BIO
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

June 14, 2012

Lonnie King, D.V.M.
Chair
Committee on Identifying and Prioritizing New Preventive Vaccines for Development
Institute of Medicine
500 Fifth Street, NW
Washington, DC 20001

Re: Ranking Vaccines: A Prioritization Framework

Dear Dr. King:

The Biotechnology Industry Organization (BIO) appreciates the opportunity to comment on the Institute of Medicine's (IOM's) new report entitled, *Ranking Vaccines: A Prioritization Framework*, which was developed for the National Vaccine Program Office (NVPO).[1] BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products. BIO membership includes both current and future vaccine developers and manufacturers who have worked closely with the public health community to support policies that help ensure access to innovative and life-saving vaccines for all individuals.

BIO commends this worthy effort to improve the process for identifying and prioritizing new preventive vaccines for development. The SMART Vaccines software has the potential to help governmental, non-governmental, and commercial enterprises reach consensus regarding mutually beneficial priorities and collaborations which will guide the future investment of resources. Today, on average, a new vaccine takes 8 to10 years and over $1 billion to develop. The advanced vaccines of today are even more challenging to make as they often require very complex technologies to address new diseases and indications that were not able to be conquered with more traditional vaccine methods. Due to high development costs and lengthy processes, BIO believes that it is critical that limited resources are spent on vaccines that are considered priorities by many immunization stakeholders.

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[1] Institute of Medicine. Ranking Vaccines: A Prioritization Framework – Phase I: Demonstrations of Concept and a Software Blueprint. May 10, 2012. Available at: http://www.iom.edu/Reports/2012/Ranking-Vaccines-A-Prioritization-Framework-Phase-I.aspx.

Recommendations

SMART Vaccines is a subjective, user-reliant model. As such, it should be used in an appropriate and transparent manner to aid and clarify the vaccine prioritization process. To help increase the utility of this tool for vaccine developers and manufacturers, BIO supports and recommends the following:

1. BIO recommends users, including the U.S. government, make inputs and rankings transparent to industry to help companies understand how major purchasers, regulators, and policy makers perceive future markets and to inform private sector investment decisions;

2. BIO recommends that the IOM Committee and NVPO carefully consider how frequently SMART Vaccines will be used to inform prioritization;

3. BIO recommends that the SMART Vaccines model be modified to account for the quality of data used;

4. BIO supports the use of a multi-attribute utility approach for the SMART Vaccines software and recommends the addition of several attributes, including "likelihood of a recommendation for routine use by the Centers for Disease Control and Prevention (CDC)"; and

5. BIO supports the public release of SMART Vaccines 1.0 to allow companies and other users to test the software using various vaccine candidates.

1. BIO recommends users, including the U.S. government, make inputs and rankings transparent to industry to help companies understand how major purchasers, regulators, and policy makers perceive future markets and to inform private sector investment decisions.

BIO strongly supports the overarching goal of SMART Vaccines, which is to serve as a decision-support tool that facilitates discussions about attributes and values among diverse users, helping them converge on a list of priority vaccines to be developed for domestic and/or international use. Vaccine companies already use internal prioritization models to direct investments in research and development (R&D), and these models include factors such as a company's product portfolio, technical and scientific expertise, and existing platforms that impact investment decisions. Yet, SMART Vaccines could provide additional utility to companies by sending a strong signal regarding the priorities of their customers, particularly governments, the World Health Organization, and non-governmental organizations (e.g. the Bill and Melinda Gates Foundation).

However, SMART Vaccines will not create one unified list of priority vaccines. In fact, it will likely create a different priority list for each user based on variations in data inputs

and the attributes selected and ranked by users when they run the software. Therefore, the development of this tool reinforces the need for vaccine companies, government agencies, and other stakeholders to continuously work together to reach consensus regarding priorities for vaccine development. To realize the full utility of this tool, users' data inputs and rankings should be fully transparent to industry to help companies understand how major purchasers, regulators, and policy makers perceive future markets and to inform private sector investment decisions.

2. *BIO recommends that the IOM Committee and NVPO carefully consider how frequently SMART Vaccines will be used to inform prioritization.*

BIO has some reservations regarding how often the SMART Vaccines tool will be used to update vaccine priorities in the context of the long development timelines for vaccines. As previously noted, vaccine development is resource and time intensive, requiring up to $1 billion over a decade. Companies assess their target product profiles at major development milestones, such as before Phase I, II, and III clinical trials, to determine whether additional investments should be made. The SMART Vaccines tool could provide helpful feedback at these points in time.

Thus, vaccine prioritization, guided by SMART Vaccines, may help inform a company's initial decision regarding development of a specific product, and updates to data inputs used in the model, such as epidemiological data, may guide critical investment decisions at later stages in the development process. However, vaccine prioritization also has the potential to derail product development and undermine the value of the prioritization process if undertaken too frequently or without good reason. Thus, it may be helpful for the U.S. government to have discussions with vaccine developers about the appropriate intervals for the reassessment of vaccine priorities through a transparent process.

3. *BIO recommends that the SMART Vaccines model be modified to account for the quality of data used.*

As acknowledged in the IOM's report, the utility of SMART Vaccines is highly dependent on the quality of data used in the model. However, vaccine development is a highly uncertain process, and this is reflected in the data related to vaccine characteristics, especially during the early stages. For instance, meaningful data on safety and adverse events is unavailable until late in development (e.g. Phase III of clinical trials) or after licensure by the U.S. Food and Drug Administration. Epidemiological data is also often uncertain or subject to change over time, especially data on emerging infectious diseases, and governments should continue to invest heavily in disease surveillance to increase the quality of this data.

To address variations in data quality, BIO recommends that the SMART Vaccines value score for each vaccine candidate be divided into two parts, as suggested by a representative member of the National Vaccine Advisory Committee at the meeting on June 5th. One part of the score could account for attributes that are more or less constant

or can be accurately projected (e.g. population data, availability of alternative public health measures). The other part of the score could include attributes that are highly variable, uncertain, and/or difficult to estimate (e.g. disease burden, adverse events, length of immunity). As more data becomes available, either through clinical, epidemiological or disease burden studies, the weight for these variables can be shifted to account for the increased certainty. This modification to the model may provide more informative and appropriate value scores and priority rankings for industry and other users.

4. *BIO supports the use of a multi-attribute utility approach for the SMART Vaccines software and recommends the addition of several attributes, including "likelihood of a recommendation for routine use by the CDC."*

BIO supports the use of a multi-attribute utility approach for the SMART Vaccines software. Compared to previous prioritization models, this modeling framework more accurately reflects the complexity of the actual decision-making process by accounting for a broad range of real-world considerations. However, the IOM's list of attributes is not exhaustive, and BIO recommends the addition of several attributes.

As BIO noted in July 2010, attributes such as "the existence of treatments" and consideration of their effectiveness, acceptability, and cost, and the "likelihood of a recommendation for routine use by the CDC" should be included among the choices. The latter is an increasingly critical business consideration for vaccine manufacturers. Unlike other U.S. healthcare markets, the government largely defines the economics and potential market for new vaccines based on recommendations made by the CDC's Advisory Committee on Immunization Practices (ACIP). The CDC's recommended immunization schedule is used by providers to guide clinical decisions regarding vaccination and by public and private insurers to determine vaccine coverage, thereby significantly impacting uptake of vaccines by patients.

ACIP recently adopted a new framework to guide the recommendation process called GRADE or Grading of Recommendations Assessment, Development and Evaluation. Like SMART Vaccines, GRADE is a decision-making tool that takes into account multiple factors, such as the expected health impacts, the balance of health benefits and risks, and health economic analyses. From the IOM's report, it is unclear how SMART Vaccines and GRADE will function in relation to each other, or how SMART Vaccines will function in relation to other international evidence-based recommendation tools. BIO believes that these tools should work harmoniously to ensure consistency in the prioritization and recommendation processes and to reduce any potential confusion among stakeholders and users.

Regarding the attributes the IOM selected for SMART Vaccines Beta, BIO strongly supports the inclusion of several attributes that represent the value of vaccination. As stated in the report, the overall value of vaccination has not been captured in previous prioritization models, as these models have looked only at short-term benefits and have

not taken into account the many intangible effects related to the long-term benefits of vaccination, such as the economic and educational benefits to individuals as well as society. When they stand alone, cost-benefit and cost-effectiveness analyses fail to capture the full return on investment in vaccination, as many of these intangible societal benefits are difficult to quantify in dollar amounts or units. BIO applauds the IOM's inclusion of multiple health and economic considerations, such as annual net workforce productivity gained and annual net direct costs or savings of vaccine use, in the model to more fully capture the value of vaccines.

5. *BIO supports the public release of SMART Vaccines 1.0 to allow companies and other users to test the software using various vaccine candidates.*

While BIO appreciates the thorough explanations related to modeling strategy and software development provided in the report, we look forward to the future release of SMART Vaccines 1.0 following Phase II of the IOM's study. The ability to test this software will allow commercial vaccine developers and other users, such as CDC and ACIP, to provide valuable input regarding the capability, functionality, and real world feasibility of this model. It would also be informative to test the model using a candidate such as rotavirus vaccine, which would facilitate an evaluation of the harmony between SMART Vaccines and recommendation tools like GRADE. Rotavirus vaccine has been widely used by the CDC to illustrate the new GRADE process and would therefore provide a useful point of comparison.[2]

Conclusion

While we anticipate SMART Vaccines informing discussions with government agencies and other stakeholders, companies are likely to continue to use their own internal prioritization models, which account for additional factors that impact investment decisions, such as a company's product portfolio, technical and scientific expertise, and existing platforms. However, SMART Vaccines could also be used by companies in the future to inform the internal prioritization process at various stages of product R&D.

BIO appreciates the opportunity to comment on the IOM report, *Ranking Vaccines: A Prioritization Framework*. We look forward to working with IOM, NVPO, HHS, and public health stakeholders during Phase II of the IOM's study and thereafter. Please do not hesitate to contact us for further information or clarification of our comments. Thank you for your attention to this very important matter.

With sincerest regards,

Kelly Cappio

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[2] http://www.rki.de/DE/Content/Infekt/Impfen/Workshops/Ahmed-ACIP-GRADE-WS-Sept-2011.pdf?__blob=publicationFile.

Manager, Vaccines & Biodefense Policy
Biotechnology Industry Organization
202.292.4681
kcappio@bio.org

cc: Dr. Bruce Gellin
Dr. Angela Shen