New Vaccines in SA

Regulatory Perspectives

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MEDICINES CONTROL COUNCIL

Reg Environment
Registration
Childhood vaccines
Clinical trials
HIV vaccines
Other vaccines
Challenges

Outline

- Regulatory Environment
- Registration of new vaccines
  - Childhood vaccines
- Clinical Trials Application procedures
  - HIV Vaccines
- Other new vaccines in development
- Challenges
- Ongoing Actions

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Regulatory Environment

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Challenges

- Act 101 of 1965 (as amended)
- Establishes Regulatory Authority
  - All medicines must be registered for use in SA
  - Quality Safety and Efficacy
- Medicines Control Council (MCC)
  - Experts and stakeholders appointed by Minister of Health
- Expert Committees (Total=9)
  - Clinical, P&A, Biologicals, Clinical Trials etc.
    - Use Policies & Guidelines → Recommendations to MCC
- New Amended Act (SAHPRA) being implemented
  - Revise MCC and decision making
  - Enhance evaluation capacity
  - Include Medical Devices and diagnostics

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New Vaccines - Registration

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Challenges

- **The Biological Medicines Committee**
  Appointed by the Minister of Health
  - **Expert evaluators in**
    - **Clinical use of biological medicines and vaccines**
    - **Manufacturing and control of biological medicines**
    - **Public Health Immunization**
- **Applications – CTD dossier (Local Module-1)**
  - **Evaluation reports – peer reviewed by BMC**
  - **Queries to applicants – consolidate report**
  - **Recommendation to MCC – Approve or Reject**
  - **Post Marketing Risk Management commitment**
  - **Evaluation and approval of amendments**
- **Timelines – variable**
  - **First response from BMC 12 – 16 weeks**
  - **Approval– usually 9 to 12 months**

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New Vaccines - Background

- No local vaccine manufacturer
  - All imports
  - Local manufacture of DTP, OPV, BCG terminated by 2000
- Clinical development mostly outside SA
  - CTD dossier – first sight for evaluators
  - Pilot IND-like procedure for local vaccine developers
  - New vaccine applications from Emerging manufacturers
- As new vaccines have become available
  - They have been registered
  - introduced into EPI when appropriate
  - NAGI & DoH decision.
- Public Health vaccine-budget doubles every few years

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Introduction of New Vaccines

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- **Childhood Vaccines** Expanded Program of Immunization (SA)
  - Included DTP, OPV, Measles & BCG for infants in 1990s
  - *Hepatitis* B sAg (recombinant) 1996
  - *Haemophilus influenzae* B PRP-conjugate 1998
  - Intradermal BCG 2000
  - Pentavalent DTP-HepB- HiB 2010
  - Rotavirus (Rotateq and Rotarix) 2012
  - Pneumococcal PS-conjugate 2013
  - Hexavalent DTaP-HepB-HiB-IPV 2013
  - Human Papilloma Vaccines (adolescents) 2014
  - Measles-mumps-rubella planned

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New Vaccines – Clinical Trials –

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Challenges

- Clinical Trials Committee
  - Evaluates applications for individual trials (not IND)
  - Evaluates amendments to approved trials
  - Recommends approval to MCC
- Applications
  - Defined format – policies and guidelines for applicant
  - Evaluation by expert – peer review of reports by CTC
  - Follow SA GCP Guidelines (2006) and policies
  - Parallel process with
    - Ethics Committee approval – required
    - GMO licence or other laws – expected
  - Investigational products require Sect 21 Permit for import & use
  - Timelines: 1st Response from CTC 8 weeks. Approval 12-16 weeks

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New Vaccines
HIV vaccine development

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Challenges

- HIV and AIDS are a major health challenge in SA
- State support for HIV-research includes
  - SAAVI - SA AIDS Vaccine Initiative
- Vaccines are developed with international support
- Many HIV Trials conducted in SA since 1999
- MCC – HIV Vaccine Task Group
  - Guidelines and policies 2003
  - Quality, Safety and ethical treatment of participants
- New and Novel Vaccines and regimens in trials
  - DNA-prime-boost, Vectored vaccines, novel adjuvants

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Other New Vaccines

- 19 new vaccine trials have been approved since Jan 2014
- Include
  - Pneumococcal conjugate vaccine in pregnant (HIV+) women
  - Meningitis PS-conjugate vaccines
  - Influenza vaccines – new formulations and in pregnant (HIV+) women
  - TB vaccines – modified BCG or MTb, Adjuvanted protein vaccines
  - HIV vaccines – DNA, Vectors and adjuvanted proteins (Clade C)
  - HPV vaccines – new formulations - regimen
  - Rotavirus vaccines – new formulation
  - RSV vaccines – early development

- HIV and TB vaccine trial sites are well established

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Current Challenges

- Each vaccine brings new challenges for MCC
  - Adaptive trial designs – defined alternatives
  - Inclusion of adolescents and infants and pregnant women
  - Dose-escalation – age-de-escalation
  - Inclusion of healthy HIV+ participants in vaccine trials
  - Calculations of power to detect AEs or protection
  - Lack of established correlates of protection
  - New immunological end-point tests – unvalidated
  - Open-ended storage of clinical samples for future research
  - Clinical trial registry
  - Inspection of Trial sites – GCP Guidelines and inspection policy
  - New vaccine applications from **Emerging manufacturers**

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Ongoing Actions

- Implementation of SAPHRA – reduce uncertainty
- Strengthened NRA
  - Improved and updated policies and guidelines
    - Emergency and Pandemic vaccine approvals
  - Improved communications with public and industry
  - Increased staff levels and training – more evaluators
  - Electronic document management system
- International and Regional cooperation
  - WHO, EU (EDCTP) and US FDA (DAIDS, NIH)
  - Developing Country Vaccine Regulators' Network
  - African Vaccine Regulators Forum
  - NGOs:- BMGF, AERAS, PATH, IVI
- Strengthened National Biologicals Control Laboratory
- Improved pharmacovigilance for vaccines use

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Thank You

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And

Colleagues from MCC