Clinical Trials Regulator's Experience and Interactions with Sponsors and Investigators- Zimbabwe

Presented by

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Presentation Outline

- Regulatory overview of Clinical Trials
- Evaluation Process of Clinical Trial Applications (CTAs)
- Interactions of Regulator, Sponsors and Investigators
- Joint Clinical Trial Application reviews & collaborations
- Regulator Experiences and Challenges

Regulatory Overview

REGULATIONS

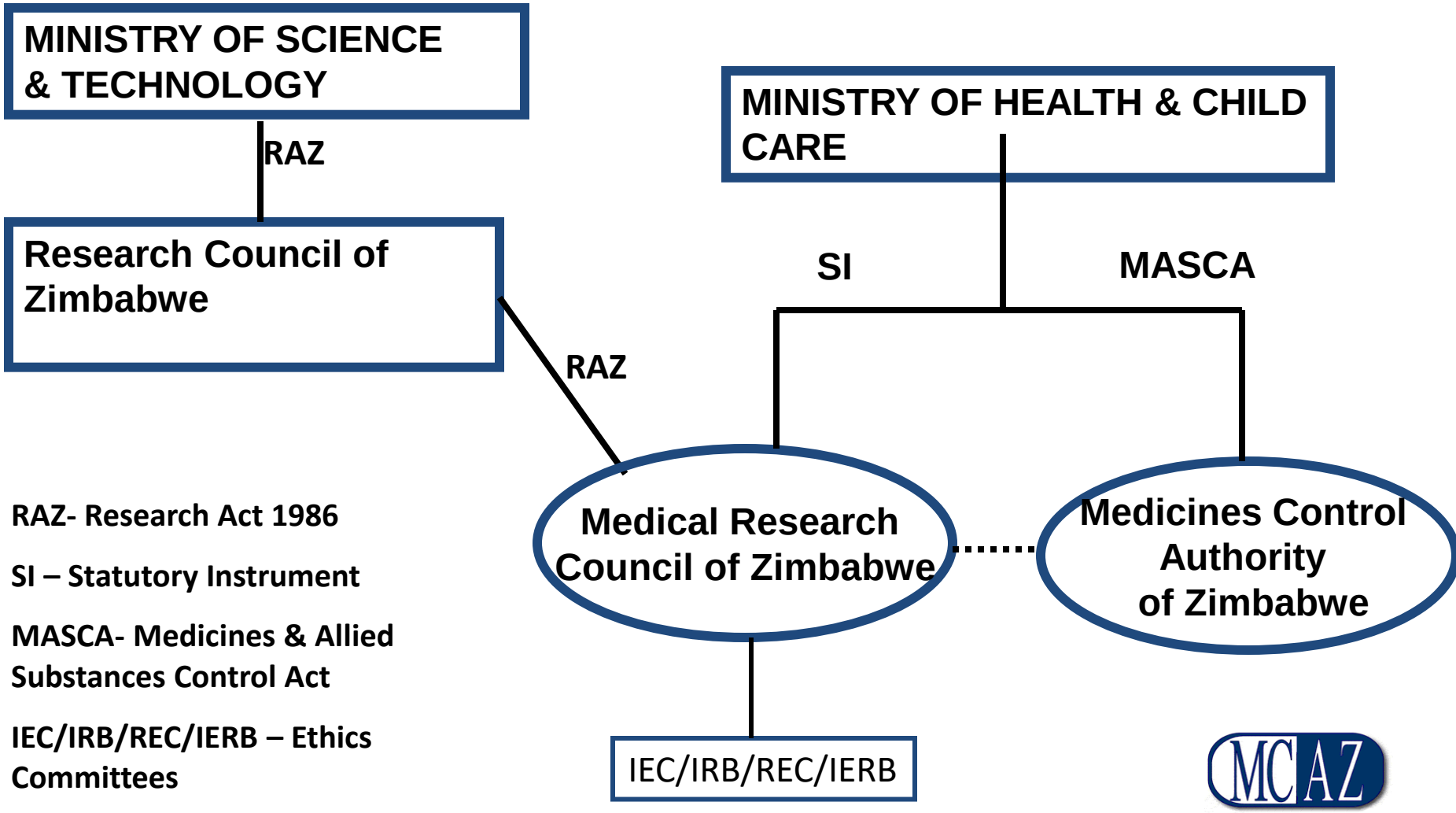
- All clinical trials conducted in Zimbabwe are regulated in terms of Part III of the Medicines and Allied Substances Control Act [Chapter 15:03] and its regulations
- no person shall conduct a clinical trial of any medicine without the prior written authorisation of the Authority, granted with the approval of the Secretary of the Ministry of Health and Child Care.

GUIDANCE DOCUMENTS

- Medicines and Allied Substances Control (General) Regulations, 1991. S.I. 150 of 1991
- Guidelines for GCP 2012 Zimbabwe – based on ICH GCP and the International Ethical Guidelines for Biomedical Research in humans(CIOMS/WHO)
- Pharmacy Guidelines for Investigational Drugs
- MCAZ Clinical Trial - SAE Reporting Guideline

http://www.mcaz.co.zw/index.php/downloads/category/14-guidelines

Research Regulatory Framework



RAZ- Research Act 1986

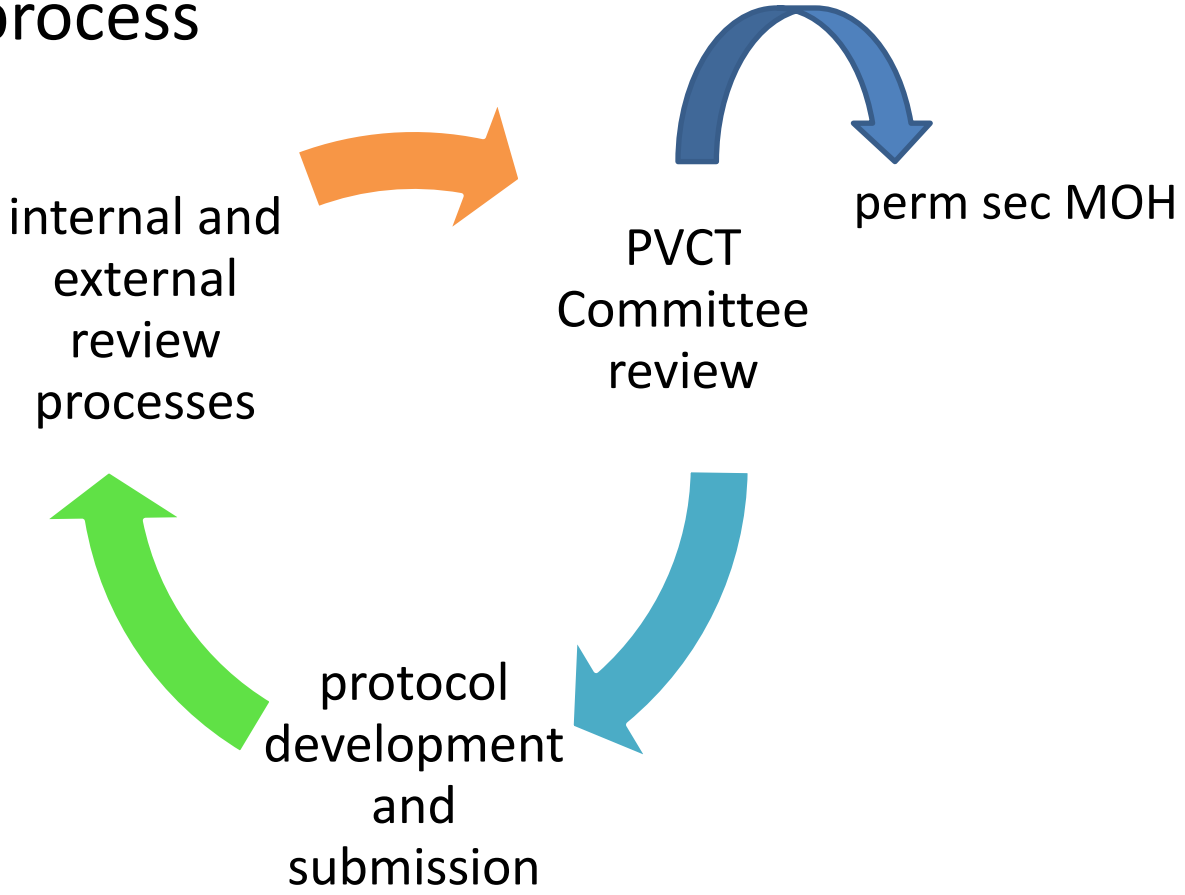
SI – Statutory Instrument

MASCA- Medicines & Allied Substances Control Act

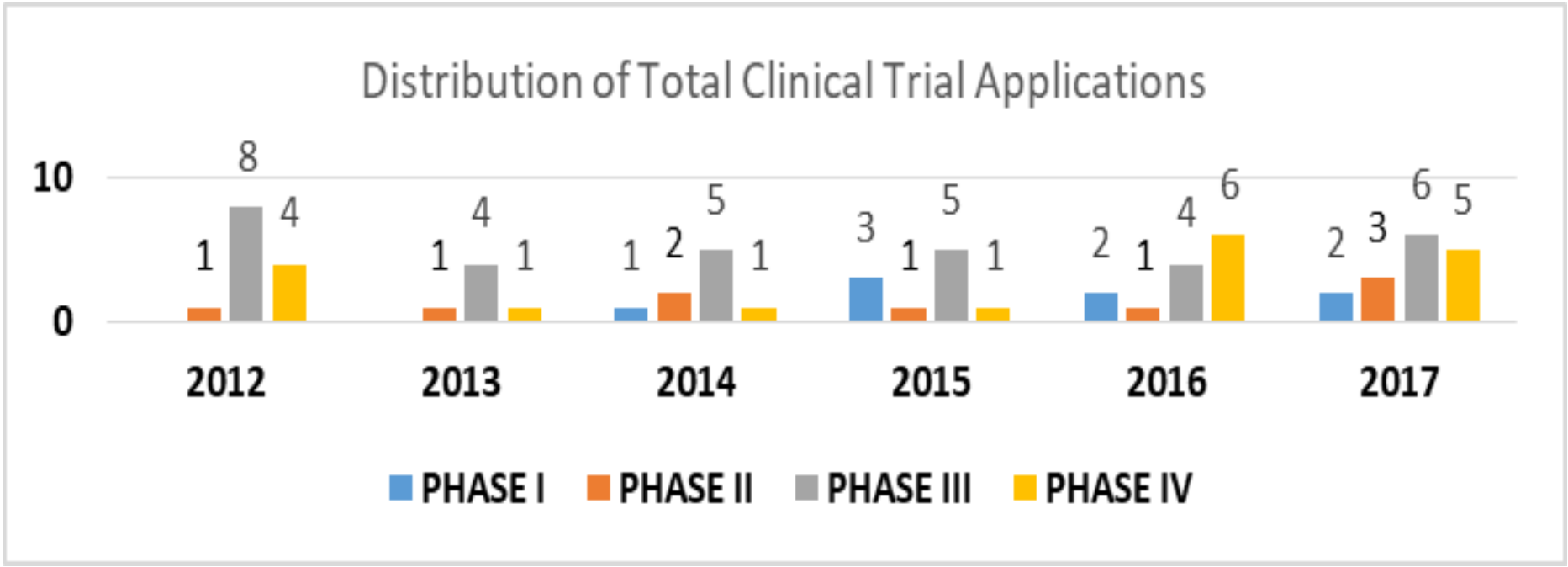
IEC/IRB/REC/IERB – Ethics Committees

Evaluation Process

an iterative process



- Target timelines for processing CTA is 90 days
- A total of 67 applications were received and approved from 2012 to 2017
- Average of 1-3 CTAs received per month



- CT timelines were improved, average processing time for authorization of a study in 2017 was 78 days against a target of 90 days.
- Developing e-Clinical trial application system and CT registry platform (≈90% complete)

Pre- CTA submission meetings

- Sponsors and/or Investigators are invited to request a pre-CTA consultation meeting.
- Particularly useful for new active substances or applications that will include complex issues eg HIV vaccines
- Essential for pivotal trials, whose results will be used for a New Drug Submission

Technical Requirements for a CTA - general

- clinical trial protocol inclusive of a statistical analysis plan
- completed MC10 form (Application form to conduct a clinical trial)
- evidence of ethics approval or application
- signed PI declaration forms and PI CVs
- signed financial declaration by Sponsor
- Participant insurance cover
- Participant recruitment materials and ICFs
- investigator brochure or package insert

Technical Requirements – IP

to ensure quality medicines are utilised, we require:

- a current and valid GMP for the manufacturer
- certificate of analysis for the IP
- stability data to support the proposed shelf life
- for IND: an investigator brochure + US FDA IND number/approval
- registered medicines: package insert/IB if necessary
- a detailed pharmacy plan describing the handling of the IP and responsible personnel

Regulator Interaction with Sponsors & Investigators

- The PI and Sponsors should observe strictly to all the conditions to which the trial was authorized
- Report all serious adverse events (SAEs)
- Seek approvals for any protocol amendments
- Report all protocol deviations
- Submit clarification memos, DSMB, progress, annual & final reports & applications to import IP
- submit safety updates and updated Investigator brochure for the study medicines if any

- Regulator provide feedback to the Investigators in writing within 30-60 days of submission depending with the report
- Feedback involves approval letters issued, letters requesting for clarifications, more information etc
- Meetings between investigators and regulator are held sometimes

Trial Inspections

- MCAZ & MRCZ joint inspections: can be routine or targeted/investigative
- MCAZ focuses on IP storage; dispensing and the conduct of the clinical trial
- MRCZ focus on ethics & may conduct participant interviews and also check ICF documentation
- We review study documents e.g. monitor reports; trial logs, pharmacy documents etc

Joint Clinical Trial Application reviews and collaborations e.g. WHO-AVAREF, ZAZIBONA

- Clinical trials regulation collaborations in African region e.g. ECOWAS, EAC & SADC
- EAC, harmonized standards for registration, clinical trials and pharmacovigilance
- SADC harmonized CTA guidelines developed
- Harmonized standards completed in ECOWAS, and partially in SADC

- AVAREF guidelines for joint & assisted reviews endorsed
- AVAREF endorsed a 60-day CTA approval timeline
- Timelines reported by 12 countries, including Zimbabwe

ZAZIBONA

- SADC –Collaborative Medicines Registration Initiative (Zazibona)
- Endorsed by SADC Ministers of Health in January 2015
- Expand to other SADC Member States beyond the 4 founding Member States
- 5 Active Participating Member States -Zambia – Zimbabwe-Botswana –Namibia-South Africa (joined June 2016)
- 1 non-active participating Member State – Swaziland (joined Nov 2016)

- Initiative to collaborate in assessment and inspections for medicines registrations with objectives to:

–Reduce workload –Reduce timelines to registrations –Develop mutual trust and confidence in regulatory collaboration –Platform for training and collaboration in other regulatory fields

- SADC/ZAZIBONA: 193 products evaluated with final joint recommendation for 123 products

Regional Centers of Regulatory Excellence (RCOREs)

- RCORE is a designated institution or partnership of institutions with specific regulatory science expertise as well as training capabilities.
- This initiative was established by the NEPAD
- MCAZ was awarded RCORE status for medicine registration and evaluation, quality assurance/quality control and clinical trials oversight
- MCAZ trains other regulators and do quality control tests for products submitted from other countries

Benefits of Collaborations

- Reduces timelines for approval of Clinical Trials
- Reduces costs of conducting clinical trials and promotes research in Africa
- Standardization of guidelines and requirements
- Enhance Expertise, Experience & work sharing

Challenges

- Lack of legal frame work for sharing of information between regulators.
- Problems with adopting regional recommendations at national level
- Different legislation and policies

Regulators Experiences and Challenges

- Provision of incomplete IP development information usually for IND making it difficulty for regulatory decisions
- lack of resources, experience and expertise eg for complex vaccine clinical trials such as HIV, Ebola vaccines
- Provision of incomplete CTA by inexperienced investigators causing delays in approvals and delay in response by investigators
- Overlapping interests-The dire need for the product versus the regulatory hurdles
- Lack of local insurance companies who offers insurance to CT participants

THE FUTURE

- SADC and AU regulatory harmonization & joint Clinical Trial evaluation reviews
- Collaboration with other International regulators
- Electronic submission of CTA applications.

THE GOAL IS TO PROMOTE RESEARCH IN AFRICA AND PROTECT SAFETY OF PARTICIPANTS

THE END

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