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Vaccine Meeting, 7/25/94

Stack:	Row:	Section:	Shelf:	Position:
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MONDAY

July 25, 1994

TIME: 3:00pm - 4:00pm

LOCATION:

EVENT: MEETING - VACCINE

HIV VACCINE EFFICACY TRIALS: SOCIAL/LEGAL/ETHICAL ISSUES

July 22, 1994

PURPOSE:

This issue paper summarizes the status of NIAID's plans to advance the most promising HIV/AIDS vaccines into efficacy trials outlines several issues concerning the conduct of vaccine efficacy trials that will require inter-Departmental coordination and collaboration, and perhaps legislative action to ensure ultimate success of the vaccine effort.

BACKGROUND:

The AIDS subcommittee of the NIAID Council and the AIDS Research Advisory Committee held a public meeting on June 17, 1994, to advise the Director, NIAID, on whether the two recombinant gp120 envelope (rgp120) candidate prophylactic HIV vaccines currently in phase II clinical trials should be advanced to expanded trials in the U.S. at this time. Their recommendation, which was accepted by the Director, NIAID, was to continue the current rgp120 program and the development of other candidates currently under study, and to proceed with expanded clinical trials of rgp120 when another HIV vaccine concept and/or compelling data from current or other studies are available. (By another vaccine concept the Committee was referring to a vaccine design other than monomeric envelope glycoprotein.) NIAID anticipates that an alternative concept could be ready for efficacy trials in approximately 2-3 years, and that sufficient information will be available in 12-18 months to judge the likelihood of this possibility.

There were major factors behind the Committees' recommendation: 1) general skepticism around the likelihood that these products produce a biologically meaningful effect; and 2) the nearly universal sentiment that communities were not yet "ready" for an HIV vaccine efficacy trial. Obviously, the successful conduct of HIV vaccine efficacy trials will require large numbers of seronegative volunteers at increased risk on HIV infection, many of whom are disenfranchised from and/or distrustful of biomedical research, including gay and bisexual men with multiple sex partners, and injection drug users (IDUs) and their partners. The future readiness of these communities will depend on several factors including the extent to which community concerns have been addressed.

In this context, there are three specific issues which lie outside the purview of the NIAID/NIH, and which are related to our successful implementation of HIV vaccine efficacy trials in these populations.

1) Discrimination arising from participation in vaccine trials

Potential volunteers are concerned about being labeled as "high risk" by virtue of their participation in an HIV vaccine trial, and/or false positive HIV/AIDS tests. Other candidate vaccines under development are likely to produce a significantly higher percentage of false positive tests. Special efforts will be required to prevent and address actual or feared discrimination by health and life insurers, employers who condition employment on negative HIV tests, emigration, and others. HIV Vaccine trial recruitment will be particularly difficult in states requiring named reporting of individuals with positive HIV tests.

2) Compensation for vaccine-induce injury

Many high risk individuals will be unwilling to participate in trials because they lack health insurance and because of concerns about the medical costs of injuries associated with experimental vaccines. Preliminary data suggests that 15-25% of potential volunteers regard guaranteed medical care for problems related to the vaccine as critical to their participation in trials.

3) Access of individuals/communities/countries to successful vaccines

Populations at increased risk may have limited access to licensed AIDS vaccines because of limited resources and/or limited access to health care. Although volunteers in a placebo arm of a trial are typically offered vaccine if it is successful, communities and countries may demand that all members have access to products after the trial ends, or to successful products from other trials. Given the general mistrust of the biomedical establishment and/or specific concerns about serving as "guinea pigs", community/country support and cooperation will be essential. Such support will be influenced by issues of access.

The attached plan summarizes NIAID's ongoing and planned activities on these three issues and, for completeness, also summarizes three other issues critical to the conduct of vaccine efficacy trials for which resolutions are already being pursued.

SUMMARY

NIAID believes that the success of our vaccine research and development efforts depends not only upon the science behind them, but also upon inter-Departmental collaboration toward complex, long-term strategies, and/or legislation to address these additional important social, legal, and ethical issues. Furthermore, given the current timeframe of vaccine development projections and the assessment of community readiness embodied in the ARAC recommendations, we believe that rapid progress is essential.

Social, Legal, and Ethical Issues
in Vaccine Efficacy Trials:

Issue 1: Trial participants may face discrimination, either from being labeled "high risk" due to trial participation or due to vaccine-induced seroconversion.

CURRENT NIAID ACTIVITIES:

- o NIAID staff will quantify, to the extent possible, the degree to which discrimination issues have arisen in NIAID's AIDS Vaccine Evaluation Group (AVEG) Protocol 201 that includes individuals at high risk for HIV infection, and how problems were resolved. The estimated completion date is 12/94.

- o NIAID staff will continue its dialogue with insurance companies, employers, etc., on an ad hoc basis as problems arise in Phase II studies.

- o NIAID vaccine trials operations contractor will continue to provide legal advice on discrimination issues that arise during Phase II trials.

- o NIAID staff will continue to highlight this issue for the PHS Task Force on AIDS' Working Group on Legal and Ethical Issues Related to HIV.

PROPOSED ACTIONS:

A) NIAID will explore the possibility of expanding its adverse events reporting (AER) system in Phase I/II/III Vaccine Trials to include adverse social events; Data and Safety and Monitoring Board (DSMB) would have to include members with appropriate expertise to review the data and provide ethical oversight of trials.

B) NIAID will provide its volunteers access to screening to distinguish true infection from vaccine-induced seroconversion upon request during the trial.

C) *Inter-Departmental coordination and collaboration will be needed.* Resolution may require education of insurers and employers, and/or changes in state HIV testing criteria and HIV reporting regulations. In addition, the CDC, in conjunction with state public health laboratories, should provide a testing service to distinguish true infection from vaccine-induced seroconversion for participants in government-sponsored HIV vaccine trials after they ends.

KEY PLAYERS: Businesses Respond to AIDS, Health and Life Insurers, HHS Office of Civil Rights, Mass Media, CDC, NIAID, AIDS Action Council, DOD, community representatives, Institute of Medicine (IOM) AIDS Vaccine Roundtable, NIH Office of Protection from Research Risks (OPRR), NIAID clinical trials investigators, community representatives, agencies that screen for HIV (e.g. Peace Corps, Job Corps, INS, etc.)

ISSUE 2: Volunteers may be reluctant to join trials unless assured of compensation for vaccine-induced injury.

CURRENT ACTIVITIES:

- o NIAID HIV Vaccine Efficacy Trial Preparedness sites will continue to estimate the extent of the concern about injury liability among potential trial participants.

PROPOSED ACTION:

A) *Inter-Departmental coordination and collaboration will be needed.* While resolution of the health care issues may occur with the implementation of a national health care plan, it is highly possible that efficacy trials will be initiated within the next 2 years and interim coverage may be necessary. The broader issue of liability may require a legislative solution.

KEY PLAYERS: Congress, Manufacturers, NIAID, HRSA, AIDS Action Council, Community Representatives, OTA, NSTC, IOM Roundtable on HIV Vaccines .

ISSUE 3: Communities and countries participating in trials may want privileged access to products after trial ends. Volunteers in early trials may want to participate in subsequent trials of more promising agents, but may be excluded for protocol reasons.

CURRENT ACTIVITIES: NONE

PROPOSED ACTIONS:

A) NIAID will facilitate interactions between communities and manufacturers in reaching agreement, prior to initiation of an efficacy trial, regarding access to products after the trial is completed.

B) *Inter-Departmental coordination and collaboration will be needed to*

seeking a written policy on access to vaccines for domestic and foreign populations.

KEY PLAYERS: Congress, Manufacturers, R&D Firms, NIAID, HRSA, AIDS Action Council, community representatives, OTA, NSTC HIV Vaccine Working Group, IOM Roundtable on HIV Vaccines, WHO.

ISSUE 4: Manufacturers and investigators may be reluctant to develop or evaluate candidate AIDS vaccines for economic and/or liability reasons.

CURRENT ACTIVITIES:

- o NIAID staff are continuing their dialogue with manufacturers to stimulate continued interest in vaccine development.

- o NIAID staff will continue to respond to requests from other government officials to provide information on liability and other private sector concerns, as they arise.

PROPOSED ACTIONS:

A) The Vaccine Efficacy Trials subcommittee of the NSTC has begun to address this issue in concert with vaccine manufacturers. Further NSTC activities to address this issue are anticipated.

KEY PLAYERS: Congress, Manufacturers, R&D Firms, NIAID, HRSA, AIDS Action Council, community representatives, OTA, NSTC, IOM Roundtable on HIV Vaccines

B) NIAID will continue its current activities in this area.

ISSUE 5: Community support will be crucial to the successful conduct of HIV vaccine efficacy trials.

CURRENT ACTIVITIES

- o NIAID is supporting the development of local Community Advisory Boards (CABs) and a national CAB through its existing vaccine clinical trials networks.

- o NIAID will ensure adequate representation of community representatives on its advisory committees and working groups, including the Vaccine Working Group, AIDS Vaccine Evaluation

Group (AVEG) Executive Committee, HIV Vaccine Efficacy Trials Network (HIVNET) Steering Committee, and Protocol Development Teams, and at key scientific meetings.

- o NIAID is funding vaccine preparatory work to educate communities and potential volunteers about HIV vaccine efficacy trials. Activities include development and evaluation of technologies such as conventional and interactive video.

- o NIAID will continue to encourage CDC's involvement in the community education aspects of vaccine trials.

- o NIAID will ensure that potential trial sites maximize opportunities for participation of minorities, women, and disenfranchised and stigmatized individuals in trials through use of culturally appropriate staff, outreach workers, transportation incentives, etc.

- o NIAID staff will continue to work with community organizations, including the AIDS Action Foundation's Working Group on the Social and Ethical Considerations in Vaccine Efficacy Trials, to address community concerns about trials.

PROPOSED ACTION:

No additional action is proposed at this time.

ISSUE 6: HIV transmission could increase in communities if trial participants increase exposure to the virus in the mistaken belief that they are protected by an experimental vaccine.

CURRENT ACTIVITIES:

- o Risk behavior is being assessed for AVEG Protocol 201 participants at each visit.

- o Vaccine preparedness sites are asking potential trial volunteers about the likelihood of behavior change in vaccine efficacy trials.

- o NIAID has added a behavioral scientist to its Vaccine Working Group.

PROPOSED ACTION:

A) NIAID will analyze data from AVEG Protocol 201, which includes individuals at higher risk for HIV infection, to assess behavior change during the trial.

B) OAR is planning a workshop with NIDA, NIMH, CDC, DOD, and NIAID to identify the most promising educational interventions for use in trials, and to help NIAID develop and validate risk assessment instruments for use in vaccine efficacy trials.

C) NIAID will define and test responsible and achievable counseling strategies.

D) NIAID will design concise and reliable risk assessment instruments. Vaccine efficacy trial sites will measure volunteer HIV-related risk behavior and decoding during trials. If risk behavior increases, counseling efforts will be intensified for all volunteers.

Author: Paul Tran
Date: 06/23/94 02:46 PM
Priority: Normal
TO: Gus Ventura
CC: Kristine Gebbie
CC: Andrew Barrer
CC: Arthur Lawrence
Subject: KG vaccine meeting

---------- Message Contents ----------

Gus, please put this date down in Kristine's schedule for the meeting: July 25, 3-4 p.m.

As of now, the meeting will include (outside of ONAP) Dr. Paul (OAR), Dr. Fauci (NIAID), and Dr. Mazzucki (DoD).

I have tried to call Dr. Burke at least three times for this meeting, but he has not returned my call. I also asked Dr. Mazzucki's secretary to include Dr. Burke for this meeting.

Kristine, Dr. Fauci asked if he could have Dr. Jack Killen (DAIDS) included in this meeting. Please let me know. Thanks.

for vaccine mtg c DOD/HHS

[39] From: Paul Tran 6/20/94 10:07AM (3680 bytes: 62 ln)
To: Kristine Gebbie, Arthur Lawrence
cc: John Gurrola, Terry Beswick
Subject: ARAC Vaccine recommendation
---------- Message Contents ----------

ARAC recommended to NIAID Director NOT to go to an expanded trial of the two current gp120 vaccines. Instead, the current gp120 programs and the development of other candidates currently under study should be CONTINUED. Expanded trials will be proceeded when another concept or compelling data from the current or other studies are available.

Out of concern of the impact the recommendation would have on vaccine industry and international collaboration, ARAC carefully crafted the language emphasizing that the decision is only true for U.S. -- not other countries, and only for these two products, at this point in time only. (During the public comment session, Don Burke read to ARAC the letter from Thai officials to NIAID Director expressing about ARAC recommendation/decision, and wanted to ensure that the decision should not have any implication on Thailand and that it should be for U.S. ONLY.)

THE PRESS: *** The NY Times, the Post, and the Philadelphia Inquirer reported this recommendation over the weekend. However, only the Times and the Inquirer included ARAC's emphasis on that its decision should not affect other vaccine development and international trials.

*** John should have received NIAID official statement on the recommendation from Laurie Doepel of NIAID Office of Communications.

REFLECTION: In view of the recommendation at the Vaccine Working Group (VWG) meeting this past April, ARAC decision was unexpected. VWG was going into the direction of having an expanded trial of smaller scale. Its members agred that "additional lab or animal model data are unlikely to add significantly to the knowledge base that would predict whether or not a recombinant gp120 candidate vaccine might afford protection from HIV infection." They concluded that the scientific rationale supports advancing and expanding clinical trials to evaluate the hypothesis further.

It was obvious that ARAC did not buy this recommendation from VWG.

ONAP: (1) Kristine, do you still want to have a meeting with DoD, NIAID, OAR (plus industry leaders?) over vaccine issues? I think there should be one. The scope of the meeting may be larger than originally intended (see below).

With press coverage lately over vaccine development, and ARAC in particular; with international concern over U.S. vaccine development strategy; with possible industry reluctance, or discontinue, to involve with AIDS vaccine R&D; with OTA soon-to-be released AIDS vaccine report; and with World AIDS Day drawing near, this would be a time for

The NIAID LAN

Kg -
F.Y.I. &
to let you
know we
included some
weblogs on
this in
Playgrounds

TO: C GEBBIE JOHN GURROLA
Fax: 82026321096
FROM: Marion Glick:31:niaid
Fax:
Voice:
DATE: 20 June 1994 11:08

The NIAID Network Mail to Fax Gateway

Date: 6-20-94 10:58am
From: Marion Glick:31:niaid
To: {Jack Whitescarver OAR \fax:22047}:fax,
{C Gebbie John Gurrola \fax:82026321096}:fax
Subj: ARAC statement
Attach: H:\aracst

Enclosed is the NIAID statement issued Friday night re ARAC meeting on HIV Vaccines.

Marion E. Glick
Chief, Information Projects Section
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June 17, 1994

NIAID Advisors Recommend Continuing But Not Expanding at This Time Ongoing Trials of Two Candidate HIV Vaccines

On June 17, 1994, the National Institute of Allergy and Infectious Diseases (NIAID) held a joint meeting in Bethesda, Md., of the NIAID AIDS Research Advisory Committee (ARAC) and the NIAID AIDS Subcommittee of the National Advisory Allergy and Infectious Diseases Council. At the meeting, NIAID solicited a recommendation from the group about whether or not to expand at this time the NIAID's U.S.-based clinical trials of the two gp120 subunit HIV candidate vaccines furthest along in development. Ashley T. Haase, M.D., ARAC chairperson and head of the Department of Microbiology at the University of Minnesota Medical School in Minneapolis, chaired the meeting.

After a full day of discussion and deliberation, these advisors recommended that the Institute continue, but not expand, the current vaccine trials of the two gp120 candidates in question and continue the development of other candidates currently under study. The committee members also recommended NIAID proceed with expanded clinical trial evaluation

when a vaccine of a different design and/or when other compelling data from current or other studies are available. In recognition of the difference in the dynamics of the epidemic throughout the world, the majority of the advisers also agreed that at the present time this recommendation applies only to studies of these two products in the United States.

The discussion and subsequent recommendation to NIAID Director, Anthony S. Fauci, M.D., is part of NIAID's ongoing decision-making process about when to begin its first efficacy trial of preventive HIV vaccines. Because of the clear, overwhelming consensus of the advisors, Dr. Fauci adopted the recommendation.

The two vaccines are based on genetically engineered forms of the major HIV surface protein, gp120, from closely related but distinct HIV-1 strains representative of most infections in North America and Europe. The Biocine Company (Emeryville, Calif., a joint venture of Chiron and CIBA-Geigy) makes its vaccine from the SF-2 strain. Genentech, Inc., (South San Francisco) bases its vaccine on the MN strain. At this time, these HIV vaccines are the only ones in an NIAID-sponsored Phase II clinical trial. NIAID began the trial in December 1992.

NIAID will evaluate data from new and ongoing HIV vaccine studies before it identifies a suitable candidate vaccine to propose for expanded trials. The Institute estimates that one to three years are needed to get such data. NIAID is committed to the development of a vaccine to prevent HIV infection and disease. This means continuing the Institute's comprehensive basic and applied program of preclinical and clinical work on candidates and concepts currently in earlier stages of development. Additional community preparedness work will also be carried out. The clinical trials conducted through NIAID's vaccine clinical trial networks are part of a broader prevention effort that includes non-vaccine prevention research.

NIAID, a component of the National Institutes of Health (NIH),

supports research on AIDS, tuberculosis and other infectious diseases as well as allergies and immunology. NIH is an agency of the U.S. Public Health Service, U.S. Department of Health and Human Services.

Prepared by:
Office of Communications
National Institute of Allergy and Infectious Diseases
National Institutes of Health
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Public Health Service
U.S. Department of Health and Human Services