Global HIV Vaccine Enterprise Annual stakeholders' meeting

HIV vaccine cannot be 'business as usual'

Fairmont Grand Hotel, Geneva, Switzerland, and virtual
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Contents

Background

The scientific challenges of developing an HIV vaccine are exacerbated by funding trends, investment patterns and the diminishing involvement of early-career researchers. The goal of the annual stakeholders' meeting is to collectively interact with the scientific community and other stakeholders involved in HIV vaccine research and development (R&D) to identify and define ways to address the ongoing challenges faced by HIV vaccine R&D. This year's meeting also aimed to revitalize and redefine HIV vaccine advocacy, with a particular focus on identifying messages to ensure sustained financial and scientific support for research globally.

Agenda

Welcome & Introduction
Marlène Bras, IAS, Switzerland

Session 1: Identifying and addressing the scientific gaps of HIV R&D

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Vincent Muturi-Kioi, International AIDS Vaccine Initiative, Kenya

Presentation 2: mRNA platform for the development of an HIV vaccine: Curb your enthusiasm?
Sheila Balinda, London School of Hygiene & Tropical Medicine, Uganda

Roundtable discussion 1: How can we foster and welcome new ideas into the field?
Moderator: *Gabriella Scarlatti, San Raffaele Scientific Institute, Italy*

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Mitchell Warren, AVAC, USA

Roundtable discussion 2: Reinventing HIV vaccine advocacy in the era of PrEP and U=U
Moderator: *Roger Tatoud, Origena Consulting, France*

Rapporteur session

- *Maureen Luba, Cooper Smith, Malawi*
- *Shan Lu, University of Massachusetts, United States*

Concluding remarks
Marlène Bras, IAS, Switzerland

Overview

Roundtable 1: How can we foster and welcome new ideas into the field?

The discussion started with a reflection on the rapid development of COVID-19 vaccines, exploring whether this success resulted from scientific advancements, policy decisions or a combination of both. Participants highlighted similarities and differences between the two responses and suggested emulating the societal responses to COVID-19 within the context of HIV vaccine R&D. The potential for biotech to contribute to R&D and the importance of conducting empirical research to advance HIV vaccine development were raised. The focus of HIV vaccine R&D was discussed, acknowledging the critical task of defining public health and research objectives recognizing the impact of pre-exposure prophylaxis (PrEP) and emphasizing the significance of inducing broadly neutralizing antibodies (bnAbs). The conversation also touched on combining B- and T-cell vaccine approaches, evaluating the role of the mRNA platform, innovative thinking beyond immunogen design, considerations for HIV vaccine studies in children, and how to envision the feasibility and potential pathways for future efficacy trials.

Participants pointed to the importance of improving communication about vaccines and heightening public awareness. Additionally, they emphasized the importance of the role of the Enterprise and donors in steering the conversation to accelerate progress in HIV vaccine R&D. Lastly, they discussed strategies for maintaining an ongoing dialogue among diverse stakeholders with diverse perspectives. A set of priorities, reflecting the topics discussed, was proposed.

Roundtable 2: Reinventing HIV vaccine advocacy in the era of PrEP and U=U

The discussion provided a thoughtful reflection on the rationale for advocating for HIV vaccine research in the era of PrEP and undetectable = untransmittable (U=U), considering both successes and limitations. Participants recognized the increasing complexity of the science, the challenge of engaging with communities whose perspectives are yet to be fully understood, and the expanding knowledge among community members; they unanimously acknowledged the imperative to improve communication and to create space and opportunities for meaningful two-way engagement. The debate extended to the role of scientists in contributing to and enhancing advocacy for HIV vaccine research. A set of recommendations, reflecting the topics discussed, was proposed.

Roundtable discussion 1: How can we foster and welcome new ideas into the field?

Gabriella Scarlatti opened the roundtable, noting that it was disheartening that no HIV vaccine had been achieved after 40 years of research. While significant progress has been made, as evidenced by the excellent presentations by Vincent Muturi-Kioi and Sheila Balinda, the commitment to developing a vaccine should be renewed.

Scarlatti noted that the 20th anniversary of the Global HIV Vaccine Enterprise was a compelling reminder of the challenges and opportunities faced by all those involved in HIV vaccine R&D. While global collaboration has been instrumental in advancing HIV research, there is a need to reignite political support and for global recognition that an HIV vaccine is still urgently needed.

As Muturi-Kioi mentioned, the HIV pandemic was now widespread globally. However, 60% of new HIV cases are concentrated in central, eastern, southern and western Africa, particularly affecting young women and adolescent girls. This highlights the urgent need for an HIV vaccine. Balinda emphasized that current prevention methods were not as successful as they should be, and the emergence of HIV variants meant that vaccine strategies would have to protect against diverse strains. The current focus on B clades underscores the importance of expanding vaccine development to address a wider array of prevalent variants. When envisioning the development and deployment of an HIV vaccine, it is crucial to consider its global reach and the unique needs of affected regions.

Both Muturi-Kioi and Balinda emphasized the urgency of developing "fast platforms" and exploring new ways to approach HIV vaccines. Scarlatti urged out-of-the-box thinking, stressing the importance of innovative approaches and a potential start from scratch. She emphasized the urgency of accelerating trial processes, with a focus on experimental medical trials. She raised questions about whether testing should involve only vaccine products or include other vaccine components. Scarlatti noted the contribution of the EHVI 2020 consortium, which conducted multiple clinical trials testing various proteins, and although they did not result in a new product, they provided a wealth of data.

Drawing a parallel with the rapid development of COVID-19 vaccines, Scarlatti opened the discussion by enquiring about the factors contributing to the success of these vaccines – whether they stemmed from scientific advancements, policy decisions or a synergistic blend of both.

Emulating the societal response to COVID-19

Shan Lu pointed out that comparing HIV and COVID-19 was challenging due to differences in transmission, pathogenesis and viral properties. However, the rapid global response to COVID-19, with countries uniting and investing billions in research, provides valuable lessons for accelerating

HIV vaccine development. The success of innovative biotech companies like Moderna and BioNtech in developing COVID-19 vaccines shows the potential of such enterprises. By emulating this societal response and investing in innovative biotech startups, we can speed up the development of an HIV vaccine and bring hope to millions worldwide.

Tomáš Hanke stated that although challenges persisted, the overall trajectory of HIV vaccine R&D was positive and achieving an effective vaccine was closer than ever. While progress remains incremental, the direction for both T-cell and antibody-based approaches is encouraging.

Johan Vekemans emphasized the value of evidence-based approaches, recognizing that HIV vaccine development would still rely on some empirical exploration of novel ideas and less well-established strategies.

Jean-Daniel Lelièvre suggested that instead of comparing vaccines for HIV with vaccines for COVID-19, a completely new pathogen, it might be more fitting to compare with malaria vaccines due to the shared complexities and historical scepticism regarding vaccine development. Both HIV and malaria pathogens are highly complex, and eliciting an effective immune response remains challenging. Despite these difficulties, there are now two vaccines against malaria. Though not 100% effective, they have made a significant contribution.

Gus Cairns highlighted the lessons learnt from the COVID-19 pandemic, emphasizing the need for equitable access to vaccines and addressing the stigma surrounding HIV. He pointed to the success of Africa in reducing HIV acquisitions while the number of HIV acquisitions was not decreasing in the WHO European region.

A greater involvement of biotech and empirical research

Lu advocated for a greater involvement of biotech in HIV vaccine research and commended the recent initiative by the IAS Corporate Partnership Programme to establish an HIV Vaccine Partnership. He encouraged more efforts such as this to promote investment in HIV vaccine research. In addition, Lu said that achieving success hinged on empirical research. Scientifically, prior to COVID-19, mRNA and DNA vaccines were often considered impractical. It is a lesson to be learnt – it is not possible to predict success, only to work towards our goals.

Hanke raised concerns about the notion that small biotech companies were solely responsible for the success of COVID-19 vaccine development. He noted that these companies relied on significant financial backing and expertise that they secured through partnerships with major pharmaceutical companies like AstraZeneca and Pfizer. These collaborations are essential for translating cutting-edge research into viable products. Moreover, the fundamental difference between HIV and COVID-19 is the relative ease with which vaccines were developed for the latter. If HIV shared the same characteristics as SARS-CoV-2, there would have been an HIV vaccine decades ago. While mRNA shows promise, the success of RNA approaches for various diseases remains to be demonstrated.

Improving communication about vaccines

Cairns expressed concerns about potential vaccine hesitancy and emphasized the need for clear communication, learning from past COVID-19 mistakes. Stressing the importance of setting realistic expectations for an HIV vaccine, Cairns highlighted the goal of a comprehensive vaccine that not only prevented illness and death but also protected against acquisition. Drawing parallels with the successful HPV vaccine, Cairns advocated for open communication and education to build public trust and acceptance of an HIV vaccine worldwide.

Daisy Ouya said that the COVID-19 experience had significantly impacted vaccine confidence, especially in regions like eastern and southern Africa. Communicating the importance of vaccines to communities is crucial to counteract mis- and disinformation and rebuild trust. In the current post-truth era, it is essential not to overlook the importance of increasing vaccine confidence as we develop new vaccines.

What should the focus of HIV vaccine research and development be in the current era?

Defining the public health and research targets for an HIV vaccine

Vekemans encouraged a review of public health targets for HIV vaccine development considering emerging technologies, such as long-acting antiretrovirals and bnAbs. He emphasized the importance of offering diverse preventive approaches to cater to various epidemiological settings and individual preferences. Vekemans advocated maintaining a long-term vision of eliminating HIV as a public health challenge and proposed extending the focus of vaccine R&D to include vaccine-based approaches to cure, aiming for a comprehensive solution to HIV eradication.

Christian Brander noted that while there was an understanding of the required protective responses, there was also a divergence in approaches on how to induce them. While some concentrate on learning from the virus, particularly in T-cell approaches, a potentially more effective strategy could involve first understanding the immune system and subsequently determining what responses to induce. The success of bnAb studies builds on studying the nature of the immune response and drawing lessons from therapeutic outcomes. Brander said that it was time to break away from the ineffective strategies of the past four decades. Credit should be given to innovative ideas outside the established norms. He expressed concern that the field was still stuck in the paths set 30 years ago, and he called for change.

Acknowledging the impact of PrEP on HIV vaccine development

Cairns noted that twice-yearly injectable PrEP was nearing licensing and that advancements in medication might render an HIV vaccine less essential, but he argued that the goal of attaining an effective, lifelong vaccine remained crucial for eradicating the virus.

Scarlatti acknowledged the challenges in developing an HIV vaccine that provided sterilizing immunity but emphasized the need to strive for such a comprehensive solution. She drew an analogy to the prevention of vertical transmission, highlighting the time and effort required to effectively implement and scale up effective preventive measures.

The importance of inducing bnAbs

Vekemans highlighted the significance of generating bnAbs in stringent animal models and then in humans. This path has been well characterized, and demonstrating its feasibility is crucial. Vekemans emphasized the need to establish R&D targets for T-cell vaccine approaches. Investigating viral control during treatment interruption studies is particularly relevant. Additionally, defining appropriate clinical and laboratory targets for T-cell vaccines would be beneficial.

Bart Haynes highlighted the challenge of developing bnAbs against HIV, contrasting it with the effective generation of neutralizing antibodies against SARS-CoV-2. While the strategy of germline targeting and B-cell lineage design holds promise for eliciting bnAbs, the substantial challenge lies in achieving sterilizing immunity, particularly given HIV's ability to integrate into the host's DNA. In contrast, the CMV T-cell vaccine, through its ability to clear the initial infection, effectively prevents persistent infection. Haynes emphasized the importance of understanding the principles guiding the humoral immune system to overcome resistance, including creating an affinity gradient between immunogens and inducing rare mutations crucial for broad neutralization. He mentioned collaboration with Hanke to integrate T-cell immunogens and with Betty Corbett's work, aiming to harness the synergy between the T- and B-cell arms of the immune system.

Brander agreed that in the context of HIV, achieving sterilizing immunity was crucial to prevent breakthrough acquisitions, which could lead to reservoir establishment and subsequent reactivation. If we consider a partially effective vaccine, its success should be evaluated based on its ability to maintain a reservoir size that ensures viral control and safety.

Combining B- and T-cell vaccine approaches

Brander highlighted the importance of combining B- and T-cell approaches for an HIV vaccine, emphasizing the need for a mechanism like T-cell immunity to prevent breakthrough acquisitions and control the reservoir. He advocated for conducting small trials to identify effective combinations, accelerating vaccine development. He said that Non-Human Primates (NHPs) trials could provide valuable insights into potential interference between vaccines, although they were not sufficient to assess efficacy in humans. Brander acknowledged that collaboration between different research teams was crucial for successful vaccine R&D and added that there was growing collaboration between T-cell, B-cell and innate immunity experts, which he believed would lead to significant advancements in HIV vaccine development.

The role of the mRNA platform in HIV vaccine R&D

Haynes said that mRNA technology offered the most rapid path for iterating vaccine designs. However, whether mRNA ultimately proves to be the ideal vaccine platform remains to be seen, as considerations such as reactogenicity and the induction of plasma cells, which are crucial for long-lasting immunity, require further investigation. The key is the design of the immunogen. Nevertheless, the rapid development cycle of mRNA vaccines compared with protein-based vaccines makes it an attractive option for iterating and evaluating various vaccine formulations. As the field moves forward, mRNA vaccines will continue to be compared with protein-based vaccines while closely monitoring their safety profiles and potential side effects.

Thinking beyond immunogen design

Hanke explained that success in vaccine development relied on aligning various factors perfectly. It is not just about the immunogen itself; the delivery method is also crucial. T-cells need to recognize the virus at multiple sites, proliferate effectively and resist redirection to non-protective sites. Timing and location in the body are critical, and if any of these elements fall short, the strategy fails. Hanke emphasized that even the best immunogen, if not delivered properly, would not induce protection if it is not presented correctly to the immune system. To achieve success, multiple factors must work in harmony, and Hanke highlighted the importance of a heterologous prime-boost strategy for non-replicating vaccine vectors. He noted the need to learn from Ad26 studies to avoid mistakes and suggested that replicating vaccine vectors, if proven safe, could offer different and more potent responses.

A role for HIV vaccine studies in children

Lelièvre suggested conducting more clinical trials in children to assess their ability to mount an immune response to HIV vaccines, as immunization in children might be more conducive to the induction of bnAbs. He noted that even a vaccine with limited efficacy, such as 30-40% protection, could be valuable in children if combined with other preventive measures. This could pave the way for a first generation of HIV vaccines that could significantly impact disease burden.

Hanke also noted that the success of childhood vaccines was often dependent on the timing of immunization, with the first half-year of a child's life being a critical period for immune system development. He suggested that this window of opportunity be explored for HIV vaccine development despite the challenges posed by vaccinating young children.

Accelerating the research process

Haynes emphasized the significance of accelerating the development and evaluation of HIV vaccines. He applauded the efforts of the HVTN and the Division of AIDS to streamline the regulatory process and promote discovery trials. The goal is to establish a common or successful platform, ultimately accelerating discovery trials from a regulatory perspective. Haynes also highlighted efforts to expedite the production and release of products. There is a collective push

globally, especially in clinical trials, to hasten the design and writing of trial protocols, traditionally a process that takes several years. The aim is to accelerate these aspects, as well.

A role for donors to drive the conversation

Margaret McCluskey acknowledged the progress made in HIV vaccine development but expressed concerns about the field's tendency to focus on a single approach instead of exploring diverse strategies. She said that better coordination could help address this issue. She urged greater collaboration in the development of bnAbs research, emphasizing the need to identify and exploit synergies across key groups. She suggested that donors and the Enterprise be more active in facilitating this coordination. McCluskey expressed frustration regarding newer vaccine platforms, particularly the germline-targeting approach, which was currently the only one on a product development path. While acknowledging the lack of enthusiasm, she said that revisiting the role of V1/V2 antibodies associated with protection in the RV144 trial still merited attention for further investigation.

Can we envision conducting an efficacy trial in the future?

Lu acknowledged the disappointment following the negative results of the Mosaico trial. However, he emphasized that setbacks were common in scientific research and that previous failures should not discourage efforts to develop an HIV vaccine. Lu drew parallels between HIV vaccine development and the progress made in TB and malaria vaccines, suggesting that HIV vaccine development might also achieve breakthroughs given the significant investment and research. In contrast to the positive outlook on scientific advancements with HIV, he expressed concern about the lack of mechanisms for efficacy trials and commitment from both government and private sectors, which hindered progress and demotivated vaccine developers. Lu encouraged the field to remain committed to moving the pipeline forward despite the challenges.

Hanke raised the possibility that small cure trials could lead to the identification of vaccines that could effectively control HIV infection. He suggested that such findings could generate momentum for larger-scale preventive vaccine trials. However, the availability of antiretroviral treatment might be closing the window of opportunity for preventive vaccine trials to demonstrate their efficacy.

Vekemans, drawing from experience with malaria and COVID-19 vaccines, stressed the necessity for a faster clinical development pathway for HIV vaccines. While acknowledging differences in funding and complexity, he emphasized the adaptability seen in regulatory and clinical approaches during the COVID-19 pandemic. Vekemans advocated for streamlined clinical testing, supporting translational medicine research with clear scientific targets, and urged a sense of urgency without hindering upstream research. He highlighted the importance of agile research spaces for collaboration, addressing immediate needs while pursuing long-term goals, and the creation of a platform to swiftly integrate scientific concepts into translational research for accelerated HIV vaccine development.

Maintaining the dialogue among a diverse range of stakeholders with different perspectives

Lu emphasized the need for more discussions and fresh ideas in HIV vaccine research. Currently, there is a trend of fewer dedicated meetings on HIV vaccines, with the topic often integrated into other gatherings. While bnAbs received significant attention, Lu pointed out the overshadowing of other immune parameters like ADCC and V1/V2 antibodies. He highlighted a recent study supporting the association between V1/V2 antibodies and protection against HIV, even in a failed vaccine candidate. Referencing unpublished data, Lu suggested that V1/V2 antibodies remain a potential correlate of protection. Stressing the importance of not dismissing ideas based on specific trial outcomes, Lu called for a more open-minded approach and additional platforms to encourage diverse scientific ideas in HIV vaccine research.

Stacey Hannah highlighted the imperative for a strategic shift in HIV vaccine R&D following the disappointing outcomes of the Mosaico trial. She emphasized the importance of articulating a clear strategy for the field, focusing on R&D targets, as mentioned by Vekemans. Acknowledging the growing complexity of the scientific landscape, Hannah pointed to the evolving nature of the field, exemplified by the USAID-funded BRILLIANT Consortium. She stressed the necessity for a well-defined strategy and proposed a systematic mapping of these targets and the various research projects and players, aiming for a more coordinated and comprehensive approach. Ultimately, she advocated a mechanism to ensure that the field collectively advances this strategy. In response to Scarlatti's question about the current role of the Enterprise, she indicated that this could be a direction for the organization to take.

Suggested priorities:

- Embrace optimism and acknowledge the remarkable scientific advancements made in HIV vaccine R&D.
- Effectively convey the message that the field is back at the discovery stage.
- Articulate and communicate the excellence of ongoing science to the public and funding bodies.
- Clearly define the need for an effective HIV vaccine and the ensuing R&D objectives.
- Adopt an open-minded approach and maintain consistency in the methodology.
- Promote and strengthen sustained collaborations, particularly to bridge knowledge gaps before proceeding.
- Enhance coordination to minimize duplication and maximize synergistic efforts.
- Explore strategies for building ecosystems around the research pipeline.
- Explore the concept of functional correlates of protection, which are key markers of effective immunity.
- Prioritize innovative trial designs as they are crucial for accelerating progress.
- Draw valuable insights from cure research to inform vaccine development strategies.
- Foster greater data sharing to accelerate knowledge accumulation and collaboration.
- Increase the diversity of people involved in HIV vaccine research to bring fresh perspectives and innovative solutions.

Roundtable Discussion 2: Reinventing HIV vaccine advocacy in the era of PrEP and U=U

Roger Tatoud highlighted the crucial role of scientists in advocating for HIV vaccine research, emphasizing that good advocacy builds on good science. Despite setbacks and a return to the discovery stage, he noted a promising pipeline with new products and approaches. However, the next HIV efficacy trial is at least a decade away, and the evolving global health landscape adds complexity to vaccine R&D. Tatoud posed the central question of how to advocate effectively for an HIV vaccine amid changing priorities, suggesting focusing on what to talk about, who to talk to, who conveys the messages, and how to convey them. He asked Cairns, who summarized recent PrEP developments, if highlighting challenges in current prevention could support strategically advocating for the necessity of an HIV vaccine.

Cairns highlighted the prolonged timeline for developing an HIV vaccine and emphasized the need for evolving arguments to support its development. He expressed concerns about the perception of PrEP as solely for gay men and cautioned against potential hurdles like stigma and funding shortages hindering fair vaccine development. Scarlatti also pondered the idea of children being better candidates for an HIV vaccine than adults, highlighting the ethical and political challenges. Surprised by limited HIV vaccine research support from Europe, Cairns questioned the comparatively modest investment despite the continent's history of groundbreaking scientific endeavours.

Tatoud noted the challenges of convincing people that there was need for an HIV vaccine. Referring to a recent meeting of European HIV vaccine R&D stakeholders organized by the HIV Vaccine Enterprise, he recalled that having good science was not sufficient to make the case and that there was a need to craft a compelling message that resonated with the intended audience. He noted that complexities of the language surrounding vaccines, such as the use of "vaccine for prevention" and "vaccine for cure" or that long-acting PrEP was "like a vaccine", could be confusing. Tatoud also suggested that we consider the broader context, arguing that relying solely on antiretroviral therapy and the U=U strategy for HIV prevention was not a sustainable solution. He echoed the sentiment of Jim Pickett, who has said that we cannot put the onus on people living with HIV to take their pills for the U=U strategy to be effective.

How can we effectively convey the message that there is a need for an HIV vaccine?

Hanke emphasized the importance of investing in HIV vaccine research, noting that the long-term costs of not developing an effective vaccine far outweighed the initial investment. He called on policy makers and economists to recognize this and support further research efforts. He expressed his frustration with the lack of information and details about the vaccine tested in clinical trials. He said that researchers should provide more information about the vaccines tested, including their components, immunogens and vectors, arguing that this information was

essential for understanding why some vaccines had failed and for improving the design of future vaccines.

Improving communication around HIV vaccine

Tatoud noted that during the meeting, "vaccine" had been used to describe very different concepts and approaches. He said he wondered about the general public's understanding of these different definitions and questioned the importance of such comprehension.

Maureen Luba shared an anecdote about a recent event in Kenya where a miscommunication about the injectable PrEP medication, CAB-LA, being referred to as a vaccine led to increased demand for the product, which is not always readily available. Luba discussed the importance of effective communication and explaining scientific concepts to community members. She emphasized the need for advocates to break down complex scientific information into more understandable terms for laypeople. She said that even with complex HIV prevention strategies, it was crucial to ensure that communities understand how these interventions work. This is essential for fostering trust and future adherence to products.

Ouya discussed the challenges of communicating about HIV vaccine research in today's world. She noted that a generation of people had not experienced the impact of HIV and AIDS, and that there were many competing priorities, such as wars, climate change, hunger and other health crises. Additionally, some well-respected organizations have sent mixed messages about the role of HIV vaccines in ending the pandemic. Ouya also queried when it was appropriate to start involving communities in HIV vaccine research and suggested that even though early-stage research might not lead to a successful vaccine, it was important to keep communities informed about the progress being made. She suggested that community engagement start early, even in the preclinical stages, to ensure that communities were aware of the research and its potential benefits.

Engaging community in HIV vaccine advocacy

Hannah added that a significant challenge lay in clarifying the concept of "community" and pinpointing specific needs within communities. She noted that the broad use of the term could lead to unrealistic expectations for community engagement. Instead, she suggested identifying the community and defining what was needed from it. Hannah pointed out that research funding for HIV vaccines had been substantial and that the science was making progress. However, she also acknowledged that conducting clinical trials in the future might be challenging and that community engagement would be needed to address these challenges.

Tatoud raised questions about the current involvement of communities in HIV vaccine research and development, contending that communities should not be merely recipients but should actively assume a leadership role in the advocacy efforts. He also wondered about the level of interest in HIV vaccine among the community. He challenged the audience to think about strategies to generate interest in an HIV vaccine and to actively engage the community in a more participatory role.

Kyle Gordon highlighted that contextualizing choice presented an opportunity for advocacy. He pointed out that some segments of the community might be hesitant to adopt existing prevention methods, such as CAB-LA, and that ways to make HIV vaccines more attractive to these underserved communities should be explored. Additionally, the HIV vaccine message should be infused into competing priorities. He pointed to the prevalence of challenges such as climate change, food insecurity and housing insecurity and argued for the importance of establishing connections between HIV prevention efforts with these issues, aiming to reach a broader audience.

Ntando Yola acknowledged that currently, the conversation about vaccine research was predominantly within the community itself and emphasized the need to expand this dialogue and involve more interested people. He noted the public's tendency to get excited about sensational events but underscored the importance of sustainable approaches to maintain interest. He highlighted the challenge of making a compelling case for an HIV vaccine amid existing interventions. Yola recognized the valuable contribution of communities engaged in research over the past 30 years and suggested leveraging this group to strengthen the case for a vaccine. Additionally, he emphasized the importance of adapting communication, messaging, and engagement approaches to the current era, highlighting the significance of artificial intelligence and social media in today's context.

Mitchell Warren, while acknowledging concerns, challenged the framing of the question, and suggested focusing on the issues at hand. He expressed confidence in the need for an HIV vaccine, citing ongoing trials and recruitment efforts. Warren highlighted conversations about local vaccine manufacturing, especially in Africa, involving civil society and advocates in initiatives like Afrigen and the WHO mRNA hub. He dismissed the idea of dwelling on the lack of vaccine advocacy, pointing to the evolving field and ongoing efforts for manufacturing capacity. Warren emphasized the need for sustained and sustainable efforts driven by communities, cautioning against flawed arguments that suggested the need for a vaccine due to struggles with other prevention methods like PrEP. Instead, he advocated for strategic advocacy, recognizing the importance of multiple prevention approaches, including treatment and PrEP, alongside pursuing an HIV vaccine.

Gaston Devisich expressed regret about the absence of a near-Phase 3 HIV vaccine trial but saw it as an opportunity to invest in preparing for one. He highlighted research challenges in regions like Latin America and the Caribbean, emphasizing the significant role of the region in studies like Mosaico. Devisich advocated for sustaining conversations about HIV vaccines proactively, avoiding the perception of failure. He stressed the importance of advocacy for diverse and accelerated research, cautioning against a one-size-fits-all approach despite the political appeal of "ending AIDS today". Emphasizing the purpose of trials in high-burden contexts, he called for urgency in developing new preventive strategies, especially for high HIV-exposure populations, noting the continued interest in combined preventive measures despite setbacks.

Jorge Sanchez highlighted the successful community participation in Mosaico across four Latin American countries. These countries, mostly inexperienced in HIV vaccine trials, performed exceptionally well, with Peru being the exception with a trial 15 years ago. Community members

actively engaged with research teams, ensuring widespread community interest and participation. The model showcased the feasibility of community-driven recruitment and demonstrated that reaching out from community to community was a viable approach, even in nations new to vaccine trials.

Approaching vaccine advocacy today

George Valiotis highlighted the role of health managers as intermediaries between policy makers and service providers and emphasized the governance aspect of healthcare decision making. Using RSV prevention as an example, he noted the limited interest in new prevention options despite availability, pointing out that established issues might receive less attention than novel challenges in healthcare. Devisich acknowledged Hanke's point on investing in healthcare for future savings but cautioned that financial arguments might not always yield expected outcomes. He discussed HIV exceptionalism and the need to make HIV more accessible for decision makers, emphasizing the importance of community input in successful implementations like Scotland's PrEP programme. Devisich concluded by addressing the prevention paradox in HIV, advocating for healthcare system redesign and thoughtful considerations for supporting community voices amid defunding challenges.

Tatoud suggested a more comprehensive approach for HIV advocacy, going beyond addressing HIV-specific challenges and aiming to tackle broader issues like antimicrobial resistance, social issues and making a positive contribution to society.

Cairns spoke about the vital role of community activism in responding to HIV and AIDS, driven by a sense of urgency and feeling under attack. He cited ACT UP's confrontational tactics to raise awareness and pressure governments and pharmaceutical companies. The Durban Moment exemplified global activism challenging government inaction. Cairns stressed the importance of alliances with scientists and policy makers. While acknowledging the effectiveness of measures like PrEP, U=U and ambitious UNAIDS targets, he expressed concerns that they might overshadow the ongoing need for an HIV vaccine, as indicated by a UK epidemic study. Aspirational goals, while supported, could impact the perception of the ongoing necessity for an HIV vaccine to eliminate the virus.

How can scientists support HIV vaccine advocacy?

Lu noted a significant communication gap between scientists developing an HIV vaccine and the broader community, including non-scientists, advocates and the public who may eventually receive the vaccine. Especially as a vaccine progresses through different phases of development, this gap has to be bridged. He highlighted the need for collaboration and shared understanding between scientists and diverse communities worldwide, which was crucial not only for the scientific aspects, but also for tailoring clinical trials and gaining community support. Lu acknowledged the inherent value in dialogue for both improving the vaccine development process and ensuring its eventual success and delivery.

Key messages from the participants:

- Effective communication:
  - Ensure sustained, clear, and two-way communication between scientists and communities, recognizing community knowledge.
- Learning and adaptation:
  - Learn from success stories.
  - Embrace effective strategies and explore innovative approaches.
- Community engagement:
  - Create ample opportunities for community engagement, fostering trust at every stage of product development.
  - Widen the "circle of trust".
- Scientific clarity and depth:
  - Dig deeper into the science, conveying a clear and hopeful message.
- Strategic repositioning:
  - Re-present the HIV vaccine to resonate differently with decision makers.
  - Define precise goals and objectives for HIV vaccine research.

Rapporteur session

Rapporteur 1: Maureen Luba

Muturi-Kioi provided a reality check on the current state of the pandemic, highlighting progress, successes and challenges, particularly new HIV acquisitions among the younger generation. Reflecting on lessons from COVID-19 vaccine development, the resounding message from the first roundtable discussion emphasized the ongoing need for an HIV vaccine, even with other interventions like PrEP being available. The optimism surrounding this necessity was tangible, underscoring the commitment to finding a vaccine despite challenges. However, a key challenge emerged – the absence of a clearly defined commitment mechanism, especially from government and the private sector in supporting HIV R&D, prompting a call for reinventing advocacy strategies.

Warren's presentation on the HIV resource tracker delved into funding and the journey of HIV vaccine research. He emphasized the need for continued conversations and highlighted the substantial funding allocated to the field. While acknowledging the well-funded nature of HIV vaccine research, he urged a strategic approach, identifying areas where additional resources could maximize impact and equally developing novel interventional strategies beyond merely seeking more funds. Additionally, he prompted reflection on the pipeline of products, noting the presence of numerous options, but underscoring the ongoing necessity for developing more options, including an effective HIV vaccine and the necessity to maintain current investment levels and diversify funding sources beyond the US government.

The live roundtable discussion, led by Tatoud, highlighted key points, including the importance of increased efforts towards creating spaces for meaningful community engagement and the need for scientists to articulate and simplify complex HIV vaccine research for communities. The discussion acknowledged the growing complexity of the field and urged heightened efforts in

community education. Defining the community and understanding its needs were crucial, as well as emphasizing the value of listening and spending time with communities. Activism in HIV vaccine advocacy was affirmed, with communities actively leading conversations and expressing eagerness for a vaccine.

The roundtable discussion highlighted the importance of advocating for combination prevention, emphasizing the need for an HIV vaccine while recognizing the efficacy of existing products like CAB-LA and providing choices for individuals. Key takeaways included the significance of messaging, particularly in the context of aspirational targets set by UNAIDS. Insightful comments were made regarding the implications of HIV vaccine R&D on healthcare systems, acknowledging the need for careful consideration of financial arguments in these discussions.

The discussion brought attention to HIV exceptionalism, challenging the notion of boxing HIV as something special and emphasizing the need to make it more accessible. The conversation also touched on the design of HIV programmes, highlighting a shift towards a new concept of "test and reach" advocated by AVAC. The key takeaway is the call to sustain current efforts and explore innovative strategies in the evolving landscape of HIV programmes.

Overall, global coordination and collaboration, as well as strengthening political commitments for effective HIV vaccine development, are crucial. Continuous engagement with communities and optimism about finding an effective HIV vaccine were key themes, acknowledging progress, complexities in the field, and a hopeful outlook for the future.

Rapporteur 2: Shan Lu

Lu thanked the IAS for its support to HIV vaccine R&D efforts and acknowledged the well-designed programme for the event, the Enterprise staff, and session leaders for their contributions, extending his thanks to all participants.

Lu commended the speakers for providing valuable insights. **Muturi-Kioi** offered a broad view of the HIV vaccine approach, and **Balinda** presented exciting advancements in mRNA vaccine research, highlighting the growth of early-career African scientists. **Lu** noted the attention to neutralizing antibodies and T-cell vaccines, suggesting more attention be paid to ADCC. He noted the challenges in GMP manufacturing for mRNA vaccines in various countries. **Warren's** summary, particularly on funding status and allocation, was valuable, emphasizing the importance of wise spending and addressing potential reductions in funding following disappointing trial results. **Warren's** summary emphasized the contributions of the HIV vaccine field to broader education and training, leading to successes in areas like COVID-19. He concluded with a call to allocate resources wisely.

The first roundtable explored challenging questions, such as why COVID-19 vaccine R&D succeeded while HIV was still struggling. A comparison of vaccines for malaria, TB and HIV suggested reasons for progress with each. The conversation touched on the role of biotech versus pharmaceutical companies, with a view that pharmaceuticals might not invest without a

suitable product. Moderna's potential interest in HIV investment was important, indicating a positive cycle coming full circle. Lu expressed optimism for the future of HIV vaccines.

The scientific discussion delved into the selection of targets, debating T-cells versus bnAbs, with a consensus that both are crucial. Progress was reported on this front, creating anticipation for further developments. The conversation shifted to mRNA vaccines and the need for accelerated progress while acknowledging safety concerns with mRNA and challenges of release manufacturing, especially when expanding mRNA vaccine production globally. Participants discussed the potential usefulness of discovery medicine trials for generating valuable information.

Participants delved into the importance of sterilizing immunity for an HIV vaccine, and reached consensus that sterilizing immunity is crucial for an HIV vaccine. The role of mutation in the context of HIV vaccine development was highlighted, with a perspective that sterilizing immunity holds greater importance for HIV than for other vaccines. Participants explored the complexity of the immune system, expressing the need for further understanding. The discussion touched on the question of whether to continue with the current vaccine approach or explore alternative systems despite the existence of knowledge gaps. Anticipation of more combination vaccines was expressed, but the challenge lies in finding platforms to exchange ideas. The value and role of the Enterprise remain to be determined in the current HIV vaccine research and development landscape and require feedback from decision makers.

Participants raised critical questions about the need for a more organized and well-managed approach in the field of HIV vaccine development, encompassing policy, priorities and technology. These suggestions emphasized the importance of adopting an industry approach for effective management. The dominant optimism was seen as a driving force for continued engagement and collaboration. Concerns were voiced about the lack of a systematic approach for efficacy trials, extending beyond funding issues to encompass the entire process. Lu noted that the roundtables were lively, with key messages emphasizing the importance of maintaining optimism, open-mindedness and exploration of topics that may have been overlooked. Lu concluded by saying that the meeting was valuable and calling for similar engagements in the future.

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