DEVELOP

Demand short-term results on the path to long-term goals

In the preceding pages, we have talked a lot about how to set and meet strategic targets. This is fairly simple for proven strategies like ART for HIV-positive individuals and VMMC. It is more complex, but doable, for emerging strategies like oral PrEP. It is hardest for strategies in development, including AIDS vaccine and multipurpose prevention technologies that would provide contraception and HIV prevention in a single product. Science doesn't run on a schedule, and a breakthrough can come at any time, or not at all. In this context, setting milestones can set false expectations. But while success resists timelines, it is possible to establish mechanisms for accountability and targets related to long-term goals. That's why our recommendation for 2015 is: ***Demand short-term results on the path to long-term goals***.

The good news is that the reason the field needs to think this way is because there is more and more clinical activity related to the "upstream" scientific agenda of immune-based strategies for preventing and/or treating HIV. Broadly-neutralizing antibodies are potent immune responses that can block the activity of many different types of HIV. The science is complex and may be a barrier to advocates following the latest developments. But now is the time to pay attention and ensure that researchers are translating scientific goals into comprehensible concepts—these products are already being evaluated in humans. There are trials of three different bNAbs for passive immunization, treatment and/or cure currently underway as well as plans to test vector-based strategy designed to generate finite supplies of bNAbs. Such strategies would require repeat dosing. This sets them apart from a vaccine regimen that seeks to provide long-term protection after a single series of immunizations. The table at right provides more detail on the differences between these and other strategies currently in development.

Decoding Complex Science; Deepening Stakeholder Engagement

As the science evolves, so do strategies for engagement and education. AVAC is proud to be part of a multi-stakeholder collaborative developing a "CUREicculum" designed to explain cure research concepts from trial design to regulatory issues. Long-time AVAC board member Steve Wakefield from the HVTN is heading up the research literacy effort focused on a planned passive immunization trial using the Vaccine Research Center's VRC01 bNAb candidate. The *Good Participatory Practice Guidelines for Biomedical HIV Prevention Research (www.avac.org/gpp)* continues to serve as the gold standard for stakeholder engagement across the research life cycle. An online curriculum launched in 2014 provides a new resource for individuals wanting to learn how to use GPP!

On the vaccine front, HVTN 100 launched in South Africa. This trial is the next in the sequence of studies designed to build on the positive results of the Thai trial known as RV144, which found modest efficacy in 2009. HVTN 100 follows HVTN 097, which found that the Thai RV144 regimen was safe and immunogenic in South African men and women. HVTN 100 will test a variation of the RV144 regimen that's been designed for increased immunogenicity and could lead to an efficacy trial as soon as late 2016 (see pages 28-29 for more details). Also in 2015, J&J and other partners will begin a Phase I/II trial of a vaccine strategy that uses an "alternative" adenovirus vector and a mosaic immunogen (e.g., one which contains genetic material from many subtypes of HIV, in hopes of providing cross-clade protection).

Much of this activity is early phase clinical research. But this doesn't mean that there isn't a role for advocacy. Particular attention needs to be paid to the decision-making processes that trigger trials and/or shelve products, and to the product development pathways for each strategy that moves ahead.

One newer challenge is to articulate the decision points and milestones in the pathways for strategies that could be used in both HIV-positive and HIV-negative individuals, such as long-acting injectable antiretrovirals or broadly neutralizing antibodies. These strategies are scientifically distinct. They work in different ways, and they are being tested with different goals. Long-acting injectables, for example, are a new formulation of a familiar product—ARVs—and they are being tested in trials leading to potential licensure. Passive immunization is unfamiliar to many people, and trials of HIV-specific antibodies won't necessarily lead to a product on the market. It is essential that the differences between these classes of interventions and the related trials are clear to the stakeholders who may be asked to participate in trials and to the broader array of stakeholders engaged in HIV prevention advocacy. Communities asked to comment on and participate in such research will want and need to know the distinctions, potential public health impact of and product-development pathways for these different products. Right now, these conversations are happening by intervention. It's important to explain the distinctions between the products, but it's also key to create opportunities to discuss multiple strategies and approaches at the same time. Trial teams and product developers should help create these forums, and look to the *Good Participatory Practice Guidelines* for a road map on structure and follow-up.

Linked conversations about these complex issues will pave the way for more in-depth, intervention-specific discussions that could emerge in the years to come.

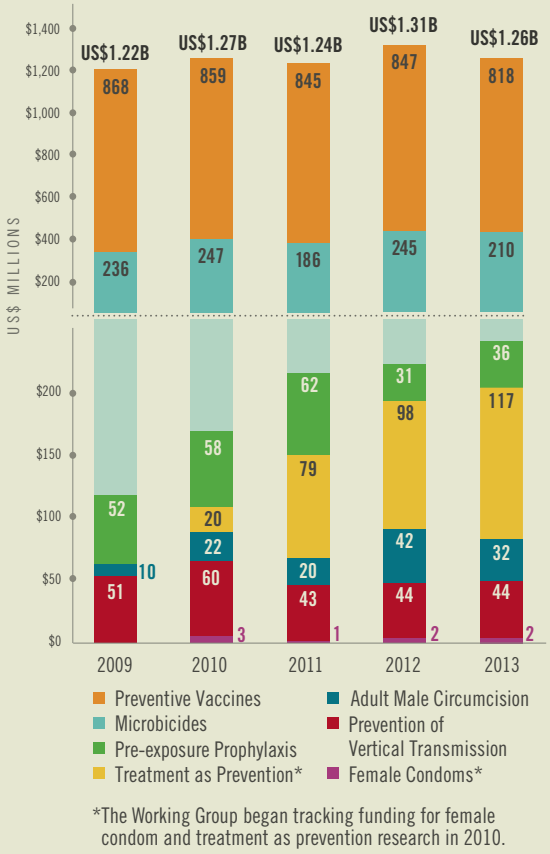
The questions that do emerge are almost certainly going to do so in the context of limited research funding. If there isn't a transparent framework for decision-making, and an agenda that looks at pathways in HIV-positive and HIV-negative individuals, then confusion will ensue. Likewise, if research funding isn't sustained—and the most recent figures show a four percent decline in AIDS vaccine funding between 2012 and 2013 (see figure at right)—then decisions will be driven by dollars, pounds and rand, and not by scientific priorities.

Cure research also requires a detailed mapping of timelines, decision points and areas for in-depth stakeholder engagement. In late 2014, the US NIH-funded IMPAACT network launched a trial that seeks to learn more about the impact of immediate treatment in infants born to HIV-positive women diagnosed at eight months of pregnancy or later, up until delivery. This trial was originally designed to attempt to replicate the "cure" seen in the child the media called the "Mississippi Baby." This child was later found to still have low levels of HIV in her blood. In scientific circles, the term cure has been replaced by "remission". This nuance is one of many that has to be translated into community understanding.

Here are some key steps to take in 2015:

- **Define accessible messages and milestones for broadly neutralizing antibody research.**
  It is tremendously complex to explain the science, purpose and possible outcomes of these trials. The field needs to ensure that this trial conduct and communications work is well-resourced and that best practices and messages are shared and adapted in real time, and for both adults and infants. Answers to key questions should be compiled into a single document that helps stakeholders sort out this complex field.
- **Ensure stakeholder engagement in cure research and passive immunization trial design.**
  It's not possible to set a deadline for having an antibody-inducing vaccine, but it is possible to have milestones for research literacy tools, documented stakeholder engagement, transparent exploration of the concerns and support for these trials, and a way forward that reflects both good science and good participatory practice.
- **Define the standard of prevention for next-generation efficacy trials, including of AIDS vaccines and multi-purpose prevention technologies.**
  This is an age-old recommendation that is made, each year, in a brand-new world. As oral PrEP is rolled out, ART guidelines change, and the world prepares for a potential microbicide ring or gel, it is essential to revisit the principles for incorporating emerging strategies into the standard of prevention for trials.

Global HIV Prevention R&D Investment 2009 – 2013 (US$ millions)



*The Working Group began tracking funding for female condom and treatment as prevention research in 2010.

Source: HIV Vaccines & Microbicides Resource Tracking Working Group. HIV Prevention Research & Development Investment in 2013: In a changing global development, economic, and human rights landscape. July 2014. *www.hivresourcetracking.org*.