

## testing vaccines in injecting drug users: VaxGen's efficacy trial in thailand

introduction by PATRICIA KAHN

---

Injecting drug use is an important component of the global AIDS epidemic. In Eastern Europe and the former Soviet Union, regions with two of the world's fastest-growing epidemics, injecting drug users (IDUs) account for the majority of people newly infected with HIV, and they are a big part of the fast-evolving epidemics in China, India and other Southeast Asian countries. Within these regions, it's common to find that 20–60% of IDUs are infected, according to UNAIDS (2004). Altogether, 136 countries reported injecting drug use within their borders in 2003, and estimates say that about 15 million people worldwide inject drugs—the majority of them living in developing countries.<sup>1</sup>

From a scientific perspective, it's not at all clear whether vaccines that work against sexual transmission will be equally effective—or will work at all—against intravenous infection (see chapter 11). And there's only one way to find out: by testing vaccines for *efficacy* in populations where one or the other risk factor predominates.

But the barriers to carrying out clinical research among IDUs are formidable. Injecting drugs is illegal everywhere in the world, and is severely punished in most countries. The result is that IDUs usually live as marginalized populations, vulnerable to human rights abuse and chronically underserved by health and social systems (see chapter 27). And few governments have taken the steps needed to reduce HIV infection risk in drug users. On the contrary, harsh criminal penalties, combined with the scarcity (and often illegality) of harm-reduction services such as syringe exchanges and long-term methadone maintenance, only fuel the fire. Yet without efficacy trials in IDUs, prospects for a vaccine that works for them could be much dimmer.

The year after VaxGen began testing its vaccine for effectiveness in a North American/European *Phase III* study (see chapter 22), a second trial was launched in an IDU population in Thailand. Under the prevailing laws, the study's prevention services could not provide clean needles. [Counseling did include information on reducing risk by injecting safely and not sharing needles or, failing this, on how to sterilize them. Safe sex information and condoms were also provided.] Another key issue was the high rate of arrest and incarceration of IDUs: Nearly 20% of the volunteers reported at the start of the trial that they had been imprisoned within the past six months. Without the ability to conduct trial visits within jails, the study would have collapsed due to loss of volunteers to follow-up.

<sup>1</sup> "Regime Change? Drug Control, Users' Human Rights and Harm Reduction in the Age of AIDS." Background paper for "Human Rights at the Margins: HIV/AIDS, Prisoners, Drug Users and the Law," a satellite meeting at the 2004 International AIDS Conference in Bangkok. [www.aidslaw.ca/bangkok2004/e-bangkok2004.htm](http://www.aidslaw.ca/bangkok2004/e-bangkok2004.htm)

For this reason, long discussion and negotiation took place between trial staff and the Department of Corrections, leading to an agreement that study visits could take place in prison for volunteers who were incarcerated during the course of the trial. Counseling remained a standard part of these visits, but the clandestine availability of drugs in prison—but not clean needles or condoms—meant an increase in the rate of infection among imprisoned volunteers, as documented earlier.<sup>2</sup>

The article which follows, by several of the trial's US and Thai researchers, describes the protocol of these prison visits and the process that led to it.

<sup>2</sup> Choopanya, K. et al., *J. Acquir Immune Defic. Syndr.* 29: 86–94 (2002).

## providing care and maintaining followup of incarcerated participants in asia's first phase III hiv vaccine trial

MICHAEL MARTIN, SUPHAK VANICHSENI, PRAVAN SUNTHARASAMAI,  
FRITS VAN GRIENSVEN, JORDAN TAPPERO and KACHIT CHOOPANYA / thailand

---

**THE FIRST PHASE III HIV** vaccine trial in Asia was completed in Bangkok in June 2003, in a population of 2,546 intravenous drug users (IDU).<sup>①</sup> Years of work by vaccine trial staff, local government officials, community volunteers, and many others set the stage for the this trial, and although in the end the vaccine did not work, the trial succeeded in giving a definitive result.

One of the biggest potential obstacles in getting this clear answer, however, emerged from a three-year vaccine preparedness study that preceded the trial. This study showed that IDU volunteers in the *cohort* were frequently arrested and incarcerated, and that incarceration was associated with an increased risk for HIV infection.<sup>②</sup> For these reasons, if the trial was to retain its participants over the full three years, vaccine trial staff would need to work with justice and prison officials in seeking permission and developing procedures for follow-up of incarcerated volunteers. In this article, we explain how these arrangements were established and how visits were conducted.

In developing a Standard Operating Guideline for working with incarcerated participants, we started from established international codes for the ethical conduct of clinical research, in particular the *Nuremberg Code* of 1947, the *Declaration of Helsinki* and *The Belmont Report*. (These documents are described in chapter 15 on ethics, and online citations listed.) We also followed the recommendations in the US Code of Federal Regulations for additional safeguards for the protection of prisoners involved in research.<sup>③</sup> Our guideline, along with the entire trial *protocol*, was reviewed by the ethical review committees of Mahidol University, the Bangkok Metropolitan Administration (BMA, which runs the city's methadone treatment programs where the volunteers were recruited, and was a partner in the trial), and the Thailand Ministry of Public Health, and by the institutional review board of the US Centers for Disease Control and Prevention (CDC). Once the trial was underway, its Principal Investigator (PI; author Kachit Choopanya) invited the Joint United Nations Programme on HIV/AIDS (UNAIDS) to carry out an ethics review, as described more fully below.

The vaccine trial preparatory study was launched in 1995. We enrolled 1,209 IDU volunteers from the BMA's methadone treatment clinics.<sup>②</sup> Participants visited the clinic every four months for three years. Since we had anticipated that a high percentage of volunteers would be incarcerated at some point during the trial, the trial PI sought the cooperation of the Department of Corrections in the study. He discussed the purpose of the preparatory study and the importance of maintaining follow-up of incarcerated participants with the Director General of the Department of Corrections. After several meetings between trial staff and Department of Correction's staff, permission for these visits was granted, procedures were established and the preparatory study was carried out as planned, including prison visits where necessary.

In preparing for the vaccine trial, the PI met again with the Director General in 1999 to review the preparatory cohort's procedures and results, and to plan for prison visits during the upcoming vaccine trial. This led to a new round of meetings between trial staff and Department of Corrections, which

involved presentations about the trial and reemphasized the importance of follow-up. Once again, the visit procedures were reviewed and revised where necessary.

From March 1999 through August 2000, we screened 4,943 potentially interested IDU volunteers from the BMA's 17 methadone treatment centers in Bangkok, and 2,546 enrolled in the vaccine trial. The median age of the enrolled volunteers was 26 years old, 93% were male, and 95% had completed primary education. A history of incarceration was reported by 78%, and 17% had been incarcerated at least once in the previous six months.<sup>4</sup>

The importance of follow-up visits during the vaccine trial was explained to potential participants as part of the *informed consent* process. Participants were asked to provide contact information, including a personal address and phone number, and to identify family and friends that trial staff could contact if the volunteer missed a visit.

When clinic staff learned through these channels that a participant was incarcerated, a study visit was scheduled and a letter requesting permission to carry out the visit was sent to the prison director. A typical visit began when the clinic team—consisting of a doctor, nurse, clinical research assistant, and counselor—arrived at the prison. The team reported to a reception area and waited for prison officials to verify their identities and escort them to the meeting point. Study visits took place in private settings, usually the infirmary. At each visit, the volunteer was reminded that he/she had the right to refuse or withdraw from the study at any time. If the volunteer agreed to continue trial participation, the standard behavioral data and blood and urine specimens were collected just as in the trial clinics, and risk-reduction counseling was carried out.

In order to maintain participant privacy regarding HIV status, all study participants received daily pills at the infirmary, HIV-negative subjects received multivitamins and HIV-positive subjects received multivitamins plus antimicrobial prophylaxis, *antiretroviral drug* treatment, or both as needed.



78% of the trial participants had been incarcerated before—17% in the last 6 months.

Research data were treated confidentially and were not shared with the prison staff. Pre-test and post-test counseling was conducted in a private setting with no correctional personnel in attendance. No study documents, complete or incomplete, or medical equipment were left behind or stored at the prison.

Trial participants all received financial reimbursement for each study visit, and this continued if and when they were in prison. During this time, the reimbursement was given to staff of the correctional facility who stored the money for the participant. The participant was able to access this money upon request and upon release from prison.

Once the trial was underway, the PI invited UNAIDS to provide an on-site, independent assessment of the ethical aspects of trial conduct. In June 2001, a UNAIDS team visited several trial sites, reviewed trial materials, interviewed staff and trial participants, and accompanied trial staff to a prison to visit an incarcerated participant. The overall conclusion of the assessment team was that the trial "...is being carried out in an ethically responsible manner."

However, the team made several recommendations regarding follow-up of incarcerated volunteers. These including that letters sent to prisons should not identify volunteers as participants in an HIV vaccine trial, IDUs or attendees of methadone clinics and that a prisoner representative (prisoner advocate with knowledge of circumstances in Bangkok prisons) should be appointed to one of the Thai Ethics Review Committees. In response to these recommendations, letters to the prison were subsequently written on health clinic letterhead (not drug treatment clinic), the letter stated the participant was in a "research study" (not HIV preventive vaccine trial), and a prisoner advocate was appointed to the Ethics Review Committee of Thailand's health ministry.

From that point on, we followed these same procedures until the trial was completed in June 2003. Overall, we conducted 3,450 visits in prison. Participant follow-up during the trial was over 90% and risk behavior monitoring during the trial showed overall reductions in reports of injection drug use and sharing of injection equipment.<sup>⑤</sup>

The first phase III HIV vaccine trial in Asia was made possible by the effort of many, many people. We would like to recognize the Department of Corrections in facilitating our visits and assisting our teams. In addition, we are extremely grateful to the participants in this vaccine trial for their patience, understanding, and selfless contributions in the search for an effective HIV vaccine.

#### references

- ① [www.biospace.com/news\\_story.cfm?StoryID=14347520&full=1](http://www.biospace.com/news_story.cfm?StoryID=14347520&full=1)  
VaxGen, Inc. (VXGN) Announces Results Of Its Phase III HIV Vaccine Trial In Thailand; Vaccine Fails To Meet Endpoints.
- ② Vanichseni S., Kitayaporn D., Mastro T., Mock P.A., Raktham S., Des Jarlais D.C., et al., Continued high HIV-1 incidence in a vaccine trial preparatory cohort of injection drug users in Bangkok, Thailand. *AIDS* 15: 397-405 (2001).
- ③ [www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm)  
Code of Federal Regulations, Regulations on the Protection of Human Subjects, Title 45, Part 46 (45CFR46), Subpart C (2001).
- ④ Vanichseni S., Tappero J.W., Pitisuttithum P., Subhachaturas W., Kitayaporn D., Raktham S., van Griensven F., Mastro T.D., Tantikul T., Vimutisunthorn E., Suntharasamai P., Kaewkungwal J., Migasena S., Gee C.C., Heyward W.L., Francis D.P., Choopanya K., for the Bangkok Vaccine Evaluation Group. Recruitment, screening, and epidemiologic characteristics of participants in the AIDSVAX B/E HIV vaccine efficacy trial, Bangkok, Thailand. *AIDS* 18: 311-316 (2004).
- ⑤ Van Griensven F., Kaewkungwal J., Vanichseni S., Tappero J.W., Sangkom U., Hiranrus K., Kitayaporn D., Pitisuttithum P., Mastro T.D., Suntharasamai P., Natrujirote P., Phasithiphol B., Luck A., Orelind K., Heyward W.L., and Choopanya K., for the Bangkok Vaccine Evaluation Group. Lack of increased HIV risk behavior among injection drug users participating in the AIDSVAX B/E HIV vaccine efficacy trial in Bangkok, Thailand. *AIDS* 18: 295-301 (2004).