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AIDS VACCINE TRIALS

'06 YEAR IN REVIEW

See inside for world map of trials launched in 2006

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 4.3 million people were newly infected with HIV last year, the majority (2.8 million) in sub-Saharan Africa. This brings the total number of HIV-infected people to 40 million worldwide. A preventive AIDS vaccine remains the greatest hope for reversing the pandemic's relentless spread, and clinical trials of vaccine candidates are now ongoing on every continent. The world is responding but more still needs to be done.

This Special Issue of *VAX* provides a review of AIDS vaccine clinical trial activity in 2006 and a comprehensive listing of all ongoing trials as of January 2007. Last year 13 new trials of preventive AIDS vaccine candidates started in 8 countries around the world. All were either Phase I or Phase I/II trials designed to evaluate the safety and immunogenicity of the candidate vaccines. The Russian Federation began its first AIDS vaccine trial and three countries in sub-Saharan Africa—Kenya, Uganda, and Tanzania—initiated new trials. The map on the inside pages of this issue focuses on these trials as well as countries that started trials in 2003-2005 that are still ongoing. The accompanying table provides information on all ongoing preventive AIDS vaccine trials. For more information, visit www.iavireport.org/trialsdb. Please email any additions, comments, or updates to iavireport@iavi.org.

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VAX is a monthly bulletin from *IAVI Report*, the publication on AIDS vaccine research published by the International AIDS Vaccine Initiative (IAVI). It is currently available in English, French, German, Spanish, and Portuguese as a downloadable pdf file (www.iavireport.org) or an e-mail bulletin.

IAVI is a global not-for-profit organization working to speed the search for a vaccine to prevent HIV infection and AIDS. Founded in 1996 and operational in 23 countries, IAVI and its network of partners research and develop vaccine candidates. IAVI also advocates for a vaccine to be a global priority and works to assure that a future vaccine will be accessible to all who need it. For more information, go to www.iavi.org.

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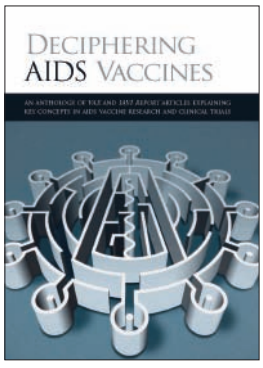
[*The publication on international AIDS vaccine research*]



Ongoing Trials of Preventive AIDS Vaccines

Trial No.	Title	Start Date	Organizer, Manufacturer	Countries (No. of sites)	Vaccine Name	Antigen (Clade)
PHASE III	**Large trials in high-risk populations to test vaccine efficacy**					
RV 144	A trial of Sanofi Pasteur live recombinant ALVAC-HIV (vCP1521) priming with VaxGen gp120 B/E (AIDSVAX B/E) boosting	Oct-03	DoD, Thailand MOPH, NIAID TAVEG, Sanofi, VaxGen	Thailand (8)	Prime: ALVAC vCP1521 Boost: AIDSVAX B/E	*env* (B,E); *gag/pol, env* (B,E)
PHASE II	**Mid-sized trials in low- and high-risk populations to test vaccine safety and immunogenicity**					
IAVI A002	A placebo-controlled, double-blind trial to evaluate the safety and immunogenicity of tgAAC09, an HIV vaccine containing clade C *gag*-PR-ΔRT DNA in an adeno-associated virus (AAV) capsid, administered twice, at three dosage levels and two dosing intervals	Nov-05	IAVI, Targeted Genetics	South Africa (3), Uganda, Zambia	tgAAC09	*gag*, PR, ΔRT (C)
HVTN 204	A clinical trial to evaluate the safety and immunogenicity of a multiclade HIV-1 DNA plasmid vaccine, VRC-HIVDNA-016-00-VP, followed by a multiclade recombinant adenoviral vector HIV-1 vaccine boost, VRC-ADV-014-00-VP	Sep-05	NIAID, Vical, GenVec	US (7), Brazil (2), South Africa (3) Later: Haiti, Jamaica	Prime: VRC-HIVDNA-016-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol, nef* (B), *env* (A,B,C); *gag, pol* (B), *env* (A,B,C)
HVTN 502/ Merck 023 (Step study)	A double-blind, randomized, placebo-controlled, IIb (proof-of-concept) study to evaluate the safety and efficacy of a three-dose regimen of the Merck adenovirus serotype 5 vaccine (MRKAd5 HIV-1 Gag/Pol/Nef)	Dec-04	NIAID, Merck	US (12), Canada, Peru (2), DR, Haiti, Puerto Rico, Australia, Brazil (2), Jamaica	MRKAd5 HIV-1 Gag/Pol/Nef	*gag, pol, nef* (B)
ANRS VAC 18	A randomized, double-blind trial to compare the safety and immunogenicity of three doses of LIPO-5 versus placebo	Sep-04	ANRS, Sanofi Pasteur	France (6)	LIPO-5	5 lipopeptides (CTL epitopes) from *gag, pol, nef* (B)
PHASE I/II	**Small trials moving into mid-sized trials in low- and high-risk populations to test vaccine safety and immunogenicity**					
HIVIS 03	A clinical trial to assess the safety and immunogenicity of a plasmid DNA-MVA prime-boost HIV-1 vaccine candidate	Dec-06	MUCHS, Karolinska Institute, SMI, Vecura, USMHRP	Tanzania	Prime: HIVIS DNA Boost: MVA-CMDR	*env* (A,B,C), *gag* (A,B), RT (B), *rev* (B); *env* (E), *gag* (A), *pol* (E)
RV 172	A clinical trial to evaluate the safety and immunogenicity of a multiclade HIV-1 DNA plasmid vaccine, VRC-HIVDNA-016-00-VP, boosted by a multiclade HIV-1 recombinant adenovirus-5 vector vaccine, VRC-ADV-014-00-VP	May-06	USMHRP, NIAID	Kenya, Uganda, Tanzania	Prime: VRC-HIVDNA-016-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol, nef* (B), *env* (A,B,C); *gag, pol* (B), *env* (A, B, C)
HVTN 042	A clinical trial to evaluate the safety and immunogenicity of the LIPO-5 vaccine and the ALVAC-HIV (vCP1452) vaccine given alone and in combination	Apr-04	NIAID, ANRS	US (10)	Prime: ALVAC-HIV (vCP1452) Boost: LIPO-5 or ALVAC-HIV (vCP1452) and LIPO-5	*env, gag, pol* + CTL epitopes from *nef/pol* (B); 5 lipopeptides (CTL epitopes) from *gag, pol, nef* (B)
PHASE I	**Small trials in low-risk populations to test vaccine safety and immunogenicity**					
HVTN 069	A Phase Ib trial to compare safety, tolerability, and immunogenicity of an adenoviral vector boost administered intramuscularly, intradermally, or subcutaneously after a DNA plasmid vaccine prime administered intramuscularly to adenovirus type 5 seropositive adults	Nov-06	NIAID	US (6)	Prime: VRC-HIVDNA-009-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol, nef* (B), *env* (A,B,C); *gag, pol* (B), *env* (A,B,C)
DHO-0586	A study to evaluate the safety and immunogenicity of a single dose of MVA expressing HIV-1 clade C *env/gag-pol* and *nef-tat* fusion genes (ADMVA), administered intramuscularly to volunteers who previously received three doses of a clade C DNA vaccine (ADVAX)	Oct-06	ADARC, IAVI	US	ADMVA	*env/gag-pol, nef-tat* (C)
HPTN 027	A study to evaluate the safety and immunogenicity of ALVAC-HIV vCP1521 in infants born to HIV-1 infected women	Oct-06	NIAID, Sanofi	Uganda	ALVAC-HIV vCP1521	*env* (B,E)
C86P1	An open label, parallel trial to evaluate safety and immunogenicity of three nasal immunizations of a fixed-dose level of HIV gp140 V2 loop deleted protein adjuvanted with LTK63, followed by intramuscular boosting with HIV gp140 V2 loop deleted protein adjuvanted with MF59	Sep-06	SGUL, Richmond Pharmacology, Novartis Vaccines	UK	Prime: HIV gp140 with LTK63 Boost: HIV gp140 with MF59	*env* (B)
VRC 011 (06-I-0149)	A clinical trial of intramuscular, subcutaneous, and intradermal administration of an HIV-1 multiclade DNA vaccine, VRC-HIVDNA-016-00-VP, and an HIV-1 multiclade adenoviral vector vaccine, VRC-ADV-014-00-VP	May-06	NIAID	US	Prime: VRC-HIVDNA-016-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol, nef* (B), *env* (A,B,C); *gag, pol* (B), *env* (A,B,C)
HVRF-380-131004	A clinical trial to evaluate safety and tolerability of administering VICHREPOL, carrying chimeric recombinant protein comprised of C-terminal p17, full p24, and immunoreactive fragment of gp41 with polyoxidonium adjuvant	Mar-06	Moscow Institute of Immunology, Russian Federation Ministry of Education and Science	Russian Federation	VICHREPOL with polyoxidonium adjuvant	*env, gag* (B)
HVTN 065	A clinical trial to evaluate the safety and immunogenicity of pGA2/JS7#2 DNA vaccine and recombinant MVA-HIV 62 vaccine	Mar-06	NIAID, Geovax	US (5)	Prime: HIVB DNA pGA2/JS7#2 Boost: MVA-HIV 62	*gag, pro*, RT, *env, tat, rev, vpu* (B); *gag, pol, env* (B)
HVTN 068	A clinical trial to evaluate immune response kinetics and safety of two different primes, adenoviral vector vaccine (VRC-ADV-014-00-VP) and DNA vaccine (VRC-HIVDNA-009-00-VP), each followed by an adenoviral vector boost	Mar-06	NIAID	US (5)	Prime: VRC-ADV-014-00-VP or VRC-HIVDNA-009-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol* (B), *env* (A,B,C) or *gag, pol, nef* (B), *env* (A,B,C); *gag, pol* (B), *env* (A,B,C)

Ongoing Trials of Preventive AIDS Vaccines

Trial No.	Title	Start Date	Organizer, Manufacturer	Countries (No. of sites)	Vaccine Name	Antigen (Clade)
PHASE I	**Small trials in low-risk populations to test vaccine safety and immunogenicity (continued)**					
RV 138	A study of Sanofi Pasteur live recombinant ALVAC-HIV (vCP205, HIV-1 *env/gag/pol*) administered subcutaneously via *ex vivo* transfected, autologous dendritic cells, intradermally or intramuscularly	Mar-06	USMHRP	US	ALVAC-HIV vCP205	*env, gag, pol* (B)
HIVIS 02	A clinical trial to assess the safety and immunogenicity of administering MVA, carrying HIV-1 genes *env, gag,* and *pol* in volunteers who previously received plasmid DNA with analogous HIV-1 genes in HIVIS 01	Jan-06	Karolinska Institute, SMI, USMHRP	Sweden	MVA-CMDR	*env* (E), *gag* (A), *pol* (E)
HVTN 064	A clinical trial to evaluate the safety and immunogenicity of recombinant protein vaccine EP-1043 and the DNA vaccine EP HIV-1090 given alone or in combination	Jan-06	NIAID, Pharmexa-Epimmune	US (3), Peru (2)	EP-1043, EP HIV-1090	*env, gag, pol, vpu* (B); *gag, pol, vpr, nef* (A,B,C,D,F,G)
IAVI D001	A randomized, placebo-controlled, dose-escalating, double-blinded study to evaluate the safety and immunogenicity of TBC-M4 MVA, HIV-1 multigenic subtype C vaccine	Dec-05	IAVI, Therion	India	TBC-M4 MVA	*env, gag, tat, rev, nef,* ΔRT (C)
IAVI V001	A randomized, placebo-controlled, double-blind trial to evaluate the safety and immunogenicity of a multiclade HIV-1 DNA plasmid vaccine followed by recombinant, multiclade HIV-1 adenoviral vector vaccine or the multiclade HIV-1 adenoviral vector vaccine alone	Nov-05	IAVI, NIAID	Rwanda, Kenya	Prime: VRC-HIVDNA-016-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol, nef* (B) *env* (A,B,C); *gag, pol* (B), *env* (A,B,C)
HVTN 063	A clinical trial to evaluate the safety and immunogenicity of HIV-1 Gag DNA vaccine alone or with IL-15 DNA, boosted with HIV-1 Gag DNA + IL-15 DNA or HIV-1 Gag DNA + IL-12 DNA	Sep-05	NIAID, Wyeth	US (7), Brazil (2)	Prime: GENEVAX Gag-2692 +/- IL-15 DNA Boost: RC529-SE + GM-CSF or GENEVAX Gag-2692 + IL-15 DNA or GENEVAX Gag-2692 + IL-12 DNA	*gag* (B); *env, gag, nef* (B) or *gag* (B)
HVTN 060	A clinical trial to evaluate the safety and immunogenicity of an HIV-1 Gag DNA vaccine with or without IL-12 DNA, boosted with homologous plasmids or with HIV CTL multiepitope peptide vaccine RC529-SE plus GM-CSF	Aug-05	NIAID, Wyeth	US (3), Thailand	Prime: GENEVAX Gag-2692 +/- IL-12 DNA Boost: DNA plasmids or RC529-SE + GM-CSF	*gag* (B); *gag* (B) or *env, gag, nef* (B)
RV 158/ WR 1143	A double-blind, randomized, dose escalating, placebo-controlled, study of safety and immunogenicity of WRAIR/ NIH live recombinant MVA-CMDR (HIV-CM235 *env*/CM240 *gag/pol*) administered intramuscularly or intradermally	Jul-05	USMHRP, WRAIR	US Later: Thailand	MVA-CMDR	gp160, *gag, pol* (A,E)
N/A	A randomized, placebo-controlled, double-blind trial to evaluate the safety and immunogenicity of a multiclade HIV-1 DNA plasmid vaccine	Mar-05	Guangxi CDC	China	DNA Vaccine	DNA plasmids (B,C)
EnvDNA	A clinical trial to evaluate the safety and tolerability of a recombinant HIV-1 multi-envelope DNA plasmid vaccine (EnvDNA)	Feb-05	St. Jude, NIAID	US	EnvDNA	*env* (A,B,C,D,E)
EuroVacc 02	A clinical trial to evaluate the safety and immunogenicity of DNA-HIV-C alone or DNA-HIV-C (prime) with NYVAC-HIV-C (boost)	Feb-05	EuroVacc Foundation	Switzerland, UK	Prime: DNA-HIV-C Boost: NYVAC-HIV-C	*env, gag, pol, nef* (C); *env, gag, pol, nef* (C)
HIVIS 01	A clinical trial to assess the safety of different modes of administering plasmid DNA with HIV genes *env, rev, gag,* and RT	Feb-05	Karolinska Institute, SMI, Vecura	Sweden	HIVIS DNA	*env* (A,B,C), *gag* (A,B), RT (B), *rev* (B)
HVTN 049	A clinical trial to evaluate the safety and immunogenicity of a Gag DNA/PLG and Env DNA/PLG microparticle vaccine and gp140/MF59 adjuvant vaccine	Jan-05	NIAID, Chiron	US (11)	Gag and Env DNA/PLG + oligomeric gp140/MF59	*gag, env* DNA/PLG, oligomeric gp140 (B)
IAVI C002	A randomized, placebo-controlled, dose-escalating, double-blinded, study to evaluate the safety and immunogenicity of a MVA expressing HIV-1 clade C *env/gag-pol* and *nef-tat* fusion genes (ADMVA) vaccine	Jan-05	IAVI, ADARC	US (2)	ADMVA	*env/gag-pol, nef-tat* (C)
HVTN 055	A trial to evaluate the safety and immunogenicity of rMVAHIV and rFPHIV vaccines, alone or in combination	Sep-04	NIAID, Therion	US (4), Brazil (2)	TBC-M358(MVA); TBC-M335 (MVA); TBC-F357(FPV); TBC-F349(FPV)	*env, gag* (B); *tat, rev, nef,* RT (B); *env, gag* (B); *tat, rev, nef,* RT (B)
RV 151/ WRAIR 984	A study of safety and immunogenicity of the WRAIR HIV-1 vaccine LFn-p24, an anthrax-derived polypeptide, adminstered intramuscularly with alyhydrogel adjuvant	Jun-04	USMHRP	US	LFn-p24	*gag* p24 protein (B)
VRC 008 (05-I-0148)	A clinical trial of a prime-boost HIV-1 vaccination schedule: multiclade DNA vaccine VRC-HIVDNA-016-00-VP, followed by multiclade adenoviral vector vaccine, VRC-ADV-014-00-VP	Apr-04	NIAID	US	Prime: VRC-HIVDNA-016-00-VP Boost: VRC-ADV-014-00-VP	*gag, pol, nef* (B), *env* (A,B,C); *gag, pol* (B), *env* (A,B,C)

NIAID: US National Institute of Allergy and Infectious Diseases. The **Vaccine Research Center (VRC)** is a NIAID intramural program that develops and manufactures vaccine candidates, conducts Phase I clinical trials, and performs comprehensive immunological analyses. The **Division of AIDS (DAIDS)** is a NIAID extramural organization that provides regulatory sponsorship and funding for extramural clinical trials. The **HIV Vaccine Trials Network (HVTN)** is a clinical trial organization funded by a cooperative agreement from DAIDS that conducts Phase I through Phase III studies and a full spectrum of immunological and statistical analyses. For more information on specific trials go to www.clinicaltrials.gov.

ADARC: Aaron Diamond AIDS Research Center; **AFRIMS**: Armed Forces Research Institute of Medical Sciences; **ANRS**: Agence Nationale de Recherches sur le SIDA; **DoD**: US Department of Defense; **DR**: Dominican Republic; **Guangxi CDC**: Guangxi Centre for Disease Control and Prevention; **HPTN**: HIV Prevention Trials Network; **IAVI**: International AIDS Vaccine Initiative; **KI**: Karolinska Institute; **MII**: Moscow Institute of Immunology; **Thailand MOPH**: Ministry of Public Health Thailand; **MUCHS**: Muhimbili University College of Health Sciences; **MVA**: modified vaccinia Ankara; **NV**: Novartis Vaccines; **RFMES**: Russian Federation Ministry of Education and Science; **RPh.**: Richmond Pharmacology; **SGUL**: St. George's, University of London; **SMI**: Swedish Institute for Infectious Disease Control; **St. Jude**: St. Jude Children's Research Hospital; **TAVEG**: Thai AIDS Vaccine Evaluation Group; **USMHRP**: US Military HIV Research Program; **WRAIR**: Walter Reed Army Institute of Research

Sources: IAVI, VRC, USMHRP, HVTN, NIH, MII, Karolinska Institute, Wyeth, SGUL, clinicaltrials.gov, http://chi.ucsf.edu/vaccines, www.anrs.fr