R&D and access measures. It is not clear how significant a role the published indicators will play in informing decision making about priorities and resource allocation. The indicators are subject to review and revision, so opportunities exist to provide advice to UNAIDS on indicators that might focus greater attention on progress in areas discussed in Part II above.

13.8 International and Regional HIV/AIDS Conferences

The International AIDS Conferences (Bangkok 2004, Toronto 2006), annual treatment, vaccine and microbicide conferences, and the regional HIV/AIDS Conferences provide an opportunity to publicize and build support for a consensus agenda on R&D and related access issues. At a minimum, coordination of planning in the lead up to the conference to ensure that the presence of global advocacy organizations (through timing of satellites etc) is complementary rather then competing would be beneficial. The media attention that the global conferences attract is an opportunity for joint media work on a single issue of agreed priority, such as highlighting successes in combining treatment scale up strategies with prevention trials.

13.9 Community education work with HIV/AIDS service organizations and people living with HIV/AIDS groups

Advocates have a common interest in translating global agendas into local action through community based initiatives such as community education that aims to put R&D agendas

[156] P Hunt, supra, note 25.
[157] UNAIDS, supra, note 35.

into a locally relevant context. This should be conducted by or in conjunction with local HIV/AIDS service organizations and people living with HIV/AIDS groups.

Treatment, vaccine and microbicide advocates emphasise the role of community education and participation in the conduct of research and access issues. AVAC has argued:

> Early and repeated educational efforts will be needed to ensure that people are informed not only about clinical trials but also about what AIDS vaccines can and cannot accomplish in terms of disease control. Integrated educational approaches that offer a full description of the biomedical and behavioural approaches to HIV/AIDS will be more successful than educational efforts that tell only part of the story.[158]

Advocates can support communities by informing them of the full range of options rather than a single focus. Initiatives seeking community participation need to invest in building the capacity of community representatives to represent interests of diverse community members, including in particular people living with HIV and members of vulnerable communities such as sex workers and drug users.

The International Council of AIDS Service Organizations (ICASO) has a strategy of supporting community education initiatives through developing community toolkits and providing NGO support. Joint efforts to support community engagement in R&D agendas could consider using ICASO's international membership structure.

Discussion points

Advocates should agree a strategy to prioritize and support coordinated efforts targeting key opportunities arising in the period 2004-2006, including

- *Building World Health Assembly support for new multilateral measures to address global equity issues relating to health R&D*
- *Submissions to the WHO Commission on Intellectual Property, Innovation and Public Health*
- *Targeting WTO delegates and WIPO to influence the evolving global IP regime*
- *Proposals for measures to expand access to existing and future global health products and for enhanced R&D support to the annual G8 summits*
- *Input to the UN Millennium Project*
- *Input to the UN Special Rapporteur on the Right to Health*
- *Work with UNAIDS to ensure monitoring of the Declaration of Commitment on HIV/AIDS supports R&D and access agendas*
- *Key advocacy messages to be delivered at Bangkok 2004, Toronto 2006 and other sector conferences*

[158] www.avac.org/actionComm.htm

- *Systematic and coordinated work with HIV/AIDS service organizations and people living with HIV/AIDS groups on community education regarding access to treatments and prevention technologies and clinical trials.*

13.10 Advocacy frameworks

To support coordinated advocacy, advocates should communicate more regularly and systematically about action on shared priorities. Advocacy organisations need to build the capacity of advocates for collaborative, mutually supportive advocacy at national and international levels. A first step in this process is the development of shared understanding amongst advocates of the nature and priorities of vaccine, microbicide and treatment fields and their respective resource needs. Advocates should engage in cross-learning to share experiences, educate each other about new challenges being confronted and lessons learnt from recent successes (and failures), and to further explore both the overlapping and divergent policy agendas of each field.

To galvanise commitment to collaboration, advocates should jointly develop a Statement of Commitment to a comprehensive, human rights based HIV/AIDS response. Advocates should collaborate in promoting this Statement amongst advocacy groups and the wider research, health and development sectors.

Advocates need to consider the full range of options for collaborative efforts. Possible actions include:

- Joint workshops, conferences or meetings alongside regional and/or global Conferences to share progress, build trust and understanding, and debate future priorities.

- Interagency links between some of the key global players to support a joint advocacy strategy eg, IAVI-AVAC-GCM-IPM-AMD-MSF-ITAC etc. Links may be formal or informal, and could be at governance levels, between chief executives and/or at the level of policy and advocacy program staff.

- Consideration of whether to focus on a single common issue to initiate a new global Campaign around (eg, a new financing mechanism for global public health goods to help support achievement of WHO's ARV scale-up targets), and whether to engage in a joint, public campaign focused on an upcoming global advocacy opportunity (eg, the 2005 G8 summit).

- Commitment to a joint work plan that establishes agreed priorities for action over the next two years.

- Establishment of task focused, time limited interagency campaign groups

- Information sharing mechanisms, such as regional summits between leading advocates, and new electronic communication channels eg, jointly sponsored campaign websites.

- Jointly supported capacity building activities for advocates and support for South-South and South-North sharing of skills and experience.

Appendices

Appendix A

Aims and remit of some of the key global organizations

AMD Alliance for Microbicide Development

The Alliance for Microbicide Development is a global, non-profit organization whose sole mission is to speed the development of safe, effective, and affordable microbicides to prevent sexually transmitted infections, most critically HIV/AIDS. The Alliance was founded in 1998 as an agent of change at a time when progress in microbicide research was slow, fragmented, and severely under-funded. A coalition of representatives from over 200 bio-pharmaceutical companies, non-profit research institutions, and health advocacy groups, the Alliance catalyzes support for its mission through advocacy, education, monitoring, research, trouble-shooting, convening dialogue around key issues, participating in dynamic and committed partnerships, and networking across constituencies, disciplines, and sectors.

GCM Global Campaign for Microbicides

The Global Campaign for Microbicides is a broad-based, international coalition of organizations working to accelerate access to microbicides. GCM's goals are to: Generate political will and increased funding for microbicide research, female condom, and cervical barrier methods; create a supportive policy environment for the timely development, introduction and use of new prevention technologies; and to ensure that, as the science proceeds, the public interest is protected and the rights and interests of trial participants, users, and communities are fully represented and respected. Activities include: awareness-raising among policy-makers, opinion leaders, the scientific community and general public about microbicides and prevention options for women; legislative advocacy and resource mobilization in donor countries; policy advocacy in government and international organizations; strengthening capacity and building consensus within the advocates community; representing user needs and interests; media and electronic outreach.

IPM International Partnership for Microbicides

The IPM was established in 2002 and aims to increase the efficiency of the development and delivery of a microbicide by expanding the breadth and level of public and private sector funding; identifying critical gaps in research and development, access, and advocacy; leveraging partnerships with both new and existing public and private players; and helping to raise awareness of microbicides worldwide.

IWGM International Working Group on Microbicides

The IWGM was established in 1994, with initial support from WHO, to ensure the closer coordination of a number of separate research programmes. It's role is to facilitate the development and approval of safe, effective, affordable and acceptable microbicides. IWGM's membership is global and includes individual members from twenty-one governmental and non-governmental organizations, from both the North and the South. IWGM is a group of experts who operate as an influential network. IWGM does not intend to have its own research programme or strategy, or funds for supporting research. IWGM's discussions are intended to foster interactions between a wide range of bodies and its deliberations feed into other partnerships/collaborations. IWGM provides a mechanism for the independent expert assessments of significant issues, which makes it possible for IWGM to develop influential 'corporate' statements without having to reflect the views of individual member organisations.

IAVI International AIDS Vaccine Initiative

The International AIDS Vaccine Initiative is a global organization working to speed the development and distribution of preventive HIV vaccines. IAVI's work focuses on four areas: mobilizing support through advocacy and education; accelerating scientific progress; encouraging industrial participation in vaccine development; and assuring global access. IAVI is financing trials of [five] vaccines candidates

AVAC AIDS Vaccine Advocacy Coalition

The AIDS Vaccine Advocacy Coalition's mission is to speed the ethical development and global delivery of preventive HIV vaccines. AVAC is a 'watchdog, educator and advocate'. AVAC addresses ethical issues, critiques the work of industry and government, provides education and mobilization services, and speaks on behalf of affected communities. AVAC is a coalition of volunteer advocates and paid staff.

ITAC International HIV Treatment Access Coalition

Formed in 2002, ITAC is a coalition of partner organizations including people living with HIV/AIDS and their advocates, NGOs, governments, foundations, the private sector, academic and research institutions and international organizations. Their shared goal is expanded access to HIV treatment for all people living with HIV/AIDS who need it. ITAC aims to mobilize and augment its partners' efforts to increase affordability, availability and uptake of HIV treatments. ITAC's priorities include: Sharing information about pilot initiatives so that lessons learnt can be applied to scale up programmes; Fostering national and international leadership and advocacy, including maintaining pressure for lower drug prices; Helping to galvanize and coordinate donor action to assist governments embarking upon treatment programmes; Supporting the implementation of national HIV treatment programmes; Disseminating information about treatment programmes, including training manuals and best practice models; Promoting an operational research agenda to improve HIV/AIDS service delivery systems (public and

private), as part of wider efforts to improve overall systems performance; Quality control including services, drug manufacturing and provider accreditation.

MSF Médecins Sans Frontières

MSF's Access to Essential Medicines Campaign is a broad effort to promote access to medicines for a range of illnesses prevalent in developing countries, including HIV. The Campaign is active in the areas of:

- advocating changes to international trade rules and patent protections to promote access;
- addressing the chronic crisis of R&D for effective, affordable and easy-to-use medicines for neglected diseases by arguing for a paradigm shift, involving increased funding, to set a needs-driven global R&D agenda, and create new mechanisms for financing sufficient and adapted R&D for neglected diseases.

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ICASO International Council of AIDS Service Organizations

ICASO is a global network of non-governmental and community-based organizations. ICASO has secretariats in five geographic regions, and a central secretariat based in Canada. ICASO conducts a program of advocacy on vaccines and microbicides, and has a long history of involvement in supporting treatment activism.

ICASO's mission is to mobilize communities and their organizations to participate in the response to HIV/AIDS; articulate and advocate the needs and concerns of communities and their organizations; ensure that community-based organizations, particularly those with fewer resources and within affected communities, are strengthened in their work to prevent HIV infection, and to provide treatment, care and support for people living with and affected by HIV/AIDS; promote the greater involvement of people living with, and affected by, HIV/AIDS in all aspects of prevention, treatment, care and support, and research; and promote human rights in the development and implementation of policies and programs responding to all aspects of HIV/AIDS.

Appendix B Global goals and indicators

Millennium Development Goals

Goal 6:	Combat HIV/AIDS, malaria and other diseases
Target 7	Have halted by 2015 and begun to reverse the spread of HIV/AIDS
Indicator 18	HIV prevalence among 15-24-year-old pregnant women
Indicator 19	Condom use rate of the contraceptive prevalence rate
Indicator 20	Number of children orphaned by HIV/AIDS
Goal 8:	Develop a Global Partnership for Development
Target 17	In co-operation with pharmaceutical companies, provide access to affordable, essential drugs in developing countries
Indicator 46	Proportion of population with access to affordable essential drugs on a sustainable basis

UN General Assembly Declaration of Commitment on HIV/AIDS (2001)

Research and development

With no cure for HIV/AIDS yet found, further research and development is crucial

70. Increase investment and accelerate research on the development of HIV vaccines, while building national research capacity especially in developing countries, and especially for viral strains prevalent in highly affected regions; in addition, support and encourage increased national and international investment in HIV/AIDS-related research and development including biomedical, operations, social, cultural and behavioural research and in traditional medicine to: improve prevention and therapeutic approaches; accelerate access to prevention, care and treatment and care technologies for HIV/AIDS (and its associated opportunistic infections and malignancies and sexually transmitted diseases), including female controlled methods and microbicides, and in particular, appropriate, safe and affordable HIV vaccines and their delivery, and to diagnostics, tests, methods to prevent mother-to-child transmission; and improve our understanding of factors which influence the epidemic and actions which address it, inter alia, through increased funding and public/private partnerships; create a conducive environment for research and ensure that it is based on highest ethical standards;

71. Support and encourage the development of national and international research infrastructure, laboratory capacity, improved surveillance systems, data collection, processing and dissemination, and training of basic and clinical researchers, social scientists, health-care providers and technicians, with a focus on the countries most affected by HIV/AIDS, particularly developing countries and those countries experiencing or at risk of rapid expansion of the epidemic;

72. Develop and evaluate suitable approaches for monitoring treatment efficacy, toxicity, side effects, drug interactions, and drug resistance, develop methodologies to monitor the impact of treatment on HIV transmission and risk behaviours;

73. Strengthen international and regional cooperation in particular North/South, South/South and triangular cooperation, related to transfer of relevant technologies, suitable to the environment in prevention and care of HIV/AIDS, the exchange of experiences and best practices, researchers and research findings and strengthen the role of UNAIDS in this process. In this context, encourage that the end results of these cooperative research findings and technologies be owned by all parties to the research, reflecting their relevant contribution and dependent upon their providing legal protection to such findings; and affirm that all such research should be free from bias;

74. By 2003, ensure that all research protocols for the investigation of HIV-related treatment including anti-retroviral therapies and vaccines based on international guidelines and best practices are evaluated by independent committees of ethics, in which persons living with HIV/AIDS and caregivers for anti-retroviral therapy participate.

Monitoring the Declaration of Commitment: Guidelines on Construction of Core Indicators (UNAIDS 2002)

Global commitment and action indicator

Public funding for R&D: amount of public funds available for R&D of vaccines and microbicides. Annual survey on financial resource flows. Survey questionnaires are distributed annually to countries with governments that provide funding to research institutions for R&D of vaccines and microbicides.

Interpretation: This indicator provides a proxy measure of the commitment of governments to HIV/AIDS research and development. Public funding from governments is only a small fraction of the total expenditure on R&D of vaccines and microbicides. Public funding for items such as drugs for the treatment of HIV/AIDS and other STDs is minimal and therefore is not included in this indicator.

HIV Treatment: antiretroviral combination therapy indicator

Percentage of people with advanced HIV infection receiving ARV combination therapy. Advanced HIV is taken to be 15% of the total no. of people infected.

Biennial monitoring of all countries. The indicator permits monitoring of trends in coverage, but does not attempt to distinguish between different forms of ARV therapy, or to measure the cost, quality or effectiveness of treatment provided.

International Guidelines on HIV/AIDS & Human Rights Revised Guideline 6: Access to Prevention, Treatment, Care and Support (OHCHR/UNAIDS 2003)

States should enact legislation to provide for the regulation of HIV-related goods, services and information, so as to ensure widespread availability of quality prevention measures and services, adequate HIV prevention and care information, and safe and effective medication at an affordable price.

States should also take measures necessary to ensure for all persons, on a sustained and equal basis, the availability and accessibility of quality goods, services and information for HIV/AIDS prevention, treatment, care and support, including antiretroviral and other safe and effective medicines, diagnostics and related technologies for preventive, curative and palliative care of HIV/AIDS and related opportunistic infections and conditions.

States should take such measures at both the domestic and international levels, with particular attention to vulnerable individuals and populations.

Appendix C National Plan precedents

The purpose of this appendix is to highlight features of existing national planning documents, such as principles, approaches and priorities. These may provide a basis for discussion on desirable features of National Plans to provide a supportive policy environment for treatments, vaccines and microbicides.

Brazil [159]

- Has a National Vaccine Plan, Microbicide Plan and AIDS Drugs Policy
- The 2001 Drugs Policy includes:
    - a program for the free and universal access to ARVs through the public health network
    - consideration of primary care infrastructure needs, national production of ARVs, adherence issues and procurement policies to reduce costs
    - creation of a Laboratory Network for viral load and CD4/CD8 cell counts
    - support to organizations of People Living with HIV/AIDS and to projects carried out by NGOs
    - committee structure to define and update clinical guidelines for ARV use
    - assistance to developing countries including technology transfer to support manufacturing capacity (technical support for the design and construction of production plant, manufacturing methods, training in quality control and analytic methods) and export of generics

- General guidelines of National Vaccine Plan and National Microbicides Plan
  • Reinforcement of existing infrastructure
  • Preference given to activities that involve technology transfer
  • Guarantee of access to evaluated products
  • Compatibility to ongoing activities
- Vaccine/microbicide preparatory infrastructure;
  • Network of HIV and reproductive health services
  • Laboratory network for serology, CD4 counts, viral load and genotyping
  • National Network for isolation and characterization of HIV (Molecular epidemiology of circulating HIV-1)
  • Anti-retroviral therapy distribution network
  • Many potential partners at Universities and Research Institutes

[159] National Drugs Policy 2001 and National HIV Vaccine Plan 1999 available at www.aids.gov.br/final/diagnostico/documentos.htm. Vaccine and Microbicide Plan summary drawn from presentation at Microbicides 2002, K Souto, H Ahrens *Brazilian Initiative on Vaccines and Microbicides for HIV/Aids Prevention* National STD/AIDS Program Brazilian Ministry of Health www.itg.be/micro2002/downloads/presentations/
:

- Vaccines and microbicides are positioned within the full spectrum of prevention strategies
- Estimation of HIV incidence in potential sites
- Feasibility studies in potential phase III sites
- Identification of partners for raising awareness and community involvement NGOs; Media; Inventory of Brazilian research institutions
- Delineation of scenarios and potential demands for tested products
- Ethical approval mechanisms stipulated
- Confirms ethical principle that the best treatment proved anywhere in the world must be provided to volunteers who become infected by HIV

Thailand

Drawn from *National Plan for HIV/AIDS Vaccine Development 1999* [160]

- The National Vaccine Plan is an operational extension of the National Plan for Prevention and Alleviation of HIV/AIDS, which is a part of the National Economic and Social Development Plan.
- Establishes a comprehensive strategy aimed at promoting the development, evaluation, and future availability of safe, effective, and affordable products for Thailand and neighbouring countries: a contribution to the global effort to develop new products with consideration of regional needs
- Promotes infrastructure strengthening, training, and transfer of knowledge and expertise in technical, managerial, and operational areas, to support the long-term involvement of Thailand in research
- Fosters and coordinates collaboration on research within different domestic institutions as well as with international institutions
- Focuses on the comparative advantage of Thailand in clinical evaluation of HIV vaccines, especially Phase III trials.
- Promotes a proactive and innovative approach aimed at identifying candidate vaccines which could be especially suited for Thailand, based on biological, epidemiological or economic considerations,
- Stimulates consensus building and collaborative work
- Bases decisions on the best scientific information available worldwide.
- Identifies all domestic HIV researchers and institutes and a process for development of policy and procedures for the planning, implementation, administration, and evaluation of R&D activities.
- Recognising expertise and know how to develop and manufacture vaccines is mostly located in the private sector, encourages partnership with the Pharmaceutical Industry
- Outlines procedures for submission/review/approval of research
- Recognises the need to resource consensus-building and training in virology, clinical trials, Good Clinical Practices, data management, and communications.

[160] Available at www.aidsthai.org/download/planvacine_eng.doc

- Commits technical and administrative support for epidemiological studies & establishment of cohorts for HIV incidence
- Supports social and behavioural research.
    - Assessment of base-line risk behaviours in potential study populations for trials and effect of preventive interventions on those risk behaviours.
    - Approaches to provide information to study cohorts and trial participants and to obtain informed consent.
    - Approaches for counselling and education of study participants.
    - Strategies to motivate participation in trials and related studies.
    - Potential social and behavioural consequences of participation in trials.
    - Impact of trials on prevention interventions in the general population
- Social, economic and operational research in relation to future vaccine use, to identify approaches for vaccine promotion and utilization, including social, behavioural and economic determinants, and strategies to reduce costs, including local production.
- Establishes communications and public information strategy to target different levels of society: general public, the medical and scientific community, political and decision makers, the media, NGOs and the private sector.
- Considers regulatory and legal issues, including compensation

Uganda

Drawn from Guidance Document for HIV/AIDS Vaccine Research, Development, and Evaluation for Uganda 2000/1 – 2005/6[161]

- Aims to promote therapeutic and preventive vaccine trials
- Government commits to actively participate in all efforts to develop and evaluate HIV vaccines that can be used in Uganda and worldwide.
- Provides national guidance for scientific, legal, ethical and policy issues in vaccine research, development and evaluation
- Guidelines and strategies for co-ordinated research, development and evaluation of the safety, immunogenicity and efficacy of therapeutic, preventive and perinatal vaccines;
- Guidelines for the selection of candidate vaccines: local HIV sub-type vaccine candidates
- Legal and ethical procedures for planning, review, approval, implementation, monitoring and administration of vaccine research.
- standards for identifying institutions capable of conducting research and trials.
- outline characteristics of potential population cohorts
- proposes ways to ensure access to vaccines to the general population.

[161] An Outline of the Guidance Document for HIV/AIDS Vaccine Research, Development, and Evaluation for Uganda 2000/1 – 2005/6 Drawn from presentation of Dr P Kadam, Health Planning Department Ministry of Health, Uganda 19 April 2000 *Aims of national strategic framework for HIV control activities in Uganda.*

- Multiple trials to be conducted simultaneously, multiple study teams
- Study sites preparations and study populations identified, cohorts for phase III and phase IV trials prepared in advance
- Capacity building for infrastructure, personnel, and information systems/procedures manuals
- strengthen institutional bio-medical research framework, build skills for clinical trials and bio-medical laboratory techniques, infrastructure up-grading with focus on laboratory support.
- Public relations and communication strategy for information processing and dissemination

South Africa[162]

Drawn from Draft National Economic Development and Labour Council Framework Agreement on a National Prevention and Treatment Plan for Combating HIV/AIDS. Dec 2002. Note that this Draft Plan was not adopted by the Government, which published its own antiretroviral delivery plan.

- Aspires to be a joint Plan of Government, business, labour and the community
- Recognises the importance of eradicating poverty to combat the spread of HIV and the impact of poverty on people living with HIV: HIV Plans must be complemented by plans to build the economy, create jobs, better housing, access to improved nutrition, clean water and welfare grants
- Recognizes that the Plan will bring about cost and social savings.
- Sets a target of allocating at least 15% of annual budgets to improvement of the health sector
- Recognises the need for ongoing research to cost the Plan and to mobilise additional sources of support, such as the Global Fund.
- a multi-sectoral plan that addresses education, awareness and prevention; procurement and production of medicines, treatment, support and care; and issues relating to discrimination and stigma (education campaigns to combat discrimination at the workplace, in commerce and services, the public sector, and in the community),
- addresses the policy, resource, organizational and legal dimensions
- implemented through partnerships between sectors at national, provincial and local government level, in urban and rural areas at workplaces and in schools
- a strong focus on education, awareness and prevention, with measurable targets and timeframes;
- Universal roll-out of treatments to prevent MTCT, and a comprehensive package of care for rape survivors, including access to ARVs in public health institutions

[162] Available via www.tac.org.za. The draft South African Plan does not address R&D, but provides a useful template for other treatment and prevention elements of a comprehensive National Plan.

- Supports people living with HIV to access: information in an understandable form; clinics that provide information on health; regular monitoring; treatment of OIs; and access to ARVs according to national standards
- Gives priority to vulnerable groups
- Requires compliance with the UN *Declaration of Commitment on HIV/AIDS* and the Abuja Declaration on HIV/AIDS, Tuberculosis and Other Related Infectious Diseases, and that the Plan be guided by the International Guidelines on HIV and Human Rights, including revised Guideline 6; and the WHO/UNAIDS/International AIDS Society commitment to mobilising the resources, infrastructure and skills needed for a massive extension in access to treatment in developing countries.
- Cooperation on improved epidemiological surveillance
- Prevention priorities
    - public education and awareness, encouraging VCT
    - resources to finance education and awareness, provision of condoms and female condoms and provision of post exposure prophylaxis for rape and occupational injuries
    - Community organizations supported to destigmatize HIV/AIDS, encourage VCT and openness within communities and families about HIV
    - the use of rapid testing
- Treatment, care and support priorities
    - continuum of care which includes:
    - support, counselling including information and advice on social grants
    - aggressive management of OIs and STI's
    - TB and PCP prophylaxis
    - public awareness and knowledge of systems for the evaluation and certification of traditional and complementary medicine;
    - a universal right to treatment for OIs: better drug supply, training of health professionals, systems for monitoring capacity, quality of care and access
    - a public sector ARV treatment programme: training patients, nurses and doctors on adherence and side-effects; strengthening public health infrastructure; private sector partnerships; reducing the costs of ARVs and diagnostics; and establishment of a pharmaco-vigilance system.
    - Government support for local production of ARVs
    - Social mobilization to break down stigma, provide treatment information and create a social climate that encourages adherence
    - community preparedness: treatment literacy & prevention information for people with HIV, and human rights information.
    - support for orphans and children
    - community home-based care program including palliative care.

Glossary of key acronyms

AMD	Alliance for Microbicide Development
ANRS	Agence Nationale de Recherches sur le SIDA
ARVs	Antiretroviral therapies
ASOs	AIDS Service Organizations
AVAC	AIDS Vaccine Advocacy Coalition
CIPRA	The NIH's Comprehensive International Program of Research on AIDS
CPTech	Consumer Project on Technology
DfID	UK Department for International Development
DNDi	Drugs for Neglected Diseases Initiative
DSMB	Data and Safety Monitoring Board
EDCTP	The EU's European and Developing Countries Clinical Trials Partnership
EMEA	European Medicines Evaluation Agency
EU	European Union, the economic and political union of 15 European states
EC	European Commission, the executive/administrative arm of the EU
FDA	US Food and Drug Administration
GATS	General Agreement on Trade in Services
GAVI	Global Alliance for Vaccines and Immunization
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GCM	Global Campaign for Microbicides
HPTN	HIV Prevention Trials Network
HVTN	HIV Vaccine Trials Network
IAVI	International AIDS Vaccine Initiative
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IFF	International Finance Facility
IP	Intellectual property
IPM	International Partnership for Microbicides
ITAC	International Treatment Access Coalition
IWGM	International Working Group on Microbicides
MAP	Multicountry HIV/AIDS Program, a World Bank initiative
MMV	Medicine for Malaria Venture
MRC	UK Medical Research Council
MSF	Médecins Sans Frontières – Doctors Without Borders
MTCT	Mother to child transmission of HIV
MDGs	United Nations Millennium Development Goals
N-9	Nonoxynol-9, a chemical trialled as a microbicide in the late 1990s
NIAID	US National Institute of Allergies and Infectious Diseases
NGO	Non-governmental organization
NIH	US National Institutes of Health
OIs	Opportunistic infections
PLWHA	People living with HIV/AIDS

PPP	Public Private Partnership
R&D	Research and development
STI	Sexually transmitted infection
TAC	Treatment Action Campaign South Africa
TRIPS	Agreement on Trade Related Aspects of Intellectual Property Rights
UNAIDS	United Nations Joint Programme on HIV/AIDS
UNGASS	United National General Assembly Special Session
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

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