expertise. Curricula cover all the regulatory functions, and new training curricula are developed as needs arise. Currently a training curriculum on testing of conjugate vaccines is being developed and the training course on lot release is being updated. A course on clinical evaluation of vaccines has been reformatted to focus on authorization of clinical trials and a new course on Good Clinical Practice (GCP) inspection has been developed by the Developing Countries Vaccine Regulators Network (DCVRN) (see below). The impact of training in raising the expertise of the NRAs and the progress of NRAs in developing their systems is measured through follow-up visits or reassessment at regular intervals. More than 2000 staff have been trained through intercountry courses that were conducted in all WHO regions and involving experts from 80 countries.

Step 5: Monitoring the Impact

GTN follow-up workshops and visits were conducted to monitor implementation of IDPs. The GTN was helpful in building a roster of regulatory experts for conducting assessments and follow-up visits and providing decentralized training. There is now a core of technical expertise from 90 countries available to other countries upon request. There is an Advisory Committee on Training that meets every two or three years to review progress in training as well as to identify improvements for strengthening NRAs. Several regulatory authorities in industrialized countries that have already implemented a strong and efficient regulatory system have reliable skills and expertise to assist developing countries. Countries from the European Union (France, Belgium, Germany, United Kingdom, Italy, the Netherlands) as well as Russia, United States, Canada, and Australia have contributed actively to this process.

On the basis of assessments, WHO can determine the impact of the NRA strengthening initiative by monitoring the number of doses of assured quality. Currently, of the approximately 12.3 billion doses of vaccine in use in the world, 8.6 billion (70%) is of assured quality (Fig. 2).

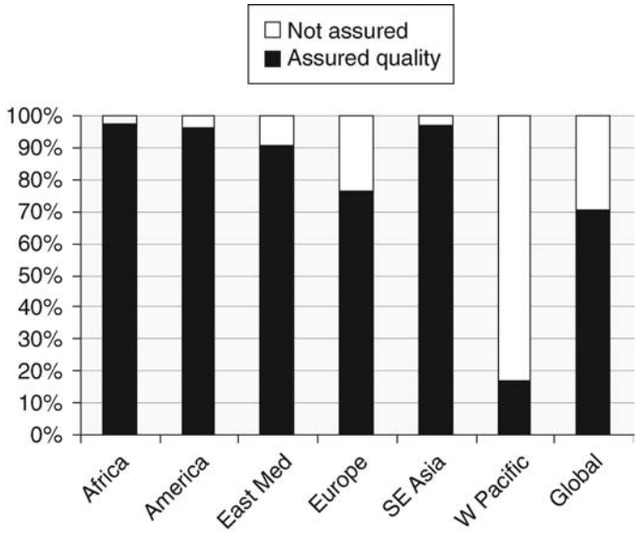

Figure 2 Proportion of vaccines of assured quality by region, 2007.

The NRA strengthening initiative has been largely responsible for the emergence of vaccine manufacturers from developing countries on the global market; in addition, the converse is true: The existence of emerging manufacturers of vaccines has triggered the strengthening of the NRAs of their countries so that production is properly regulated.

PREQUALIFICATION OF VACCINES

The vaccine prequalification system was formally put in place within WHO in 1987 to provide advice to UN procuring agencies on the quality, safety, and efficacy of vaccines for purchase. Currently, a total of 124 countries are served by UN procurement agencies, 90 through UNICEF Supply Division, and 34 through the PAHO RF. This accounts for approximately 58% of the total population receiving vaccines of assured quality.

Because of the importance of oversight of the manufacturer's NRA for prequalification of a product, a new policy endorsed by an expert committee in 2004 requires a mandatory assessment of NRAs in all the countries for which prequalified vaccines are listed and in countries where manufacturers intend to apply to WHO for vaccine prequalification. The steps of the current prequalification process, described in a WHO publication (22), begin with an assessment of the overseeing NRA, to ensure that it is functional. If it is, WHO reviews the manufacturer's product summary file, which describes the product, the production process, the facilities, the quality system, and clinical and nonclinical data generated to demonstrate its safety and utility for the intended purpose in the target group. The written standards developed by the ECBS are one of the bases for developing specifications for the procurement tender document. WHO provides independent testing to confirm consistency of final product characteristics and to ensure that the product meets the specifications in the relevant tender, and organizes a site visit to the manufacturing facilities to assess compliance with GMP and to verify the information in the file. Agreements are reached with the manufacturer and the NRA on continuing responsibilities, reporting requirements, and shipping and packaging specifications. Figure 3 shows the current dependence of the prequalification process on NRA status.

Once prequalification status has been conferred, the continuing oversight of the prequalified vaccine falls under the responsibility of the relevant NRA. When the vaccine is reassessed, a process that happens at prescribed intervals to maintain prequalification status, by a WHO team of experts, generally NRA representatives participate either as observers or as team members during the site visit. The information gathered during the reassessment both from review of an updated product summary file and at the time of the site visit serves as feedback on the NRA performance with regard to the oversight of the specific product and leverages further improvement.

In the past, most prequalified vaccines were produced in industrialized countries. An outcome of the prequalification process is that it sets up an independent and unbiased method to evaluate vaccines proposed for purchase no matter where they are produced—thus allowing emerging suppliers to compete on the international market. The result of this is that the number and percentage of vaccines, both traditional and new, coming from emerging suppliers, whose prices may be lower, and who may be able to supply basic vaccines in larger