Vaccine Licensure: African Perspective

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Outline

- Introduction to International Vaccine Development and Licensing
- National Regulatory Authorities (NRAs)
  - Responsibilities
  - Challenges
- National Immunization Technical Advisory Groups (NITAGs)
- Collaborative Efforts
  - WHO, SIVAC, DCVRN
- Issues to address
International Vaccine Development and Licensing

- **In country vaccine development**
  - Oversight of clinical trials depends on national regulatory authority
  - Evaluation of safety, immunology, public health, ethics, and finances depend on country regulatory authority

- **Out-of-country vaccine development**
  - Individual trials need not be carried out in each country
  - Vaccine *does* require licensure in each country
  - WHO can ‘pre-qualify’ vaccine for licensure
  - National Regulatory Authority (NRA) must meet with WHO, review license, & authorize
  - Ministry of Health must sign off on project of licensing decree
Important factors in process:

- When NRA reviews ‘pre-qualified’ license, it must take into account implementation factors unique to its needs
  - Labeling (appropriate languages)
  - Instructions for use (appropriate for staff to administer vaccine)
  - Thermal indicators
  - Etc

The time between NRA approval and MOH approval may be lengthy

- Special license for introduction may be given to expedite introduction of first batch of vaccines
Responsibilities of NRAs

- The NRA must ensure the quality, safety, and efficacy of vaccines used in the country.

- Functions include:
  - Laboratory access
  - Regulatory oversight of clinical trials
  - Licensing activities
  - Marketing authorization
  - Lot release
  - Post-marketing surveillance (including adverse events)
  - Regulatory inspections
Responsibilities of NRAs (2)

- According to WHO, African NRAs need to be able to complete these steps efficiently:
  - Establish regulatory strategies to regulate clinical trials taking place in their country
  - Perform a regulatory review of clinical trial applications
  - Assess clinical data and product characteristics to respond to license application
Responsibilities of NRAs (3)

- Licensure requires evidence of safety and efficacy in target population

- The recommended use of product is outlined in prescribing information
  - This is defined in license application (by manufacturer)

- NRA is not responsible for recommending vaccine for public health program
  - It can push manufacturer to provide evidence of suitability in target population
Challenges faced by NRAs (1)

Rapid Scientific Advances

- New, complex products
- Complex quality concerns
- New technical issues
- Training may be lacking
Challenges faced by NRAs (2)

2. Expanding global market

- Increased volume of products crossing borders
- Establishment of more clinical trials in developing countries
- Necessity to share and standardize evaluation of products with other countries in region
Challenges faced by NRA (3)

Lack of Authority

- Legal basis to authorize/review trial may not be in place
- Another institution may be issuing clearance for clinical trials (i.e. scientific council)
- Conflict of interest between NRA and Scientific Council/ethics committee may interfere with objectivity
National Immunization Technical Advisory Groups (NITAGs)

- NITAGs provide recommendations to NRA based on evidence and unbiased scientific review.

- NITAGs should be neutral and credible advisors.

Responsibilities include:
- Provide technical and scientific expertise as developments in vaccines and vaccine-preventable diseases arise
- Advise immunization policies in context of local conditions
- Analyze immunization and safety data through monitoring of national immunization program
Challenges faced by NRAs (4)

- **Conflicting evidence**: Manufacturer evidence may not agree with
  - Biomedical evidence from external source
  - Licensing/policy conditions
  - Public health mandates

- NRA may not be communicating with a national immunization technical advisory group (NITAG)

- NITAG may not exist
Challenges faced by NITAGS

Global survey of existing NITAGs identified key challenges:

1. NITAG members not independent from national immunization program
2. Difficulty in recruiting sufficiently broad and knowledgeable expertise
3. Lack of cooperation of private health delivery systems
4. Lack of declaration of potential conflicts of interests
5. Need for public transparency in decision-making
6. Need for more interactions between NITAG and NRA

NITAGS in Africa (2011)

Based on data from WHO vaccine-preventable diseases: monitoring system 2012 global summary
Measures of NITAG standards

- Are there legislative or administrative basis for the advisory group?

- Does core membership include:
  - Pediatrics?
  - Public health professionals?
  - Infectious disease experts?
  - Epidemiology experts?
  - Immunology experts?
  - Other experts?

- Does the advisory group have formal written Terms of Reference?
NITAGS in Africa (2011) that Meet Required Standard

- No NITAG exists
- NITAG exists
- Existing NITAG meets all standards

Based on data from WHO vaccine-preventable diseases: monitoring system 2012 global summary
Supportive activities of WHO

- Establish regulatory mechanisms for licensing of new vaccines (not registered in the country of manufacture)
- Exchange experiences on evaluation and regulatory review of new vaccines
- Collaborating with the European Medicines Agency
  - vaccines manufactured in Europe for exclusive use in developing countries
- Collaborate with NRAs in developed countries to develop new regulatory strategies to facilitate licensing of novel vaccines
Supportive activities of WHO (2)

- Facilitate establishment of regional networks of regulatory authorities and research centers
  - address short term need for review of clinical protocols, monitoring trials and evaluation of trial data
- Discuss the specific regulatory needs for the authorization of clinical trials of vaccines in development
  - develop guidelines for the review of clinical trial applications
  - define training needs
- Supporting NRAs which have not yet fully developed the expertise for the review of license applications
  - workshops and technical assistance.
Supportive activities of SIVAC Initiative:

- Aim to help establish/strengthen national NITAGs
- Regional approach to NITAG development paired with cross-national collaboration
- Organize regional technical workshops
- Create tools and learning modules to strengthen and connect NITAGs

The SIVAC Initiative was established in 2008 as a 7-year project funded by the Bill & Melinda Gates Foundation and is implemented by the Agence de Médecine Préventive (AMP) in partnership with the International Vaccine Institute (IVI).
Supportive activities of Developing Countries’ Vaccine Regulators Network (DCVRN):

- Annual meeting of NRAs
- Exchange scientific information and expertise with regulators/manufacturers from well-sourced countries
- Strengthen procedures for review of clinical trial protocols and data for new vaccines

The DCVRN was established by WHO in 2004.
Issues to Address:

- How can African countries with less-developed NRAs and NITAGs take full advantage of collaborative efforts?
- How can regional regulatory advisory groups be successfully established when countries have different regulatory processes?
- How can we encourage better cooperation between NRAs and NITAGs within country?
- How can we expedite the regulatory process regarding clinical trial review and vaccine licensure?
- How can we recruit or train experts to NITAGs and NRAs?