Regulatory Challenges and Constraints when Evaluating Vaccine Clinical Trials

Global Vaccine and Immunization Research Forum
15-17 March 2016; Johannesburg, South Africa

WHO Regulatory Strengthening Update
&
LMICs Challenges in Vaccine Clinical Trial Regulation

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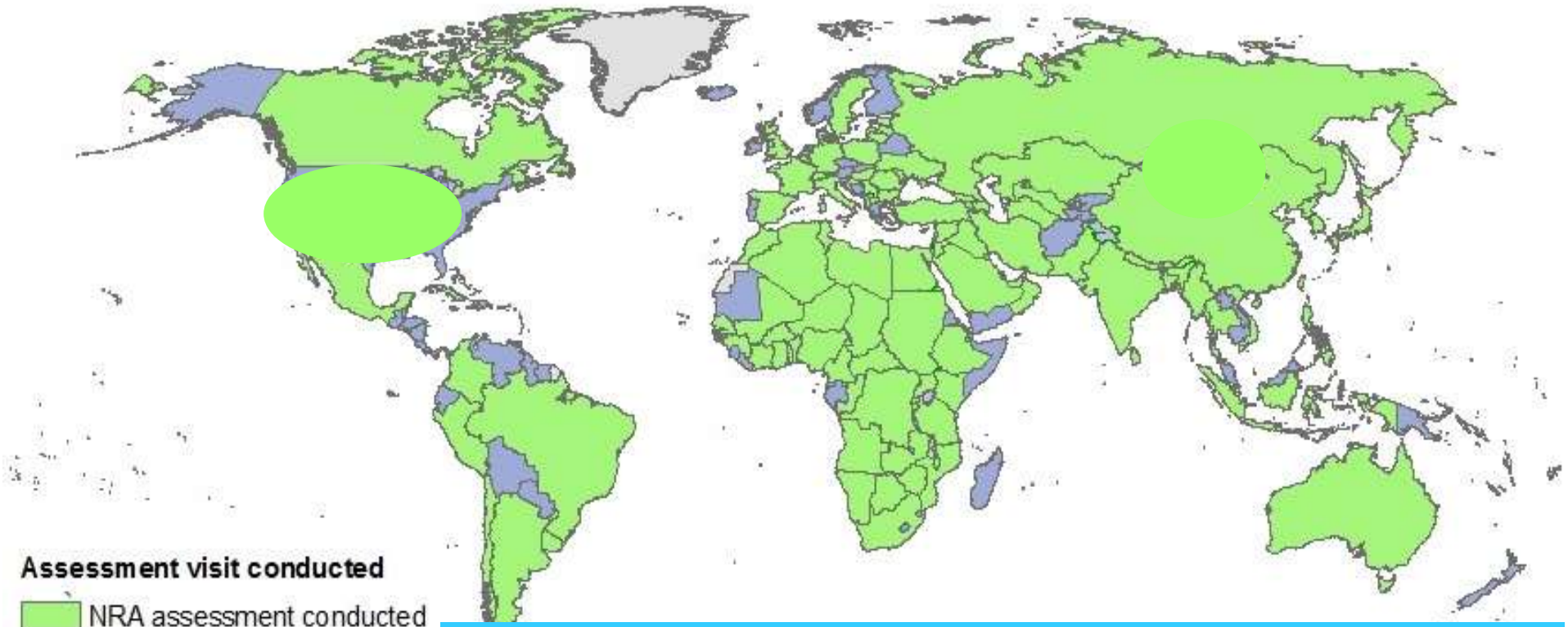
OUTLINE

1. **Global Update on WHO NRA Strengthening**
    1. NRA Strengthening-Update
    2. NRA Strengthening-Functions
    3. Research Regulatory Framework-One Model
    4. Clinical Trial Evaluation Process

2. **Challenges in Vaccine Clinical Trial Regulation**
    1. CT Regulatory Framework (Zimbabwe Model)
    2. Evaluation Process
    3. Challenges: Study product, NRA, EC Oversight, Participants
    4. Opportunities

1997-2014: WHO assessed 114 out 194 countries



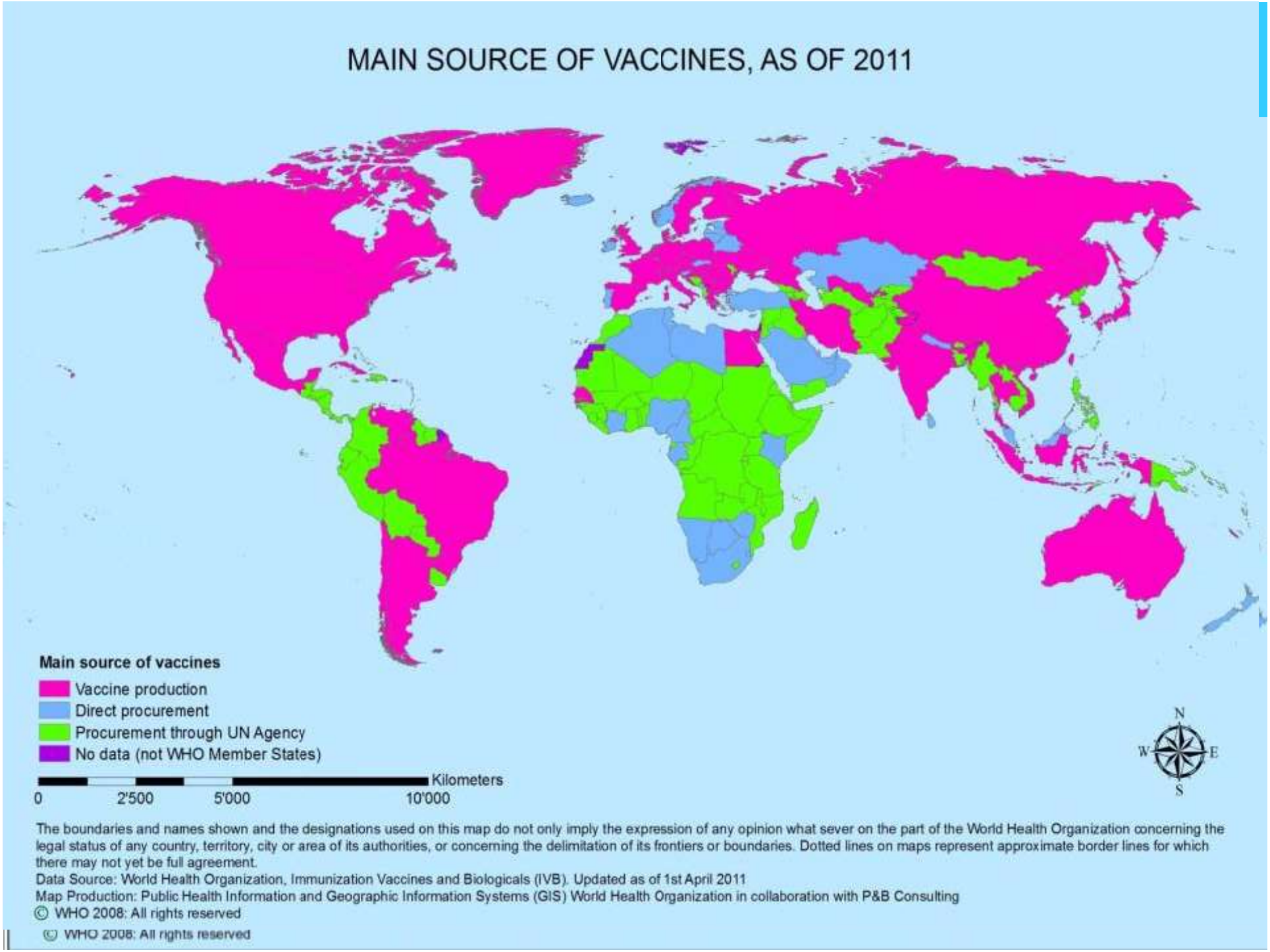
World Health Organization

- 7 international consultations of experts

(1997, 1999,2001,2002,2004,2007,2011, 2014)

- 950 regulatory experts, + 350 assessors

MAIN SOURCE OF VACCINES, AS OF 2011



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Data Source: World Health Organization, Immunization Vaccines and Biologicals (IVB). Updated as of 1st April 2011

Map Production: Public Health Information and Geographic Information Systems (GIS) World Health Organization in collaboration with P&B Consulting

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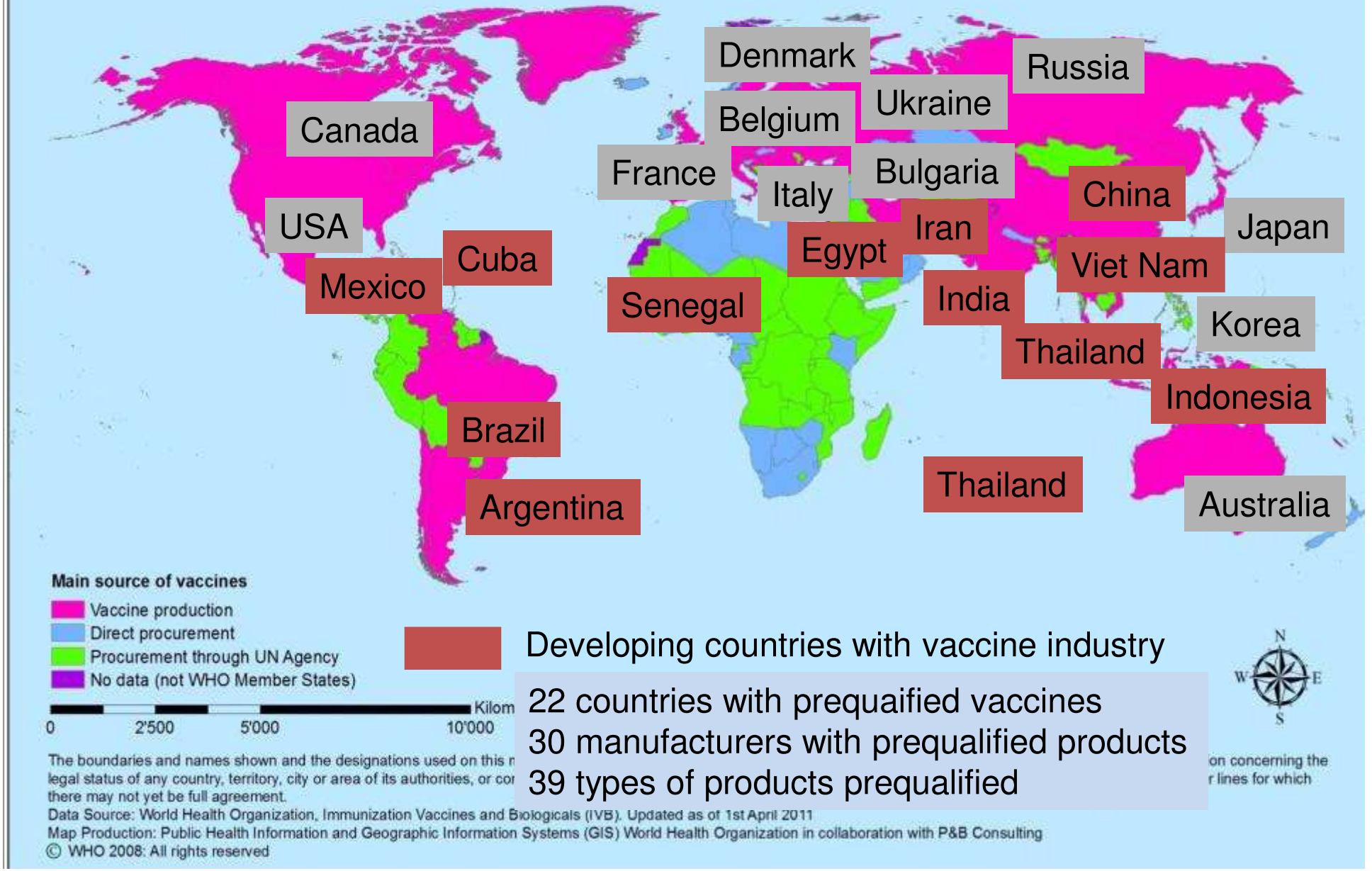
44 vaccine producing countries, 2014

146 vaccine manufacturers, 90% global production in 25 countries



Developing countries with vaccine industry

22 countries with prequaified vaccines
30 manufacturers with prequalified products
39 types of products prequalified

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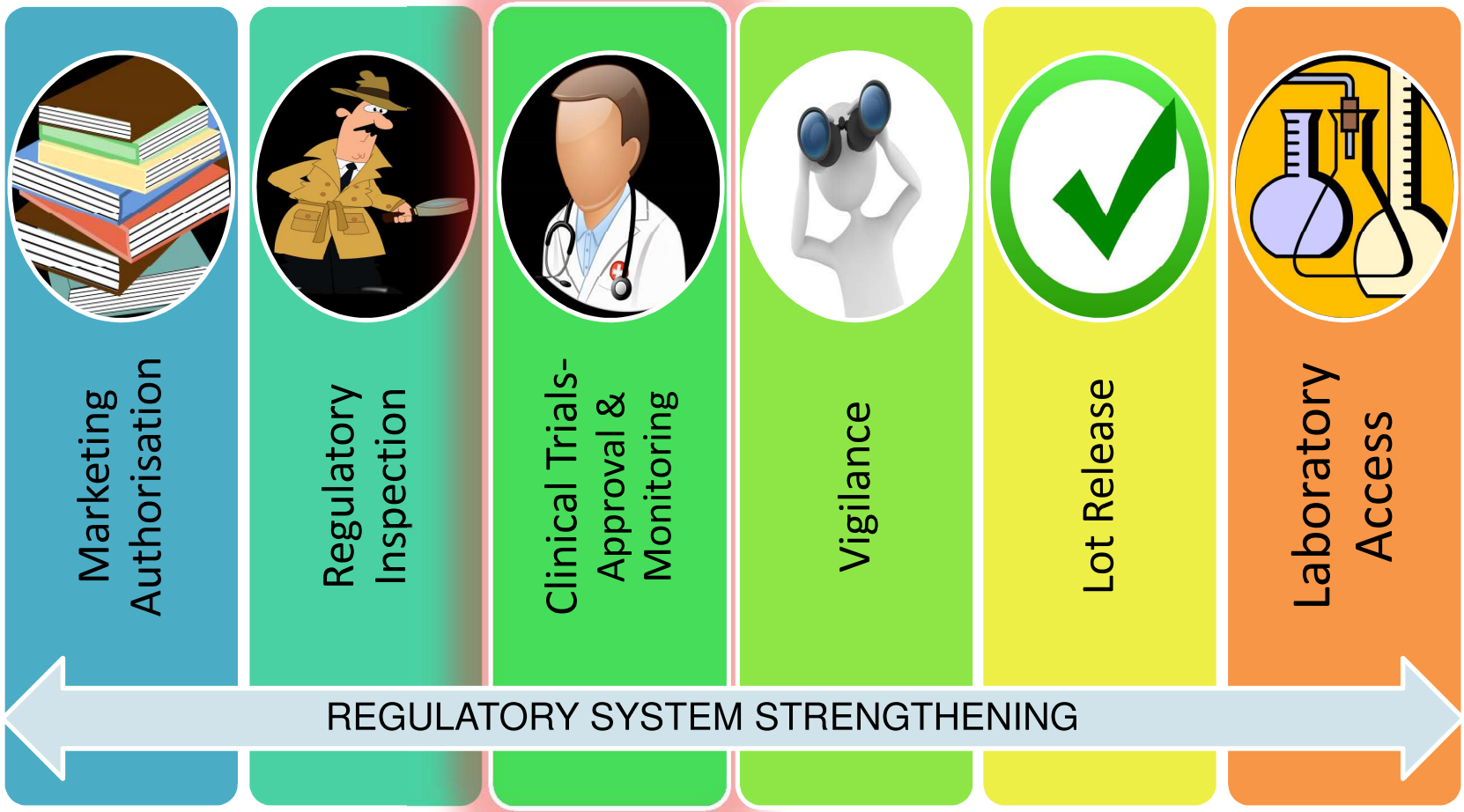
NRA Assessment & Strengthening



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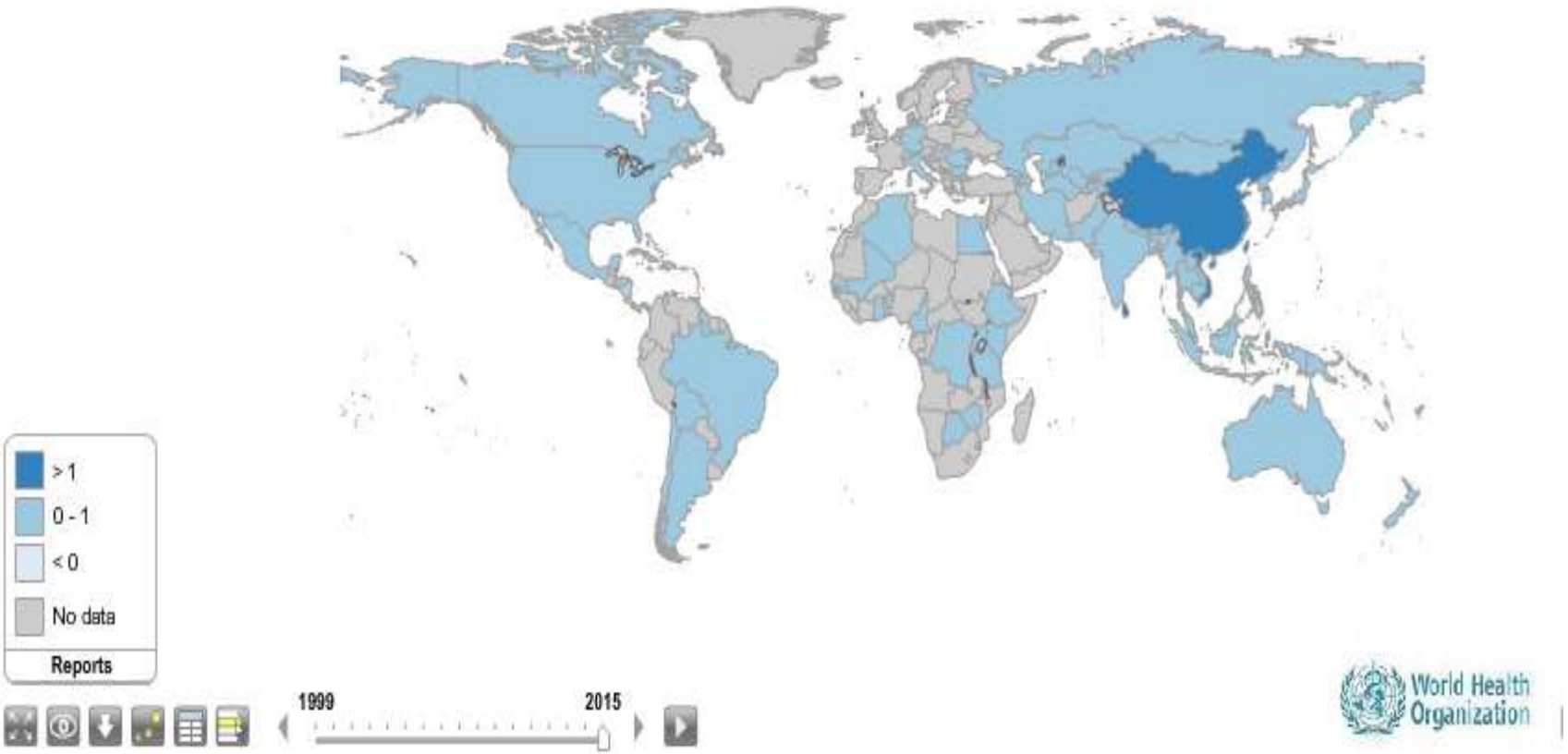
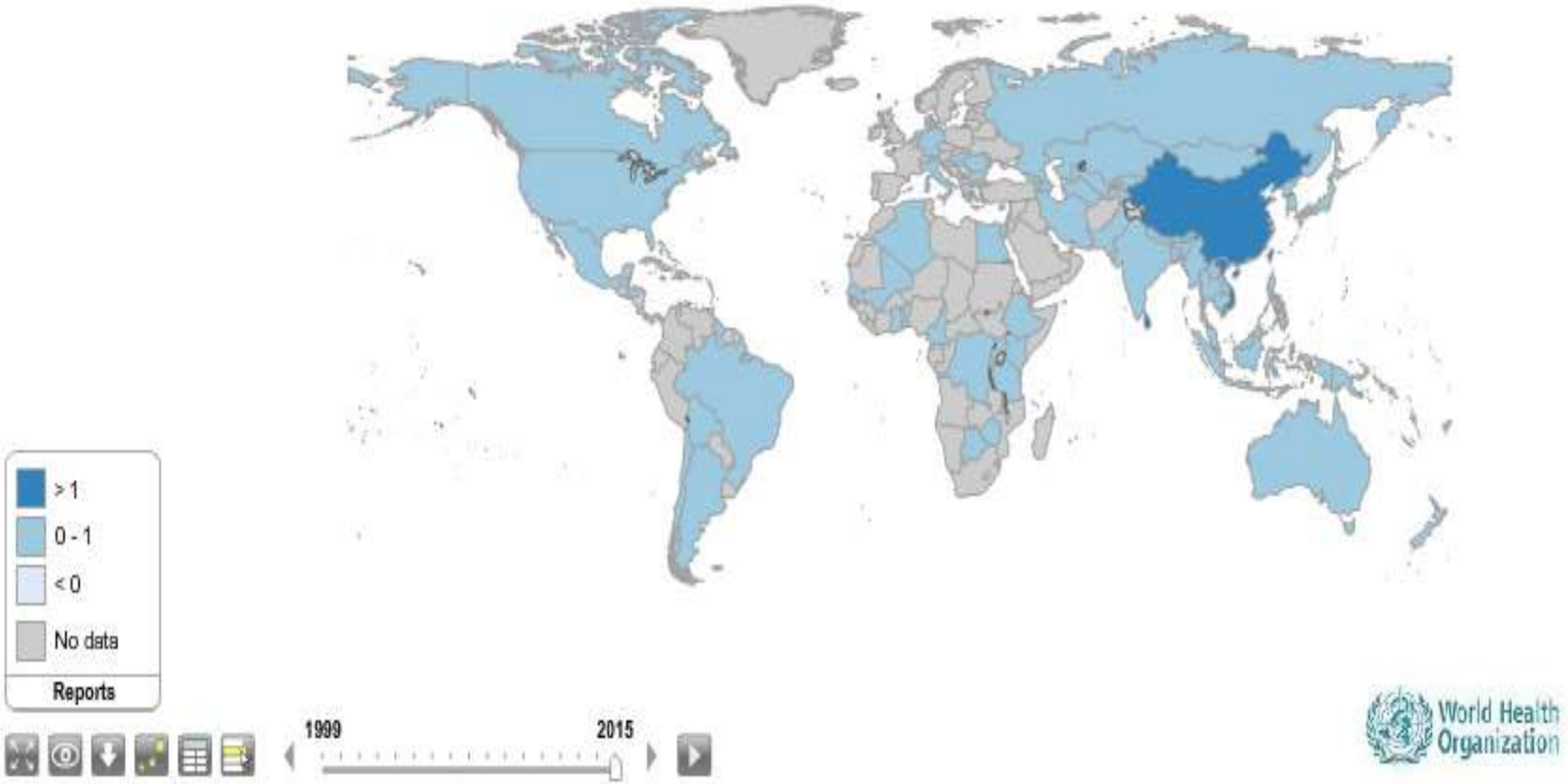
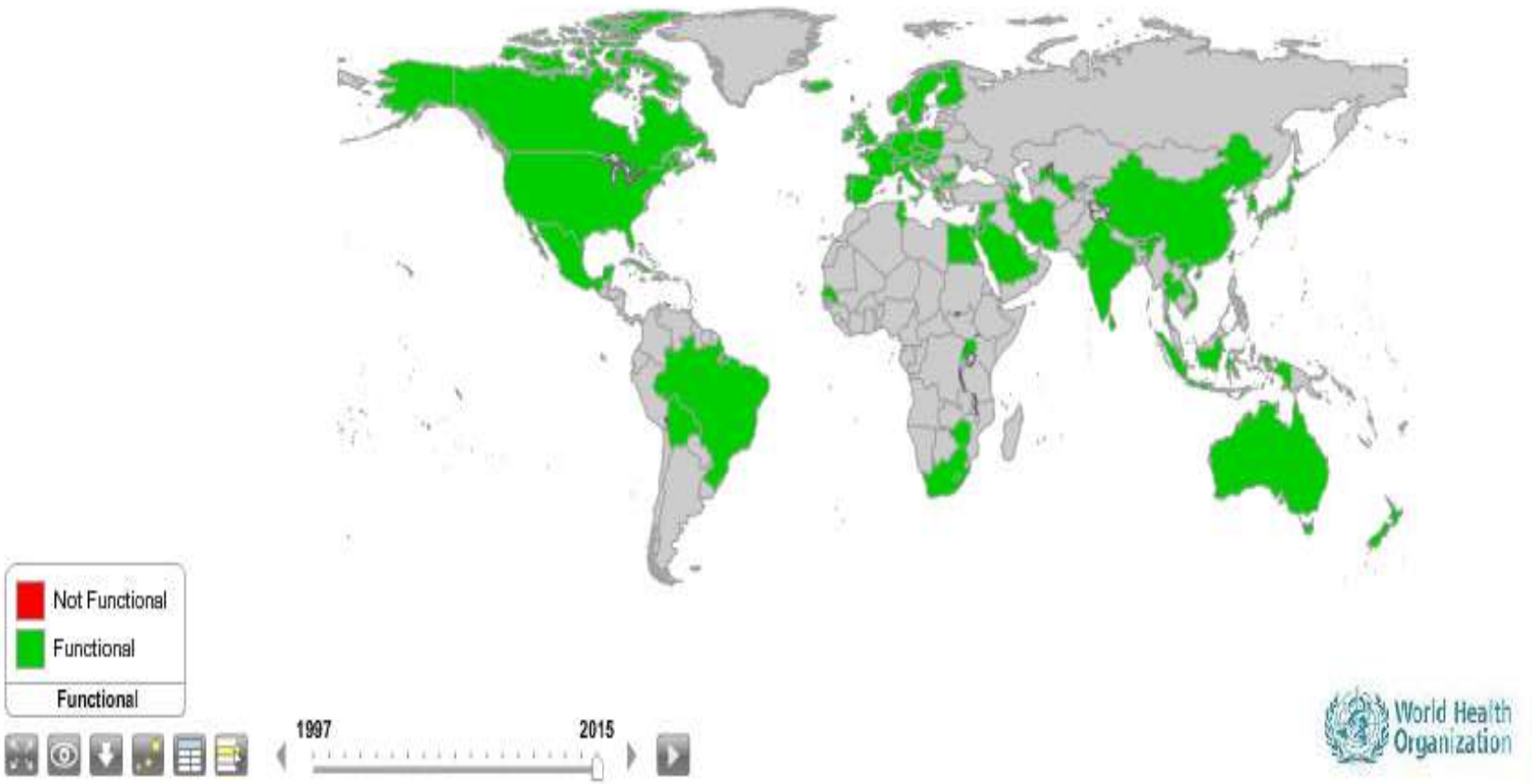
NRA Visits 1997-2015



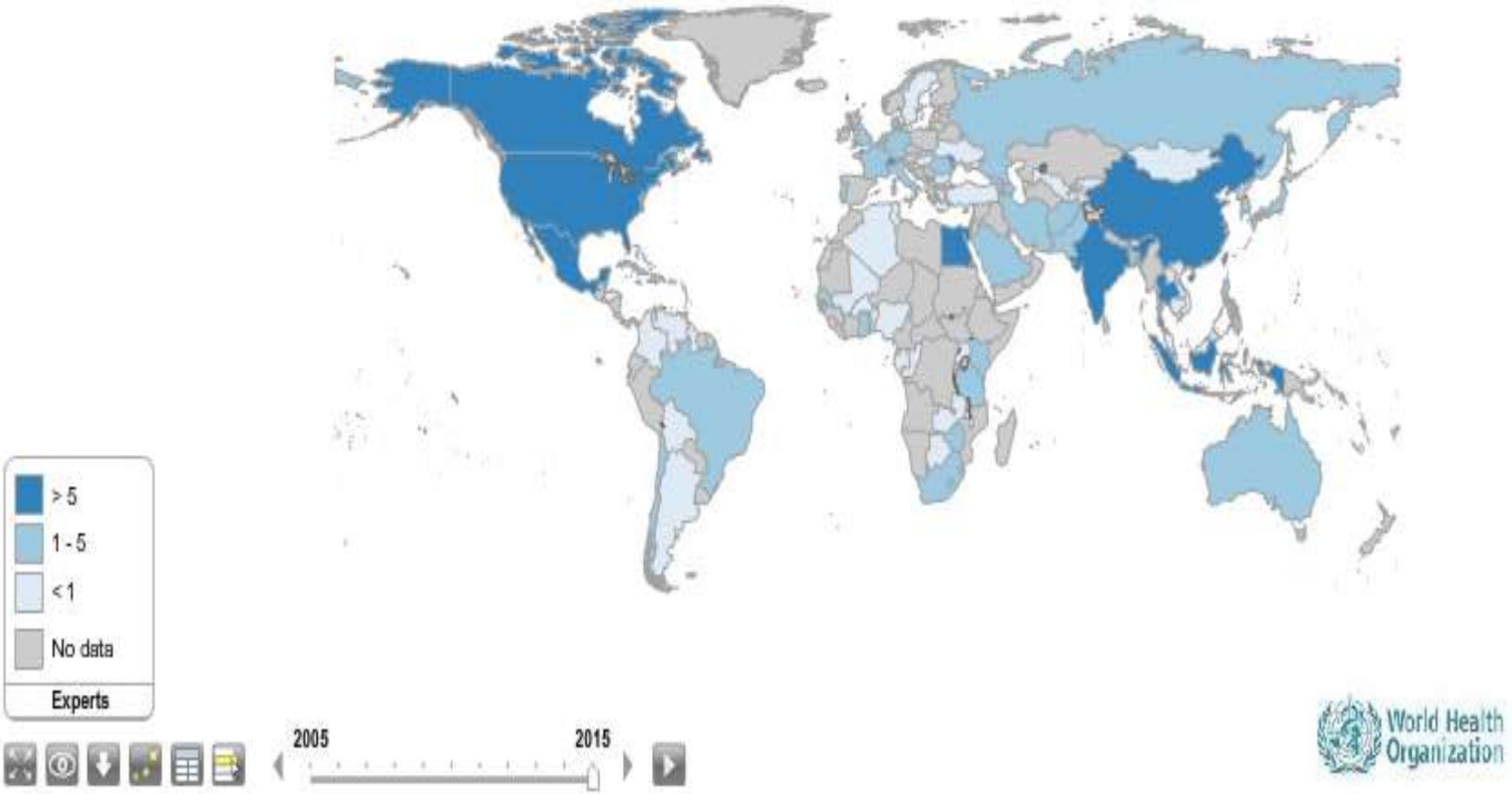
NRA/GLO Training 1999-2015



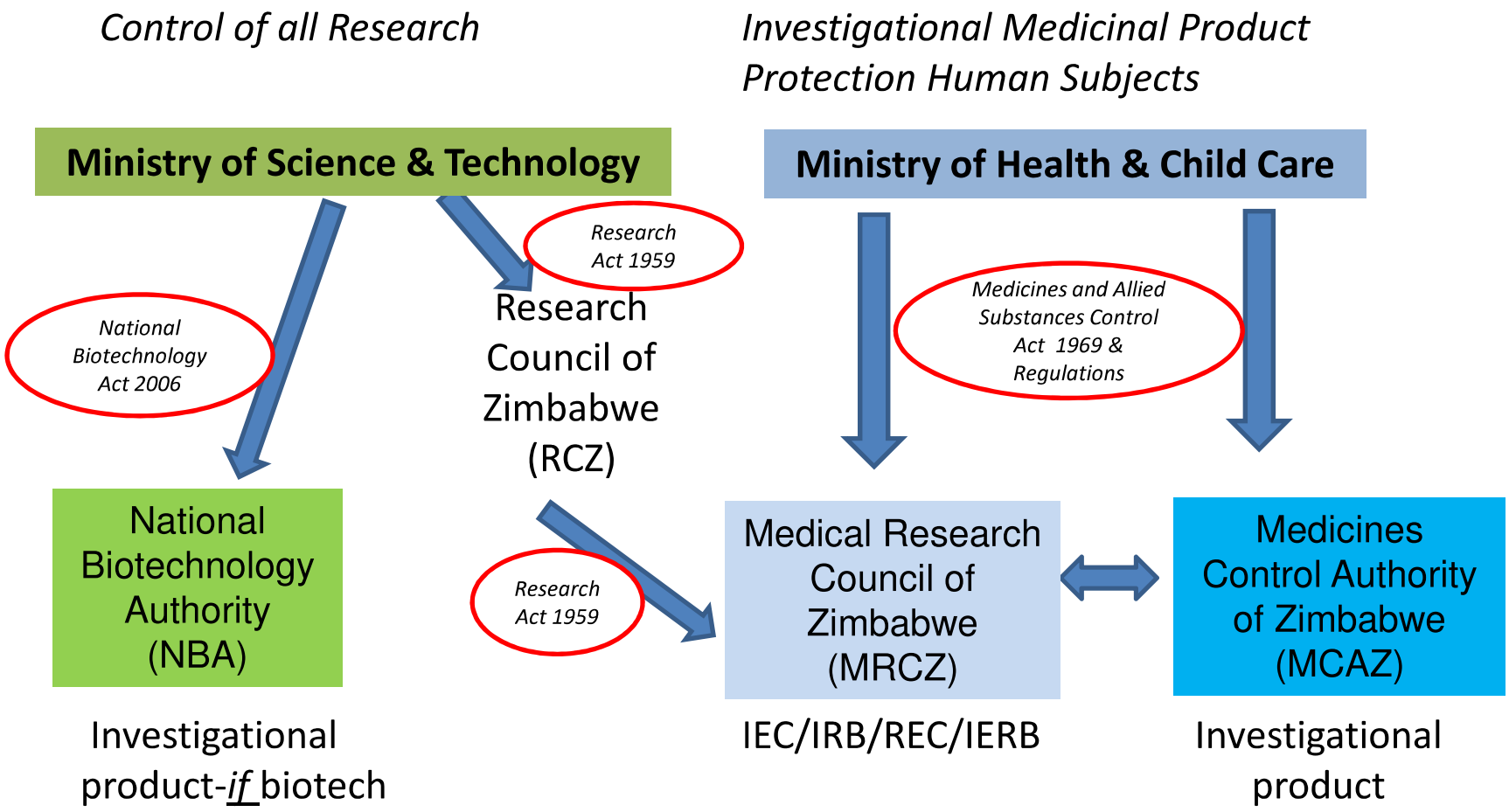
NRA Status 1997-2015



NRA In-country Expertise



RESEARCH REGULATORY FRAMEWORK



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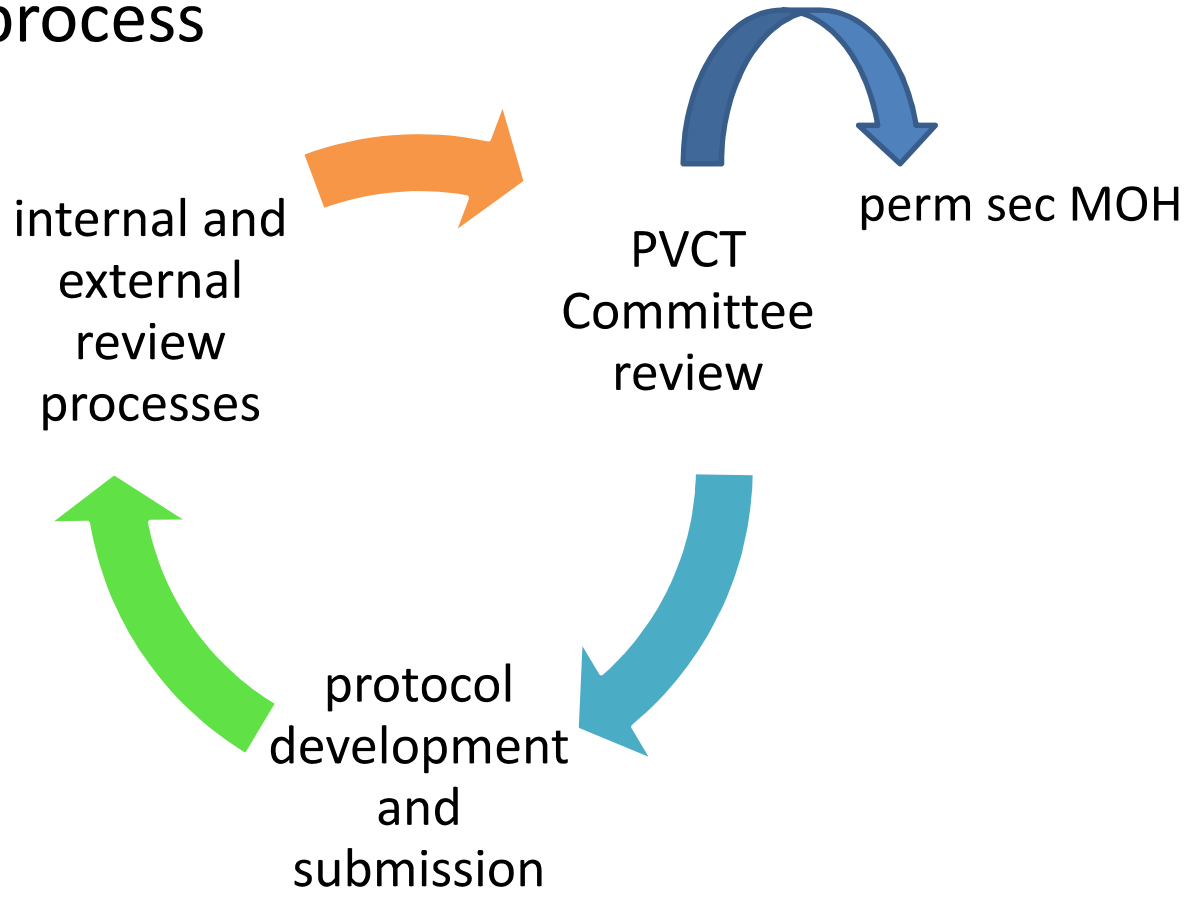
EVALUATION PROCESS

an iterative process



CHALLENGES WITH VACCINE TRIALS

National Regulatory Authority:

- Lack of resources to validate the quality of the medicine
- Difficult to implement similar standard of care e.g. no Prep in HIV vaccine trials
- Limited technical capacity in-house and external resource persons.

CHALLENGES WITH VACCINE TRIALS

Ethical Oversight:

- Limited technical capacity in-house and external resource persons.
- Limited numbers of experts in Human Clinical Trials network-potential conflict of interest.
- Involvement of higher policy levels than ECs on trials for new vaccines (HIV, EBV, malaria).

CHALLENGES WITH VACCINE TRIALS

Study Product:

- incomplete information *(formulation, stability data, GMP of manufacturer)* on investigational medicinal product development (IMP) in the investigators brochure (IB)
- Inadequate knowledge on immunogenicity and immune protection correlations for novel vaccines-no IND in originator country
- Reliability of animal models to humans

CHALLENGES WITH VACCINE TRIALS

Participants:

- Low vaccine literacy in community
- False sense of protection
- Difficult consent process

  - vaccine induced seropositivity-stigmatisation
- Insurers not interested in underwriting clinical trials
- Co-morbidities (HIV, TB): impact on adverse events

CHALLENGES WITH VACCINE TRIALS

Systematic:

- Coordination between NRA and EC
- Involvement of National Biotechnology Authority if vaccine is produced by genetic engineering processes
- Safety-disposal of waste

OPPORTUNITIES WITH VACCINE TRIALS

Capacity Building:

- WHO Vaccine PQ Capacity Building
- NRA Assessment and Strengthening-predicated on NRA responsiveness

  -regulatory framework

  -collaboration

  -peer to peer learning
- Global Learning Opportunities-evaluation of Clinical data
- HCanada vaccine regulation *(annual forum Ottawa and regional workshops in Africa)*

OPPORTUNITIES WITH VACCINE TRIALS

Collaborations

- AVAREF
- Regional Economic Grouping: EAC, SADC (ZAZIBONA), UEMOA, WAHO, COMESA
- Continental: African Medicines Regulatory Harmonisation
- Expert Opinion (Article 58 or similar)

Regional Centres of Regulatory Excellence (ReCoRE)

- African Union NEPAD designated ReCoRE *(Burkina Faso, Ghana, Zimbabwe, RSA)*

Bridging the Gap-

- Regional Scientific Workshops WHO: Rota, HIV, Malaria, EBV, HPV, Polio End Game

AMRH NEPAD RECORES

	RCORE Applicant Institution(s)	Designation
1	Direction General de la Pharmacie du Medicament et des Laboratoires / University of Ouagadougou Burkina Faso <rsemde@yahoo.fr ; rasmane.semde@univ-ouaga.bf ; rasmane.semde@@dgpml.sante.gov.bf>	RCORE in clinical trials oversight
2	Food & Drugs Authority (FDA) Ghana <http://www.fdaghana.gov.gh>	RCORE in medicine evaluation and registration and clinical trials oversight
3	Medicines Control Authority of Zimbabwe (MCAZ) <http://www.mcaz.co.zw>	RCORE in medicine registration and evaluation, Quality Assurance/Quality Control and clinical trials oversight

Ref: <amrh.org/wp.../NEPAD-Agency-Designated-RCOREs_May-2014-.pdf >

ACKNOWLEDGEMENTS

1. WHO NRA Strengthening-Status update and regulatory functions

2. MCAZ Pharmacovigilance & Clinical Trials Division- Challenges in CT regulation in LMICs, CT regulatory framework, CT evaluation process a

3. WHO PQ Capacity Building-AVAREF/DCVRN

4. RECORE-African Union NEPAD African Medicines Regulatory Harmonisation (AMRH) initiative

5. WHO & BMGF

6. Clipart

Thank you!!

William Wekwete 14 March 2016

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