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Report on the Immunization and Vaccines Related Implementation Research (IVIR)

Advisory Committee Meeting
Geneva, 25-26 September 2012

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1. Executive Summary

- The sixth meeting of the IVIR advisory committee was held 25-26 September 2012 in Geneva, Switzerland. The name of the advisory committee has now been changed from QUIVER (Quantitative Immunization and Vaccines Related Research) to IVIR (Immunization and Vaccines related Implementation Research) so that it can incorporate immunization systems issues as well as quantitative methods in evaluating vaccine performance.

- WHO is in the process of developing an Implementation Research priority setting framework. They have set up an ad hoc working group and are in the process of prioritizing the research questions. IVIR is positive about the priority setting approach and methods used. However, the members feel that more thought should be given to whether or not to shorten the list of proposed research questions to be prioritized (currently 86 priority questions) and reformat the questions to reduce the burden on the respondents. In addition, IVIR believes that a wide number of stakeholders should be involved, particularly from the countries and each of the six WHO regions.

- The Johns Hopkins School of Public Health International Vaccine Access Center is using Value of Statistical Life (VSL) to value a fatality or injury prevented through vaccination in monetary terms. IVIR members believe that Cost Benefit Analysis (CBA)/Value of Statistical Life (VSL) and Cost-Effectiveness Analysis (CEA) address different questions and that VSL has not been as widely used in the health sector. They believe that there are technical challenges to the measures that have not been fully addressed. The committee believes that VSL may provide valuable complementary information, but should not be used as the primary basis for priority setting in vaccines at this time. In theory, the VSL method is appropriate to decide whether a vaccine should be introduced, but empirical evidence is lacking, particularly in low- and middle-income countries (LMICs). The IVIR-AC recommends conducting case studies using both CBA/VSL and CEA for economic evaluation of vaccine introduction using similar datasets in LMICs.

- WHO established a working group to assess yellow fever disease burden. Improving evidence on yellow fever will help inform decisions about vaccination as well as GAVI decisions about investment. The working group is tasked with providing information on published and unpublished sources of yellow fever data and to provide input into the methods used to estimate burden in Africa. Imperial College London was commissioned to coordinate and carry out the work. The working group proposed two approaches to estimate burden of disease: (1) estimate the annual risk of infection from the age distribution of observed cases; and (2) estimate the basic reproduction number from reported outbreak sizes. Preliminary estimates are expected to be presented to WHO and

partners in late October with final estimates by the end of 2012. Next steps will be the evaluation of yellow fever control strategies, support policy-making, and peer-review publication. It was noted that it will be important to distinguish between yellow fever and jaundice possibly due to other causes.

- Work on the broader benefits of vaccination addresses requests from external stakeholders as well as in-country decision-makers, such as Ministers of Finance, for outcomes of economic evaluations beyond traditional measures (e.g., cost per QALY/DALY). The intended outcome is to develop tools and methods that could capture broader impacts of vaccination in a way that is useful to stakeholders and feasible to measure. So far, this work has involved two expert consultations (Toronto 2011 and Geneva 2012), a stakeholder survey, and a literature review. In addition, four groups have responded to a request for proposals to develop innovative tools and have begun conducting their proposed packages of work. IVIR members recognize that measurement of broader economic impact of vaccines is important to estimate and thinks that the proposed theoretical framework is appropriate. However, it is more difficult to estimate indirect effects of vaccines – i.e., the specific mechanisms to deal with confounding have not yet been worked out and there are deficiencies in basic data. IVIR recommends that there should be a continued effort to try to find better mechanisms to measure these causal relations. It is also important to think about including variables that measure broader impact in the design of RCTs to improve the likelihood that indirect effects can be evaluated.

- WHO is continuing to support an investment case for measles and rubella eradication. IVIR is encouraged by the investment in properly modeling eradication before the measles end game is reached. However, they continue to emphasize the need to consider heterogeneity in vaccine uptake, which is a key driver during the eradication phase. This requires models that do not simply aggregate entire populations, as well as exploration of the behavior of vaccine refusers and hard-to-reach groups within individual countries. It is also important to conduct an assessment of risks associated with elimination campaigns, issues associated with first dose vs. second dose, and costs of outbreaks. IVIR suggests that data from the experience of the Americas in eliminating measles and rubella could be evaluated and used for some of these risk assessment analyses.

- WHO has developed a cervical cancer prevention and control costing (C4P) tool. IVIR reviewers believe that the methods used in the WHO C4P tool are appropriate. They feel that the costing tool could be very helpful for national program managers in planning for the introduction of HPV vaccination, as well as screening and treatment once that module is completed. They suggest some modifications that could further enhance the tool: (1) include an optional module for capturing societal costs (user and indirect/productivity costs); (2) provide a sensitivity or scenario analysis, including allowing for different vaccination schedules; (3) include more monitoring and evaluation costs, particularly for cancer registries for the screening and treatment module; (4) include an optional module for local data collection for countries that have decentralized health systems; and (5) add more information on cost calculations to the user guide.

- A proposal to use emulation in order to incorporate transmission dynamics (herd immunity) into static models of immunization (such as WHO-CHOICE's PopMod, PAHO's TriVac, and LiST) was presented. The plan is to use PopMod as an exemplar, and incorporate herd effects from a dynamic model of rotavirus vaccination into PopMod. An emulator would then be used to allow PopMod to model parameter sets that had not been explicitly used in the original dynamic model. IVIR members believe that both static and dynamic models have benefits and drawbacks. The proposed approach is to merge the emulator with the static model. This approach has promise but also has some drawbacks. IVIR members suggest that the model be pilot tested. They also feel that there should be some exploration of what would be required to provide the kind of modeling tool that will incorporate the benefits of static and dynamic modeling.
- WHO commissioned a study on the burden of disease of varicella and herpes zoster. IVIR members believe that the proposed methods to investigate the burden of disease of varicella and herpes zoster are appropriate but are concerned about the lack of data, especially in African countries. For this reason, they suggest that the working group evaluate other existing seroprevalence data, as well as data from Latin American countries that have introduced varicella vaccine. Even in the absence of hard data, modeling can play a role in estimating the impact of vaccination. IVIR members also suggested some medium-term solutions to the lack of data: (1) include zoster in existing surveillance systems; and (2) test for varicella antibodies in existing serum samples in Kenya and other countries.