The World Health Organization (WHO) convened a three days informal consultation of experts from 17 to 19 December 2007 in Geneva. The meeting examined progress that has been made over the past 10 years (1997-2007) in a WHO project, managed by the Immunization, Vaccines and Biologicals Department, to strengthen vaccine regulatory capacity in countries, and to provide guidance for the future of the project. The participants were from National Regulatory Authorities (NRAs), National Control Laboratories (NCLs), national pharmacovigilance centers, and national immunization programmes representing 25 countries, all WHO regions, together with representatives from institutions such as the European Medicines Agency (EMEA), the Pharmaceutical Inspection Convention/Scheme (PIC/S), and the Government of Canada.

Over the 10 year period, the vaccine regulatory system has been reviewed in 86 countries; some of these countries have had more than 10 WHO visits. More than 1 000 technical personnel have been trained through a Global Training Network (GTN), that was initiated in 1996. On the basis of this experience, a robust system of evaluation and documented methodologies to conduct an assessment of a national vaccine regulatory system has evolved, and is now available for countries to use for self-assessments. Over 400 regulatory experts have been identified to conduct assessments and a global database has been compiled for these people to serve on a roster for WHO. The impact of the vaccine NRA strengthening project has been twofold – the establishment and strengthening of functional NRAs (Table) according to their respective levels of need, and a flourishing number of manufacturers particularly in the developing world capable of supplying vaccines of assured quality. The programme now supports the United Nations vaccine prequalification system. Indeed, it is a mandatory pre-condition for prequalification of a vaccine that the producing country has an assessed and functional NRA before prequalification can start.

For the future, five main themes were identified that, if addressed, will build upon the achievements outlined above, and will strengthen the project, and hence regulatory oversight of vaccines within countries. These are:

1) to develop a process to ensure appropriate and consistent training of newly recruited experts for the WHO assessments since the standards of the experts, and their experience and understanding of the vaccine regulatory process, inevitably vary.

2) to increase harmonization of the WHO assessment procedures for national regulatory oversight of vaccines and for drugs. A dual system of assessment (drug and vaccines) will create confusion amongst the NRAs and those who have to make policy decisions, and there will be fatigue, confusion and frustration amongst those reviewed. On the other
hand, increased harmonization will potentially benefit countries, simplify the process and facilitate synergies in management of both projects.

3) The institutional development plan (IDP) is an important and necessary outcome of the review process. It has considerable potential for increasing the capacity of individuals within the NRA and for training them. It also has bearing on improvement of systems, and within-country management. The IDP needs to contain commitment from countries regarding human resources, development of facilities, sustained financial support, political involvement and buy-in. The IDP should specify follow-up, with specific timelines, and it should be based on sound practices such as the GTN and other training activities. The IDP also places obligations on WHO to facilitate follow-up activities and more recognition of the role of the WHO Regional Offices is encouraged. For this purpose, WHO/HQ and regions should use these IDPs to a greater extent to monitor progress and coordinate support to national vaccine regulatory systems. Joint ownership of the IDP, between the country and WHO, is the best assurance for achieving sustained improvement.

4) There is need to continue to increase the involvement of the WHO Regional Offices in the vaccines NRA strengthening project. It is not suggested that NRA assessments for WHO vaccine prequalification purposes should be a regional activity; that is the responsibility of WHO at headquarters. However the WHO regions have much to contribute to the NRA assessment review process, especially assessments that are primarily intended for capacity building.

5) Vast amounts of data have been generated during the course of the project. These data are a valuable research resource, potentially for health systems strengthening research, and should be further analysed. The computerized database has an enormous potential, particularly for planning, understanding resource needs, and for developing evidence to guide policy makers.

The WHO NRA assessment process depends on the quality of it's assessors and it was recommended to assess the assessors in order to sustain the system credibility. In general, the competence of the experts has been high, and their approach objective. However, there is more to be done to assure that in the future a thorough understanding of the tools and their application, and consistency between assessors are sustained. It was noted in the meeting that the WHO is not the only institution with experience in capacity building of vaccine NRAs. The delegate at the meeting from the EMEA shared the experience with the European Union/European Economic
Area Benchmarking of European Medicines Agencies (BEMA) project. A concept of performance maturity levels is applied by the BEMA. The merits of this approach are that it allows for standardization across disciplines and activities, and it's success depends on training and uniformity of standards. Most importantly, it addresses consistency of assessment approach and of the assessors. The applicability of these approaches will be explored for the WHO model especially concerning guidance to and training of assessors.

Every NRA assessment requires a team leader. Traditionally, that function has been assumed by a WHO staff member with a thorough knowledge of the system. The team leader minimizes subjectivity and ensures standardization. S/he ensures that the team is well briefed beforehand and properly informed regarding the background to the assessment and the health systems and health status in the country. Participants in the meeting recommended to increase the number of team leaders and were unanimous that the team leader should be a WHO staff member and not an invited external expert.

The meeting reviewed in depth the assessment tools that are used by WHO. Participants considered that Quality Management Systems should be an indicator for all regulatory functions. This at present is an aspiration since very few countries have a thorough Quality Management System governing all their NRA activities. Elements for assessment of Quality Management Systems governing all functions should be clearly defined for future plans of NRAs. The participants stressed that this should not be confused with a requirement to establish an ISO 9001 Quality Management System which would set the bar unrealistically and unnecessarily high in many countries. Moving towards ISO 17025 accreditation for laboratories activities was also expressed as a desire rather than a requirement at the present time. The WHO assessment tool will be modified to reflect these desires.

The meeting considered a number of other related issues concerning revision of the WHO assessment tool and methodologies as well as the project's future steps. For this purpose, three working groups were established, each of which made recommendations. After discussion, overall recommendations were agreed by participants. They include the need to finalize the review of the WHO assessment tool, including functions, indicators, sub indicators and to link indicators with the scoring systems for prequalification assessments and capacity building assessments, and development of a comprehensive guidance document for countries to help preparations for assessments. The participants also recommended a revision of the standard operating procedures (SOPs) for the selection of experts and for ensuring the overall competence of the assessment team. Countries have the right to decline an individual as a member of the expert team; if they do so, however, adequate reason should be provided.
The meeting considered a vision for 2012, five years hence. A competent NRA is central to these objectives. It would require, *inter alia*, the following: strengthening of the prequalification process based on the premise that there should be independent and functional NRAs in all countries, respectively, to the level necessary; strong regional participation in the process; reliance on the IDP which would serve as the ongoing terms of agreement between the NRA and its political authority on the one hand and the WHO on the other; systems for retrieval and analysis of the assessment data; and an ongoing system of robust external review of the programme provided either by an independent external advisory committee (advisory to the Director of IVB and through the Director to the Director-General of the WHO or through *ad hoc* committees called together from time to time to address particular issues.
Number of Member States that have a functional National Regulatory Authority (NRA) according to their main source of vaccines, December 2007
(totals Member States = 193 Member States)

- **83 countries** are functional.
- **71 countries** are functional for UN Agency Procuring.
  - **12 countries** are not functional for UN Agency Procuring.
- **51 countries** are functional for Procuring.
  - **15 countries** are not functional for Procuring.
- **13 countries** are functional for Producing.
  - **31 countries** are not functional for Producing.