How South Africa regulates medicines and vaccines

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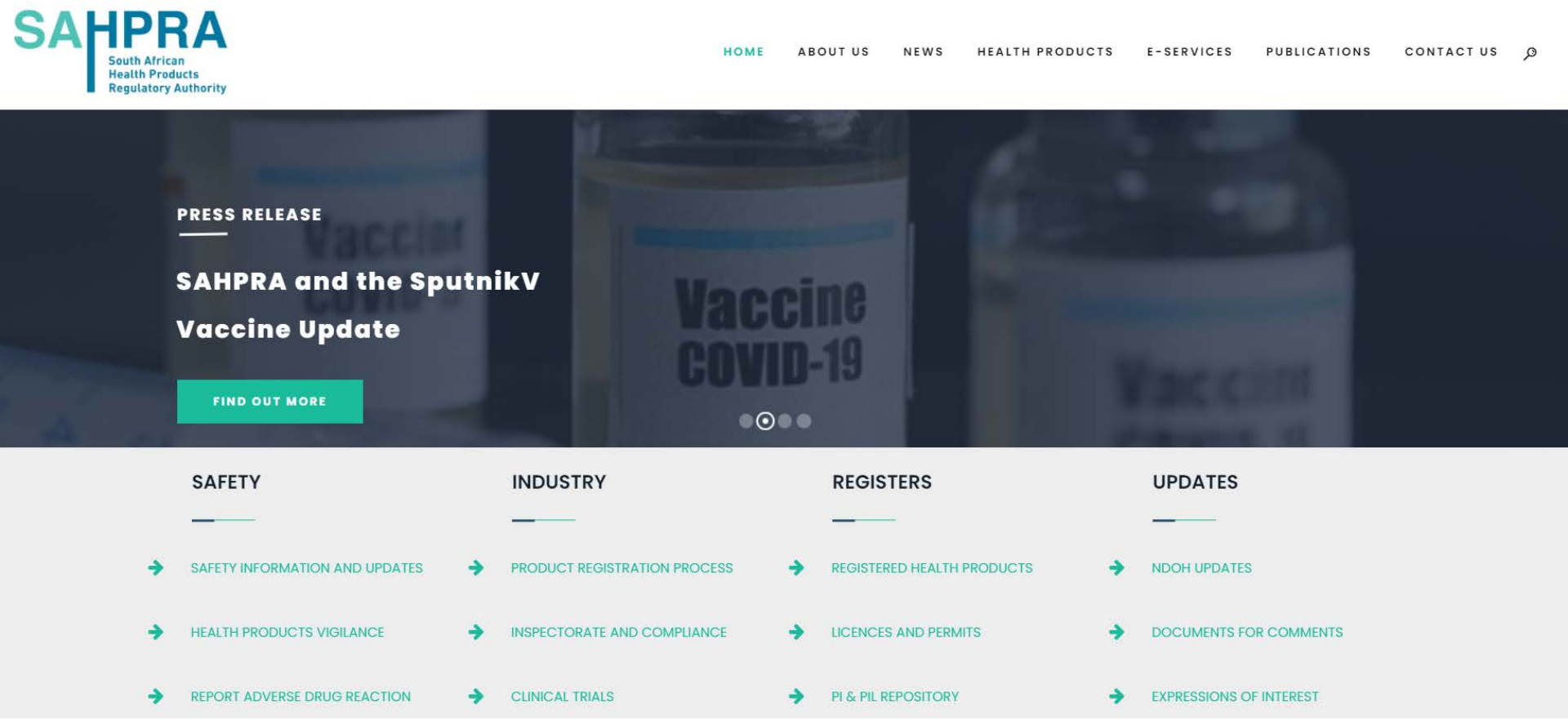
Webinar arranged by:

SAHPRA – SA's national medicines regulatory authority (NMRA)



Human medicines | Veterinary medicines | Medical devices (incldg IVDs) | Clinical trials | Radionuclides

Medicines and Related Substances Act (Act 101 of 1965)

- **14. Prohibition on the sale of medicines, medical devices or IVDs which are subject to registration and are not registered.**—
  (1) Save as provided in this section or sections 21 and 22A, no person shall sell any medicine, medical device or IVD which is subject to registration by virtue of a declaration published in terms of subsection (2) unless it is registered.
- (2) (a) The Authority may from time to time determine that a medicine, medical device or IVD, or class or category of medicine, medical device or IVD or part of any class or category of medicine, medical devices or IVDs mentioned in the declaration, shall be subject to registration in terms of this Act.

Implications

- **All** category A medicines (human use, apart from complementary medicines; including biological medicines) have been the subject of a "call-up notice", so have to be registered before they can be sold.
- **Section 21** allows for access to unregistered medicines for individual patients or in clinical trials. Some provisions for "bulk" approvals (e.g. out of stock; emergency use of colistin and ivermectin).

eCTD - dossier structure (Module 1)

Directory Structure – Part 1

- 0000 of 'MCC01'
  - 1 Administrative Information and Prescribing Information
    - Envelope
    - Module 1 ZA
      - 1.0 Letter of Application
      - 1.2 Application
        - 1.2.1 Application Form
        - 1.2.2 Annexes
          - 1.2.2.1 Proof of payment
          - 1.2.2.2 Letter of Authorisation
          - 1.2.2.3 Dossier Product Batch Information
          - 1.2.2.4 Electronic copy declaration
          - 1.2.2.5 Curriculum vitae of the person responsible for pharmacovigilance
          - 1.2.2.6 API Change Control
          - 1.2.2.7 EMA certificate for a Vaccine Antigen Master File (VAMF)
          - 1.2.2.8 EMA certificate for a Plasma Master File (PMF)
      - 1.3 South African labelling and packaging
        - 1.3.1 South African Package Insert
          - 1.3.1.1 Package Insert
          - 1.3.1.2 Standard References
        - 1.3.2 Patient Information Leaflet
        - 1.3.3 Labels
        - 1.3.4 Braille
      - 1.4 Information about the experts
        - 1.4.1 Quality
        - 1.4.2 Non-clinical
        - 1.4.3 Clinical
      - 1.5 Specific requirements for different types of applications
        - 1.5.1 Literature based submissions
        - 1.5.2 Amendments/Variations
          - 1.5.2.1 Tabulated schedule of amendments
          - 1.5.2.2 Medicines Register Details
          - 1.5.2.3 Affidavit by Responsible Pharmacist
        - 1.5.3 Proprietary name applications and changes
        - 1.5.4 Genetically modified organisms
        - 1.5.5 PI and PIL amendments/updates

Directory Structure – Part 2

- 1.6 Environmental risk assessment
  - 1.6.1 Non-GMO (genetically modified organisms)
  - 1.6.2 GMO
- 1.7 Good manufacturing practice
  - 1.7.1 Date of last inspection of each site
  - 1.7.2 Inspection reports or equivalent document
  - 1.7.3 Latest GMP certificate or a copy of the Appropriate licence
  - 1.7.4 Release
    - 1.7.4.1 API
    - 1.7.4.2 IPIs
    - 1.7.4.3 Finished Product Release Control (FPRC) tests
    - 1.7.4.4 Finished Product Release Responsibility (FPRR) criteria
  - 1.7.5 Confirmation of contract
  - 1.7.6 CPP (WHO certification scheme)
  - 1.7.7 SAPC registration
  - 1.7.8 Registration with Registrar of Companies
  - 1.7.9 Other documents relating to the Applicant/PHCR
  - 1.7.10 Sample and Documents
    - 1.7.10.1 Confirmation of submission of sample
    - 1.7.10.2 Batch manufacturing record of the sample
    - 1.7.10.3 CoA of the sample
  - 1.7.11 Certified copy of a permit to manufacture specified Schedule 5, Schedules 6, 7 and 8 Substances
  - 1.7.12 Inspection flow diagram
  - 1.7.13 Organogram
- 1.8 Details of compliance with screening outcomes
- 1.9 Individual patient data - statement of availability
- 1.10 Foreign regulatory status
  - 1.10.1 List of countries in which an application for the same product as being applied for has been submitted
  - 1.10.2 Registration certificate or marketing authorisation
  - 1.10.3 Foreign prescribing and patient information
  - 1.10.4 Data set similarities
- 1.11 Bioequivalence trial information
- 1.12 Paediatric development programme
- 1.13 Risk management plan

Module 2 – summaries; Module 3 - Quality; Module 4 – Non-clinical; Module 5 - Clinical

Assessment focuses on:

- **Quality**
  - How is the medicine made and how will quality be assured during production and distribution?
- **Safety**
  - Are the expected adverse effects proportional to the proposed use? Pregnancy/lactation?
  - How will further data on safety be gathered? Adverse events following immunisation (AEFI)? Risk management plan?
  - How will access be controlled (scheduling)?
- **Efficacy**
  - Does the medicine achieve its proposed purpose (in preventing or treating a disease or symptom)?
  - Are there important differences in effect between patient groups (age/sex/co-morbidities/other medicines)

Who does the assessment and who makes the decision?

- Internal screening
- External evaluator/advisory committee member review (primary)
- Peer review (secondary), with the possibility of committee discussion
- Recommendation to the Authority
- Final decision is taken by the Authority (CEO + staff)

- Certificate of registration + conditions + PI/PIL
- Single exit price (if sold to the private sector) set by the manufacturer/importer; recorded in the Medicines Price Registry; subject to annual maximum SEP adjustment by the MoH

The possibility of reliance

- **2B. Functions of Authority.**—
  (2) The Authority may—

  (*a*) liaise with any other regulatory authority or institution and may, without limiting the generality of this power, require the necessary information from, exchange information with and receive information from any such authority or institution in respect of—

  (i) matters of common interest; or

  (ii) a specific investigation; and

  (*b*) enter into agreements to cooperate with any regulatory authority in order to achieve the objects of this Act.

Specific biological medicine issues

- Batch-by-batch testing at the National Control Laboratory for Biological Products (UFS)
  - Applied to all current vaccines
  - Possibility of reliance options
- Genetically Modified Organisms Act (Act 15 of 1997), in the case of adenovirus-vectored vaccines

A new option: “rolling reviews”

What is a rolling review?

A rolling review is a regulatory tool that EMA uses to speed up the assessment of a promising medicine or vaccine during a public health emergency. Normally, all data on a medicine’s effectiveness, safety and quality and all required documents must be submitted at the start of the evaluation in a formal application for marketing authorisation. In a rolling review, EMA’s human medicines committee (CHMP) reviews data as they become available from ongoing studies, before a formal application is submitted. Once the CHMP decides that sufficient data are available, the formal application can be submitted by the company. By reviewing the data as they become available, the CHMP can reach its opinion sooner on whether or not the medicine or vaccine can be authorised.

During the rolling review, and throughout the pandemic, EMA and its scientific committees are supported by the COVID-19 EMA pandemic task force (COVID-ETF). This group brings together experts from across the European medicines regulatory network to advise on the development, authorisation and safety monitoring of medicines and vaccines for COVID-19 and facilitate quick and coordinated regulatory action.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

http://www.icmra.info/drupal/en/covid-19/vaccines_confidence_statement_for_hcps

ICMRA

International Coalition of Medicines Regulatory Authorities

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ICMRA statement for healthcare professionals: How COVID-19 vaccines will be regulated for safety and effectiveness

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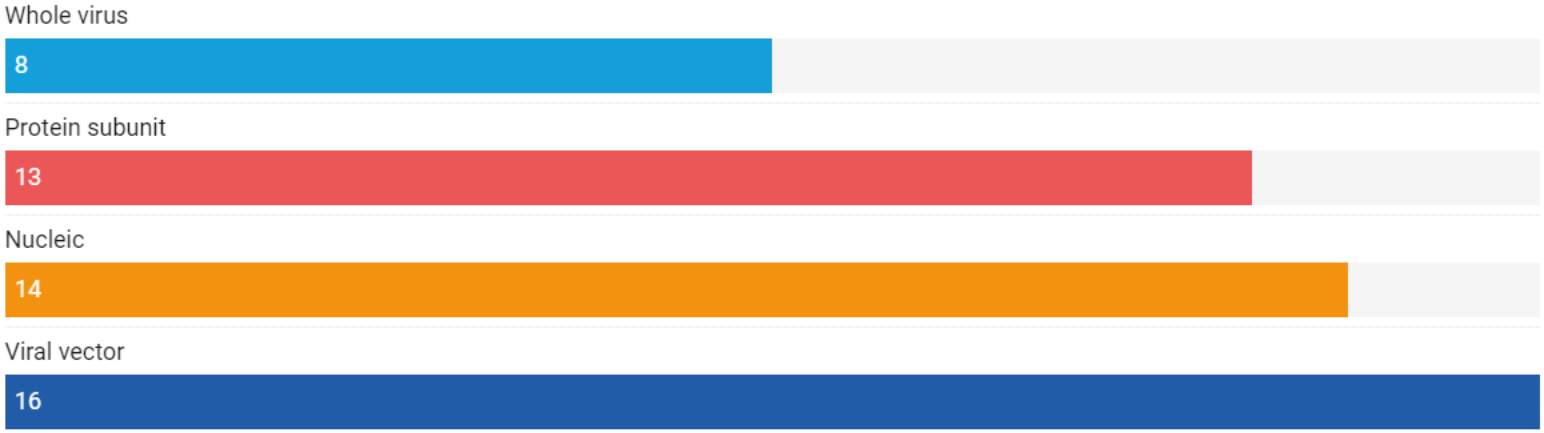
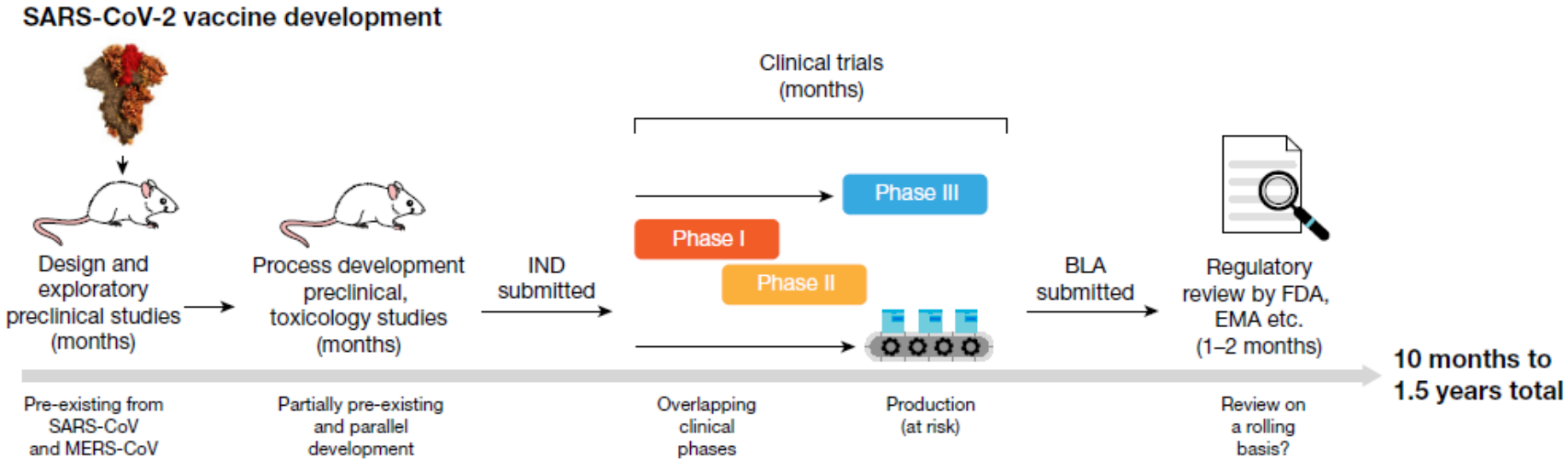
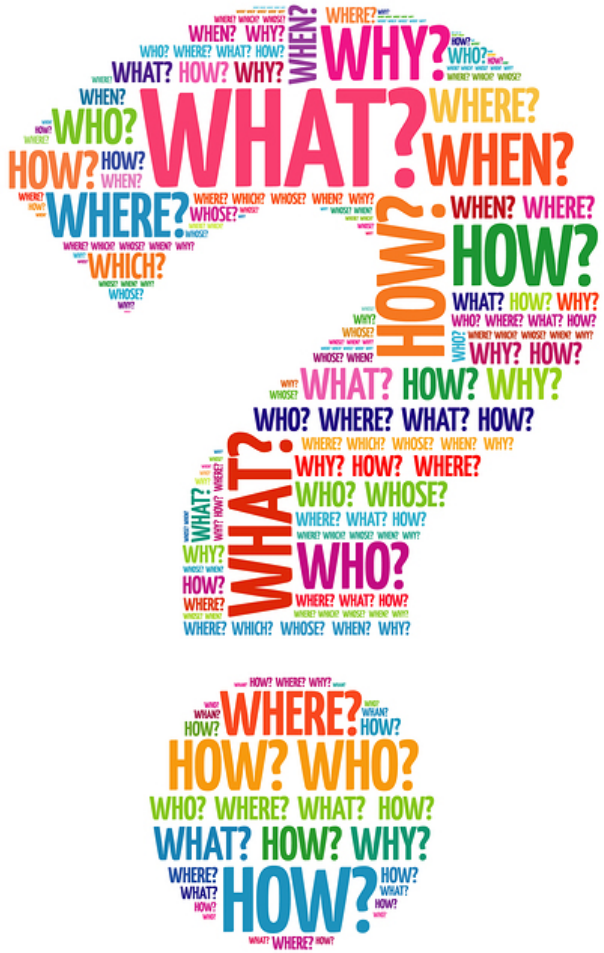


As of 15/12/2020

Source: WHO: Draft landscape of COVID-19 candidate vaccines • Created with Datawrapper

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