INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

IPM's Perspective as Regulatory Sponsor

Dr Annaléne Nel, Chief Medical Officer

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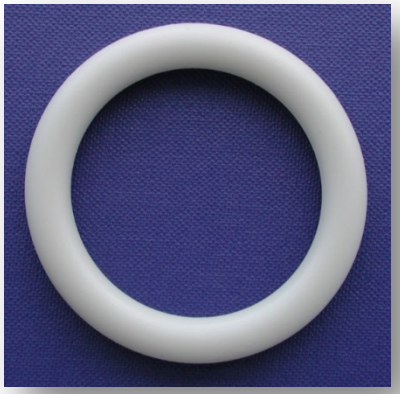
Developing HIV Prevention Products for Women worldwide

A Regulatory Sponsor

- The person / company who applies for
  - FDA, USA: Investigational New Drug (IND)
  - EMA, Europe: Medicinal Investigational Product (IMP)
  - MCC, SA: New Chemical Entity (NCE)
- The regulatory sponsor applies for authorization from a NRA to administer an new investigational drug or biological product to humans
- All regulatory sponsors are held to the same standards and requirements for conducting research with an investigational drug or device

Regulatory Considerations: Dapivirine

- Dapivirine is a new chemical entity (NCE)
- Approval pathway for a NCE for HIV prevention is more complex than for an already approved treatment drug being used for prevention (like Truvada for PrEP use)
- Need to include more comprehensive safety and quality data



Dapivirine Ring-004 Development Path

Drug Discovery:

Dapivirine

Preclinical:

- Lab/Animal studies
- Chemistry, Manufacturing Control

IND

Phase I

Clinical

Regulatory Review

Post Licensure

- IPM holds the worldwide rights to dapivirine

- IPM regulatory sponsor
- FDA IND for Dapivirine Vaginal Ring:
  - IND 108743, submitted Apr 25th, 2011
- Communication and consultation with regulatory authorities

Regulatory Sponsor
Quality Assurance and Quality Control

RESPONSIBILITY:

Implementing and maintaining QA and QC systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements

Dapivirine Ring-004 Development Path

Drug Discovery

Preclinical

IND

Clinical

Phase I

Phase II

Phase III

Regulatory Review

Post Licensure

- Ensure clinical trial is conducted according to signed investigator agreement
- Protecting the rights, safety and welfare of participants under the investigator's care
- Control of the investigational product
- Record maintenance and retention
- Management of site-based finances, records, and quality assurance
- Accommodating NRA inspections

Dapivirine Ring-004 Development Path

Drug Discovery

Preclinical

IND

Clinical

Phase I

Phase II

Phase III

ASPIRE (MTN-020

The Ring Study (IPM 027)

Regulatory Review

Post Licensure

- Critical path with two pivotal Phase III trials
  - Comparable data from two similar protocols required to demonstrate reproducibility of results
  - Summary of Clinical Safety
  - Summary of Clinical Efficacy
- Alignment of clinical trial conduct at research centres
- Standardisation of external service providers operational execution (CROs, central laboratories, data management, biostatistics)

Regulatory Sponsor

Quality Assurance: Audits

PURPOSE:

Independent of and separate from routine monitoring or quality control functions, to evaluate trial conduct and compliance with the protocol, SOPs, GCP, and the applicable regulatory requirements

Dapivirine Ring-004 Development Path

Drug Discovery:

Dapivirine

Preclinical:

- Lab/Animal studies
- Chemistry, Manufacturing Control

IND

Clinical

Phase I | Phase II | Phase III

Art 58 (EMA)
NDA (FDA)

Regulatory Review

Post Licensure

- Pharmacovigilance
- Access

- IPM global licensure holder

- IPM regulatory sponsor
- FDA IND for Dapivirine Vaginal Ring:
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- Preparation of regulatory dossier
  - Electronic Common Technical Document (eCTD)
- Submission of application for marketing approval
- EMA: Article 58 submission
  - First step to seek marketing approval from African regulators
  - WHO Pre-Qualification
- MCC, SA: in parallel to EMA submission
  - Inspections most likely for South African research centres (both ASPIRE and The Ring Study)
- FDA
  - New Drug Application (NDA)

In conclusion

- Inspections are usually triggered by
  - o release/publication of trial results
  - o submission of marketing application
- Passing an inspection proves:
  - o compliance with international ethical and scientific standards
  - o adequacy of research sites/sponsor quality systems
  - o the integrity of the data
  - o protection of the rights, safety and well being of trial participants