

# THE REGULATION OF BIOLOGICAL MEDICINES IN SOUTH AFRICA: STATUS OF *IN VIVO* TESTING

National Control Laboratory for Biological Products

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HSI Symposium on Global Harmonization of Vaccine Testing Requirements.

March 19, 2019



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March 25, 2019



# NATIONAL DOH

## National Drug Policy: DoH, 1996

- Adequate and reliable supply of safe, cost effective medicines of quality to all citizen
- Availability and accessibility of Essential Medicines to all citizens
- **Safety, efficacy and quality of medicines through evaluation, testing, registration and post-registration variation and surveillance**
- Good Dispensing and Prescribing Practices
- Rational use of medicines
- Individual responsibility for health, preventive care and informed decision making



# **LEGISLATIVE FRAMEWORK: TWO GOVERNMENT DEPARTMENTS**

## **(National Department of Health)**

### **South African Health Products Regulatory Authority**

MEDICINES AND RELATED SUBSTANCES ACT 101 OF 1965

Human medicines

Animal medicines that would be prescribed by a veterinarian

## **Department of Agriculture, Forestry and Fisheries**

FERTILIZERS, FARM FEEDS, AGRICULTURAL REMEDIES AND STOCK REMEDIES ACT, 1947 (ACT NO. 36 OF 1947)

So-called 'over the counter' products. This would include veterinary vaccines for production animals and also 'medicines' for conditions recognisable by the farmer.

# SA NATIONAL CONTROL LABORATORY



The laboratory is authorized under The Medicines and Related Substances Act, 1965 (Act 101 of 1965), as amended by Act 72 of 2008, together with Act 14 of 2015, regulation 15

- ISO/IEC 17025:2017
- GMP compliant
- Licenced as a testing laboratory by SAHPRA
- WHO Testing laboratory

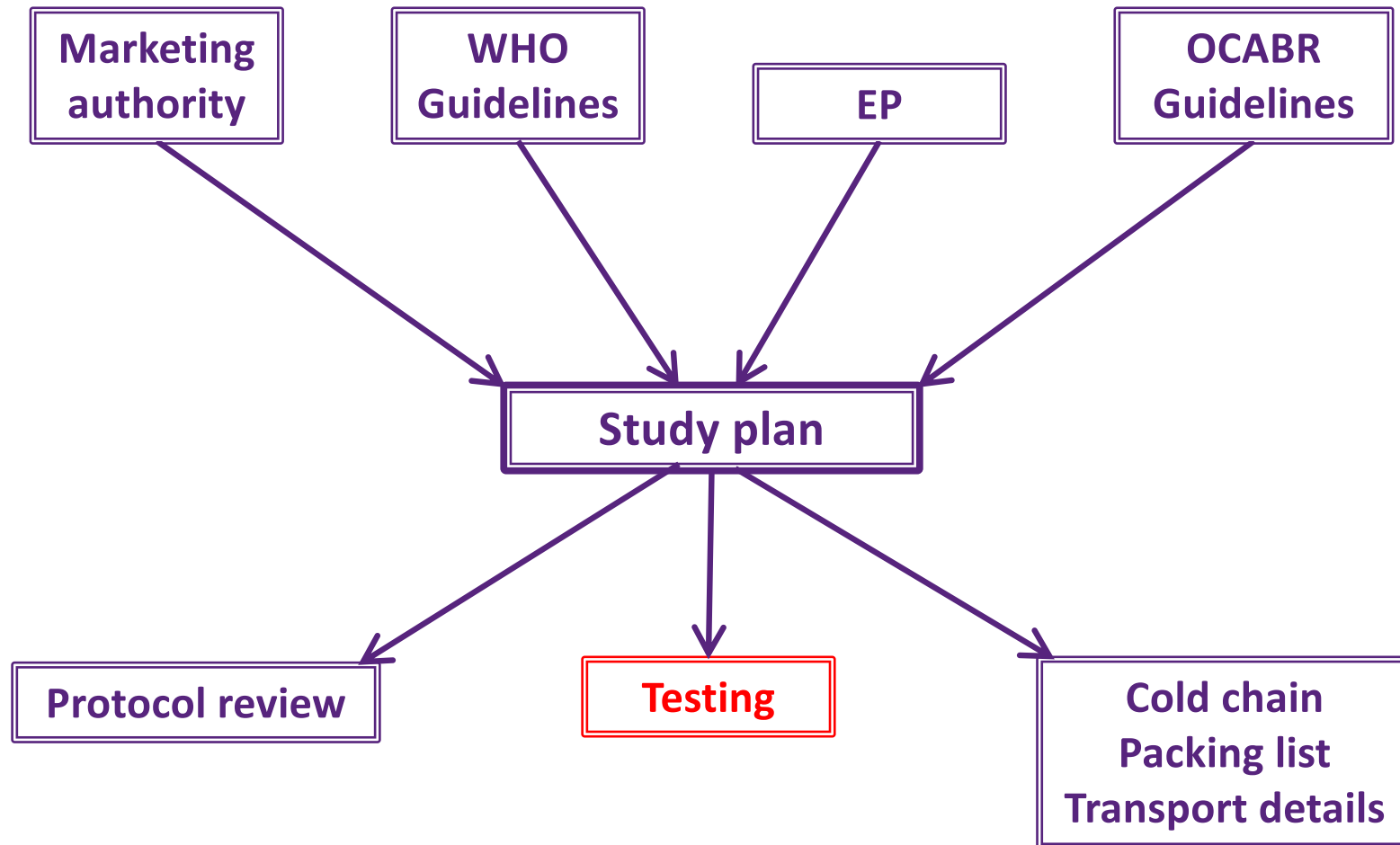


## REFERENCE DOCUMENTS USED

- Manufacturing protocol and QC of batches
- Eur. Ph. Monographs
- ICH guidelines
- OCABR guidelines
- WHO Guidelines for Independent Lot Release of Vaccines by Regulatory Authorities
- WHO Technical Report Series
- Marketing Authorisation Dossier
- NCL guidelines, SOPs etc.



# THE NCL LOT RELEASE PROCESS: STUDY PLAN



# TESTING POLICY

- Batches are selected for testing by considering the following:
- Batches received with low frequency ( $< 6/\text{year}$ ) which require specialist methodology will usually not be tested for identity or potency
- All batches from new manufacturers will be tested until proof of consistency of production has been demonstrated
- In the case of a manufacturer with a proven record, not all batches of the particular product will be tested if the number of batches received for lot release exceeds the NCL testing capacity. In this case, batches will be selected for testing based on their composition as described in the summary protocol
- For products produced by new manufacturers the NCL considers consistency of production only to be demonstrated after testing a minimum of 30 batches without incident
- In the case of a valid out of specification (OOS) test result, an investigation of the OOS test result is initiated. If the OOS test result has convincingly been attributed to a failure in the production and QA release of the product on the part of the manufacturer, all subsequent batches of that product will be tested until consistency is again demonstrated

# ***IN VIVO* TESTING POINTS TO CONSIDER**

- 1. Ethics and the 3R principle** - elimination of all unjustified *in vivo* testing
- 2. The scientific merit of *in vivo* testing for lot release** - New, complex formulations, which have specialised *in vivo* testing protocols are almost impossible to replicate by the NCL of an importing country.
- 3. The WHO NCL network for Biologicals** - South Africa is a full member of the WHO NCL Network for Biologicals. The Network has accepted the principle of promoting the development of harmonised common standards and best practice, including the use of 3R principles amongst NCLs of countries manufacturing prequalified vaccines



# ***IN VIVO* TESTING POINTS TO CONSIDER**

**4. High cost**

**5. The status of the abnormal toxicity test -**

- deletion from European Pharmacopoeia
- WHO Expert Committee on Biological Standardization held from 29 Oct to 2 Nov 2018

**NCL recommended termination of all *in vivo* testing for lot release purposes**

# ACT NO. 36 OF 1947

## REGISTRATION OF ANIMAL VACCINES

FERTILIZERS, FARM FEEDS, AGRICULTURAL REMEDIES AND STOCK REMEDIES ACT, 1947 (ACT NO. 36 OF 1947)

Meant for so-called 'over the counter' products. This would include veterinary vaccines for production animals and also 'medicines' for conditions that a farmer can recognise him/herself.

**'stock remedy'** means a substance intended or offered to be used in connection with domestic animals, livestock, poultry, fish or wild animals (including wild birds), for the diagnosis, prevention, treatment or cure of any disease, infection or other unhealthy condition, or for the maintenance or improvement of health, growth, production or working capacity, but excluding any substance in so far as it is controlled under the Medicines and Related Substances Control Act, 1965 (Act 101 of 1965);

# ACT NO. 36 OF 1947

## REGISTRATION OF ANIMAL VACCINES

### Safety studies should include:

- Single dose studies
- Repeat single dose studies (where applicable)
- Overdose studies 2X for inactivated vaccines and 5X or 10X (depending on

**No lot release by NCL**

**No post importation testing**

**No TABST anticipated in future**

- Environmental effects.
- Data in non-target species (if available).

# ACT NO. 101 OF 1965

## REGISTRATION OF ANIMAL VACCINES

### WHEN A VETERINARY PRODUCT SHOULD BE REGISTERED

A veterinary product is liable for registration with the Medicines Control Council if any of the following apply.

- i) Any of the ingredients of the veterinary product is listed in one of the Schedules to the Act;
- ii) The product is a veterinary medicine by virtue of the definition of a veterinary medicine in the

**No lot release by NCL**

**No post importation testing**

**No TABST anticipated in future**

# SAHPRA STRATEGIC PLAN

- 5.3.3.1 Veterinary medicines and biologicals Veterinary services must enhance coordination and communication with DoH in veterinary drug control (scheduled and over-the-counter medicines).
- A Single Veterinary Medicine Act will be compiled, in order not to duplicate resources and capacity needed and prevent the two regulators being played up against one another and to address the issue of antimicrobial resistance.

**Dr Nick Nwankpa is the Director of the African Union  
Pan African Veterinary Vaccine Centre in Debre Zeit,  
Ethiopia**



**Waiver of Target Animal Batch  
Safety Test (TABST) VICH  
Guideline**

**Nick Nwankpa**

*The VICH 6 Public Conference, Cape Town South Africa  
26 – 28 February 2019*

## Opportunities for Waiver of TABST in Africa



AU-PANVAC

1. Harmonization of Vaccine Registration in ECAS and Centralization of registration in West Africa
2. Adoption of the OIE Standards for the implementation of Safety tests
3. Use of AU-PANVAC as an independent provider of qc services
4. Laboratories eager to comply with international standards
5. It is time to do the right thing !

## The way forward for the waiver of TABST Africa



1. Create awareness on the need for waiver of TABST
2. Engage all Stakeholders in the drive for adoption: The OIE, PANVAC and Vaccine Manufacturers
3. Provide credible alternatives to TABST
4. Support laboratories in Africa to comply with international standards
5. If possible provide necessary incentives for implementation



# Thank You

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