THE OPPORTUNITIES AND CHALLENGES OF INTRODUCING ANTI-RETROVIRAL THERAPY (ART) IN RESOURCE-POOR SETTINGS

A consensus statement by organisations delivering AIDS projects for the Canadian International Development Agency (CIDA)

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Background

On September 4-5, 2001, the Canadian Public Health Association (CPHA) convened a meeting of clinicians and public health experts working with major CIDA-funded AIDS projects in West, East and Southern Africa, and in India. The purpose of the meeting was to elaborate a technical consensus on major issues related to the introduction of anti-retroviral drugs in resource-poor settings, particularly in the context of Canadian international development programming in Africa. The consensus presented in this document is based on principles of public health and the field experience of the organisations participating in the meeting. The participants acknowledge that policy issues related to access to ART require a much wider social consensus. Such a consensus should, however, be informed by the best possible technical assessment of critical issues of public health and health care systems development.

The participants acknowledge that the situation is extremely dynamic and that our knowledge about the use of ART is incomplete. We are dealing with a rapidly developing medical technology whose long term costs and benefits have not yet been fully assessed. The consensus is based on what is presently known about ART. It will have to be updated periodically.

The use of anti-retroviral drugs

Maintenance of anti-retroviral therapy (ART)

At the present time, ART involves the daily administration of three or more anti-retroviral drugs to people infected with HIV in order to suppress viral replication. When optimally applied, ART results in dramatic decreases in viral load, recovery of the immune system, and improvements in general health. There are indications that, for some individuals, life-time adherence to this regime may result in a normal healthy life-span, although it will not eliminate HIV infection.

Experience with triple therapy ART in its current form dates back only about five years. Some ART regimes are complicated, involving as many as 20 tablets per day taken at precise intervals. Development of newer combination drugs has made it possible to administer some triple-drug combinations as one tablet taken twice daily. Once-daily regimes are under study.

Close to 20 different anti-retroviral drugs are currently being marketed. Short-term adverse side effects, as well as serious and life-threatening long-term complications have been documented for practically all of these drugs. Adherence to ART is a major issue in all settings. Current research in some resource-poor countries is evaluating the use of community volunteers to supervise daily drug administration, similar to a procedure developed in tuberculosis therapy (Directly Observed Treatment – DOT). Irregular adherence to ART can lead to the rapid development of drug resistant strains of HIV. Long term benefit with currently available regimes appears to be associated with

adherence rates of 90 percent or greater. This means that three drugs must be taken daily in the right combination at the right time with less than 10 percent error.[1]

The possibility of "pulsed ART" or structured treatment interruption (STI) is under investigation to determine whether patients on ART may be able to interrupt treatment periodically for periods of one month or longer. When the results of current STI trials are confirmed, guidelines on the frequency of "drug holidays", the length of interruption, the therapeutic efficacy of this strategy and when to start and stop pulsed therapy will be developed.

ART in Canada is monitored every three to six months using laboratory investigations of viral load and immune status (lymphocyte CD4 count). These tests are costly and require specialised laboratories that are available in very few centres in resource-poor countries. An alternate laboratory monitoring strategy, using total lymphocyte count as a proxy indicator for the CD4 lymphocyte count is showing promise in initial trials. While this will be helpful to adapt laboratory monitoring to resource-poor settings, many regional and district health facilities in Africa are not able to consistently perform accurate and timely lymphocyte counts.

Until recently, ART was not an issue of much interest in resource-poor settings because the cost of the drugs was prohibitive. Nevertheless, private clinics delivering state-of-the-art ART have been operating in almost all countries of the world for as long as ART has been available. Low-cost generic copies of some anti-retroviral drugs have been available for at least ten years. There has recently been a flurry of exposure of this fact in the international news media.

An effective international lobby has succeeded in producing a spectacular reduction in the prices of anti-retroviral drugs in resource-poor countries. Until recently, the drug costs for this type of treatment have been in excess of CAD $20,000 per person per year. Generic drug manufacturers can now deliver the drugs necessary for maintenance ART at a price of CAD $400 to $900 per person per year. Additional costs would be incurred for clinical and laboratory monitoring and treatment of complications. In Brazil, a country which is widely acknowledged as a world leader in delivering low-cost ART through the public sector, the cost of ART per patient in 2001 was estimated at USD 2,530 per year. (Reference: Ministry of Health, National AIDS drugs policy, 2001)

Prevention of mother to child transmission (MTCT) of HIV

Mother to child transmission of HIV can occur during pregnancy, labour and delivery, or breast-feeding. This is sometimes referred to as parent to child transmission (PTCT) to acknowledge the role of the father in this process. While this is a useful concept for counselling, the biologically more precise term MTCT is preferred in a discussion of prevention strategies using anti-retroviral drugs.

[1] *Adherence has been difficult to measure in industrialised countries in the absence of DOT. This provides additional reason to explore DOT and to generate better information about short and medium term clinical benefits of ART as well as long term survival benefits in resource constrained settings*

Mother to child transmission of HIV has been recorded in up to 40 percent of infants born to HIV positive mothers in some African settings. About one third to one half of these infections are transmitted through breastfeeding. The balance of infections can potentially be prevented by providing a single anti-retroviral drug to the mother shortly before delivery and to the infant shortly after birth. Drug regimes of proven efficacy using *zidovudine* or *nevirapine* can prevent about half of the HIV infections that take place during delivery. The drugs are easy to administer and the drug costs for the *nevirapine* are less than CAD $3 per intervention. However, when no postpartum ART is provided, HIV infection may still be transmitted thorough breastfeeding.

There are high expectations of the benefits of providing anti-retroviral drugs for the prevention of MTCT. However, research projects that have introduced these regimes in regular maternal health services have so far recorded very disappointing results. This is primarily because in the environment of stigma and discrimination of people living with HIV that persists in many countries, there is a high loss to follow-up of expectant mothers during the process of counselling, testing, revealing the test results, prescribing the drugs, and obstetric delivery, especially among mothers who are HIV positive. The limited number of studies have so far not been able to show a benefit above ten percent of cases of HIV infection averted.

Moreover, the very limited success of the above mentioned studies have required major improvements in the provision of maternal health care. More staff had to be hired, premises had to be improved, and the quality of services vastly improved, with more individual attention paid to women before, during, and after obstetric delivery. Most such programmes have also failed to emphasise the need to provide additional resources for the children who are protected from HIV transmission but who will experience the profoundly negative personal and economic consequences of losing one or both parents during childhood. It is conceivable that the promise of prevention can be more fully realised with concerted effort to strengthening maternal health services. Improvement of maternal health services is an urgent need in many resource-poor countries, especially in Africa. It does not require specialised training or the creation of specialised services; it can be achieved by improving and expanding what exists already.

Post-exposure prophylaxis (PEP)

In Canada, it is common practice to provide three-drug anti-retroviral therapy for a period of one month to individuals who have been exposed to HIV infection either through an injury (usually in a health care setting) or through sexual intercourse (usually in the case of rape). Very little is known about the effectiveness of this intervention to prevent HIV infection. The adherence rate in Canada, i.e. the proportion of people who actually complete the full treatment, is low, especially in the case of PEP after rape because of side effects and the perceived low likelihood of HIV infection in the assailant. Health care workers

have high rates of completion of the one month course when the source patient is known to have HIV infection.

There are no reliable data on occupational HIV infection among health care workers in some resource-poor countries. However, given the deplorable state of many health centres and hospitals, particularly in Africa, the absence of effective infection control, the absence of appropriate containers for sharp instruments, etc., the infection rate may be quite high. The first step in reducing occupational exposure to HIV should be better training in infection control and improvement in health facilities and their infection control procedures. Adding access to anti-retroviral drugs for PEP may provide the incentive for these improvements. It would also require that any health care staff who wanted to benefit from access would have to consent to voluntary counselling and testing for HIV. It would therefore greatly increase the personalisation of HIV risk among health care staff and thereby potentially have a major prevention benefit.

The provision of anti-retroviral drugs for PEP after rape requires the existence of rape crisis counselling and support services. There is a tremendous need for this type of service in many countries. Rape intervention services are very rare in resource-poor countries, and are practically non-existent in sub-Saharan Africa with the exception of pilot projects in South Africa. PEP with anti-retroviral drugs, although still of questionable usefulness, may be the stimulus for the creation of a needed social service.

Current status of access to anti-retroviral drugs

The discussion of this topic focused on sub-Saharan Africa as the region where most participants in the meeting were working or have worked.

Anti-retroviral drugs are widely available in sub-Saharan Africa through a variety of channels. Anti-retroviral drugs are imported by international development organisations and multi-national companies to use for their personnel or within specific projects. ARV drugs are obtained through solidarity networks of people living with HIV, and drugs are imported by private pharmacies for resale. A recent independent survey of pharmacies in Kenya found that 15 of the existing 17 anti-retroviral drugs were readily available in all regions of Kenya. There are anecdotal reports that anti-retroviral drugs are entering informal drug distribution channels operated by itinerant drug sellers and cross-border traders.

While there are numerous international projects providing anti-retroviral drugs for the prevention of MTCT, most of the private and informal sector drugs are used for ART. None of the participants at the meeting was aware of any drugs provided for PEP other than in the Central Plateau PEP Programme in Haiti for health care workers and rape survivors which began in 1997 and the South Africa rape centre pilot projects. Access to ART is largely limited to urban areas. Most patients on ART buy treatment at the quality and quantity they can afford. There are numerous reports of people selling their property in order to buy ART of questionable quality for a limited amount of time. Families are plunged into poverty as men spend the family capital on a few months of ART.

International humanitarian aid and research projects providing ART free of charge according to need are plagued by queue jumping, influence peddling, and resale of donated drugs by the people who are supposed to use them. In most countries, a very small number of the urban elite have access to high quality ART, and an increasingly larger number of people, primarily urban men, have intermittent access to some drugs. In the Kenyan survey, 33% percent of physicians prescribing ART in Kenya did not have any training in appropriate use of these drugs. Of 101 patients on ART surveyed in Kenya, only 5 were using triple therapy, i.e. more than 90 percent of prescribed ART in this survey was inadequate according to the accepted standard of treatment at the time of the survey.

The consequence of irregular and uncontrolled use of ART is the rapid emergence of drug-resistant viral strains. There are already published reports of a very high prevalence of resistance to multiple anti-retroviral drugs in Abidjan, Cote d'Ivoire.

The current political environment

International development projects, including the projects represented at this meeting, are coming increasingly under pressure from governments and NGO partners to support the establishment of MTCT prevention and ART delivery programmes. This is particularly the case in sub-Saharan Africa where one pharmaceutical company has offered drugs for MTCT prophylaxis free of charge for 5 years to any country wishing to implement MTCT prevention programmes. Many government AIDS programmes are visibly shifting their emphasis towards the procurement and provision of ART. A medicalisation of national AIDS commissions is evident in several countries of Southern Africa.

Possible reasons for this shift include pressure from HIV positive government officials and politicians who are buying ART at high cost on the open market and would personally benefit from publicly funded ART. We are aware of at least one country in Africa where this was stated to be the main reason for policy initiatives to introduce ART by the National AIDS Control Programme. Another reason may be the relative ease with which money can be spent on procurement of drugs as compared to prevention programming.

International development agencies are also coming under pressure from domestic NGOs and treatment access activists who are demanding that additional development funds be allocated to the procurement of ART. A very effective alliance of First World NGO's and urban activists from developing countries has organised itself around the battle over drug prices and patent rights with the pharmaceutical industry. Having won this battle, this alliance is now taking on governments and international agencies to step up drug procurement and delivery. Influential groups such as the African First Ladies are mobilised to add their voice to greater access to drugs for ART and MTCT prevention.

Meanwhile, it appears that the stake-holders of the newly created Global Health Fund are separating into two camps. On one side is a group including many African countries that would like the Fund to be used for the procurement of anti-

retroviral drugs. On the other side is a group of countries who believe the Fund should be used for improving the health care service infrastructure in the poorest countries.

Within this highly politicised national and international field, the pharmaceutical industry stands to make significant gains as the potential in their market share increases, with many of the costs borne by the international development community.

Issues to consider

The following are key issues that should be considered in the discussion on access to ART. Agencies like CIDA, which potentially have an important voice in international decision forums dealing with this subject, should be well informed on the status of arguments on these issues.

Prevention of HIV infection

The main response to the global pandemic of HIV infection must remain the prevention of new infections. Statements that "prevention has failed" are inaccurate and irresponsible. Prevented cases of HIV infection cannot be registered. There are however, countless examples of successful HIV prevention programmes including many that were documented by the projects and organisations present in this meeting. These include the SAT Programme's success in supporting the local response to AIDS in Zambia which has contributed to a 50 percent decrease in HIV prevalence among urban adolescent girls over the last six years. Also, the successful intervention of the West Africa AIDS Project among sex workers in Benin and Ghana which has recorded a steady reduction in HIV prevalence among this group, and contributed to the continuing low HIV prevalence among the general population in Cotonou and Accra and the marked reduction in HIV risk behaviour and in the incidence of sexually transmitted diseases observed by the Manitoba-Nairobi STD Project in Kenya.

Two important points are:

- HIV prevention efforts in some part of the world have not been conducted with sufficient energy and resources, or have started too late in the epidemic
- The dichotomy set up early in the pandemic between "prevention" and "care" is false and has fragmented the response to AIDS in many locations. It risks to be revived in the current discussion on treatment access.

The availability and the use of ART is most certainly influencing prevention programming. The interaction is complex and mostly unknown. The main elements of this interaction are:

Possible positive outcomes

- People who receive appropriate ART have lower viral loads and are, therefore, less likely to infect others
- Access to ART encourages people to seek voluntary counselling and testing and to discuss AIDS more freely. It could reduce the stigma of AIDS, leads to greater personalisation of risk, and stimulates a shift in the behavioural profile of the population, thereby reducing overall susceptibility to HIV infection.

Possible negative outcomes

- People who receive inappropriate ART may have a transient clinical recovery and resume sexual activity while they continue to have high viral loads. They may be highly infectious and may in addition harbour drug resistant strains of HIV
- The availability of ART will be interpreted by many to mean that AIDS is no longer a threat to life and will result in a decrease in attention to HIV prevention. Condom use may become less consistent.

All four effects are likely and have already been observed. How important one is over the other, and how the different effects interact, will differ from location to location and is largely unknown.

As agencies and organisations charged with the responsibility of social programming, we cannot assume the complacent position that increased access to ART will automatically reinforce HIV prevention. Since increased access to ART may potentially have a negative effect on HIV prevention, increased programming in HIV prevention must accompany any initiatives to widen access to ART. In order to avoid diversion of scarce international and national public resources for integrated community AIDS care and HIV prevention initiatives to the simple procurement of anti-retroviral drugs and creation of ART facilities, additional resources are required from governments and the international community.

Social equity and challenges to ART delivery

The global inequity between societies where most people have access to ART and societies where few people have access to ART is mirrored in local inequity where small social and demographic groups have access to health care while large segments of the population do not.

Some middle-income countries with HIV prevalence of one or two percent are able to provide publicly funded ART to all citizens who require it. However, almost all African countries have very low incomes and higher HIV prevalence. These countries lack the personnel and health system capacity to deliver ART to everybody in need, even if all the drugs were provided free of charge by the international community. Building up the necessary health care infrastructure is a task that will take years, even if it is attacked with unprecedented vigour.

Using national and international public funds to provide ART in poor countries with high HIV prevalence therefore invariably raises the question: “who will

benefit?" If universal access cannot be achieved in the short or medium term, selections will have to be made. Not targeting ART will invariably result in a consolidation of the current status quo, i.e. the urban elite, senior civil servants, and formal sector employees will receive ART. Men will receive ART in much higher proportion than women. The rural and urban poor who should be the main focus of publicly funded social programmes will have no chance of access and indeed may be worse off because of diversion of scarce funds for basic health care to the purchase of ART.

In the entirely appropriate international response aimed at decreasing global inequity, we must under all circumstances avoid unwittingly increasing inequities and social injustices at the country and local level.

Proposals of how to target ART discussed at the meeting included:

Provide ART according to need: Since the need is large, this is essentially no targeting at all. Need is dependent on the availability of voluntary counselling and testing services that make the need apparent. As long as these are underdeveloped, the identified need will be restricted, largely to the urban groups who already have limited access to ART. This option would, in fact, only dress up the status quo into something that looks a little more palatable.

Provide ART to HIV positive women who have participated in an MTCT prevention programme: This is theoretically an attractive option because it targets women and it requires no additional counselling and testing programme (the women have already been tested and counselled). It also has benefits in preventing HIV transmission during breastfeeding and it could prevent early orphanhood of the newborn child. Current recommendations are that women wean their infants at the age of four to six months. When breastfeeding ends, ART could be stopped in asymptomatic women and started again when there is a clinical progression of AIDS. In practice, MTCT prevention programmes may find it difficult to exclude the husbands of mothers from access to ART. It may prove difficult to prevent women from sharing or handing over the drugs to their husbands, voluntarily or under duress. In the event that a breastfeeding mother is entered into a long-term ART programme, it would be justifiable to offer ART to fathers as well. This may provide an incentive for some fathers to come forward for voluntary counselling and testing.

Provide ART to HIV positive female sex workers: This is also theoretically attractive from a public health point of view. Many of these women are already participating in STD surveillance and treatment programmes. They are often highly motivated for HIV prevention. Lowering their viral load could have a major prevention benefit because of their large number of partners. Keeping well established and skilled sex workers alive and active may reduce the recruitment pressure. But, in practice it will be impossible to convince governments and the public that a much coveted,

expensive and life-saving service should be made available free of charge to female sex workers, a group that is involved in an activity that is stigmatised and illegal in many countries.

It is highly unlikely that the objective of providing equitable access to ART to people in resource-poor settings will be met through any targeted public sector programme. Universal access is the only option. The necessary resources and infrastructure to provide universal access exist in some middle income countries with low HIV prevalence. It can potentially be created through a fast track approach in a few countries like Botswana. However, in the majority of African countries it will require long-term massive investment in building up the basic health care delivery system.

Safety issues regarding viral resistance and adverse effects of ART

We know that inappropriately applied ART leads to rapid emergence of drug resistant strains of HIV. We also have the first data showing that drug resistance is rising rapidly in some locations in Africa. Since people starting on ART require the drugs for the rest of their lives, the emergence of resistance will not only affect new patients entering therapy but it will continue to make life more and more difficult for those already on treatment. Monitoring for the emergence of resistance and for break-through viraemia is expensive and would be very difficult to introduce in most resource-poor settings. The two drugs most useful for the prevention of MTCT, *zidovudine* and *nevirapine*, are unfortunately also the two drugs to which drug resistance appears to develop fastest.

Some experts maintain that resistant strains of HIV are "defective" and therefore, less infectious and less likely to cause major epidemics. This may be true, but we cannot assume that all drug resistance is linked to lower virulence or infectivity.

In addition to the public safety issue of resistant strains of HIV, there is also the personal safety issue of adverse drug effects in people receiving ART. Even in sophisticated health care settings people on ART sometimes die of liver failure or other complications. Given that there has only been 5 years experience with triple therapy regimens, complications which have not yet been recognised to date, may occur. As well, the long-term consequences of some of the observed metabolic abnormalities have yet to be determined. The probability of a person on ART having complications that are not recognised at an early stage is much greater in health care settings where there are few physicians (e.g. Malawi with 3 physicians per 100,000 population) than in settings where there are proportionately many more (e.g. Canada with 183 physicians per 100,000 population).

The overriding ethical maxim of medicine, to do no harm, would be seriously compromised by implementing a programme of widespread publicly funded access to ART now in many resource-poor settings given the current status of health care infrastructures in these countries.

Opportunity costs

The newly established Global Health Fund for the control of AIDS, malaria and tuberculosis as well as new policy directions in Official Development Assistance (ODA) raise the hope that additional funds will soon be available for health and development. However, no matter how generous the international development assistance to a country is, the country itself will still have to carry most of the cost of strengthening its health care infrastructure.

An international agency that decides to provide a large grant for the procurement of anti-retroviral drugs and for the establishment of an ART delivery programme should therefore be conscious of the high opportunity costs it may be generating for the grant recipient. Tanzania, for instance, has 4 physicians per 100,000 population; Zimbabwe once had as many as 14 but the number is shrinking. If a significant number of these physicians become trained in the delivery of ART and recruited into specialised ART clinics, other important health sector tasks may suffer. The same argument applies to nurses, administrators, laboratory technicians, health facilities, etc. It is therefore, critical that the forces that are put into action to facilitate the delivery of ART are used to leverage increased support to the health care system as a whole, including increased support for the training of new health care workers and retention of existing staff.

In other words, the amounts of human and financial resources required for ART provision by an individual country will likely be more than can be sustained with internal resources. It will be important not only to safeguard other health and development programmes and create synergies with them but also to focus any additional resources on strengthening the health care system as a whole for long term sustainability.

International agencies and funds may decide to carry much of the direct cost of making ART accessible to resource-poor countries for the foreseeable future. They should, however, be aware that these countries may experience unaffordable opportunity costs without the addition of resources to strengthen and benefit the health care system as a whole.

The margin for action

The presentations made by the meeting's participants revealed dearly that there can no longer be a discussion of whether ART should be introduced into resource-poor countries or not. National Ministries of Health and their international supporters no longer have a choice whether or not to address issues related to ART. It is no longer a question of "if", but rather a question of "how".

The rapid growth of more or less uncontrolled marketing and use of anti-retroviral drugs throughout the world is revealing a serious weakness in the national control of pharmaceuticals in many countries. Unless there is a major investment in drug regulation, quality control, and procurement systems, we are poised to see much suffering caused by injudicious use of anti-retroviral drugs. For the

same reason, Governments will have to make major investments in drug security to stop leakage from public pharmacies into the informal sector.

Large company health services and specialised university clinics are already providing quality ART. We can assume that staff in these facilities is well trained and competent. However, a growing number of poorly trained health professionals and para-professionals are becoming involved in the lucrative business of providing ART and are likely providing sub-standard treatment. This is an enormous challenge to many national health authorities. It can only be addressed through a combination of judiciously targeted training programmes, licensing controls, and professional regulations.

Ignoring ART in international health and development programming is no longer an option. However the emphasis should be on strengthening the systems that are necessary to regulate and control a potentially harmful technology, rather than on weakening these systems further by dumping drugs into poorly organised public pharmacies and delivery systems.

Recommendations

Based on an assessment of the situation and taking into consideration the issues listed above, the meeting participants formulated a number of recommendations addressed to Canadian public programmes and agencies, including CIDA.

1. We recommend that any official position on ART be informed by sound principles of public health and health systems development with specific attention to the status of issues discussed in this document: the prevention-care continuum; social equity; safety; opportunity cost; and margin for action.
2. We recommend, that any official Canadian support for, or investment in ART delivery in resource-poor countries will only be considered if it can conclusively demonstrate that it:
   - Contributes to HIV prevention programming;
   - Improves social equity in access to health care; and
   - Strengthens the basic health care delivery system by assuring
     - Widespread availability and universal access to voluntary and confidential HIV testing and counselling services
     - An uninterrupted supply of medications (through strictly managed procurement and through close regulation)
     - Adequate clinical monitoring and treatment and care of complications
     - Adequate laboratory services to monitor ART and its potential complications
     - Effective nation-wide control and treatment of sexually transmitted diseases and tuberculosis.

3. Given that relatively low-cost interventions can be made that have the potential to stimulate major collateral improvements in maternal health services, infection control services, or rape crisis intervention services it is, therefore, recommended that any official Canadian support for, or investment in, MTCT prevention or PEP programmes using anti-retroviral drugs be considered where there is assurance that the drugs are safe from diversion and that the utmost care is taken to prevent the development of drug resistance through misuse, and that these programmes conclusively demonstrate that they are linked to:
   - comprehensive improvements in maternal health services
   - the improvement of infection control and occupational safety in health care settings
   - the creation of quality community services for rape crisis intervention, and

- strengthened support for AIDS orphans.

4. Given the important role of ART in the response to AIDS, and given that current ART regimes are poorly adapted for use in resource-poor settings, we furthermore recommend increased Canadian public investment in research on anti-retroviral drugs in resource poor settings, including the support of ART trial centres. The objectives of this research should be to:
    - develop drugs that are more appropriate for use in resource-poor settings;
    - develop ART regimes and laboratory monitoring regimes that are more appropriate and feasible for application in resource-poor settings;
    - develop monitoring systems for uptake, adherence, effectiveness, drug resistance, cost, and benefit of ART;
    - facilitate evaluations at country level of the legal and social impediments to reducing the discrimination and stigma experienced by people living with HIV which hinder uptake of both HIV prevention and care initiatives
5. Given the importance of ART in the response to AIDS in developing countries, we urge the Government of Canada to formulate a position on this issue. This position should be integrated into the official Canadian HIV/AIDS strategy and be reflected in the official Canadian position in the discussions of the priorities and objectives of the Global Health Fund. This strategy is to be updated regularly, and it should be binding for official Canadian delegations to international organisations, funds, and forums.

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