A photograph showing a row of small, clear glass vials with black caps, arranged in a line on a reflective surface. A blue syringe with a needle is positioned in the foreground, angled towards the vials. The background is softly blurred.

Harmonisation and
improvement of
registration, distribution and
quality control of vaccines in
the Middle East

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**Training OIE Focal points on Veterinary
Medicinal Products**
Casablanca, 6-8 Dec 11

Introduction

In a world that has complicated routes and means of transportation, the handling and transfer of biological products and materials, becomes a very critical process to be carried out safely. It becomes, sometimes, a considerable risk as it was not ever before. The intended and unintended mishandling and misuse of these substances can pose threat and lead to harmful consequence over unlimited areas and people.

Biological materials (including specimens for testing, reagents, disease agents, vaccines, etc.,) should be carefully collected, packed, labeled, stored, shipped and received according to specific regulations and conventions established by International and regional agencies.

Introduction

The consequences of the introduction into a country of an infectious disease or an animal pathogen or new strain of animal pathogen from which it is currently free, are potentially very serious.

However, there is also the risk that disease may occur as a result of the accidental release of animal pathogens from laboratories that are using them for various purposes such as research, diagnosis or the manufacture of vaccines. Such pathogens may already occur in the country or they may have been imported deliberately or inadvertently. It is therefore necessary to have in place measures to prevent their accidental release.

These measures may be applied either at national borders by prohibiting or controlling the importation of specified pathogens or their carriers (see Article 5.8.4.) or within national boundaries by specifying the conditions under which laboratories must handle them.

Role of the OIE

The OIE, as the world setting-standards organization for animal health and trade in animals and animal products, is well placed to lead the international and regional efforts for setting up guidelines and recommendations for safe handling and transport of veterinary biologicals including vaccines and disease agents.

OIE International Standards



Terrestrial Animal Health Code – mammals, birds and bees

Aquatic Animal Health Code – fish, molluscs and crustaceans

Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Manual of Diagnostic Tests for Aquatic Animals



**Trade standards
(Codes)
Biological standards
(Manuals)**

Role of the OIE

- **Chapter 1.1.7.**
[Biotechnology in the diagnosis of infectious diseases and vaccine development](#)
- **Chapter 1.1.7a.**
[The application of biotechnology to the development of veterinary vaccines](#)
- **Chapter 1.1.8.**
[Principles of veterinary vaccine production](#)
- **Chapter 1.1.9.**
[Tests for sterility and freedom from contamination of biological materials](#)
- **Chapter 1.1.10.**
[Guidelines for international standards for vaccine banks](#)
- **Chapter 1.1.11.**
[The role of official bodies in the international regulation of veterinary biologicals](#)

Veterinary Biological Products

Biological products are those products derived from living organisms which are manufactured and distributed in accordance with the requirements of appropriate national authorities, which may have special licensing requirements, and are used either for prevention, treatment, or diagnosis of disease in humans or animals, or for development, experimental or investigational purposes related thereto. (CDC).

They include, but are not limited to, finished or unfinished products such as vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, immunostimulants, certain cytokines, antigenic or immunizing components of live organisms, and diagnostic components that are of natural or synthetic origin ...

Certain Basic Criteria

Veterinary biologicals must meet certain basic criteria, regardless of the Regulatory Agency overseeing their production. These criteria include:

- **Safety**: *the product must be safe in the target species and, if live, in species exposed to shed organisms;*
- **Efficacy**: *the product should be effective according to claims indicated on the label;*
- **Quality**: *includes purity, potency and consistency;*
- **Purity**: *the product must be free from contaminating agents;*
- **Potency**: *each batch of product should be formulated, and tested, to ensure effectiveness and reproducibility of activity as demonstrated in the registration data.*

Classification of Infectious substances



- *Infectious substances, are divided into a two-tiered classification system; Category A and Category B.*

For shipment purposes, all biological materials fall into one of the following categories:

- *Category A infectious substances*
- *Category B infectious substances*
- *Patient specimens*
- *Biological products definition*
- *Unregulated biological materials*
- *Regulated medical waste*
- *Genetically modified organisms or materials*

Category A

- **Category A is defined as an:** *“Infectious substance, which is transported in a form that when exposure to it occurs, is capable of causing permanent disability, life threatening or fatal disease in otherwise healthy humans or animals.*
- **Infectious substances** meeting this definition that affect humans, including zoonotic agents, are designated UN 2814 and given the shipping name of ***“Infectious substance, affecting humans”*** **those affecting** animals only are designated UN 2900 and given the shipping name of ***“Infectious substance, affecting animals”***.

**indicative list of pathogens that must be assigned to UN 2814 or UN 2900)
The pathogens on these lists cannot be assigned to UN 3373 (7, 13).**



- **Infectious substances affecting humans that must be designated UN 2814**

Cultures Only:

- Bacillus anthracis, Brucellas, Pseudomonas pseudomallei, Clostridium botulinum, Coccidioides immitis, Crimean-Congo hemorrhagic fever virus, Escherichia coli, Hepatitis B, Herpes B virus, Highly pathogenic avian influenza virus, Mycobacterium tuberculosis, Rabies virus, Rift valley fever virus, Tick-borne encephalitis virus, West Nile virus, Yersinia pestis...

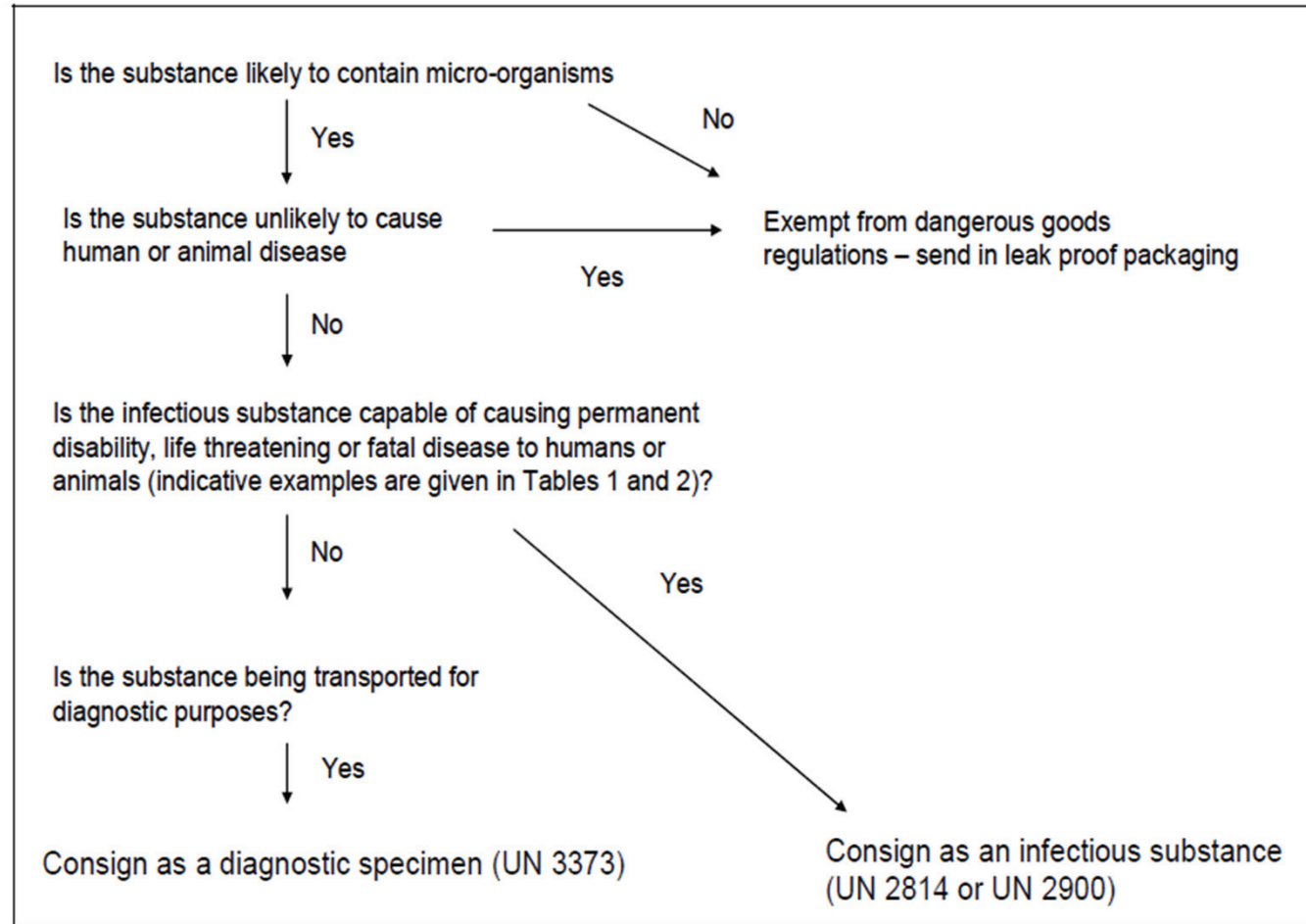
Virus:

- Ebola virus, Hantavirus, Lassa virus, Monkey pox virus, Nipah virus, Variola virus...

- **Indicative examples of animal pathogens forbidden as diagnostic specimens that must be shipped as infectious substances affecting animals (UN 2900)**

- African swine fever virus, Peste des petits ruminants virus, Avian paramyxovirus Type 1 – Velogenic Newcastle disease virus, Rinderpest virus, Classical swine fever virus, Sheep-pox virus, Foot and mouth disease virus, Goatpox virus, Lumpy skin disease virus, Swine vesicular disease virus, *Mycoplasma mycoides* – *Contagious bovine pleuropneumonia*, Vesicular stomatitis virus...

Biological Substances, Category B.



The Role of Official Bodies in the International Regulation of Veterinary Biologicals



The Veterinary Services should develop and document appropriate procedures and standards for all providers of relevant activities and associated facilities. These procedures and standards may for example relate to:

- programming and management of activities, including international veterinary certification activities;*
- diagnostic tests for animal diseases;*
- preparation, production, registration and control of biological products for use in the diagnosis or prevention of diseases;*
- border controls and import regulations;*
- disinfection and disinfestation;*
- treatments intended to destroy, if appropriate, pathogens in animal products.*

The Role of Official Bodies in the International Regulation of Veterinary Biologicals



The official control of veterinary biologicals is vested in various national and regional organizations that differ in their approach to ensuring the quality, safety and efficacy of the products.

World-wide harmonisation of standards for veterinary biologicals will be of help to Chief Veterinary Officers who must follow the instructions given in the OIE International Animal Health Code, as they apply to all biological products for use in international trade.

It will also be of assistance to vaccine producers, who have expressed their wish for world-wide harmonisation of registration rules so as to simplify and facilitate marketing of their products.

The Role of Official Bodies in the International Regulation of Veterinary Biologicals



- ***Application for approval and License***
- ***National Assay***
- ***Re-Examination and Re-Evaluation***
- ***Minimum Requirement of Veterinary Biological Products***
- ***Cases of Rejection of Approval***
- ***Cancellation of Approval***
- ***Procedure for Marketing Approval***

Veterinary Authorities of importing countries shall make available specific procedural requirements for approval or licensing of biologicals for veterinary use. They may limit supply to registered institutions or *in vitro* use or for nonveterinary purposes where such assurance cannot be provided.

Role of the VS

Ensure biologicals are free of disease producing agents

Issue licenses and permits

Monitor and inspect products and facilities.

Control field tests and release of biologicals.

It is needed:

In order to maintain the original quality of the product

- Which originally manufactured under appropriate standards of good manufacturing practice***

With increasing globalization of the manufacturing sector

- The need to transport products for greater distances between source and customer***

Role of VS

The objective is to ensure that the high level of product quality achieved by

- observing good manufacturing practices is maintained throughout the distribution chain.***

Good distribution practice guidelines (GDP)

- Cold storage***
- Controlled RT storage***
- Cold-chain transportations***
- System check and calibration***

Role of VS

Risks from infection are reduced by good laboratory techniques and secure facilities, which aid in the containment of pathogens. It is important to understand that containment of pathogens can be used for two purposes.

- *One is to prevent disease in humans in the laboratory;*
- *the other is to prevent the release of the pathogen into the environment and causing disease in animals or humans.*

Registration

Registration of the fabricant company

- Accredited by competent authorities
- Site Master file
- GMP
- Free sale certificate/Certificate of pharmaceutical product (WHO)
- Certificate of analysis and release certificate (certified by competent authorities)

Registration of vaccines in the Middle East

Special Measures

- Vaccines produced outside the origin of fabricant
- Some vaccines should be registered (if not used in country of origin) in 2 or 3 other countries
- VS Visit and evaluation of the factory
- WHO checklist and OIE standards

Good distribution practice (GDP)

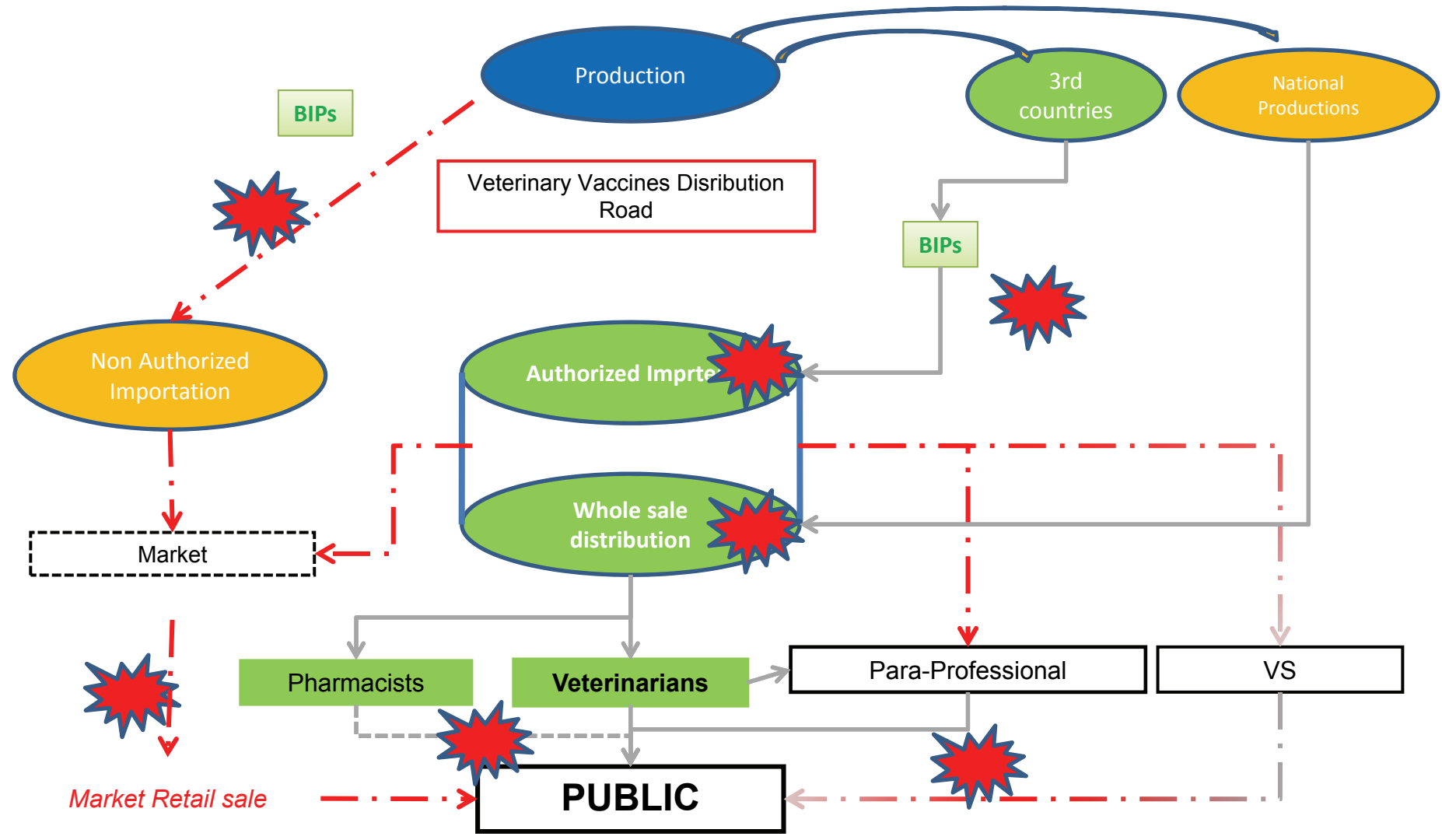
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Control of vaccine distribution

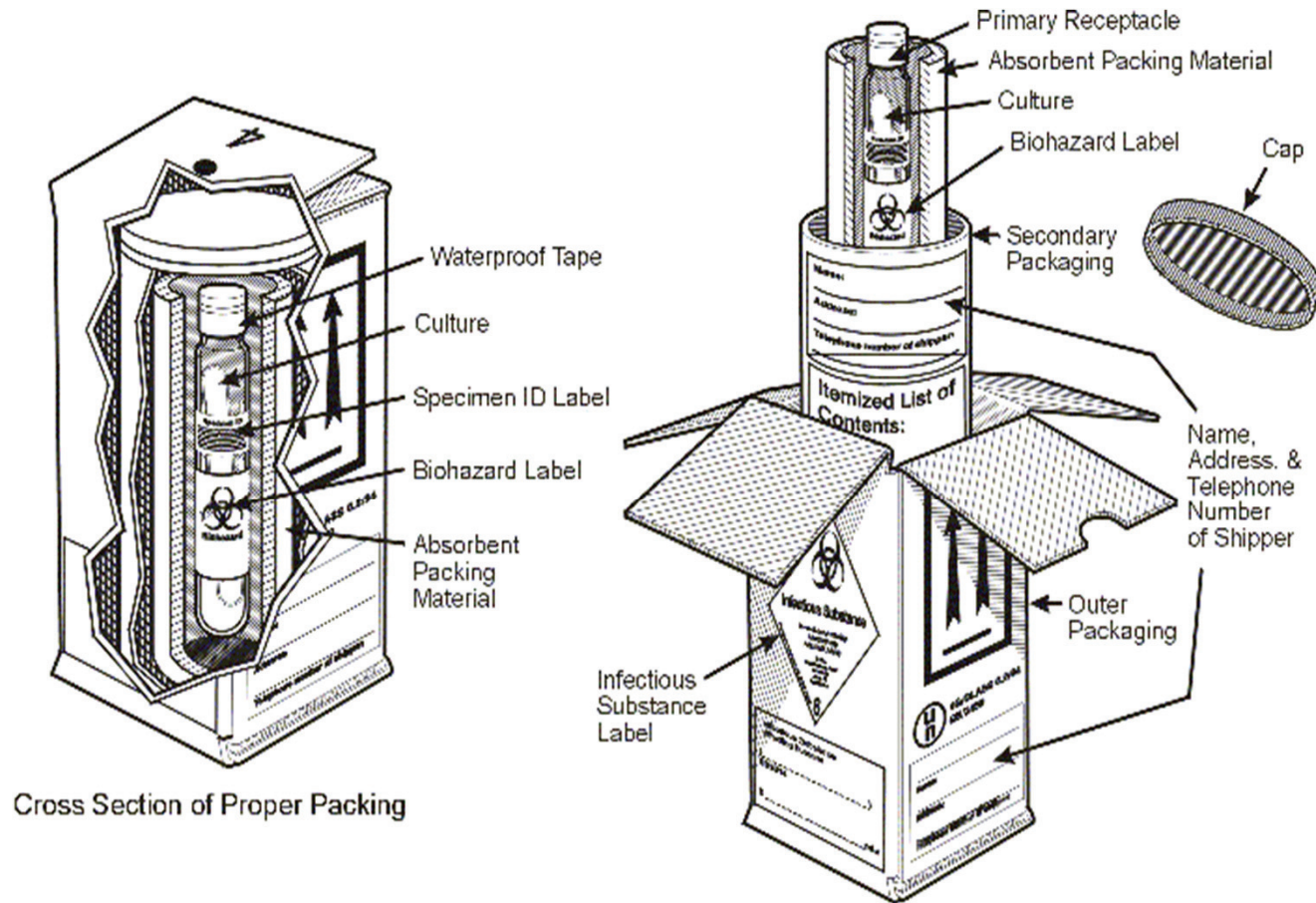


Packaging and Transportation

- *Packaging and transportation of biological materials are subject to strict national and international regulations.*
- ***Individuals** involved in the packaging, transportation and shipment of infectious substances **must receive training** on proper packaging, labeling, and documentation according to the applicable regulations and requirements before shipping such materials.*
- *UN 2814, UN 2900 (Category A)*
- *UN 3373 (Category B)*

Packaging

- *Infectious substances must be packed in good quality packaging, which must be strong enough to withstand the shocks and loadings normally encountered during transport.*
- ***Packaging must consist of three components:***
 - *A securely closed, watertight primary container (test tube, vial or ampoule)*
 - *A durable watertight secondary container*
 - *A tertiary or outer shipping container*



Cross Section of Proper Packing

Packing and Labeling of Infectious Substances

vaccine storage and transportation

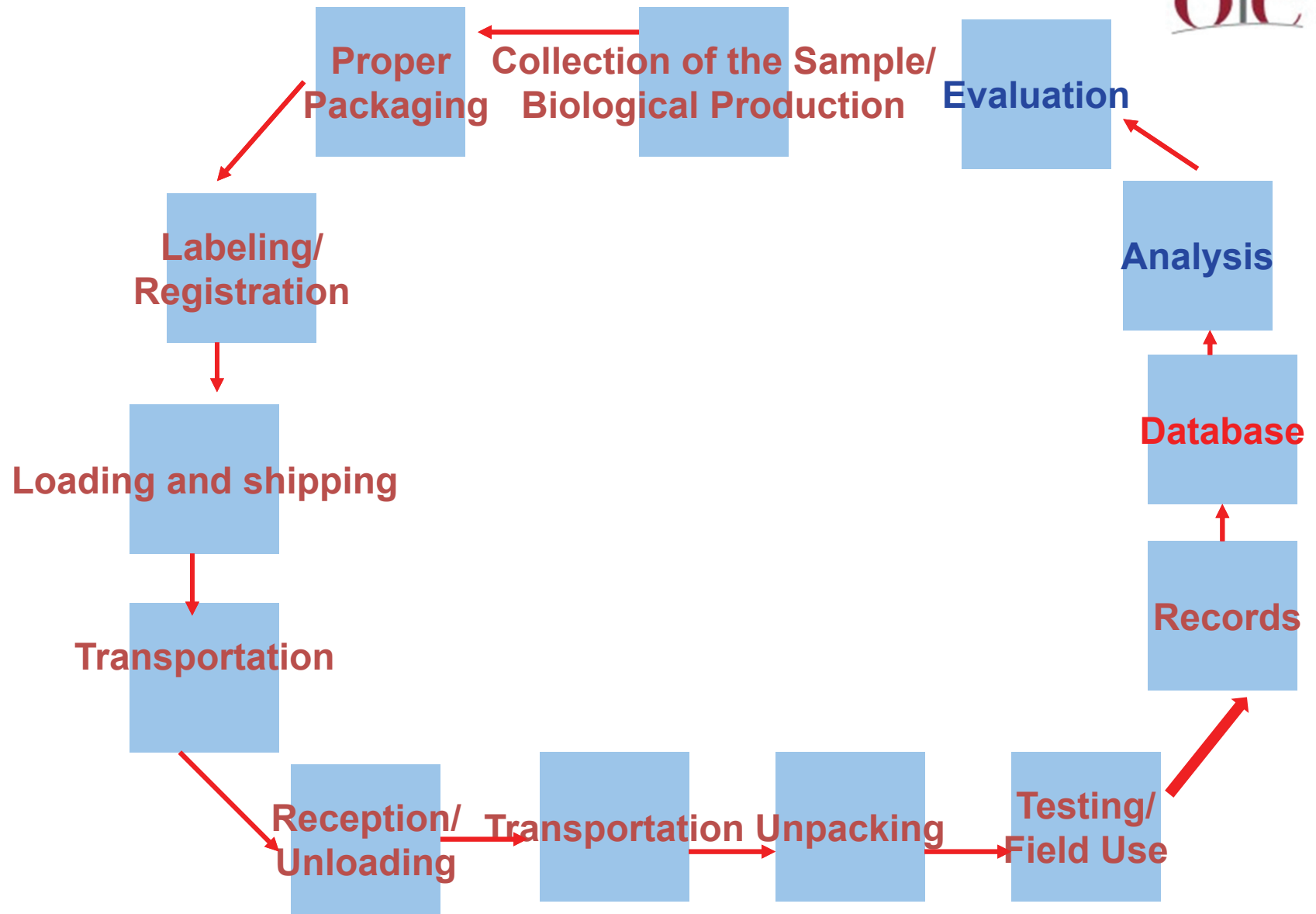
- *Maintaining vaccines at the appropriate temperature from the time they leave the manufacturer to the time of administration, i.e., **maintenance of the cold chain**, is a very important aspect of proper immunization delivery programs.*
- ***Lack of** adherence to the **cold chain** may result both in lack of vaccine effectiveness, undue vaccine failures, and an increased rate of local reactions after vaccine administration.*
- ***Damage** can be done by exposure to heat or freezing of the vaccine depending on the nature of the product. Recent studies have highlighted major deficiencies with respect to the cold chain.*
- ***Records** should be kept of doses received, including lot numbers for each vaccine shipment, and of wastage after vaccine expiry dates have passed.*

Recommendations for storage

- 1. Vaccines should never be removed from the refrigerator except for the following reasons: withdrawing a dose(s); shipping to clients; or transporting to immunization clinics. The refrigerator door should not be opened too frequently.*
- 2. Vaccines should be stored in the refrigerator as soon as they are received.*
- 3. All persons responsible for handling vaccines should know the correct storage temperatures for the various vaccines.*
- 4. All vaccine storage refrigerators should have a maximum-minimum thermometer or, if large quantities of vaccines are stored, a continuous temperature recording device.*
- 5. Two daily temperature readings for the vaccine refrigerator should be taken and recorded.*
- 6. All staff handling vaccines should have training about the importance of good vaccine storage and transportation techniques.*
- 7. Vaccines should never be stored on refrigerator door shelves because temperatures are warmer there than on the shelves of the refrigerator.*

Recommendations for transportation

- 1. Manufacturers and central pharmacies should place both heat and cold monitors in their shipments of vaccines.*
- 2. Central pharmacies and manufacturers who make long distance shipments should periodically use electronic monitors to detect possible problems and their location.*
- 3. Shipping boxes for most vaccines should be clearly labelled as containing perishable goods that have to be stored between 20 C and 80 C and must not be frozen.*
- 4. All transport companies carrying vaccines should be advised that the product is perishable and should be refrigerated immediately on receipt.*
- 5. Manufacturers should obtain written documentation from transport companies concerning the handling of perishable products (transportation, warehouse storage conditions, length of time between pick up and delivery, etc.). Refrigerated vehicles should be equipped with temperature monitoring Devices.*
- 6. All vaccines should be transported in an insulated container with an appropriate number of ice packs (except when shipped under refrigerated transit).*
- 7. When vaccines sensitive to freezing are to be shipped in outside temperatures of less than 20 C, they should be shipped in a vehicle in which the temperature should be kept higher than 20 C.*



Receiving and Unpacking Vaccine Shipments



Conclusion



- *The region continues its effort for establishing a Middle Eastern mechanism for handling veterinary biologicals. This mechanism should consider the existing capacity(ies) of the involved regional countries,*
- *Efforts should be made, with the support of the OIE Collaborating Centers and relevant international organizations, such as the International Cooperation on Harmonization of Technical Requirements for the Registration of Veterinary Medicinal Products (VICH), to develop OIE standards and guidelines for the registration of veterinary biologicals and medicinal products within national or regional mechanisms.*
- *The registration of these products should be based on sound scientific principles to ensure the protection of animal and/or human health, as well as the environment, and not unnecessarily hinder free trade.*

Conclusion



- *The handling , packaging, storing and transport of infectious materials is mainly described in the related chapters of **the OIE manual of diagnostic tests and vaccines** in which high standards of laboratory safety and containment requirements, that will ensure healthy working conditions for laboratory staff and protection of the environment, are described and defined as the greatest priority.*
- *Emphasis should be placed on the registration of the establishments used for storing and distributing veterinary medicinal products and biologicals.*

Conclusion



- *Countries should consider the reference role of the World Organization for Animal health as the reference standards setting organization relevant to the regulation of veterinary biologicals and to consider the rule of “One World One Standard” (OWOS).*
- *Veterinary authorities are the only authorities for the control and supervision of the use, transfer and distribution of the veterinary biologicals.*



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