


PATIENT’S BILL OF RIGHTS AND RESPONSIBILITIES
(THOMAS KERNS)
Patient’s Bill of Rights and Responsibilities

(Thomas Kerns)

YOU HAVE THE RIGHT TO

• Be treated with respect by app persons connected with the research team.

• Be fully informed about:
  - The purposes, nature and methods of the research in which you are participating;
  - All possible risks, inconveniences, hazards or discomforts of any kind related to your health or well being that might result from your participation in the trial;
  - Any changes in knowledge about the vaccine being studied which could materially affect your decision to continue participation in the trial.

• Have all information relating to your participation in the trial, including whether or not you are a volunteer in the trial, and all records relating to your medical condition or sero status, kept fully confidential and released to no one except to persons whom you explicitly, in writing, authorize to receive it.

• Be reimbursed for transportation, meals and other out of pocket expenses that result from your participation in the trial, as well as to be given a small stipend for your time involvement as described in the consent form.

• Participate in support groups, counseling sessions and classes designed for you and your family and/or partner.

• Be protected (to the fullest extent that the research team is able to protect you) from all harms, physical, psychological, social, economic and legal, which might result from your participation in these trials.

• Have the research team be on your side and looking out for your well-being.

• Be compensated for any accidental injuries which may result from your participation in the trial (as described in the consent form).

• Not to be manipulated or coerced by any one on the research team into doing anything against what you consider to be in your own best interests.
• Ask questions to the research team about anything regarding any aspect of your participation in this project.
• Quit your participation in the trial at any time you wish, for any reason.

YOU HAVE THE RESPONSIBILITY TO

• Keep your appointments with the research team, to the best of your ability.
• Be fully truthful with the research team in your reports about risk behaviors.
• Provide fully truthful responses to counselor’s questions about matters relating to your participation in the trial.
• Provide fully truthful responses on any tests or questionnaires that are part of the research.
• Keep the research team apprised of any changes in the state of your health.
• Keep the research team apprised of any changes in the medications you are taking.
• Keep the research team apprised of any drugs you are taking.
• Keep the research team apprised of any changes in your residence or living situation so they can communicate with you if they need to.
• Not ‘unblind’ yourself. ie; not secretly attempt to learn whether you have received the candidate vaccine or the placebo.
• Inform your counselor as soon as possible if you do inadvertently become unblended.

________________________________________

Signature of the Investigator
Date

Subject’s Statement :
The rights and responsibilities described above have been explained to me. I have had an opportunity to ask questions. I understand that future questions I may have about my rights or responsibilities as a subject can be answered by one of the investigators.

______________________________

Signature of Subject
Date
Ref: NARI/Admin/708/RTI/14-15/002/869

Date: 29/04/2014

To,
Mrs. T.S. Saritha,
House No. 80-A, Sector A,
Opp. Shopping Complex,
Chandimandi, Chandigarh,
Panchkula – 134 107, Haryana State,
Email id: sarithas@yahoo.co.in.


Sir,

With reference to your letter dated 03/04/2014, the information regarding Vaccine Clinical Trials is furnished herewith in the enclosed statement.

Yours Sincerely,

Dr. Nita Mawar,
Scientist B and CP10

Encl 1. Question Answer sheet from A to V
2. Screening Informed Consent Document
3. Enrollment Informed Consent Document

Copy To:
1. The Director, NARI, Pune
Specify the particulars of Information required:

a) What procedure is adopted in selecting subjects for HIV Vaccine Clinical Trials?

For our trials, we adopted the procedure of community based recruitment. Meetings to provide information about trial were conducted in the community. Those who showed interest in participation contacted study team on their own. This was followed by two contacts with the participants to give detailed information. The participants who expressed interest in participation after third contact were enrolled for screening.

b) What are the details of the ethical committees that reviewed and approved the HIV Vaccine Clinical Trials?

NARI has an independent ethics committee formed as per national guidelines of ICMR. Details of NARI's ethics committee are available in all the annual reports website (http://www.nari-bmc.in). The annual reports are available on NARI's website. ICMR's Central Ethics Committee also reviewed the protocol.

c) What are social, educational and economic background of the subjects participated in HIV Vaccine Clinical Trial, in general?

The participants in the HIV vaccine trials in India belonged to all socio-economic status. All participants were literate and many had college and above level education/technical education.

d) What are the motives identified for participation in the HIV Vaccine Clinical Trials?

Mostly altruism and a few wanted to know about HIV vaccine trial through direct experience

e) What remuneration was offered to the participants of HIV Vaccine Clinical Trials?

No remuneration was paid. Rs. 300/- per scheduled study visit was paid as compensation for loss of wages and travel as per approval by the Ethics Committee.

f) Any difficulty was faced in retaining the subjects of HIV Vaccine Clinical Trials? If so, how was it solved?

There was no difficulty.

g) Were the subjects participated in HIV Vaccine Clinical Trials advised about ongoing management of their condition, especially through provision of local standard of care?

The vaccine trial participants were uninformed healthy adult individuals and hence question is not relevant.

h) How was the informed consent procedure carried out for participants of HIV Vaccine Trials? Kindly furnish a copy of Blank informed consent form and patient information sheet.

Informed consent process was performed by trained counsellors in a confidential setting. There was also a test of comprehension administered by an independent person (other than counsellor). An individual passing the test was then requested to make decision about the participation and signing the informed consent form accordingly.
i) What standard operating procedures were carried at the institutional level except review by ethical committee and informed consent procedures, in connection with the HIV Vaccine Trials?

The mandatory regulatory approval was also obtained from CDSCO (then DCGI), Scientific Advisory Committee of NARI and GEAC. The trial was performed as per prefixed protocol and all investigations were trained in Good Clinical Practices.

j) What complications are expected in the participants of HIV Vaccine CTs?

No complications other than those normally seen with any other licensed vaccine were expected.

k) What complications are observed in subjects of HIV Vaccine Clinical Trials?

There were no safety issues in these trials. Vaccines were found safe. The safety data is published and available openly.

l) How many years of follow up is offered to the Trial participants of HIV Vaccine Clinical Trials?

It depends on the trial period as per protocol, one year of follow up after the last study injection.

m) Is there any system for surveillance of long term complications of the trial participants, once after the HIV Vaccine Clinical Trial is completed?

No, there is no such system.

n) What compensation will be given to those trial participants of HIV Vaccine Trials, in whom complications are identified?

The vaccine trial participants were provided medical insurance for complications. Arbitration board was established to address the issues related to compensation. No case was required to refer to the board.

o) Any health insurance is offered to the Trial Participants of HIV Vaccine Trials. If so kindly give details?

Medical insurance was provided to all volunteers deciding and consenting to participate in the trial.

p) Any vaccine injury compensation program exists for HIV Vaccine Trial participants?

No

q) Any measures are taken to reduce the non medical social harms of HIV Vaccine Clinical Trials, if so kindly elaborate.

Yes, Community education program and created awareness about phase 1 HIV vaccine and helped in gaining community support for vaccine trial participation. Counseling support was provided during the entire period of trial participation.

r) What regulations are binding on the ethical conduct of HIV Vaccine research in India?

CDSCO guidelines, ICMR biosafety guidelines

s) What measures are undertaken to maintain confidentiality of subjects of HIV Vaccine Trials?

Each study participant is only identified by unique ID number and none of the data is linked to her name. The informed consent forms had their signatures were kept separately under lock.
ENROLLMENT INFORMED CONSENT DOCUMENT

Volunteer Information

Enrollment visit for Phase I Prime-Boost HIV vaccine trial

Sites of research protocol

National AIDS Research Institute (NARI), Pune, India
Tuberculosis Research Centre (TRC), Chennai, India

Protocol Title: A Phase I Double-Blind, Placebo-Controlled, Randomized Trial to Evaluate the Safety and Immunogenicity of TBC-AM1, a multigenic MVA HIV Vaccine vs ADVAX, a multigenic DNA HIV Vaccine followed by TBC-AM1, a multigenic MVA HIV Vaccine

Protocol Number: SAVI P001
Protocol Date: 2 Apr 2006
Protocol Version: 2.0
Sponsor: International AIDS Vaccine Initiative
Principal Investigators: Dr. Suraj Mohanty, MD, MPH
TRC, Dr. V.D. Ramamurthi, MD, PhD

Introduction
On your first visit to this clinic, you were screened to assess your eligibility for the AIDS vaccine trial. You were found eligible. Today, you will be given an opportunity to participate in the AIDS vaccine trial using a "Prime-Boost" schedule. The purpose of this trial is to evaluate the safety of the vaccines included in the prime-boost regimen and their ability to generate immune responses in HIV-uninfected, healthy volunteers who are at low risk for HIV infection. The information about this trial is given in this informed consent document and in a separate document called the Volunteer Information Brochure, which explains in more detail the procedures of this trial. The clinic staff will discuss the information with you and will answer any questions you may have about any aspect of the vaccine trial. Once you understand the trial and if you agree to take part, you will be redirected to sign this consent form. Your individual

[Signature]

[Date]

[Chairman, Ethics Committee]
1. One of the two experimental vaccines being tested is TBC-M4. TBC-M4 was made from weakened live virus particles called Modified Vaccinia Ankara or MVA which is related to the smallpox vaccine. TBC-M4 contains DNA, which contains some of the genetic information of the HIV. International scientists developed this AIDS vaccine which has already been tested in India as a collaborative effort between the Indian Council of Medical Research, National AIDS Control Organization, and the International AIDS Vaccine Initiative (IAVI).

2. The other experimental vaccine being tested is ADVAX. This vaccine is made using RNA (genetic instruction code for part of HIV. ADVAX has been tested in humans in the United States.

Some people in the study will receive placebo only. Placebo looks similar to the vaccine but has no active ingredient. There is a different placebo for each vaccine.

This is a preventive vaccination regimen under evaluation intended for people who are not infected with HIV. It is NOT a drug for AIDS or HIV infection.

**Trial Procedures**

1. We will enroll 32 HIV-uninfected, healthy male or female volunteers between the ages of 18 and 59 who are at low risk of HIV infection to participate in this trial.

2. **Trial Groups**: There will be 2 different groups (A and B). Lucky group will receive a vaccination regimen as described here: Volunteers in Group A will receive DNA vaccine or placebo followed by MVA vaccine or placebo. Volunteers in Group B will receive only MVA vaccine or placebo regimen. Below is a table showing the regimens for Groups A and B. Enrollment into Group A will be completed first followed by enrollment into Group B. You will not know if you are assigned to Group A or Group B, but you will not know if you receive the experimental vaccine(s) or placebo(s).

![Signature]

R.K. Mutatkar
Chairman, NIMR
Chairman, NARC, Pune

NABH PC-13 Enrol and Consent

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3. Regimen: In group A, 12 volunteers will receive two injections of the DNA vaccine followed by two injections of the MVA vaccine, and 4 volunteers will receive 4 placebo injections. In Group B, 12 volunteers will receive three injections of the MVA vaccine and 4 volunteers will receive 3 placebo injections. If you are assigned to group A, you will receive your first injection on the day of enrollment and subsequent injections after 1, 3, and 6 months from the first injection. If you are assigned to Group B, you will receive your first injection on the day of enrollment and subsequent injections after 1 and 3 months. The injections will be given on your back, side, or arm in alternate sites over time depending on your choice. If you agree to participate in the trial, pass the assessment of understanding, and sign the Informed Consent Document, you will receive the first injection today after completing the enrollment process.

4. Knowing group assignment and double-blind: You will know if you have been assigned to either group A or B, but you cannot opt for a particular group. Knowing your group means you will know the number of injections you will get. You will not know whether you are receiving the vaccine(s) or the placebo(s). The treatments will be assigned randomly, like by the toss of dice, this is known as randomization. The assignment will not know this information either. This procedure is known as double-blind. It ensures that your reporting of the reactions and symptoms is not influenced by your knowledge whether you have received the vaccine regimen or the placebo. Similarly, it will not influence the assessment of the same by the researchers.

5. Observation: After each injection (see table below), you will be under observation for 1 hour at the clinic. Over the next two weeks, you will be required to come for 3 additional follow-up visits for clinical examination, assessment of risk behavior, psycho-social issues related to trial participation and blood tests at specified intervals as mentioned in
the Volunteer Information Brochure. Each visit at which you receive an injection may last for approximately 3-4 hours. Other visits may last up to 2 hours. You may also call or visit whenever you feel like it.

2. Study Venues: Starting with the vaccination visit, the visit schedule will depend on your group and would include 16 visits for Group A and 16 visits for Group B. These visits at the clinic for medical evaluation will be spread over a period of 16 months. The schedule of the visits is given in the Volunteer Information Brochure and will be explained to you by the counselors. Returning for follow-ups at the specified timings is very important. If you do not return at the scheduled time, we will need to contact you in a manner in which you agree. The counselor will document the mode of contact agreeable to you in the Informed Consent Form. During this period, HIV testing, including pre and post-test counseling, will be performed 7 times. Counseling and blood collecting will also be available throughout the trial. Any doubts or questions you may have will be clarified at any time.

Possible Risks and Alternatives

Blood Collection

Between approximately 30 ml and 105 ml of blood will be collected at each of the times indicated in the schedule given in the Trial Brochure. Blood collection may, in some cases, cause pain and swelling at the puncture site. Sometimes, you may feel dizzy. Efforts will be made to make the participants feel relaxed and comfortable. You will be seated in a comfortable position while trained staff collects the blood samples. All this will help minimize discomfort during the blood draw. Please understand that the donated blood volume will be naturally replaced by the body within a few hours without any special diet.

Risks Related to the Vaccines

Careful review of data from animal and laboratory studies as well as from human studies has demonstrated that each of the vaccines used in this trial was safe, generally well tolerated, and generated immune responses, allowing initiation of this trial in human beings. In the previous tests in India, the TRC-M4 vaccine was tested at a lower dose and a higher dose. Volunteers in this trial will receive the lower dose.

Local reactions at the site of the injection may include redness, swelling, pain, tenderness and in very rare cases, the formation of a scar, skin discoloration and muscle damage. Participants...
Reimbursement for Your Participation
There will be a total of either 10 or 19 scheduled study visits (depending on your assigned group), including today. To compensate you for your time and cost of transportation, we will provide you Rs. 1,000/- for each visit. The amount is expected to cover the expenses you incur for travel as well as loss of daily wages. You will be given reimbursement in the event of unscheduled visits for problems requiring attention by the research team.

Trial-Related Injuries
If you suffer from any adverse events or disabilities directly due to the trial vaccine, the study sponsor will ensure the provision of comprehensive care, support, and treatment. Should you become HIV-infected during the course of the trial, the study sponsor will ensure active follow-up care, support, and treatment, including free access to antiretroviral therapy (ART) for a period of 2 years from the point of eligibility and when medically recommended by existing clinical treatment guidelines. The sponsor will advocate for the best available HIV care and treatment that is provided by the national government or by alternative mechanisms beyond the covered period. You will also be provided medical insurance for vaccine-related and medical events (not covering HIV infection and vaccine-related events) for the duration of the trial period.

Storage of Samples
We would like to store your blood and blood cells for a maximum period of 10 years for possible use in new investigations or tests related only to AIDS vaccine research and development in the future. A number rather than your name will be used to label this blood. The stored and coded samples may be used in the future only for tests related to approved AIDS vaccine research and development. Stored coded samples may be shipped to independent national or international laboratories.

Genetic Testing
A test may be conducted to determine your HLA type or other genes that might control or influence your body's response to the vaccine. HLA is a specific marker on the surface of your body's cells. The result of this test will be kept strictly confidential.

[Signature]
04 JUN 2009
Peer, R.K. MUTAYIAR
GM, ISVAC, New Delhi
Independent Consultant on Medical Ethics, India
who did not receive the vaccine. You must also know that by receiving these vaccines you may not be able to participate in other AIDS vaccine trials in the future.

**Important:** You should not consider yourself protected from HIV after receiving these vaccines. It is very important that you avoid any behaviour that would put you at risk of contracting HIV infection. Counsellors have given you and will continue to give you information and education material about HIV risk reduction behaviour.

**Vaccine induced antibodies:** After the study injections, you may test positive for HIV antibodies. This does not mean that you are actually HIV-infected; rather the antibodies might have been induced by the test vaccine. If others come to know about your HIV antibody positive status, they may treat you unfairly. You will not be able to donate blood. You may also have difficulties with getting insurance, hospitalization, travelling to other countries, employment and joining the military service as long as you are HIV antibody positive. We do not know how long this HIV antibody will persist. Most likely this is a temporary condition. However, there are very reliable additional tests to differentiate whether you are actually infected or you are only antibody positive. This additional testing will be done free of cost. Upon your request we will provide you a certificate of participation in the AIDS vaccine trial mentioning the result of additional tests whenever you request. The certificate would state that the HIV antibody positive test results are due to participating in an AIDS vaccine trial and not due to infection with HIV.

Should you require any testing including HIV, for whatever reason, we strongly recommend that you contact the study team here and we will advise you accordingly. The study team will arrange for follow-up HIV testing.

**Pregnancy:**

Women are advised to avoid getting pregnant during the trial for up to 4 months after the last injection by using a reliable method of contraception because we do not know whether the experimental vaccines might cause some unforeseen harm to the fetus. You must discuss this with our staff and take all necessary precautions while in the trial. Particpating men are also advised to use condoms. If women participating in the trial or wives/partners of male trial participants become pregnant, the pregnancy should be reported to our clinic for immediate counselling and medical advice. Vaccine injections would be stopped in the pregnant women.
and the study team would follow her until delivery. The newborn baby would also be examined and followed up appropriately.

If you face any of the problems or difficulties described above, help is available from the trial staff upon your request.

Emotional and Social Risks
Some of the social and emotional risks to you as a participant are that you may feel uncomfortable while discussing sensitive information about sexual health and risk behavior. You may experience criticism, resistance, and/or withdrawal from family members when they know about your AIDS vaccine trial participation. Stigma and discrimination may also result from participation. Your community, for example, may believe that you are interested in such a trial because you practice risky behavior, and this may lead to emotional and social stress. You may also worry about possible long-term adverse effects of the vaccine. Follow-up counseling will be provided by trained counselors throughout the trial, and they may help in preventing and/or reducing such stress.

Benefits
There is no direct benefit to you by participating in this trial. Participation in the vaccine trial is a voluntary act, and you will contribute toward the global effort to find a safe and effective vaccine against AIDS. Throughout the trial you will receive information about your general health and HIV status. You will receive self-risk reduction and family planning counseling. The results of this trial will be used for the development of vaccines and will help to assure whether the experimental vaccines being tested are safe in human subjects and capable of inducing immune responses against HIV subtype C. This might enable the scientists to further evaluate these vaccines. At this moment no vaccine has been shown to prevent HIV infection or AIDS.

New Findings
You will be given any significant new information learned about the vaccine(s) during the course of the trial. It is possible that this information may influence your willingness to continue as a trial participant. At the end of the trial, you will be informed of the final trial results and whether you received vaccine or placebo.

Confidentiality of Records

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Your personal and medical records from this study will be kept confidential to the extent permitted by law. They will be identified by a code. Personal identifier information from the records will not be released to anyone except to those who are involved in conducting the study. You will not be personally identified in any publication about this trial. Only the Principal Investigator and the staff that is authorized by the Principal Investigator of the trial will have access to the clinical records that will otherwise be kept under lock and key. Your clinical records may also be reviewed by the Drugs Controller General of India, the International AIDS Vaccine Initiative (IAVI), the Safety Review Board (SRB), Ethic Committees, study monitors, national or international government regulatory agencies and auditors to make sure that the trial was conducted properly. They are equally bound to respect your confidentiality. Since the consent form will have your signature and your name, it will be kept securely under lock and key. The study staff will sign an agreement that will require them to maintain confidentiality of study records. In case of a dispute, the matter can be taken up with the arbitration board comprised of legal, social and medical experts. We request that you allow us to obtain medical information about you from your doctor in case you fall ill during the trial. This will help us to assess any adverse events approximately.

Discontinuation of Your Participation

Your participation is voluntary and you may withdraw at any time from this study without giving a reason. You will continue to have access to medical care and facilities that are routinely provided at this clinic. The trial-related specific investigations and medical evaluations will not be available after you have stopped your participation. If you decide to discontinue your participation in the trial, please contact the trial center and inform us of your decision.

You may be asked to discontinue receiving vaccinations or participation in the trial for the following reasons:

- If you are unable to keep appointments or are unable to follow trial procedures
- If the trial protocol, vaccine manufacturer, Safety Review Board, Drug Controller General of India or other regulatory agencies decide to stop or amend the study
- If your physician feels that staying in the study is harmful to your health
- If you become pregnant
- If you become HIV-infected

However, to enable us to complete the study documentation you will be asked to make a final visit to the study clinic.

NARH CONS Enrollment Consent

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PROF. R. K. MUTATKAH

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Reimbursement for Your Participation

Tigaca will be a total of either 15 or 19 scheduled study visits (depending on your assigned group), including today. To compensate you for your time and cost of transportation, we will provide you Rs. 500/- for each visit. This amount is expected to cover the expenses you incur for travel as well as loss of daily wages. You will be given reimbursement in the event of unscheduled visit for problems requiring attention by the research team.

Trial-Related Injuries

If you suffer from any adverse events or disabilities directly due to the trial vaccine, the study sponsor will ensure the provision of comprehensive care, support, and treatment. Should you become HIV-infected during the course of the trial, the study sponsor will enable access to care, support, and treatment, including free anti-retroviral therapy (ART) for a period of 5 years from the point of eligibility as and when medically recommended by existing national treatment guidelines. The sponsor will advocate for the best available HIV care and treatment that is provided by the national government or by alternative mechanisms beyond the covered period. You will also be provided medical insurance for unforeseen good medical events (not covering HIV infection and vaccine-related events) for the duration of the trial period.

Storage of Samples

We would like to store your blood and blood cells for a maximum period of 10 years for possible use in new investigations or future research, as related to AIDS vaccine research and development in the future. A number higher than your name will be linked to label the blood. The stored and coded samples may be used in future studies for issues related to approved AIDS vaccine research and development. Stored coded specimens may be shipped to independent national or international laboratories.

Genetic Testing

A test may be conducted to determine your HLA type or other genes that might control or influence your body's response to the vaccine. HLA is a specific marker on the surface of your body's cells. The result of this test will be kept strictly confidential.

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PROF. R. K. MUTATKAR
Gorab B. M. F. C. O. R. C. O
University of Calcutta

04 JUL 2009

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Long term follow-up study:

When the vaccine trial is complete, another study will be proposed to follow vaccine trial volunteers for a period of 5 years after the last vaccination. Participation in the Long Term Follow-Up study is optional, and you do not need to make the decision to participate or not participate in the study now. The decision will not affect your ability to re-enroll in the present FluVac Boost vaccine trial.

Copy of Informed Consent Document for your Records:

A copy of the Informed Consent Document will be provided to you. If you do not wish to take your copy of the Informed Consent with you, the investigators will keep your copy at the study site in a safe and secure location. You may obtain your copy at any time.

Problems or Questions:

Should you have any questions about the rights of the trial participants, please contact Prof. R.K. Mutatkar, Chairman, NARI Ethics Committee (Phone: 191 70 271 1719).

If you have any questions about the trial, trial-related work or side effects, please contact Dr. Sanjay Meendale, Trial Principal Investigator (Phone: +91 20 2712 1230, Fax: +91 70 2712 1071).

84 Jul 2019

Prof. R. K. MUTATKAR
Chairman, Ethics Committee
National AIDS Research Institute Pune
Declaration of Consent

[Participant's name and address]

Agreed to take part in the enrollment for the research project entitled:

A Phase I Double-Blind, Placebo-Controlled, Randomized Trial to Evaluate the Safety and Immunogenicity of TBC-1M4, a multigenic MVA HIV Vaccine vs ADVAX, a multigenic DNA HIV Vaccine followed by TBC-1M4, a multigenic MVA HIV Vaccine (JIVI PC01)

[Selections: YES or NO]

[Selections: YES or NO]

I agree that the investigator can obtain medical information from my doctor to help him/her assess any adverse events.

[Selections: YES or NO]

[Selections: YES or NO]

I agree to be contacted by the study staff

[Selections: YES or NO]

[Selections: YES or NO]

[Selections: YES or NO]

[Selections: YES or NO]

I agree to store some of my blood samples for future use in AIDS vaccine research for a maximum period of ten years

[Selections: YES or NO]

I wish to take a copy of the signed and dated informed consent form with me

[Selections: YES or NO]

I have read this Informed Consent Document and have discussed with the study investigator about the purposes of the study, the procedures involved, the anticipated risks and benefits involved, and other safety procedures and rights of study subjects. I have been given the opportunity to ask questions, which have been answered to my satisfaction. I understand that any questions that I might have will be answered.

[Signature]

04 Jun 2009

Prof. R. K. Mutatkar
Re: Request for opinion on issues related to HIV Vaccine Clinical Trials

Friday, 20 February, 2015 12:03 PM
Mark as Unread

"Amar Jasani" <amar.jasani@gmail.com>

"Santhia S" <sanitha1@yahoo.co.in>

Dear Santhia,

You may go thru the following editorial and debate on it - they provide answer to most of your queries:


In addition if you search the past issues of the IJME, you will find articles by the PI of the AIDS vaccine trial in India and others.

Amar

Amar Jasani:
Independent Researcher and Teacher (Bioethics, Public Health)

Editor: Indian Journal of Medical Ethics (https://ijme.in)
Visiting Professor: Centre for Ethics, Yenepoya University, Mangalore.
(http://www.yenepoya.edu.in/colleges.php?id=41&org=center)

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Address (Office): C/O CEHAT, Survey no. 2804-D5, Aram Society Road, Vakola, Santacruz East, Mumbai 400055, State: Maharashtra, India

Email: <amarjasani@gmail.com> & <amarjasani@yahoo.co.in>

On 19 February 2015 at 12:59, Santhia S <sanitha1@yahoo.co.in> wrote:

Sir,

I have tried you on the land line number available, but could not. I am a research scholar at National Law School of India University Bangalore. My research project is on HIV Vaccine
Clinical Trials in India. As part of academic interest, I have few queries which I would like to forward to you. Your experience in the field of medical journalism, with your keen interest in the ethical aspects of clinical trials in India is noteworthy. I undertake that your views/response will only be used for research/academic purpose. I hope you would reciprocate at the earliest. I would be highly obliged, if you could take some time out of your hectic schedule to share your views on the following issues:

1. In your view, how prepared is India to conduct III V vaccine clinical trials balancing the interest of the trial participants as well as the investigators and sponsors?
2. Do you think, India’s move to start the first ever Phase I trial at NARI-Pune was ethical, particularly when the results of failure of similar trials in two countries were already known?
3. What is your opinion about regulatory framework pertaining to HIV vaccine research in India, as it stands today? What are the lacunae in the existing regulatory mechanism, even after the recent changes? Do you suggest any solution to it? If so, kindly elaborate.
4. Do you think placebo trials are ethical in HIV vaccine trials?
5. Do you think the informed consent process of HIV vaccine clinical trials in India adequate especially in view of the recent guidelines to record the process on audio/video recording? If not, how can we address these issues in a better manner?
6. Is it required to have Health Insurance for these trial participants, for a long term basis, at the cost of the sponsors of the Clinical trials?
7. What is your opinion about standard of care issues related to HIV vaccine trials?
8. Do you think economically vulnerable subjects were induced in these HIV vaccine clinical trials?
9. Do you think that obtaining informed consent in HIV vaccine trials is truly possible?
10. What are your suggestions to improve the existing scenario of HIV vaccine trials in India?

I look forward to hear from you,

with regards

T S Saritha,
Cell: 09874786244
RE: Ref: Question on Interpretation of GCP

Friday, 27 February, 2015 11:51 PM

Mark as Unread

"CC CCP Questions" <gcp.questions@fda.hhs.gov>
"Santha G" <santha.l@gmail.com>

Good afternoon,

In regards to your questions concerning the guidance on Transferring Clinical Investigation Oversight to Another IRB, I am providing the following responses:

(a) Can the submitting IRB review the research protocol and documents, for a second time, even though it was cleared by the first IRB?

Because the regulations do not address transfer of IRB oversight, it is left to the receiving IRB to decide whether to conduct a review of the clinical investigation prior to the next continuing review date established by the original IRB. In practice, most IRBs often choose to perform some type of review before accepting responsibility for a study.

(b) If the second IRB has a conflict of views on the decisions and approval of the first IRB, will it resolve further issues?

IRBs have the authority under 21 CFR Part 56.113 to suspend or terminate approval of research in circumstances where the clinical investigation is not being conducted in accordance with the requirements of the IRB's requirements or has been associated with unexpected serious harm to subjects. The receiving or second IRB must promptly report any suspension or termination of IRB approval, including the reasons for the action, to the clinical investigator, appropriate institutional officials, and FDA.

(c) Is there any appeal provision to FDA in such kind of situation?

Again, the IRB has the authority to suspend or terminate approval of the study received. As far as I am aware, there is an appeal provision to FDA that is available regarding this type of matter.

I hope that this information is helpful. Please contact us at gcp.questions@fda.hhs.gov if you have further questions. Since many questions and answers regarding good clinical practices have been addressed over time, some individuals may find it useful to access a set of related GCP questions found at the following web address: https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ReplicatingInquiriesFDAandGCP/CLINICALPRACTICE/important.htm.

Sincerely,

Shelley A. Fultz, MS, M1 (ASCP)
Policy Analyst, Office of Good Clinical Practice
Office of the Commissioner, Food and Drug Administration

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(h) which represents the best judgment of the employee providing it. This information does not, necessarily reflect the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.
Original Message

From: Saritha S [mailto:saritha1@yahoo.co.in]
Sent: Thursday, February 19, 2015 1:58 AM
To: OC GCP Questions
Subject: Ref: Questions on Interpretation of GCP

Madar\' Sir,

Ref: Guidance for IRBs, Clinical Investigators, and Sponsors Considerations When Transferring Clinical Investigation Oversight to Another IRB.

Let me introduce myself as a research scholar on legal and ethical issues in HIV Vaccine Clinical Trials in India. As a part of my research, I have gone through various Federal Regulations and FDA Guidance documents.

It is very interesting that your esteemed office has issued a non-binding recommendation on Transferring Clinical Research oversight from one IRB to another IRB, which is not very common in other countries.

However, on going through the documents, one doubt arose in my mind which may require clarification.

(a) Can the second IRB review the research protocol and processes, for a second time, even though it was cleared by the first IRB?

(b) If the second IRB has a conflict of view on the decisions and approval of the first IRB, will it vitiate further research?

(c) Is there any appeal provision to FDA in such kind of situations?

It will be great if you could be very kind enough to respond and clarify my doubts.

with regards,

1. S. Saritha
Regarding your query to IAVI - Request for opinion on issues related to HIV Vaccine Clinical Trials in India

Wednesday, 4 March, 2015 7:15 PM
Mark as Unread
Submit

"Smiti Bhagi" <Sbhagi@avi.org>

"sarihais1@yahoo.co.in" <sarihais1@yahoo.co.in>

From:

To:

Full Headers "Printable View"

Dear Smiti,

Thank you so much for your mail. It's wonderful to learn if your area of interest and we would certainly try and help you with your research to the best of our abilities. However for us to be able to do so, we would need to request you to share some more details on your research and the purpose of the same including explaining how and where these responses would be used. Given we don't work in isolation and have partners who work closely with us in this field, including Governmental institutions, we would have to follow necessary protocols before we share any information.

I hope you would understand and share some more details, for us to be able to help you suitably.

You can reach me on mobile if you may so desire.

Thank you!

Warm regards,

Smiti Bhagi, Program Specialist
IAVI, the International AIDS Vaccine Initiative
+91.11.4737.0025 (office) +91.981.124.2140 (mobile) IAVI.org IAVI AIDSVaccine

The World Needs an AIDS Vaccine
Dear Sir,

I am a research scholar at National Law School of India University Bangalore. My research is on HIV Vaccine Clinical Trials in India. As part of academic interest, I have few queries which I would like to forward to you. I undertake that your views / response will only be used for research / academic purpose. I hope you would reciprocate at the earliest.

1. What do you think on the present scenario of regulatory framework of clinical trials in India? Kindly elaborate your opinion on regulatory framework pertaining HIV vaccine clinical trials in India? Do you think it is adequate? If not, kindly suggest the policy reforms.

2. How prepared is India for HIV vaccine clinical trials? How much do you score the preparedness of India for Global vaccine trials in a scale of 10, even after the recent changes?

3. Do you consider that Indians are being treated as guinea pigs by developed nations, conducting clinical trials in India?

4. Do you think economically vulnerable subjects were induced in many of these trials and how it can be prevented?

5. Is it ethical to carry out placebo controlled HIV vaccine clinical trials?

6. Do you think that obtaining informed consent in HIV vaccine trials (both preventive and therapeutic vaccine trials) is truly possible?

7. In your view and experience how was the informed consent process carried out in HIV vaccine clinical trials? I would be greatly obliged if you could kindly furnish a copy of informed consent form.

8. In your experience what were the motivations of the trial participants of the HIV vaccine trials (both preventive and therapeutic vaccine trials)?

9. What measures are taken by sponsors/CRCs/Investigators/Ethics Committee(s) for surveillance of long term adverse vaccine effects specific to HIV vaccines?

10. What measures are undertaken to address issues like vaccine related malignancy etc... Do you feel the compensation formula adopted for the trial related injuries and death are adequate?

11. What is your opinion about health insurance being offered to these trial participants on a long term basis with the facility covering the cost of any follow up treatment for a period post trial? If so, who should fund it if the sponsor is unable to discharge the obligations to compensate any trial related injury (due to any reason like bankruptcy, ceased to be in business etc.)?

12. What measures are taken to reduce the non medical social harms of these subjects?

13. How practical it is to develop and implement Participants Bill of Rights in India for trial participants of HIV vaccine trials?

Best regards

From: Saritha S
To: Rajal Goyal
Subject: Request for opinion on issues related to HIV Vaccine Clinical Trials in India

Sent: Thursday, February 19, 2015 1:51 PM

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PROPOSED BILL
HIV Preventive Vaccine Clinical Trial, Protection of Participants Bill, 2015

A Bill to provide for the protection of persons participating in the HIV Vaccine Clinical Trial in India and for matters connected therewith or incidental thereto.

Be it enacted by Parliament in the Sixty Sixth Year of the Republic of India as follows:

CHAPTER I PRELIMINARY

1. Short Title, Extent, Commencement and Application

(1) This Act may be called the HIV Preventive Vaccine Clinical Trial, Protection of Participants Act, 2015

(2) It extends to the whole of India, except the State of Jammu and Kashmir.

(3) It shall come into force on such date as the Central Government may, by notification in the Official Gazette, appoint.

(4) It applies

(a) to every establishment, which conducts preventive HIV vaccine clinical trials, including establishments where a Clinical Trial is pending.

(b) any Sponsor, Investigator, ethics committee involved in conducting preventive HIV vaccine trials

2. Definitions

(1) In this Act, unless the context otherwise requires,—

(a) AIDS means.—Acquired Immune Deficiency Syndrome, a condition in humans characterized by a combination of signs and symptoms, including progressive failure of the immune system caused by Human Immunodeficiency Virus, which attacks and weakens the body’s immune system making the HIV-positive person susceptible to life threatening conditions or other conditions, as may be specified from time to time;

(b) Clinical Trial shall have the meaning assigned to it in Rule 122 DAA of the Drugs and Cosmetics Rules, 1945

(c) Competent Authority shall mean the Drug Controller General of India.

(e) HIV is a lentivirus (a subgroup of retrovirus) that causes HIV infection and AIDS

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(f) “Informed consent” means consent given by any individual or his representative specific to a proposed intervention for testing the HIV preventive vaccine, without any coercion, undue influence, fraud, mistake or misrepresentation and such consent obtained after informing such individual or his representative, as the case may be, such information, as specified in the guidelines, relating to risks and benefits of, and alternatives to, the proposed intervention in such language and in such manner as understood by that individual or his representative, as the case may be;

(g) Vaccine means and includes a HIV Preventive Vaccine

(h) Vulnerable Population means and includes children, adolescents, women, individuals who are commercial sex workers, men who have sex with men, injection drug users, lesbians, Gay, individuals whose ability to protect himself is absent or diminished on account of his social, educational, and economic backwardness.

(2) All other words and expressions used herein and not defined but defined in the Drugs and Cosmetics Act, 1940 (23 of 1940), Drugs and Cosmetics Rules, 1945 shall have the meanings respectively assigned to them in the said Act and Rules.

Chapter II

The Advisory Boards

3. Clinical Trial Advisory Board.- (1) The Central government shall, as soon as may be constitute, a board to be called a HIV Preventive Vaccine Clinical Trial Advisory Board (hereinafter referred to as Advisory Board) to advise the Central Government on such matters arising out of the administration of this Act as may be referred to it and carry out other functions assigned to it under this Act. The Advisory Board shall be a body corporate by the name as aforesaid having perpetual succession and common seal, with power to hold the property both movable and immovable and to contract, to sue or be sued,

(2) The Advisory Board shall consist of--
(a) a Chairman to be appointed by the Central Government;

(b) such number of members, not exceeding Ten but not less than six, as the Central Government may nominate to represent, HIV Preventive vaccine clinical trial participants, Sponsors, Investigators, members of Research Ethics Committee and any other interests which, the opinion of the Central Government, ought to be represented on the Advisory Board. The members representing HIV preventive vaccine clinical trial participants shall be non-technical members and the remaining members may be technical members, who have necessary qualifications as may be prescribed under the Act.

(3) The number of persons to be appointed as members from each of the categories specified in sub-section (2), the term of office and other conditions of service of, the procedure to be followed in the discharge of their functions by, and the manner of filling vacancies among, the members of the advisory Board shall be such as may be prescribed:
Provided that the number of members nominated to represent the HIV preventive vaccine trial participants shall not be less than one third of the number of members nominated to represent the Sponsors, Investigators, members of research ethics committee.

(4) The head office of the Advisory Board shall be at such place as may be notified by the Central Government.

(5) All questions came up before any meeting of the Advisory Board shall be decided by majority vote of the members present and voting, and in the event of an equality of votes, the Chairman or in his absence the person presiding shall have a second or casting vote.

4. Qualifications, Terms of office, conditions of service of Chairman and other members

(1) A person shall not be qualified for appointment as the Chairman or technical members of the Advisory Board, unless he

(a) in case of Chairman, is or has been, a Judge of High Court or an Advocate qualified to be a judge of High Court,

(b) in case of technical member, who has necessary qualifications and experience in the field of medical research ethics, HIV Vaccine clinical research, or conduct of clinical trials

(c) in case of non technical member, has been a Clinical Trial participant, or has worked in the field of counseling, rehabilitation, or representing HIV patients, or HIV vaccine clinical trial participants, and shall not be directly or indirectly associated with any Sponsors of HIV vaccine clinical trials,

(d) The tenure appointment shall be for a period of three years with eligibility for reappointment for a maximum period of three year.

5. Functions of the Advisory Board

(1) Notwithstanding anything contained in the Drugs and Cosmetics Act, 1944, the functions of the Advisory Board shall be to –

(a) Make recommendations, either suomoto or on request from the Competent Authority on the following matters, namely,

(i) on the monitoring of the process of selection of participants for HIV preventive vaccine clinical trials including persons belonging Vulnerable Population, measures to prevent inducement for participation in the HIV preventive vaccine clinical trial,

(ii) on the informed consent process to be followed by the Sponsors, research ethics committee and the Investigators, to maintain confidentiality and privacy of the trial participants,
(iii) the time limit for monitoring the trial participants post conclusion of the clinical trial, any general or special compensation payable to the HIV preventive vaccine clinical trial participants (iv) Compulsory Clinical trial insurance to be taken in case of HIV preventive vaccine clinical trials, the coverage and the permissible exclusions, and period of coverage required,

(v) on implementation of compulsory free medical aid, and compulsory HIV tests to distinguish the issues related to Vaccine induced seropositivity,

(vi) counseling for the HIV preventive vaccine trial participants including any their partners, family members etc,

(vii) on laying down code of conduct for Investigators, Sponsors, research ethics committee and other key support professionals involved in the conduct of HIV vaccine clinical trials, disciplinary actions required in case of any clinical or scientific misconduct,

(viii) on the standard of care to be provided for any clinical trial participant who was injured during the participation in the clinical trial or in connection with his participation in the clinical trial,

(viii) issue necessary guidance documents, and on any other matters for the efficient management and conduct of HIV preventive vaccine clinical trials and or for the special protection of vulnerable population and other clinical trial participants,

(xi) on training on research ethics, conduct of clinical trials and on all policy matters touching the conduct of HIV preventive vaccine clinical trials,

(2) The Advisory board shall ensure transparency while discharging its powers and functions and shall issue or hold a consultation process after giving opportunity to all stakeholders before issuing any recommendations, which shall not be not less than 15 days time to respond once a consultation process is issued.

(3) The recommendations of the advisory board shall be binding on the Competent Authority unless returned within a period of thirty days,

(4) During the pendency of a Consultation process or recommendations, the Advisory board may

(i) orders investigations on the conduct of any HIV preventive vaccine clinical trials

(ii) pass necessary orders to redress the grievance of any Clinical Trial participant

(iii) take immediate steps and or pass necessary interim orders for protection of the Clinical Trial participants,

Provided that no final orders in any of the matters shall be passed without affording the affected parties an opportunity of being heard.

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(6) Any dispute as to whether an injury caused to the clinical trial participant of HIV preventive vaccine clinical trials, during the trial or the injury detected after the trial or the injury has any direct or proximate connection with the Clinical Trial, the decision of the Advisory Board shall be final and binding on the Sponsor unless the Sponsor files an appeal before the High Court, as per this Act.

7. **Fund, Levy and collection of cess.**—

(1) There shall be constituted a fund to be called HIV Preventive Vaccine Clinical Trial Participants of India General Fund and there shall be credited thereto

   (a) all grants, fees, and charges by the Advisory Board received under this Act or from the Central Government or from any International Organizations subject to the approval of the central government,
   
   (b) all cess levied and collected under this Act, and

   (c) all sums received by the Advisory Board, as may be decided by the Central Government.

(2) There shall be levied and collected a cess, which shall not be less than two percent of the cost of the HIV vaccine clinical trial incurred by the Sponsor, as the central government may, by notification in the official gazette, from time to time specify.

(3) The cess levied under subsection (1) shall be deposited by the Sponsor as a precondition for grant of permission for conduct of HIV preventive vaccine clinical trial.

(4) The Fund shall be applied for the benefit and protection of HIV Preventive Vaccine Clinical Trial participants and for the objects authorized under this Act. The Advisory Board may from time to time order utilization of such Fund collected for the purposes of the medical treatment, protection and rehabilitation of the HIV preventive vaccine clinical trial participants, who faced discrimination or isolation from the community, or where the Sponsor is unable or not available providing medical treatment, for the HIV preventive vaccine clinical trial participants.

8. **Compulsory Clinical Trial Insurance**

(1) The Sponsor of the Clinical Trial shall take compulsory clinical trial insurance for the protection of HIV preventive vaccine clinical trials, for such periods as may be prescribed by the Advisory Board from time to time, and submit a copy of the Insurance contract before the Advisory Board, before the conduct of a Clinical Trial.
Chapter III – Miscellaneous

9. Power to call for information, appoint Inspectors, order Audit

(1) The Advisory Board shall have the power to call for information from any person in connection with the conduct of a HIV preventive vaccine clinical trial, or to appoint Inspectors and order Inspection on the conduct of any HIV preventive vaccine trials, if it is of the view that such Clinical Trial is conducted in a manner detrimental to the interest of the Clinical Trial participants, or without providing or ensuring sufficient protection to the Clinical Trial Participants.

(2) The Advisory Board shall have the power to order Audit of the affairs of any HIV preventive vaccine clinical trial, to verify whether the Clinical Trial is conducted in compliance of the ethical guidelines issued, orders of the Advisory Board or in consonance of the recommendations of the Advisory Board as accepted by the Competent Authority or in accordance with the provisions of this Act.

10. Power to Issue Directions, for providing Vaccine free of cost and other matters,

(1) The Advisory Board shall have the power to issue directions to Sponsors, for providing the HIV preventive Vaccine free of cost, to the HIV Preventive Vaccine Clinical Trial Participants once such Vaccine is approved under the Drugs and Cosmetics Act, 1944.

(2) The Advisory Board shall have the power to impose additional conditions for the conduct of HIV preventive vaccine clinical trials under this Act, in addition to the compliance requirements under the Drugs and Cosmetics Act, 1944 for the conduct of a Clinical Trial, which may include provision of HIV Preventive Vaccine at a concessional rates to the people of India.

(3) The Advisory Board shall have the power to issue directions to Sponsors, Clinical Trial Investigators, Research Ethics Committees in connection with the conduct of a preventive HIV vaccine clinical trial.

11. Penalty for Contravention of directions of the Advisory Board

(1) If a person violates directions of the Advisory Board, such person shall be punishable with fine which may extend to Ten lakh rupees and in case of second or subsequent offence with fine which may extend to twenty lakh rupees and in the case of continuing contravention with additional fine which may extend to twenty lakh rupees for every day during which the default continues.

12. Bar of jurisdiction

(1) No civil court shall have jurisdiction in respect of any matter which the Advisory Board is empowered by or under this Act to determine.
13. Cognizance of offences

(1) No court shall take cognizance of any offence punishable under this Act or the rules or regulations made there under, save on a complaint made by the Advisory Board.

(2) No court inferior to that of a Chief Metropolitan Magistrate or a Chief Judicial Magistrate of first class shall try any offence punishable under this Act.

14. Appeal to High Court

(1) The orders or directions issued by the Advisory Board, except any interim orders shall be appealable before the High Court. An appeal has to be filed within 30 days from the date of the order or direction as the case may be, provided the High Court may entertain an appeal after the expiry of the said period of 30 days, if it is satisfied that the appellant was prevented by sufficient cause from preferring the appeal in time.

15. Power to make rules

(1) The Central Government may, by notification, make rules for carrying out the purposes of this Act.

(2) In particular, and without prejudice to the generality of the foregoing power, such rules may provide for all or any of the following matters, namely,- (a) the salary and allowances payable to and the other conditions of service of the Chairman or other members of the Advisory Board
       (b) any other matter which is to be, or may be, prescribed, or in respect of which provision is to be made, by rules.

16. Application of certain laws

(1) The provisions of this Act shall be in addition to the provisions of the Drugs and Cosmetics Act, 1944 and, in particular, nothing in this Act shall affect any jurisdiction, powers and functions required to be exercised or performed by the Drugs Controller General of India or Licensing Authority under the Drugs and Cosmetics Act, 1944, in relation to any area falling within the jurisdiction of such Authority, so far as it is not inconsistent with this Act.

17. Power to Remove Difficulties

(1) If any difficulty arises in giving effect to the provisions of this Act, the Central Government may, by order, published in the Official Gazette, make such provisions not inconsistent with the provisions of this Act as may appear to be necessary for removing the difficulty:

(2) Every order made under this section shall be laid, as soon as may be after it is made, before each House of Parliament.