

Malaria Vaccine Technology Roadmap Stakeholder Meeting III Summary Report



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Please submit comments to:

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This report presents a summary of discussions that occurred at the third Malaria Vaccine Technology Roadmap Stakeholder Meeting. This meeting was held on August 23, 2005, in Oxford, United Kingdom, in conjunction with the 2005 Gordon Research Conference on Malaria. During the meetings, speakers shared preliminary Roadmap results and facilitators solicited input from a broad group of stakeholders. In total, more than 60 stakeholders from 16 countries participated in this meeting. The contents of this report reflect the opinions and comments heard during this meeting. The PowerPoint presentations given at the meetings are not summarized in this document but are posted separately at <http://www.MalariaVaccineRoadmap.net>.

Inputs gathered during the meeting will be combined with other input gathered as part of the overall roadmap process. This information will be used to create a draft Malaria Vaccine Technology Roadmap that will be circulated later in 2005 for community discussion and review.

Speakers

- Dr. Andy Waters, Chair, 2005 Gordon Research Conference on Malaria
- Dr. Ruth Branston, Scientific Programme Officer, The Wellcome Trust
- Dr. Doug Holtzman, Senior Program Officer, Infections Diseases, The Bill and Melinda Gates Foundation
- Dr. Zarifah Reed, Initiative for Vaccine Research, World Health Organization
- Mr. Jack Eisenhauer, Senior Vice President, Energetics Incorporated

Summary of Key Themes

While the TRM process may be useful in sharing information and bringing scientists together to improve progress toward a malaria vaccine, more funding is needed to affect real change in the rate of progress. Hopefully the Roadmap can be used to attract more funding to malaria vaccine research.

The Roadmap specifies that it stops short of considering vaccine delivery issues. This statement refers to delivering vaccines to people, as opposed to vaccine delivery systems, which are within the scope. This statement should be clarified in the Roadmap.

The Roadmap specifies goals for producing a vaccine with efficacy against severe disease. Clinical trials that can measure severe disease will require very large trials (5,000-6,000+ participants). The step from trials measuring clinical disease to those measuring severe disease is huge in financial terms and the number of trial participants required. However, Phase 2b trials can be done to screen out candidates that can't deliver efficacy against clinical disease. It is reasonable to assume (but not guaranteed) that these candidates are unlikely to offer protection against severe disease if they do not protect against clinical disease. Further, surrogate markers (e.g., severe anemia) can be used to measure severe disease in proof-of-concept trials. The Roadmap should explicitly state that surrogate markers will likely be needed to measure vaccine candidates' protective efficacy against severe disease.

Poverty is a critical problem in many malaria endemic areas. Malnourishment hinders parasite clearing by weakening immune systems. Measles is an example of this problem. A vaccine for child-bearing age and pregnant women may be able to protect unborn children.

We have heard in 1970, 1980, and 1990 that a malaria vaccine is 10 years away. A new approach is needed to prevent us from making the same empty promise again today. The roadmap would benefit from more skepticism to avoid hype.

Discussion of Initiative #1: Improve Understanding of Immune Response and Parasite-Host Interactions

- All can agree that there is a great need to improve the understanding of immune response and parasite-host interactions. During the last few years the amount of information available through genomics and other new techniques have greatly expanded knowledge in this area. This knowledge will lead to an explosion in new and deeper understanding of parasite biology and parasite-host interactions.
- The real challenge is converting this new understanding into criteria that help to prioritize vaccine candidates by distinguishing the most promising candidates. The connection between a more complete understanding of parasite biology and distinguishing promising malaria vaccine candidates is not obvious. This connection will be increasingly important as new vaccine concepts and candidates emerge. Scientists cannot test the handful of vaccine candidates existing today due to the time, costs, and other resources required; as the number of potential vaccine candidates grows this limitation will become increasingly significant. A method for applying limited knowledge in an open way to establish criteria and move those that rate highly into Phase 2b trials is urgently needed. Such a process should be open and consultative, and it should employ a healthy dose of skepticism while avoiding individuals promoting their preferred candidates. Independent advisory committees may be the best way to proceed with this process. The criteria should themselves be regularly questioned and reconsidered as trials occur and new information is available.

Discussion of Initiative #2: Identify Correlates of Protection

- “Correlates of protection,” as written, is too narrowly defined. It should refer to how to induce appropriate immune responses, including induction of memory. The goal is effective mechanisms of inducing an immune response that improves upon natural resistance.
- Many small studies have been done that examined responses to one or two antigens. Such studies have been limited in value as isolated studies, in part because of their small size. A systematic review (e.g., “Cochran” review) could yield additional information. Protein arrays can help scientists identify a range of responses and increase overall learning. Good epidemiological data for the past studies is needed to get the most out of such an analysis.
- The use of high-quality antigens and standardized functional assays (e.g., growth inhibition assays) across studies could facilitate the identification of correlates of protection. Such assays may be housed in a central facility to encourage accessibility; this facility would likely not be affiliated with an academic institution. Similar centers have been established in other areas and could serve as models; the group strongly agreed on the need for such an approach. New standard assays are also needed for new antigens that are emerging as possible vaccine candidates. Further, while functional assays to identify antibody response have been done in bulk, assays to measure cellular response are more challenging but also needed.
- Revisiting passive antibody transfer work (McGregor) using well-characterized monoclonal antibodies could help scientists identify protective antigens. Many studies done on MSP-1 in natural infection have not yielded clear results.
- There are two needed growth inhibition assay reagents: transvectants that would enable detailed examination of fine specificity of polyclonal responses, and more human monoclonal reagents to define in functional assays for growth inhibitors.

Discussion of Initiative #8: Balanced Global Portfolio

- The balanced global portfolio is intended to create a balanced scientific approach. There are many opinions on what the best scientific approach to malaria vaccines is today. This balance will be driven by funding organizations. European government funders have lagged behind American agencies in investing in malaria vaccine research. However, European funders tend to invest more heavily in field research. These differences factor into the overall global portfolio balance. Individual funders will of course remain in control of their own funding decisions in support of their missions. The Roadmap can help to point out where their missions fit into the overall malaria vaccine research and development universe.
- The Roadmap is expected to help the malaria vaccine community develop a more balanced global portfolio of vaccine candidates. However, how it does so remains to be seen. There may be a need for independent advisory committee structures, peer reviews, and coordination among funders and other stakeholders on the supply side. Incentives, price, and other economic actions needed to stimulate demand for a malaria vaccine should be considered now so they are in place when a vaccine becomes available.
- Another unresolved question is determining how any new resources attracted to malaria vaccines by the Roadmap is allocated and spent. It is clear that the Roadmap is *not* attempting to establish a centralized enterprise that has a common pool of money.

- Within a managed, balanced global portfolio, how will the tension between collaboration and competition amongst scientific groups be handled and maintained?
- The Roadmap puts forth two goals, one for 2015 and a second for 2025. Care should be taken to ensure these goals are pursued in a complimentary manner and that the risk of success or failure in reaching the first goal by 2015 is properly considered. Additional milestones may help to further clarify the progress sought between now and 2025 in pursuit of both goals.

Group Discussion: Roadmap Implementation

The Roadmap can lead to several outcomes, including:

- attracting new funds from current and new funders
- informing current funders about the scientific community's priorities
- providing a stimulus and incentive for people to aggregate into consortia to achieve critical mass needed to pursue biggest issues
- self-justifying the work researchers are already doing, without actually changing behavior
- showing researchers how their work fits into the bigger picture and leads to product development, helping to make their work more relevant
- encouraging collaboration by linking researchers that may be working on related problems
- sharing information about what other researchers are doing and where progress stands in a dynamic way over time

The issue of creating an organization to guide and manage the Roadmap's implementation has been discussed at previous TRM meetings. Many in the community have advocated a coordinating role rather than a centralized enterprise model that directly control funds. A "lighter touch" that goes beyond ad hoc coordination is most likely. The MALVAC group of malaria funders is in the process of discussing how best to implement the roadmap from an organizational standpoint. It was recognized that funders are likely to maintain their individual funding processes while acting together in a more coordinated way toward shared goals.

Bringing independent working groups together to develop more detailed plans around the initiatives may be a logical first step. Others noted that some activities called for in the TRM are already being addressed (e.g., standardization and development of assays).

The HIV Vaccine Enterprise has in the last year issued two new calls for applications, leading to large amounts of new funding. While the hope is that new funding will become available through the Roadmap process, the HIV experience was different. With the HIV Enterprise, funding was made available first and technical plans developed to determine how best to utilize that funding. The scientific plan developed in that exercise has many similarities to the Roadmap. However, the approach taken here was to identify the important issues first and then approach funders to frame resources based on the consensus of the scientific community. This process must also consider how funding malaria vaccines will affect malaria research collectively. Funders can't be led to believe vaccines are the only answer – other interventions must be acknowledged.

The TRM process does not end with the publication of the Roadmap document. One key to success will be maintaining the dialogue among the scientific community.

Other Comments

- Some participants feel the Roadmap was a plan set in stone and are wary of “grand schemes” that have failed in the past. This is not the case for this Roadmap effort, a point that should be strengthened in the front of the document when explaining the purpose of the effort. One key to success will be continual dialogue with the community.
- The front end of the Roadmap should more clearly describe that this Roadmap addresses only one piece of the overall malaria problem. The malaria community recognizes that other issues (e.g., vector control, pregnancy vaccines, drugs) are also important and will likely make greater impacts on reduction of malaria in the near term. The Roadmap should avoid implying that vaccines are the only answer and emphasize that other techniques should be supported as part of a comprehensive approach to malaria control and prevention.
- Some participants were concerned with the Roadmap’s focus being too prescriptive and threatening to the academic base research in this area. Strong academic structures are needed to bring new minds into the malaria vaccine field. People were concerned that the TRM will perturb this process. Others felt that academic research would benefit from greater focus while maintaining a degree of academic freedom. The Roadmap may end up favoring a quasi-industrial approach to big science that individual academic groups may or may not wish to pursue. The TRM identifies the activities that will feed into product development, but it makes no judgment on the validity or appropriateness of all other activities that are ongoing. Further, the ten initiatives call for a great amount of innovative research and should not be expected to seriously distort funding.
- Greater involvement in the malaria vaccine community from endemic countries, both in terms of funding and performing work, is needed. It is critical to engage with the leadership and decision-makers in endemic countries so they are prepared for a malaria vaccine once it becomes available. One way to stimulate this involvement is by continuing to engage endemic country representatives in the TRM process.

List of Participants

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