Regulatory Challenges and Constraints when Evaluating Vaccine Clinical Trials

Global Vaccine and Immunization Research Forum
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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 of 194 countries
- 950 regulatory experts, + 350 assessors
Vaccine producing
1990: 63 countries
2012: 44 countries

Vaccine demand is increasing
However number of producing countries is decreasing
44 vaccine producing countries, 2014
146 vaccine manufacturers, 90% global production in 25 countries

Developing countries with vaccine industry
22 countries with prequalified vaccines
30 manufacturers with prequalified products
39 types of products prequalified
NRA Assessment & Strengthening

Marketing Authorisation
Regulatory Inspection
Clinical Trials Approval & Monitoring
Vigilance
Lot Release
Laboratory Access

REGULATORY SYSTEM STRENGTHENING

Protecting Your Right to Quality Medicines and Medical Devices
NRA Visits 1997-2015
NRA Status 1997-2015
NRA In-country Expertise
RESEARCH REGULATORY FRAMEWORK

**Control of all Research**
- Ministry of Science & Technology
  - National Biotechnology Authority (NBA)
    - Investigational product- *if* biotech
  - Research Council of Zimbabwe (RCZ)
    - Research Act 1959

**Investigational Medicinal Product Protection Human Subjects**
- Ministry of Health & Child Care
  - Medical Research Council of Zimbabwe (MRCZ)
    - IEC/IRB/REC/IERB
  - Medicines Control Authority of Zimbabwe (MCAZ)
    - Medicines and Allied Substances Control Act 1969 & Regulations

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EVALUATION PROCESS

an iterative process

internal and external review processes

PVCT Committee review

protocol development and submission

perm sec MOH

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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

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## AMRH NEPAD RECORES

<table>
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<tr>
<th>RCORE Applicant Institution(s)</th>
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<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>

[Logo: MCAZ]

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4. RECORE-African Union NEPAD African Medicines Regulatory Harmonisation (AMRH) initiative
5. WHO & BMGF
6. Clipart
Thank you!!