Regulatory pathways to improve vaccine access in developing countries

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The New Regulatory Reality

- National Regulatory Authorities (NRAs) are on the critical path to innovation and access to safe and effective medical products
- Degree to which NRAs fulfill their mandates in an effective, efficient and transparent manner has a direct impact on innovation, access and public health
- At the same time, NRAs must consider more modern and intelligent models of regulation that consider resource constraints, increasingly complex technologies, globalization and public expectations

Regulatory Convergence

- Represents process whereby regulatory requirements across economies become more aligned over time as a result of the adoption of internationally recognized technical guidances, standards and best practices
- Does not require the harmonization of laws and regulations
- Broader concept than “harmonization” which is commonly meant to mean the same standard or process

-> Example: Good Review Practices

Current Scene

- Increasing prevalence of harmonization, convergence and other forms of cooperation at both regional and international level
- Examples abound: ICH/IPRF, IMDRF, ICMRA, PIC/S, IGDRP, APEC, ASEAN, AMRH (EAC, SADC/ZaZiBoNa, ECOWAS), GCC, PANDRH etc….
- What is becoming increasingly apparent is that intended objectives cannot be achieved unless products of harmonization and convergence implemented in consistent and intended manner
- Requires common understanding and preparation (legal amendments, complementary guidance, SOPs, training, resourcing, infrastructure, etc.)

WHO's role in promoting access to quality medical products

- WHO has long supported regulators in LMICs in fulfilling their mandates through:
  - Developing norms and standards
  - Promoting regulatory convergence and harmonization
  - Training and capacity building
  - Supporting information and work sharing arrangements
- Experience to date has helped characterize the benefits, challenges and potential evolution of such initiatives in accelerating in-country regulatory decisions

An Apparent Dilemma

- WHO supports the strengthening of regulatory systems in accordance with numerous WHA resolutions
- WHO also promotes access to essential medical products as one of the key enablers of health and equality
- The challenge: Strengthening the capacity of regulatory authorities to regulate in a manner that is consistent with timely access to priority medicines

Considerations

- Weak regulatory systems do not serve interests of consumers, patients, industry nor the health care system

- At the same time, as countries develop regulatory capacity it is important that regulatory systems be science based, respect international standards and best practices, and adopt an approach that focuses on what cannot be done by others while leveraging the work of other trusted NRAs and regulatory networks for the rest

Global Regulatory Scenarios

NRA Maturity Level

Well resourced SRA	Robust registration system: 'Full service" regulator Serve as a reference for emerging systems
Functional- formal system	• Technical registration system in place, however may be challenged to balance responsibilities with resources and expertise • Should consider collaborative approaches and referencing whenever possible to effectively meet these challenges
Administrative system	Administrative registration system: rely on and adopt decisions of other NRAs
No formal system	No registration system: rely when possible on UN procurement of PQ'ed products, or accept products already approved in SRA countries

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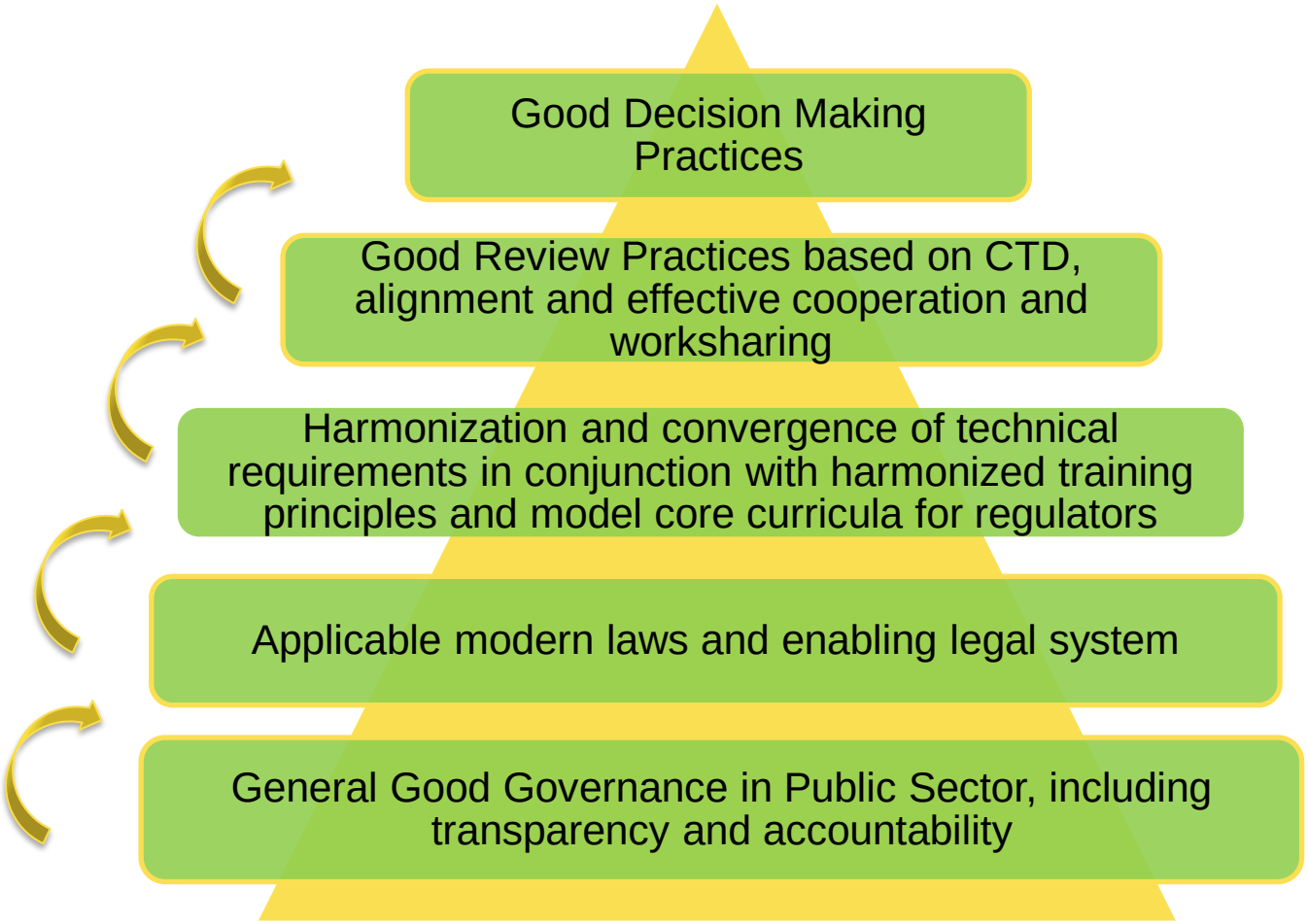
An Effective Approach to Regulation

- Some elements of regulatory oversight can be shared
  - Evaluation of quality, efficacy and safety
- Other elements of regulatory oversight must be local
  - Licensing decision
  - Local manufacturing oversight
  - Pharmacovigilance
  - Appropriate distribution controls (stability and cold chain)
  - Product security (protection against counterfeiting and adulteration)
- Regulatory framework should also be flexible, providing for expedited or waiving of registration in the case of emergencies or other important public health situations

Hallmarks of a modern regulatory system



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Elements of a Good Regulatory Framework

- A set of common elements are shared by effective regulatory frameworks:
  - Science-based
  - Risk-based
  - Flexible and adaptive to evolving needs
  - Streamlined and efficient
  - Harmonized and aligned with international standards
- Efficiency increased by leveraging work of WHO, trusted NRAs and regulatory networks
- Good regulatory framework must begin with an overarching strategic direction

Flexibility

- Regulatory oversight must be risk-based to achieve a balance between appropriate controls and timely access to medical products
- Circumstances will arise where accelerated access is applicable
  - Emergencies of Public Health Concern
  - Drug shortages
  - Innovations in treatment of critical illness
- Increase in regulatory oversight is vulnerable to the implementation of overly rigid constraints
- This can be exacerbated by existing legal frameworks
  - Some requirements may already be enshrined in law
- A spectrum of risk-based options could include waivers, highly accelerated evaluation pathways or provisions to accept expert recommendations

WHO Joint Review Workshops: Facilitating registration of IPV

- Under the polio eradication endgame strategy, 23 countries participated in joint reviews with WHO:
  - AFRO selected countries for expedited procedure joint review (20-24 Oct 2014 Turkey)
  - SEARO selected countries for expedited procedure joint review (10-14 Nov 2014-Bangkok)
  - EMRO selected countries for Full registration joint review (20-24 Oct 2014 Morocco)
- Regulators found exercise very helpful to improve the quality of the review process: facilitated the review of the science-based sections of the dossiers
- However, registration depends on administrative procedures as well, which vary from country to country and may include additional requirements

RSS Survey

- Recent survey conducted to better understand currently available regulatory pathways in countries
- Survey requests information on:
  - Standard, expedited and emergency pathways for medicines and vaccines licensure
  - Clinical trial application pathways
  - The legislation or guides that regulate these pathways
  - The timelines associated with the reviews

WHO Prequalification of Priority Health Products

Action plan of UN for expanding access to selected health products – medicines, vaccines, in vitro diagnostics/medical devices

Objective

- To ensure quality, efficacy (performance) and safety of health products procured using international funds (e.g. GFTAM, UNITAID, UNICEF, UNFPA etc.) to serve patients in developing countries

Components

- Scientific assessment of Quality, Safety and Efficacy of prioritised health products and technologies, inspections of manufacturers and monitoring of the products after their prequalification
- Prequalification of quality control laboratories
- Building capacity of regulators, manufacturers and quality control laboratories

Prequalification process for vaccines

http://www.who.int/immunization_standards/vaccine_quality/pq_system/en/

- Scientific review of quality dossier
- Scientific review of clinical data
- Testing of samples
- Consultation with responsible NRA
- Site audit to manufacturing facilities

Prerequisite*: The National Regulatory Authority responsible for the product is "functional" as per assessment performed using the WHO assessment tool and established indicators

* - *not for medicines and diagnostics/devices at this stage*

Revised procedure in place from January 2012

Collaborative registration of WHO-prequalified products

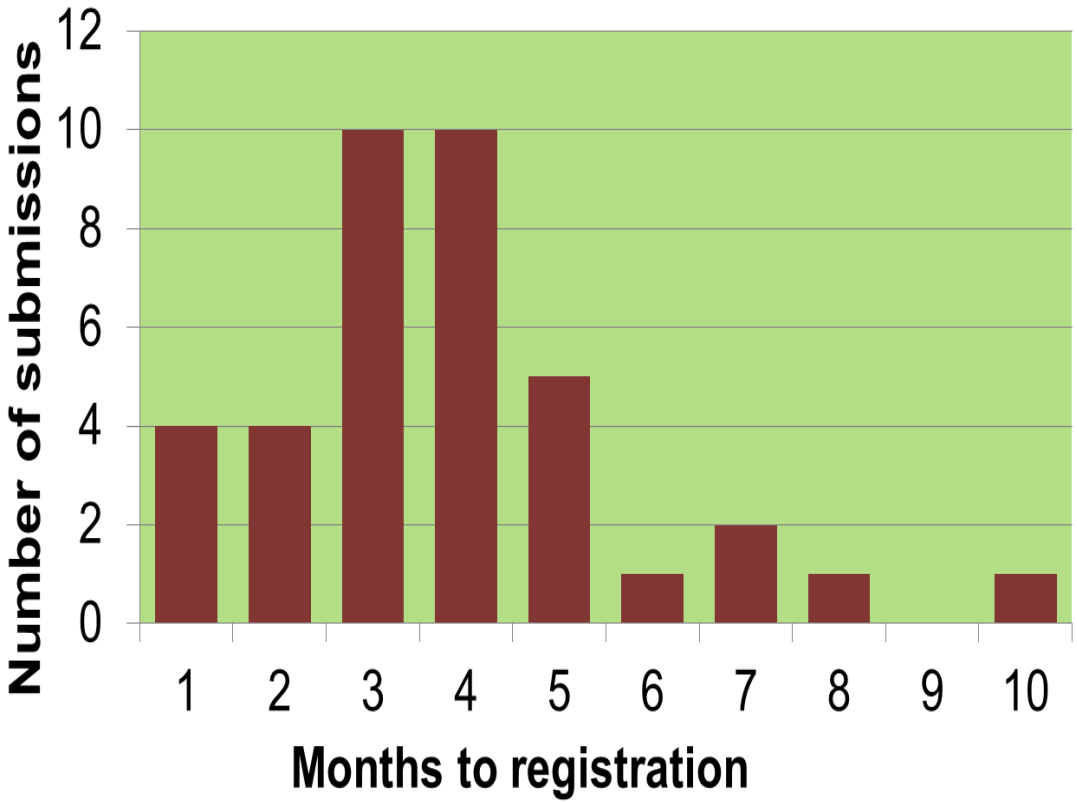
- To be used, prequalified medicines must be authorised for use (registered) by national regulatory authorities.
- In many countries that are recipients of prequalified medicines, regulatory systems are either weak or lack capacity to manage effectively applications, delaying accessibility of essential medicines.
- PQT strives to facilitate the process in co-operation with involved manufacturers and regulators.

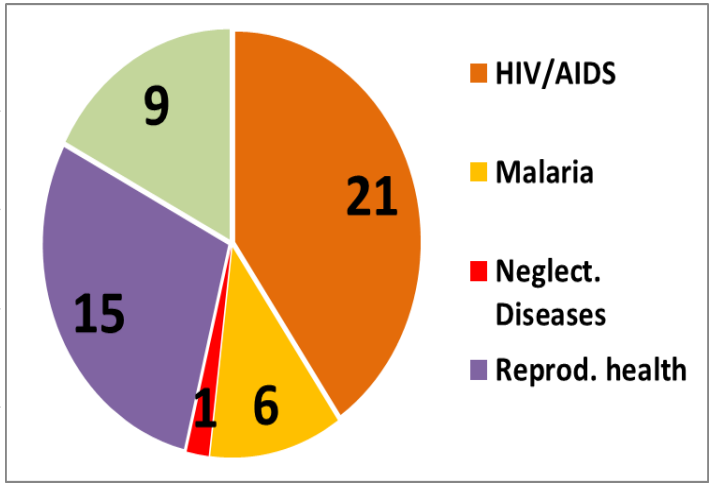
Principles of WHO Collaborative Procedure

- Voluntary for manufacturers and NMRAs and does not interfere with national decision making process and regulatory fees
- WHO-PQT shares with interested regulators detailed outcomes of its assessment and inspections to support their decision making in exchange for accelerated registration process
- Product and registration dossier in countries are 'the same' as approved by PQP. Co-operation among PQ holder (manufacturer), NMRA in interested country and PQT overcomes confidentiality issues, ensures information flow and product identity

WHO Collaborative Procedure

(47% approved within 3 months, 74% approved within 4 months by national authorities)





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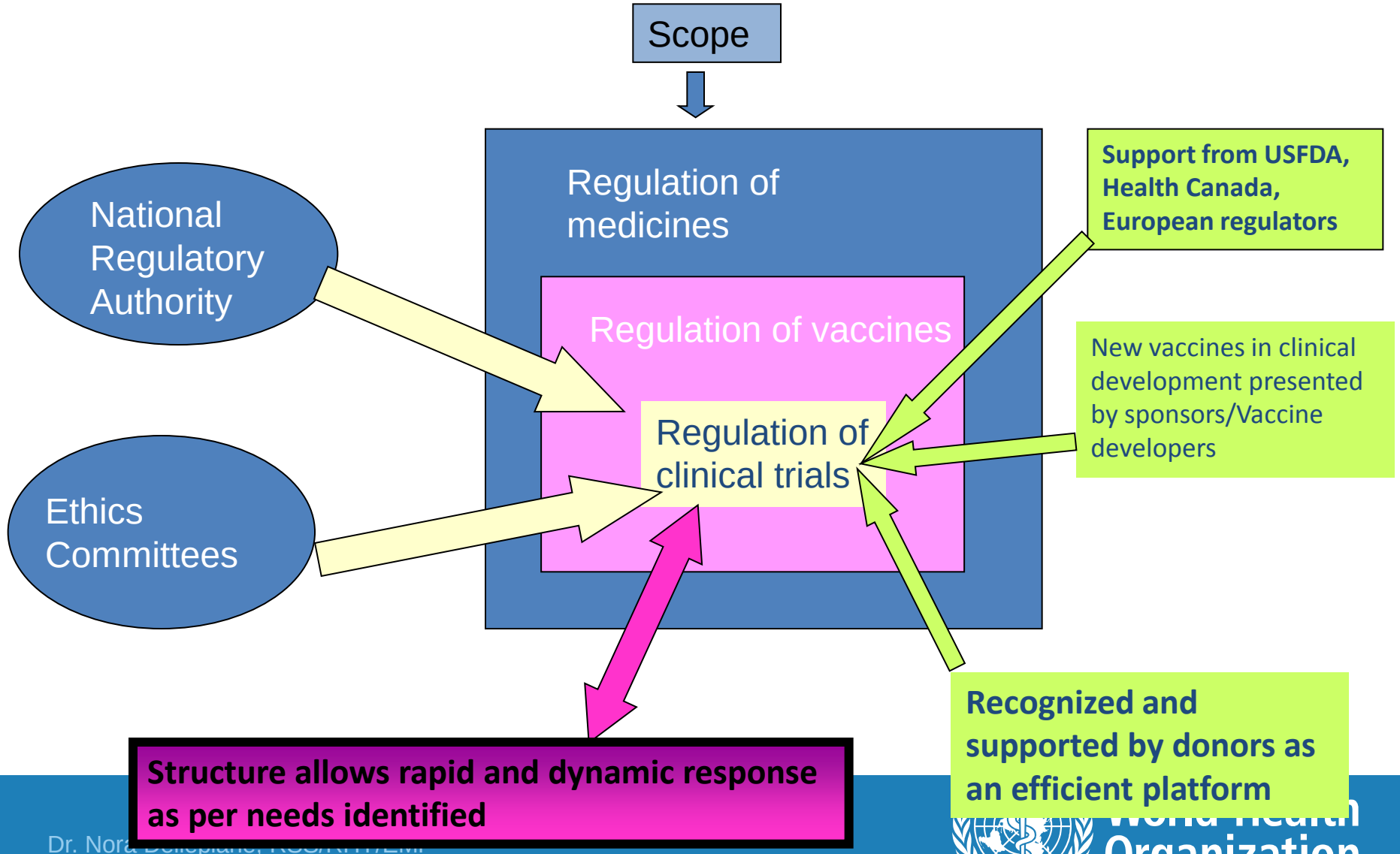
AVAREF-African Vaccine Regulatory Forum

Network approach to regulation of clinical trials in Africa



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WHO assisted Ebola candidate vaccines CT applications joint assessments using African Vaccines Regulatory Forum (AVAREF)

- Joint Review of GSK ChAd3 Ebola Phase II Vaccine trial submission - 15-16 December 2014, Geneva, Switzerland
  - Submission: Ghana, Nigeria, Mali, Senegal and Cameroon
  - Supporting agencies: USFDA, Health Canada, EMA, Swissmedic
- Joint Review of the Janssen Ebola Zaire Phase I Vaccine Clinical Trials Application – 3-4 February, Arusha, Tanzania
  - Submission: Ghana, Kenya, the United Republic of Tanzania and Uganda
  - Supporting agencies: USFDA, Health Canada, EMA
  - Total time from review to approval: average 30 days (one exception)
- Assisted Review of the Janssen Ebola Zaire Phase III Vaccine Clinical Trials Application – 8-10 April, Accra, Ghana
  - Submission: Sierra Leone
  - Supporting agencies: USFDA, HC, EMA
  - Outcome: 2 waves of submissions; all NRAs committed to review documents within 10 working days from receipt

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The next DCVRN meeting

- Next meeting to be hosted by WHO and CDSCO 16-20 November 2015 in New Delhi
- Key focus of meeting will be future vision and operating model for the Network
- DCVMN's views important to informing discussions

Concluding remarks

- All regulators have a duty to ensure the efficiency, effectiveness and transparency of operations
- At the same time, not all regulators have the resources or capacity to perform all regulatory functions: decisions have to be made nationally on which areas to focus and build capacity, and in which areas rely on other regulator's work
- Good regulatory practices and flexible regulatory frameworks a must for meeting the challenges of an increasingly complex global regulatory environment

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Thank you for your attention

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