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Preparing for the availability of a partially effective HIV vaccine: Some lessons from other licensed vaccines

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Introduction

The 2009 RV144 trial in Thailand shows that a partially effective vaccine against human immunodeficiency virus (HIV) acquisition is possible (1). Past mathematical models have shown HIV vaccines with partial effectiveness (assuming availability and no compensatory risk behavior) may have important public health impact (2). While we are still many years away from a licensed HIV vaccine, what might be some of the "downstream" considerations for the implementation of a partially effective HIV vaccine in the developed and developing world in the current era? Are there any changes since the HIV domain last considered this issue in anticipation of the results of the first Phase III trials of HIV vaccine (Vaxgen gp120) a decade earlier? (3, 4).

During the Acquired Immunodeficiency Disease Syndrome (AIDS) Vaccine 2010 Conference, a satellite symposium cosponsored by AIDS Vaccine Advocacy Coalition (AVAC), the U. S. Centers for Disease Control and Prevention (CDC), Gates Foundation, the Joint United Nations Programme on HIV/AIDS (UNAIDS), US Agency for International Development (USAID), US Military HIV Research Program (USMHRP), World Health Organization (WHO) took advantage of the conference location in Atlanta to draw upon some of the experience of CDC and its associated partners in preparing for the availability and implementation of newly licensed vaccines to further this dialogue. This paper summarizes the presentations on some lessons for future HIV vaccine implementation from the introduction of hepatitis B vaccine, human papillomavirus (HPV) vaccine, the annual influenza virus vaccine strain selection, a potential annual HIV vaccine strain selection, as well as planning for next steps in Thailand in response to the RV144 trial, and highlights

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from the moderated discussions with the audience on issues relevant to low/middle income countries and developed countries (Table 1). Hopefully these ideas will facilitate preparations for the introduction of a future licensed HIV vaccine.

Introduction of hepatitis B vaccine (Dale Hu)

Hepatitis B virus (HBV) is transmitted in similar ways as HIV and also has an enormous global burden of disease. However, there are some important differences between vaccine development for the two pathogens. One important difference was that once the hepatitis B surface antigen (HBsAg) was identified in 1965, vaccine development proceeded fairly quickly (5). The fact that humoral immunity as manifested by antibodies to HBsAg is highly protective allowed clear demonstration of the effectiveness of hepatitis B immune globulin and early vaccine candidates in chimpanzees. Once controlled trials demonstrated high efficacy, hepatitis B vaccine was licensed in the United States in 1982 after only 13 years of research (5). In contrast, the major challenges to HIV vaccine research and development included the lack of clearly identified human immune correlates of protection from HIV infection or disease, the incompletely understood significance of HIV genetic diversity, the absence of an ideal animal model, and the complexities of developing new vaccine approaches (6).

Although adults at high risk [e.g., health providers, injection drug users (IDU), men who have sex with men (MSM)] were initially targeted to receive the newly licensed hepatitis B vaccine, coverage rates remain unacceptably low and impact on HBV incidence minimal (7). There was also increasing recognition during the 1980s of the burden of chronic liver disease from infections acquired during childhood – including among infants born to HBsAg negative mothers, particularly among high risk immigrant populations. These two considerations plus availability of new data on long term protection and cost-effectiveness culminated in 1991 to expand hepatitis B vaccine recommendations in the US beyond high risk groups alone to include: (a) routine infant and childhood hepatitis B vaccination, enforced via school entry immunization laws, and (b) prevention of perinatal HBV transmission (8). After some years of delay, including initial concerns by some providers their patients were at low risk, hepatitis B vaccine coverage in the U.S. pediatric population now exceeds 90% (9). Most other developed countries have also expanded efforts on targeted high risk groups to a more comprehensive strategy of universal perinatal and childhood hepatitis B immunization (10).

Given the current epidemiology of HIV in the United States, the resources to implement an HIV vaccine of low to moderate efficacy may be very challenging, especially among persons at higher risk for HIV infection (e.g., MSM, IDU, and heterosexuals at high risk), and would need to be integrated into a comprehensive HIV prevention program.

Current funding and support for vaccination in the United States is limited and is primarily available to children [through the Vaccines for Children (VFC) program] and the elderly (though Medicare) and to individuals covered by some private insurance plans or by occupational safety programs (e.g., hepatitis B vaccination for health care workers) (11).

Furthermore, efforts to increase immunization coverage of high risk populations (MSM, IDU, prisoners) with hepatitis B vaccines have achieved modest success (12–15).

Nearly 20 years after hepatitis B vaccine was first licensed, several factors converged to allow less developed countries with a high prevalence of chronic HBV infection to begin to increase hepatitis B vaccine coverage and decrease the burden of disease.(16–18). These include (1) increase in number of hepatitis B vaccine manufacturers, including those from countries like South Korea and India; (2) decrease in hepatitis B vaccine cost for countries procuring vaccine from UNICEF from $3–6/dose in 1990s to $0.18–0.40/dose in 2010 (19); (3) availability of combination HBV and routine pediatric diphtheria-tetanus-pertussis (DTP-HepB) vaccine; and (4) the advent of the Global Alliance on Vaccines and Immunization (GAVI) to finance introduction of new and underutilized vaccines (20).

Successful and sustainable implementation of a future HIV immunization program will require (1) preparation of medical providers, the general community and high-risk populations to create an environment favorable to immunization, (2) development of a medical infrastructure that can access and follow these varied high-risk populations, (3) expansion of comprehensive, ongoing prevention programs, for which vaccination would be one component of the prevention effort and (4) establishment of funding mechanisms for adult vaccination in non-elderly populations.

The ongoing effort to increase hepatitis B vaccine coverage will be useful for future HIV vaccine efforts to: 1) identify access points for high risk populations, clarify barriers to successful immunization, and identify mechanisms to overcome these barriers, including appropriate incentives for providers and patients, 2) develop model programs for delivering vaccine to high-risk populations building on the example and infrastructure of current pilot programs for hepatitis B immunization, and 3) engage the private medical sector through professional societies to educate providers and develop partnerships for delivering immunization to adults and adolescents, including those at high risk.

In summary, although HBV has a similar epidemiology to HIV, hepatitis B vaccine development proceeded relatively rapidly after understanding the correlates of immunologic protection. As the cornerstone of hepatitis B prevention and an eventual goal for future HIV vaccines, increasing hepatitis B vaccine use has resulted in marked decreases in infection and disease rates in many parts of the world. Nevertheless, despite the availability of a highly effective and safe vaccine, coverage rates in many high risk populations remains less than optimal. Therefore, the ongoing promotion of hepatitis B vaccination and other adult immunization will be efforts well spent in preparation for future HIV immunization.

Introduction of HPV vaccine (Eileen Dunne and Lauri Markowitz)

Two HPV vaccines are available, one that prevents HPV 6, 11, 16, 18 and another which prevents HPV 16, 18. In the US, either vaccine is recommended routinely for girls aged 11 or 12 years; vaccine can be given at 9 years of age (21, 22). Vaccine is also recommended for females 13 through 26 years who have not started or completed the vaccine series (21, 22). One vaccine (quadrivalent) may be given to males aged 9 through 26 years. Prophylactic HPV vaccines are targeted to young adolescents as this common sexually

transmitted infection (STI) can be acquired soon after sexual debut. Despite availability of a vaccine with high efficacy, and recommendations for routine vaccination of females, HPV vaccine implementation has had some specific challenges in the US and globally, in part due to the targeting of adolescents. In 2009, three years after licensure of the first HPV vaccine, 44% of adolescent girls aged 13–17 years had initiated HPV vaccination, and 26.7% had completed the three dose series in the US (23). Some fundamental lessons learned from implementation of HPV vaccine may offer insights for a future HIV vaccine, particularly if the vaccine is to be targeted to adolescents. Issues that provide insights may be broadly categorized as vaccine delivery, acceptability, cost barriers, and policies that support vaccine programs.

One of the principal challenges to implementing HPV vaccine is reaching adolescents. The primary setting for vaccine delivery in the US is the medical home, but many adolescents do not routinely visit a provider for a prevention visit (24). Even when adolescents visit the medical home, there are missed opportunities for HPV vaccination (24). One specific challenge to HPV vaccination is the requirement for 3 doses, requiring multiple visits (25). Some countries such as Australia, the United Kingdom and parts of Canada, are achieving high HPV vaccine coverage through school located immunization programs (26, 27). However, these programs may not be as feasible in the US as vaccine is not routinely delivered in schools, there are few schools with health clinics, limited availability of personnel to vaccinate, and complicated reimbursement issues (28).

Another important component to implementation success is provider, parental and adolescent acceptability of the vaccine. Although many studies found overall acceptability of HPV vaccine, vaccine uptake has been found to be higher in older adolescents compared to younger adolescents (29, 30). As HPV vaccines target adolescent girls and prevent an STI, some parents and providers may be more comfortable vaccinating older adolescents, when discussions about sexual behavior may arise. Furthermore, some have hypothesized that vaccinating adolescents against HPV would lead to increased sexual risk behavior because of the belief that the vaccine protects them from an STI. However, adolescent sexual behavior is shaped by a complex interplay of individual, family, peer, school and community factors, and it is unlikely HPV vaccine would have a direct influence on this process. There are also questions that arise about a new vaccine that may impact acceptability, including those related to duration of protection and vaccine safety (31).

Vaccine costs can also impact successful implementation. In the US there is a federal entitlement program in place for eligible adolescents <19 years of age, the VFC program. Although this program provides vaccine without cost to eligible adolescents, not all uninsured or underinsured adolescents receive vaccine through this program. The private sector cost for the vaccine is approximately ~US$130/dose not including administration fees (32).

Vaccine policies such as school immunization requirements may impact implementation. State-based school immunization requirements are credited, in part, for high childhood vaccine coverage (33). All states have elementary school requirements for at least one vaccine; most have middle school requirements for some vaccines. However, these policies

for HPV vaccine have generated substantial debate about the public health versus individual rights. Supports for these policies are facilitated by the appropriate climate and timing of their initiation. Only two jurisdictions at present have school requirements for HPV vaccine, Virginia and the District of Columbia; both have broad opt out provisions (34). An early push for HPV vaccine requirements primarily supported by vaccine manufacturers soon after vaccine licensing caused considerable controversy; at this time there are few settings willing to consider initiating these policies (34).

In summary, while progress has been made in introduction of HPV vaccine in the US, important challenges remain in vaccine implementation. These challenges may offer insight into key issues for other prevention efforts directed to adolescents, including a potential future HIV vaccine. It is important to note that an HIV vaccine may have different issues depending on vaccine efficacy, acceptability, doses required, and ages or subgroups targeted for immunization. However the ongoing experience with HPV vaccine may provide insight and opportunities for a future HIV vaccine.

Influenza vaccine strain selection (Michael Shaw)

Influenza vaccines have been used for the prevention of influenza virus infections since the first inactivated, whole virus vaccine formulations were tested in the late 1930's (35). However, it soon became obvious that antigenic changes in circulating strains required frequent reformulation in order to ensure the closest match possible between the vaccine strains and those circulating in the human population to optimize vaccine effectiveness (36, 37). The current WHO Influenza Surveillance Network was established in 1952 upon the recommendation of a WHO Expert Advisory Committee that an international network of laboratories be set up to coordinate the collection and exchange of information related to the characteristics and epidemiology of the viruses (38). The Network has since evolved to also serve as a global alert system to identify emerging influenza viruses with pandemic potential. The system currently collects more than 150,000 patient samples from more than 100 countries each year and extensively analyzes thousands of virus isolates submitted to one of five WHO Collaborating Centers for Influenza Reference and Research located in Australia, China, Japan, the United Kingdom, and the United States.

Whether inactivated or live-attenuated, current influenza vaccines must be regularly reformulated to incorporate clinically relevant antigens. There are several factors that must be considered when recommendations are made for new influenza vaccine strains:

1. *Are there new antigenic variants?* The surface glycoproteins of the virus, the hemagglutinin (HA) and neuraminidase (NA) undergo continuous change manifested as "antigenic drift" as circulating strains evolve to escape host immunity; both types A and B influenza viruses undergo antigenic drift (39, 40). This type of variation requires regular assessment of circulating strains to monitor the extent of change relative to previous strains. Type A influenza viruses are also capable of undergoing "antigenic shift" where entirely new HA and/or NA glycoproteins are acquired either through a reassortment event with a non-human strain (41) or due to the introduction of an entirely new strain from an animal host (42). The analyses performed are both antigenic, to measure reactivity to antibody,

and genetic, to correlate antigenic changes with molecular characteristics. Since more labs are now capable of genetic analyses than can perform detailed antigenic characterization, correlation of antigenicity with genetic sequence allows more rapid and extensive data collection.

2. *Are these new variants spreading in the human population?* Influenza activity is monitored and representative strains analyzed to detect any trend in circulating strains that might indicate a new variant is becoming established. Antigenic variants appear frequently but are only of concern for the purposes of vaccine strain recommendations if they are deemed likely to displace the predominant strain. An extensive and geographically representative surveillance system is needed for this type of data to be accurate. The rapidity with which influenza viruses spread within a vulnerable population also requires timely submission of strains for evaluation.

3. *Do current vaccines induce antibodies effective against the new strains?* Part of the regular assessment process is the serological evaluation of individuals vaccinated against the current vaccine strain to see if the response is capable of protecting against the newly identified variant(s). If cross-reactivity is sufficiently high, a change in vaccine strain might not be necessary.

4. *Are there new variants suitable for vaccine production?* Vaccine production methods and technology impose certain constraints on the choice of strain beyond the antigenic characteristics of the virus. A vaccine strain must be capable of growth without change in antigenic characteristics in an approved substrate such as embryonated hens' eggs (in the US) or certified cell line cultures (approved in certain non-US markets and pending approval in the US). In addition, type A influenza vaccine strains are often high-growth reassortant viruses having surface antigens from the new variant strain expressed in a background of a high yield strain adapted for growth to high titer in the desired substrate (43). These reassortants must be produced for any new type A virus being considered in order to be feasible for large scale production.

All of these factors must be evaluated and data available with sufficient lead time for vaccine production, licensure, and distribution before influenza season. In the Northern Hemisphere this means vaccine virus recommendations must be issued by mid-February and the specific viruses must be made available for manufacturers by March in order to allow reassortant virus production and distribution to manufacturers by the end of May. This is followed by a testing and licensure process in June and July, filling and packaging in August, and vaccine release and shipment in September for the beginning of vaccination in October and November. Similarly, for the Southern Hemisphere the vaccine virus recommendations must be made mid-August to September in order for vaccine to be available for the next year's influenza season. The risk of a new variant appearing after the selection has been made is an incentive for devising new vaccine technologies with shorter lead times so the strains chosen can be as current as possible.

Will annual consensus strain antigens improve HIV vaccine formulations? (Jim Mullins)

Several features distinguish the patterns and levels of genetic variation in influenza A versus HIV. Influenza A infections are transient, with new strains circulating the globe through human populations annually. The amount of genetic variation that accrues within the days to weeks in which flu viruses typically replicate within one human before passing the virus along to another human is small. In contrast, HIV infections are permanent, giving HIV an greatly extended period for intrahost evolution, measured at about 0.2–1%/year, depending on the gene (44, 45). Consequently, the evolution of HIV continues apace in all infected individuals throughout their lifetime, until and unless successfully suppressed by antiretroviral therapy. Overall, the level of global diversification of the influenza A HA (haemagglutinin) gene that occurs over ten years is approximately the same as that which occurs over one year in a single person infected with HIV-1.

Sequential infection with HIV strains, termed superinfection, is not rare, and superinfecting strains sometimes recombine to form novel genomes with superior growth properties in the host and wide transmissibility in populations. Viral diversification of HIV-1 is also accelerated by recombination between superinfecting strains. In parallel, dual infection of cells by two flu strains is famously associated with genome segment reassortment, leading to strains with pandemic potential, especially if derived from strains from different host species.

HIV-1 evolves in a star-like phylogeny, that is, within each host it explores new evolutionary space, finding new ways to evolve away from structures attacked by host immune responses. Each individual HIV strain evolves sequences that are maximally divergent from other circulating strains (46). This is the crux of the problem for producing HIV vaccines that are temporally specific, much less based on annual consensus sequences, as is done so successfully for annual influenza A vaccines. Obtaining an efficacious HIV vaccine of any sort is beyond our grasp currently, thus definition and use of a “circulating strain” is not likely to be useful concept in the production of HIV vaccines in the middle term future.

A likely important component of HIV-1 evolution that permits exploration of so much evolutionary space is the development of compensatory mutations. As mutations that result in escape from immunologic targeting, viral fitness can be impaired; hence, compensatory mutations are selected for that permit maintenance of escape while improving viral fitness (47, 48). More than two dozen compensatory mutations have been identified using computational methods in influenza (49). Again, however, hundreds of interacting, potentially compensatory amino acid changes have been identified in individual HIV genes (50, 51). Hence, fitness of HIV can apparently be maintained while continuing to adopt increasingly diverse primary structures.

There are several current approaches to HIV vaccine design and implementation. The focus here will be on variables in immunogen design (52, 53). Strains of convenience, essentially laboratory strains, sometimes matched by genetic subtype to the test population, have been

used in each of the large scale Phase III and Phase II HIV vaccine trials to date. More recently, several approaches have been put forward for selection of the viral strain sequences to be used in vaccine formulations. These include:

1. "Circulating strains", discussed above.
2. Founder strains, those found to clonally dominate early in infection, have garnered considerable attention since these viruses may well embody important characteristics, potentially reflected in antigenic characteristics that confer a replication advantage in an exposed host (54–57).
3. Computationally derived central strains, in particular, consensus, ancestor and center of tree sequences (58–63). Since HIV envelope gene sequences recover some ancestral features early in infection (46), the use of an evolutionarily central strain may have the advantage of being able to block the outgrowth of evolutionarily favored structures as well as more commonly encoded epitopes than any given natural strain. Studies to date indicate that central state immunogens give rise to immune responses with enhanced breadth of recognition of natural strains (58–61, 64).
4. Variation inclusive antigens represent an exciting current approach. The use of multiple natural strains (65), computationally designed Mosaics (66) and COT+ antigens (65, 67, 68) have been proposed. In addition, Mosaic antigens have produced encouraging results in macaque studies (69, 70) and prototype immunogens are now in clinical development.
5. Given that it may not be possible to block most of the viable escape pathways HIV can evolutionarily transit to elude immune suppression, a renewed focus on composing vaccines from conserved components of the viral proteome are a particularly exciting possibility (71–73) for the development of broadly applicable immunogens with the capacity to direct immune responses to only those elements of the virus critical to its survival.

The utility of determining annual consensus HIV strains is nonetheless manifold. For example, continued molecular epidemiologic study of the global pandemic will continue to remain valuable to identifying new outbreaks with divergent viral strains, to defining host population immunologic imprinting on the virus (74), identification of changes to conserved regions, and ultimately, to identification of the limits to evolutionary expansion. Combining these surveys with co-variation analysis should also help deconvolute primary and compensatory mutations resulting in preserved viral function.

Post-RV144 planning in Thailand (Supachai Rerks-Ngarm)

After learning in September, 2009 that the RV144 study demonstrated the first-ever report of a limited degree of protection against HIV acquisition in a preventive HIV vaccine efficacy trial in humans (1), the Thai Ministry of Public Health (MOPH) and the US Military HIV Research Program (with support from WHO/UNAIDS and Global HIV Vaccine Enterprise) hosted an International Consultative Meeting in Thailand on March 16–18, 2010, to consider issues concerning the next steps that should be taken following this

major scientific milestone. The issues discussed among local and international experts were utility of RV144 vaccines regimen, further studies for more information on the vaccines regimen, the HIV vaccine development policy and other relevant issues. Table 2 summarizes the recommendations to the Thai MOPH, from the four meeting workgroups spanning four broad (and frequently intersecting) themes: Public Health and Future Access; Ethical, Regulatory and Community Issues; Science and Vaccine Development; and Clinical Trial Design and Statistics. The full report is available free online (75).

Several of the recommendations have been or will soon be implemented, they include most notably:

1. Search for correlates of protection. Working groups in four categories (a) humoral and innate immunity, (b) cell immunity, (c) host genetics, and (d) animal model have been formed to identify the most promising candidate studies to test the limited quantity of patient samples from the RV144 trial participants in an effort to define the immune mechanisms mediating the protection against HIV infection.
2. Assessing the impact of a late boost to the RV144 regimen. The RV305 late boost study is recruiting uninfected RV144 study participants and administering a late boost regimens consisting of the RV144 combination regimen or one component of the combination (AIDSVAX® B/E or ALVAC-HIV). Cellular and humoral immune responses following the different boost regimens will be characterized and compared.
3. Increasing our scientific understanding of the RV144 regimen. The RV306 immunogenicity trial will enroll new vaccinees to the RV144 regimen and obtain enough samples to better characterize systemic and mucosal immunity of the ALVAC/AIDSVAX combination or AIDSVAX alone or ALVAC alone. It will also characterize the innate, humoral and cellular immune responses after late boosting with ALVAC/AIDSVAX or AIDSVAX alone or ALVAC.
4. In the longer term, plan for follow-on Phase IIb trials using an updated poxvector prime and gp120 protein boost regimen in a higher HIV incidence population in Thailand and South Africa.

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Table 1

Key Issues raised during moderated audience discussion at AIDS Vaccine 2010 Satellite Symposium "Preparing for the Availability of a Partially Effective HIV Vaccine", Atlanta GA, September 28, 2010.

Considerations for low and middle income countries:	
1.1	Need help with algorithm for introduction of HIV biomedical interventions; need to start by identifying gaps in knowledge in each country/setting.
1.2	The lesson from hepatitis B vaccine that there was poor availability in countries at greatest need for decades; this was only solved by manufacturing in the region.
1.3	Access to licensed vaccines is still poor in many countries; what will be the impact of the current funding gap for Global Alliance on Vaccines and Immunizations (GAVI) and advanced market initiative on future HIV vaccines?
1.4	Adult vaccination programs need improving globally in each country.
1.5	Countries differ in their risk groups for HIV and the relative maturity of their national immunization program; probably won't be single size fits all.
1.6	The health care workers are already overworked; therefore the logistics of a future HIV vaccine will be critical (e.g., multiple doses in high risk groups => low coverage)
1.7	Need to better translate meaning of "partial" efficacy for the general public
1.8	Consult community more with messaging on the results before dissemination
Considerations for high income countries:	
2.1	Much practical/implementation resource already available in the routine immunization program.
2.2	Mostly an issue of competing priorities, especially if HIV prevalence/incidence is low.
2.3	Funding for childhood vaccines well established; adolescents/adults more challenging.
2.4	Need to think about incentives vs. removing barriers to immunizations.

Table 2

Recommendations for the Future Utility of the RV144 Vaccines to the Thai Ministry of Health from joint Consultative Meeting, Bangkok, Thailand, March 16–18, 2010(75)

1	The Thai Ministry of Public Health, researchers, and sponsors have no obligation at this point in time to offer the RV144 vaccine regimen to the placebo group in the trial.
2	Re-vaccination of a small subset of HIV-uninfected RV144 vaccine recipients with ALVAC-HIV [vCP1521] and AIDSVAX B/E, alone and in combination. This study should comprehensively assess the effect of such late boosting on immune responses.
3	A separate immunogenicity study of HIV-uninfected volunteers should be conducted to further characterize the immune responses induced by the RV144 vaccine regimen.
4	Consideration should be given to comparing the RV144 vaccines with related vaccines in intensive immunogenicity studies.
5	Efforts should be made to improve and extend the results of the RV144 trial.
6	Discussions for future HIV vaccine efficacy trials should begin within the global context of HIV vaccine development.
7	The use of a placebo control in future HIV vaccine trials is warranted and ethically acceptable.
8	It is not currently necessary to include the RV144 vaccine regimen in a prevention package.
9	Future vaccine protocols should anticipate and explicitly state benchmarks (such as the level of efficacy) and also describe the strategy that will be used for un-blinding of the trial and vaccination of the control group.
10	Future phase III or later-stage trials should maintain individual HIV infection control observation periods for at least 2 years after initiation of the vaccine sequence with duration examined for at least 1 year after the last vaccination.
11	Improved and standardized methods for characterizing transmission route in infected participants should be included in future trials.
12	Multi-arm studies must be designed with incidence rates in mind, and are probably not applicable in low incidence, general-risk populations in Thailand.
13	The Thai Ministry of Public Health in its capacity of overseeing research in Thailand should ensure that researchers “consult communities through a transparent and meaningful participatory process, which involves them in an early and sustained manner in the design, development, implementation, and distribution of results of biomedical HIV prevention trials.”
14	More intensive studies of increased risky behavior post-vaccination would be valuable, and consideration could be given to inclusion of the RV144 placebo group participants in such studies.
15	Improved data collection methodologies and validation measures should be developed to improve accuracy of behavioral risk assessments.
16	Several modelling teams should be encouraged to estimate the cost and impact on the HIV epidemic of vaccine regimens with varying efficacy and durability (including a 31% efficacious general population vaccine with 1-year duration of protection).
17	Better estimates are needed of what will happen in the Thai population when preventive HIV vaccines are introduced, including the acceptability of these vaccines.
18	Public health decisions related to preventive HIV vaccines must start with a focus on the current context of public health prevention and care and treatment.
19	The pathways to licensure for preventive HIV vaccines in general should be defined and the role of regulatory bodies, both national and other bodies, explored.
20	A plan should be developed to ensure access to preventive HIV vaccines post-licensure.
21	The Thai Ministry of Public Health, in its capacity of overseeing research in Thailand should seek to ensure that vaccine trial results and implications are communicated to the public in clear and understandable language.
22	There are compelling scientific and ethical reasons to continue further vaccine research that may benefit the Thai people.