Transportation and Handling of Biological products in the Middle East

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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.

National and International organizations have found it necessary to develop recommendations and guidelines to safeguard production, handling and transportation of hazardous materials.
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.
Biologicals

- Biological materials
- Biological substances
- Biological products
- Biological specimens
- Biological agents
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 or that are derived from synthesizing or altering various substances or components of substances such as microorganisms, genes or genetic sequences, carbohydrates, proteins, antigens, allergens, or antibodies.
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.
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.

International harmonization of regulations concerning biological products did not begin until well after those concerning chemically defined products.
World Organization for Animal Health (1924)  
175 Member (2009)

Five permanent Regional Representations: Bamako, Buenos Aires, Tokyo, Sofia and Beirut

Five Sub-regional Offices: Bangkok, Brussels, Gaborone, Panama, and Tunis

Five Regional Commissions: Africa, America, Asia-Pacific, Europe and Middle East
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.
The OIE’s objectives

- to ensure transparency in the global animal disease and zoonosis situation
- to collect, analyse and disseminate scientific veterinary information and disease control methods
- to provide expertise and encourage international solidarity in the control of animal diseases
- to improve the legal framework and resources of national Veterinary Services
- Within its WTO mandate, to ensure sanitary safety of the global trade of animals and animal products while avoiding sanitary barriers, by publishing health standards
- to provide a better guarantee of the safety of food of animal origin at farm level, and to promote animal welfare, through a science-based approach
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)
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*
- *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.

Is the substance likely to contain micro-organisms

Yes

Is the substance unlikely to cause human or animal disease

No

Is the infectious substance capable of causing permanent disability, life threatening or fatal disease to humans or animals (indicative examples are given in Tables 1 and 2)?

No

Is the substance being transported for diagnostic purposes?

Yes

Consign as a diagnostic specimen (UN 3373)

No

Yes

Exempt from dangerous goods regulations – send in leak proof packaging

Consign as an infectious substance (UN 2814 or UN 2900)
Packaging

• 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
Packing and Labeling of Infectious Substances
Packing and Labeling of Clinical Specimens
Packaging Critical Biologic Agents

a. Biological agents include infectious agents of humans, plants, and animals, as well as the toxins that may be produced by microbes and by genetic material potentially hazardous by itself or when introduced into a suitable vector. Biologic agents and infectious substances are closely related terms that are found in the transfer and transportation regulations. Biological agents may exist as purified and concentrated cultures but may also be present in a variety of materials such as body fluids, tissues, soil samples, etc.

b. Critical biologic agent is defined as related to Biological and Chemical Terrorism:

c. Transportation refers to the packaging and shipping of these materials by air, land, or sea, generally by a commercial conveyance.

d. Transfer refers to the process of exchanging these materials between facilities.
Biologicals and production

Ensure biologicals are free of disease producing agents
Develop appropriate standards and procedures for product release.
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
Good distribution practice (GDP)

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
Storage Conditions

**Controlled Temperature**
- Some products require narrow temperature ranges
- Minimal intervention

**Sufficient Space**
- To permit adequate air circulation
- Place susceptible good in strategic location
  e.g. away from airflow from the refrigerator unit

**Refrigerators site**
- Avoid environmental extreme temperature which affect performance
  - <10 C or >30 C

**Record keeping**
- Electronic temperature recording device
  - Several locations depend on the size of the unit
  - Temperature alarm
- Temperature mapping
  - Present risk areas
  - Distributions under extreme external temperature
  - Repeated mapping every 3-4 years
Protection is achieved through:

(a) the requirements for rigorous packaging that will withstand rough handling and contain all liquid material within the package without leakage to the outside;

(b) appropriate labeling of the package with the biohazard symbol and other labels to alert the workers in the transportation chain to the hazardous contents of the package;

(c) documentation of the hazardous contents of the package should such information be necessary in an emergency situation; and

(d) training of workers in the transportation chain to familiarize them with the hazardous contents enabling response to emergency situations.
Transportation

- The following are suggested items that should be addressed. It would be advisable to contact the receiving laboratory to determine if it has a submission form that it would like to have submitted with the samples or if it needs other information.

  - i) Name and address of owner/occupier and geolocation (latitude and longitude, if available) where disease occurred, with telephone and fax numbers.
  
  - ii) Name, postal and e-mail address, telephone and fax numbers of the sender.
  
  - iii) Diseases suspected and tests requested.
  
  - iv) The species, breed, sex, age and identity of the animals sampled.
  
  - v) Date samples were collected and submitted.
  
  - vi) List of samples submitted with transport media used.
Importation of animal pathogens

• The importation of any animal pathogen, pathological material or organisms carrying the pathogen should be permitted only under an import licence (IP) issued by the relevant authority.

• The IP should contain conditions appropriate to the risk posed by the pathogen and, in relation to air transport, the appropriate standards of the International Air Transport Association (IATA) concerning the packaging and transport of hazardous substances.

• When considering applications to import pathological material from other countries, the authorities should have regard to the nature of the material, the animal from which it is derived, the susceptibility of that animal to various diseases and the animal health situation of the country of origin.

• It may be advisable to require that material is pre-treated before import to minimise the risk of inadvertent introduction of a pathogen.
TRANSPORT OF INFECTIOUS MATERIAL

- **Great care** must be taken when preparing and packing diagnostic specimens, infectious materials and pathogens for transport, to ensure that there is no breakage of containers or leakage of contents that could put at risk personnel in the transport system or animals that may come in contact with contamination.

- **Applicable local, national and international regulations** for the transportation of dangerous goods (diagnostic or clinical sample and infectious materials) and importation of animal pathogens must be followed. These are summarised in Chapter 1.1.1 Collection and shipment of diagnostic specimens.
Groups of Animal Pathogens

a) Group 1 animal pathogens
Disease-producing organisms that are enzootic but not subject to official control.

b) Group 2 animal pathogens
Disease-producing organisms that are either exotic or enzootic but subject to official control and that have a low risk of spread from the laboratory.

c) Group 3 animal pathogens
Disease-producing organisms that are either exotic or enzootic but subject to official control and that have a moderate risk of spread from the laboratory.

d) Group 4 animal pathogens
Disease-producing organisms that are either exotic or enzootic but subject to official control and that have a high risk of spread from the laboratory into the environment and the national animal population.
IATA Regulations

- [http://www.iata.org/whatwedo/cargo/dangerous_goods/infectious_substances.htm](http://www.iata.org/whatwedo/cargo/dangerous_goods/infectious_substances.htm)
- Infectious Substances
- Guidance:
  - Download the Guidance Document (pdf) developed by ICAO DGP for complying with the 50th edition of the DGR on:
  - Definitions, classification, exceptions, prohibitions
  - Packaging for a number of specific substances
  - Passenger Provisions
  - Training and Emergency Response
- Classification:
  - Download the excerpt of DG Regulation on the Classification of Infectious Substances (pdf)
- Packing:
  - Download Packing Instructions 650 in English (pdf), applicable to UN 3373 on passenger and cargo aircraft and CAO.
CONTAINMENT GROUPS

1. The principal purpose of containment is to prevent the escape of the pathogen from the laboratory into the national animal population. Some animal pathogens can infect humans. In these instances the risk to human health may demand additional containment than would otherwise be considered necessary from purely animal health considerations.

2. The level of physical containment and biosafety procedures and practices should be not less than the Group into which the pathogen has been placed and the detailed requirements should be appropriate to the type of organism (i.e. bacterium, virus, fungus or parasite). The lowest containment level will be required for pathogens in Group 1 and the highest level for those in Group 4.

3. Arthropods may be pathogens or vectors for pathogens. If they are a vector for a pathogen being used in the laboratory, the appropriate containment level for the pathogen will be necessary in addition to the containment facilities for the arthropod.
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 about 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 2o C and 8o 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 2o C, they should be shipped in a vehicle in which the temperature should be kept higher than 2o C.
Standard Operating Procedures (SOPs)

• **Vaccine may be transported by either hand carrying or shipping to another site. In both cases, the cold chain must be maintained.** It is important to establish a routine, systematic process for handling vaccine shipments and vaccine transport. Each facility should develop its own written standard operating procedures (SOPs), covering every aspect of vaccine shipping: receiving, storing, packing, and transportation.

• **The SOP should specify that the vaccine is:**
  1- Attended at all times during transport.
  2- promptly placed into appropriate storage units upon arrival.
  3- Transportation in the minimum needed quantity to avoid unnecessary loss of expensive vaccine.
Collection of the Sample/Biological Production

Proper Packaging

Evaluation

Analysis

Database

Records

Testing/Field Use

Unpacking

Transportation

Reception/Unloading

Loading and shipping

Transportation

Labeling/Registration

Proper Packaging

Collection of the Sample/Biological Production

Evaluation

Analysis

Database

Records

Testing/Field Use

Unpacking

Transportation

Reception/Unloading

Loading and shipping

Transportation

Labeling/Registration
Receiving and Unpacking Vaccine Shipments
Assessment of Risk from Pathogens

Laboratory work of the type described in this Terrestrial Manual should be carried out with a minimum of risk to the health of the staff (biosafety) and the environment (biocontainment). This requires careful consideration of the risks involved in a particular procedure, followed by appropriate measures to minimise the risk of human disease and of possible release into the environment.

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.
Guidance from Understanding Risk

Provides a **useful tool kit** for dealing with **uncertainty and complexity**

*Does not make difficult problems simple,*
  
  – especially where societal values are involved.

**Inform** the interested and affected parties among the public

**Respect** differences in values and cultures

**Seek flexibility**

**Seek progress**, rather than seeking overall solutions.
If a man will begin with certainties he shall end in doubts, but if he will be content to begin with doubts, he shall end in certainties.

» Francis Bacon *The Advancement of Learning*, 1605.
Risk assessment in transportation and storage

Result in a decision being reached on the preferred type of shipping system.

- The degree of temperature control necessary
- The load size
- Whether the products are to be shipped by land, sea, air or a combination of these
- Transit times and locations effect
Example

Risk assessment and analysis for vaccines, other biological products and products of biotechnology revealed:

– Most stable between 2°C and 8°C

– The majority of these are susceptible to storage temperatures below 0°C because:
  
  • this may denature proteinaceous material
  • resulting in a reduction of effectiveness
  • less soluble components may crystallise out of solution at low temperatures
  • Some changes in physical characteristics (for example, particle size).

– Alternate freezing and thawing will result in even greater damage to these products.
Modes of Transport

Air freight provides a relatively rapid and reliable means of shipping temperature-sensitive medicines across large distances.

Planned or unplanned deviations occur that have not been addressed during qualification.

- Changes in pre- and post-flight arrangements that may result in delays or unexpected variations in

- Changes in the storage environment
  - unheated aircraft hold
  - effects of radiation during flights at the time of abnormal solar activity

- Goods not shipped on the intended flight,

- Delays in obtaining customs clearance

- Exposure of some materials of biological origin to radiation from x-ray scanners at airports
Modes of Transport

The security of medicines being transported by road is of concern to regulators

- Trucks may need to be fitted with heaters in order to maintain the load temperature
- Temperature controls must be tamper-proof.

Sea crossings present a major challenge.

- The temperature inside a large steel box on the deck of a container ship in the tropics can be excessive.
Training Requirements

- Some countries have established regulations for domestic of hazardous materials by rail, air, vessel (ships), and motor carrier (ground).

- IATA has established guidelines exclusively for the transport of dangerous goods by air (both domestic and international).

- National regulations require that anyone wishing to ship infectious materials must first receive function-specific shipping training.

- Individuals wishing to ship infectious materials classified as hazardous material (dangerous goods) must receive certified shipping training every 2 years.
Training Requirements

**General Awareness Training**

*Online Training for categories A and B has been developed. It is entitled as:*  

**Awareness Training for the Transport of Hazardous Materials; Transportation of Infectious Substances, Category B**

*These trainings cover how to classify biological materials, select proper shipping names, select approved packaging materials, mark and label packages, and complete all required documentations.*

*To ship an infectious substances that qualifies at category A material, it requires more comprehensive certified training and documentation than category B.*
Role of VS

• The Veterinary Services should define and document their policy and objectives for, and commitment to, quality, and should ensure that this policy is understood, implemented and maintained at all levels in the organisation.

• Where conditions allow, they may implement a quality system corresponding to their areas of activity and appropriate for the type, range and volume of work that they have to perform. The recommendations for the quality and evaluation of Veterinary Services propose a suitable reference system, which should be used if a Member choose to adopt a quality system.
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;
- prevention, control and notification of disease outbreaks;
- risk analysis, epidemiological surveillance and zoning;
- inspection and sampling techniques;
- 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.
Conclusion

- The region should start by 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.

• Also appropriate training and competence has been demonstrated and documented to be the essential means required for the protection of involved people in handling, packaging and shipping of biological materials mainly veterinarians and laboratory personnel.

• Emphasis should be placed on the registration of the establishments used for storing and distributing veterinary medicinal products and biologicals.

• Middle Eastern countries should take appropriate actions to evaluate veterinary medicinal products and biologicals of national and international origin before release, using OIE standards, wherever applicable, and the expertise of OIE Reference Laboratories, if necessary.
Conclusion

- The uncontrolled transfer of biological materials by individuals, groups and organizations which sometimes may lead to bioterrorist actions which may destroy all efforts that have been made by other countries to achieve safeguarded transfer of biologicals.

- 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.
Presentation References

OIE Manual of Diagnostic tests and vaccines (2008)
http://www.oie.int

Center for Disease Control (CDC)
Transport of Infectious Substances
http://www.cdc.gov/od/ohs/biosfty/shipregs.htm

World Health Organization (WHO)
Guidance on Regulations for the Transport of Infectious Substances 2007-2008

USDA-APHIS
http://www.aphis.usda.gov/import_export/

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THANK YOU