New regulatory pathways for vaccine registration

Summary of ad-hoc presentation at the MSF/Oxfam Consultation "improving access and stimulating vaccine development for use in resource poor settings" by Gillian Chaloner-Larsson, PhD Jan 26, 2010

WHO has been active since the early 1990s in training and developing the expertise of national regulatory authorities in developing countries, both in vaccine manufacturing countries and in vaccine procuring countries. I have been involved in most of these projects as a consultant on regulatory affairs and GMP (Good Manufacturing Practice) for the WHO Vaccine Quality groups (various acronyms: VSQ, V&B, IVB, ATT, QSS) and IVR (Initiative for Vaccine Research).

1.Early 1990s: CVI: Children's Vaccine Initiative

- WHO expert teams visited developing county manufacturers for basic assessment of compliance with GMP.
- Resulted in clear instructions for separation of quality control and manufacturing functions

2.Public Manufacturers Consortium: 1995 meeting

- Meeting to discuss cooperation among public manufacturer for improvement of manufacturing in developing countries
- Decision on membership to be based on adequacy of the National Regulatory Authority (NRA)
- Resulted in recognition that training of NRAs was a priority
- Eventually the Developing Country Manufacturers Network (DCMN) was established and is still active

3.Establishment of the six critical functions for vaccine regulation and corresponding indicators: 1996

- Licensing
- Lot Release
- Laboratory Access
- Post marketing survelliance
- GMP inspections
- Clinical trial evaluation

4.GTN: Global Training Network: 1997 – present (since 2009 GLO: Global Learning Opportunities)

- Training of several thousand NRA staff from many countries (vaccine producers and vaccine procurers) in all of the 6 critical functions.
- Recent training of training staff to ensure the information is presented in an effective manner

5.WHO PreQualification:

- WHO programme to evaluate vaccines against WHO recommendations to be eligible for sale to UN Agencies
    - Site visit by WHO with contracted expert team
    - Testing of samples of vaccine by WHO accredited laboratory
    - Review of the PSF (product Summary File)
    - Formal guide for information to be submitted and format of the PSF.
- Manufacturer applies for prequalification.
- Individual vaccines prequalified, not the manufacturer.
- Initially traditional vaccines were reviewed usually long after the vaccines had been produced and used in country. Recent developments in novel vaccines and new combination vaccines have resulted in the potential for some parallel review by NRA for licensing and WHO review for prequalification.

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6.NRA Assessment programme

- Separate assessment based on critical functions and corresponding indicators to determine if an NRA is "fully functional"
- NRA must be fully functional for manufacturers in the country to obtain WHO prequalification for one or more vaccines.
- Training arranged for countries with sublevel functions.

7.New Regulatory Pathways:

- Recognition in 2002 that new regulatory pathways for licensing will be needed for vaccines needed in developing countries manufactured by developing country manufacturers.
- Proposals for such new regulatory pathways covered. Possible approaches: Licensing in the country of manufacture; Proposal to the European Commission (scientific review of products not for license in EU); Export provisions; Shared manufacturing with licensing in the country of final manufacture; Contract non-profit organization
- GTN training has been satisfactory on manufacturing aspects but the evaluation of proposals for in-country clinical trials and for analysis of clinical trial data from other countries required input
- Developed a network of developing country NRAs for training on clinical trial evaluation

8.Contract Manufacturers Database (IVR)

- Identification, assessment and registration of several dozen contract manufacturers with abilities in one or more aspects of GMP which could be contracted to aid vaccine developers to manufacture suitable GMP clinical trial material for phase I and II clinical trials (2001 – 2004).
- Database on WHO website

9.Partnership between WHO and other NGOs to promote and manage developing country vaccines in clinical trials in-country"

- E.g. Meningitis vaccine project in India, Measles aerosol vaccine project in India (IVR).
- Followed international regulatory norms to ensure the vaccine manufacturing, preclinical and clinical studies and clinical reports would be meet international acceptance criteria.

10.References:

- Regulatory pathways for vaccines for developing countries. Julie Milstien& Lahouari Belgharbi, Bulletin of the World Health Organization 2004;82:128-133.

NOTE: not in presentation

- Guidance for Industry: General Principles for the Development of Vaccines to Protect Against Global Infectious Diseases. U.S. Department of Health and Human Services, Food and Drug Administration. Center for Biologics Evaluation and Research, September 2008
- Report on the meeting on national regulatory authority (NRA) networking for new regulatory pathways. Geneva, 27–28 November 2002. WHO/V&B/03.17
- Guidelines on clinical evaluation of vaccines: regulatory expectations. WHO Technical Report, Series No. 924, 2004 Annex 1.
- WHO guidelines on nonclinical evaluation of vaccines. WHO Technical Report Series, No. 927, 2005, Annex 1