SA vaccine trials launched, but future funding not secure

Craig McKune

Following a decade of research, the first two South African-developed HIV vaccines went into clinical trials in July. The two vaccines are both being tested in phase I safety trials in 36 local volunteers at two sites: the Emavundleni Centre in Cape Town and Chris Hani Baragwanath Hospital in Soweto. But the launch of the South African trials has been overshadowed by a funding crisis at the South African Aids Vaccine Initiative (SAAVI), which developed the vaccines but has had its funding from the Department of Science and Technology (DST) terminated.

The new vaccine trials, known as SAAVI 102/HVTN 073, follow on the heels of disappointing 'Step' trials of a candidate vaccine developed in the USA by pharmaceutical company Merck, which were called off in 2007 after it was found the vaccine failed to prevent HIV infection or reduce viral load (see SAJS 105, 168–169; 2009). Testing the same product, the South African Phambili trials were also subsequently dropped. But as the HIV epidemic in southern Africa is dominated by a particular strain of the virus (subtype-C), it was predictable that vaccines developed against other strains would not work optimally here.

As part of the SAAVI initiative to develop a vaccine specifically for subtype-C, virologist Carolyn Williamson and her team at the Institute of Infectious Diseases and Molecular Medicine at the University of Cape Town (UCT) surveyed HIV from newly infected patients and selected genes that best represented local strains. Building on this, she and Anna-Lise Williamson, from the same institute, refined two vaccines—the two now on trial—by incorporating additional subtype-C genes and modifications to make them more effective.

The new trials are using what is known as a prime-boost response: the synthetic DNA vaccine is given to prime the body’s immune response, followed by the MVA vaccine which should boost the immune response. MVA is made from the Modified Vaccinia Ankara virus, similar to the smallpox vaccine—so volunteers must not have received the smallpox vaccine before.

The SAAVI 102/HVTN 073 vaccine trials aim to test if the candidate vaccines are safe for people and how their immune systems respond. Trial participants also have to be HIV-negative and at a low risk of becoming infected. If the results are promising, phase II trials will be conducted also to test vaccine safety and immune response, and phase III trials would test if the study vaccine is effective in preventing HIV infection or slowing its progression to Aids.

The two MVA and DNA study vaccines, however, are all that remain of a pipeline of vaccines that was being developed by SAAVI researchers. As a consequence of the DST withdrawing funding, only seven of SAAVI's former vaccine team of 39 researchers remain employed by the initiative.

Based at the South African Medical Research Council, SAAVI was formed in 1999 with the goal of producing a viable HIV vaccine through coordinated research, development and testing. It was backed by the South African government and local and international donors including Eskom, the US National Institute of Health (NIH) and the HIV Vaccine Trials Network (HVTN).

SAAVI first ran into trouble when Eskom cut its R15-million grant at the end of 2007, citing its own financial difficulties as the reason. Then in February last year DST announced that it was terminating its contract with the initiative. According to the department (http://www.dst.gov.za/Sharp.pdf), the SA government is ‘revisiting’ its expectations of HIV vaccine research in favour of ‘a strategic combination of interventions’, and accordingly has allocated R45 million over the next three years to fund the new South African HIV/AIDS Research (and Innovation) Platform (Sharp), which is to focus more ‘holistically’ on HIV prevention and treatment research.

The DST website reports that SAAVI has been guilty of under-spending, and ‘issues’ had been raised in independent audits in 2005 and 2006. Neither SAAVI interim director Elise Levendal nor the DST
would give details of these issues, but
Levendal said that only very minor con-
cerns had been reported.

In the case of the SAAVI 102/HVTN 073 trials, DST’s health innovations director
Glaudina Loots says that now that the
DNA and MVA vaccines had entered
clinical trials, the department’s job was
done. ‘DST’s responsibility is up until the
phase I clinical trials, and that’s it,’ she
said. Another reason for the cut cited on
the DST website was that ‘the lion’s share’
of the funds had gone to Anna-Lise Wil-
liamson, but department spokesman
Lunga Ngqengelele declined to elaborate
on this.

In an effort to keep SAAVI’s vaccine
effort alive, as the DNA and MVA vaccines
were so close to clinical trials, UCT vice-
chancellor Max Price met with deputy
minister of science and technology Derek
Hanekom. ‘Hanekom made funds avail-
able to continue the project for another
year’, according to deputy vice-chancellor
Danie Visser, and the department has
provided an additional R6.6 million since
March 2008.

Anna-Lise Williamson argues that it
does not make sense for the DST to fund
the candidate vaccines only up until the
phase I safety trials. ‘This is questionable
logic. The way a vaccine pipeline works,
this vaccine that is going on trial is
unlikely to be the last version. We need to
see if we are getting a decent immune
response, then we must take it back to the
labs for more research.’ Regular potency
assays are still needed to assess the stability
of the products.

‘[And] we may wish to combine this
product with other products to see if we
could increase the breadth of responses,’
says Carolyn Williamson. ‘We could pos-
sibly improve the insert to increase
immunogenicity. We could use the DNA
vaccine as a primer for other vaccines to
prime the MVA. All of these things require
laboratory investigation to see if they
would hold any promise in clinical trials.’
But the DST has left the trials—and any
future work on the DNA and MVA
products—to be funded by international
donors and the Department of Health.

‘The impact of DST withdrawing its
funding has been huge,’ said Levendal.
‘There are very promising young scientists
who have been retrenched, many of
whom have still not found new positions.’
She said SAAVI has been forced to operate
at a more modest level than before. ‘We
are basically coordinating vaccine research
and development now, and we will do
that through small grants to basic science,
ethical research and community research.
It’s a major blow, but we’re using the
limited amount of money we have as well
as we can.’—‘We had huge capacity that
is now gone,’ says Anna-Lise Williamson.
‘For vaccine research we need to have
sustainable money. Vaccine projects take
over 15 years to come to fruition so we
have to have buy-in on a different level.’

SAAVI is trying to secure alternative
funding in a difficult environment: global
spending on HIV vaccine research has
fallen for the first time since 2000. A report
released in July, ‘Adapting to Realities:
Trends in HIV Prevention Research
Funding 2000 to 2008’ (http://www.
hivresourcetracking.org) by the HIV Vac-
cine and Microbicide Resource Tracking
Working Group, found that HIV vaccine
research spending had dropped 10% be-
tween 2007 and 2008. The report sug-
gests this relates to shifting scientific
priorities, the declining economy and
competing health priorities globally.

But Levendal said the Italian national
health department had pledged R38
million dedicated to strengthening
existing clinical trial sites, and to help
build vaccine manufacturing capacity in
South Africa. And SAAVI was waiting for
the Department of Health to sign an
agreement to fund R35 million over the
next three years. While Levendal would
not elaborate on how this money would
be spent, she said part of it would go to the
DNA and MVA vaccines, and once it was
approved, SAAVI would announce a new
call for proposals.

According to Carolyn Williamson, the
initiative has provided strong negotiating
power with international scientists.

‘South Africa is a highly desirable location
for HIV vaccine research. The disease has
a high impact and rate of spread, it is a
unique strain, and the country has good
scientific and infrastructural capacity.’—
‘SAAVI gave South African researchers
incredible leverage. Researchers knew
that if they wanted to work in South
Africa, they also had to contribute to the
country,’ she said.

Following its first call for proposals in
February this year, Sharp now supports
nine research projects, which are expected
to come up with a new diagnostic test to
detect HIV drug resistance; possible new
drug targets; potential biomarkers to be
used to inform control of HIV infection;
and finding molecules or a neutralising
antibody which could be used in a vaccine.
The intention is to develop an approach
to HIV prevention and treatment research
that will help to reduce the rate and risk of
transmission in the short term ‘while
awaiting the development of an effective
vaccine’, reports the department’s website.

But Carolyn Williamson said that in
terms of producing an actual vaccine
product that can be clinically tested, these
programmes do not compare to SAAVI’s.
‘They’re funding only basic science in
isolation but it is not obvious from the
outside what their long term strategy is,’
she said.

‘If the DST’s mission is product develop-
ment,’ she adds, ‘I don’t think it has a
sensible approach. If you develop a
product and go all the way to trial and
then just dump it, what kind of a science
and technology department are you?’

Craig McKune is a science journalist based
in Cape Town.