

CHAPTER 1.1.10.

VACCINE BANKS

SUMMARY

Vaccine banks provide antigen or vaccine reserves, either of ready-to-use vaccines or of antigenic components that can be quickly formulated into the final product for emergency use or other vaccination campaigns. They may be established for national or international use. For some international banks in particular, it is important to define the drawing rights of the members of the controlling consortium, and to establish clear governance mechanisms. For banks managed by intergovernmental organisations such as the OIE, appropriate financing should be in place, together with eligibility criteria for access to the bank. Vaccine banks may be deployed by Veterinary Authorities for different purposes ranging from systematic mass vaccinations, to emergency vaccinations, or to strategic interventions.

Vaccine banks can be classified by their geographical coverage as well as by the nature of product stored.

The advantages of antigen banks include the ability to store vaccine antigen as concentrated stocks with prolonged retention of potency in low temperature storage. Appropriate serotypes can also be selected from the bank according to the needs at the time of deployment. The disadvantage of antigen banks is the delay between the decision to deploy and the availability of the final formulated vaccine. This can, to some extent, be fast-tracked by pre-testing of the antigen components before storage, and provided the Competent Authority is able to provide early release certification.

Ready-to-use formulated vaccines can be deployed rapidly and are available for immediate use for the full duration of the shelf life of the vaccine. When not used a disadvantage is the defined shelf life, often shorter than for banked antigens. Also for diseases that have several serotypes and show broad strain variation in their antigenic characteristics the fixed formulation may not sufficiently protect against the strain involved in a given outbreak.

For some banks, whether storing antigen or ready-to-use formulated vaccines, plans should be in place to replenish stocks before the end of the shelf life. Shelf life expired products are not acceptable for use and must be discarded and destroyed.

Planning for the components of a vaccine bank, and for the quantity of material to be stored, should involve all relevant stakeholders including the Competent Authorities, vaccine bank administrators, vaccine manufacturers and reference laboratories. Relevant information to inform the planning should include the epidemiology of the disease in question, its geographical occurrence, the nature of the pathogen, patterns of animal production, movement and trade, pre-existing vaccine coverage of the population and the logistics of deployment of the banked vaccine.

The regulatory principles of vaccine production apply equally to vaccine banks and should comply with the requirements of Chapter 1.1.8 of the Terrestrial Manual and the disease-specific OIE standards in Part 2 of the Terrestrial Manual.

A. DEFINITION OF A VACCINE BANK

Vaccine banks are defined as antigen or vaccine reserves, which can be of different types. They may be operated as a bank that holds the antigen component, or a ready-to-use formulated vaccine, or both. The vaccines may be deployed for different purposes ranging from systematic mass vaccinations, to emergency vaccinations, or to strategic interventions. Service contracts are a specific mechanism for accessing antigen or vaccine reserves.

B. TYPES OF BANKS

Vaccine banks can be classified by their geographical coverage as well as by the nature of product stored.

A country may hold its own national bank, or it may be part of a larger group of countries that share a bank, which either have predefined drawing rights, or an *ad hoc* mechanism to determine these drawing rights. Such international consortia are based on shared risk and may share a common geographical region, or have similar disease status and approach to preventing and controlling a given disease. The bank may be held on the territory of one or several of the group members or be retained by the manufacturer(s). An adequate system of governance should be established for all vaccine banks.

Certain vaccine antigens can be stored as concentrated stocks and retain potency for several years at temperatures below -70°C , depending on the stability of the antigen. Such antigens have to be formulated into vaccines before deployment, in which case the vaccine composition, including potency, can be adjusted according to the need. Formulation of antigens for use may be done either by the manufacturer or in a dedicated facility maintained by the bank members. In the latter case, the facility should be licensed to formulate the final product and it will assume pharmaceutical responsibility for the final vaccine. However, in an emergency vaccination-to-live scenario, licensing authorities may demand that all vaccines meet the same standard as the commercial vaccines used in food-producing animals.

The arrangements for vaccine banks need to clearly define all the essential requirements including: time between reception of order and delivery, import permits, customs clearance, transportation, appropriate cold chain, vaccine labels and inserts, and directions for use. In the case of an antigen bank, specific arrangements are recommended to contract the supply of the antigen(s) together with control samples (see Sections D. *Quantities of vaccine required in a bank* and F. *Acquisition of antigens or vaccines for a bank*). These arrangements include storage, formulation, availability of reagents and suitably sized vials, and the supply of formulated vaccines.

The main advantages of vaccine banks holding antigens are the speed that antigens can be turned into the final licensed vaccine when compared with vaccine production beginning from the working seed, the long shelf life of the antigen, the flexible combination of antigens for different vaccination strategies. However, there is always a necessary time delay between giving the order for formulation and the availability of the ready-to-use formulated vaccine, which may not be suitable for rapid vaccination in emergency situations. Under well-specified circumstances in an emergency situation (for example an outbreak of foot and mouth disease in a country previously free of that disease), in a quality controlled manufacturing system in accordance with OIE standards (OIE *Terrestrial Manual* Chapter 1.1.8 *Principles of veterinary vaccine production*), and because the antigen has been fully tested before storage, it may be possible to deliver the vaccine before the final product testing is finished, provided that special authorisation, frequently referred to as early release certification, is received from the Competent Authority of the country of destination.

Ready-to-use formulated vaccines can be deployed rapidly and have a pre-determined formulation with a finite shelf-life, usually indicated in the product registration (as validated by appropriate testing) depending on the characteristics of the vaccines, when stored in appropriate temperature-controlled facilities.

The main advantage of ready-to-use formulated vaccines is the availability for immediate use for the full duration of the shelf life of the vaccine. One disadvantage of such vaccines is the defined shelf-life, often shorter than for banked antigens. Another inconvenience of ready-to-use formulated vaccines for diseases that have several serotypes and exhibit broad strain variation in their antigenic characteristics is that the fixed formulation may not sufficiently protect against the strain involved in a given outbreak.

For all banks, whether storing antigen or ready-to-use formulated vaccines, there is the need to renew the stocks at the end of the shelf life of the product at the latest. Shelf life expired products are not acceptable for use and must be discarded and destroyed in appropriate specialised facilities (Lombard & Fuessel, 2007). Renewal orders and the process between the expiry date of the current stock and the arrival of new stock should be considered in a timely manner. Alternatively, stocks of antigen or ready-to-use formulated vaccines could be rotated and replenished to ensure there is a continuous supply of product within shelf life.

C. SELECTION OF VACCINES FOR A BANK

Depending on the disease targeted and the likely contingency requirements, a range of vaccine strains may be required. Competent Authorities in consultation with the vaccine bank administrators and relevant reference laboratories must decide which vaccine strains should be held and whether they should be stored as a separate antigen component for subsequent formulation, or as a ready-to-use formulated vaccine. The value of any

vaccine bank is dependent upon the appropriateness of what it holds for field application, particularly in respect of diseases that have several serotypes and exhibit broad strain variation in their antigenic characteristics.

The potential for an outbreak not adequately covered by a banked vaccine must be alleviated by continual monitoring of the global disease situation, taking into account animal health information systems such as OIE's WAHIS and disease-specific updates in the periodic reports by international reference laboratory networks, and supported by laboratory genetic and antigenic characterisation facilitated by reference and other suitable laboratories. Additional vaccine strains may need to be included in the banks' portfolio or, where no suitable vaccine strain is available, developed as quickly as possible for subsequent inclusion in the bank.

The world is an interdependent community that encompasses rapid and extensive movement of people, animals and animal products, and the increasing awareness of deliberate release of a pathogen through bioterrorism, heightens the risk of disease incursion and makes prediction of a specific threat difficult. Increased cooperation and collaboration between different international, regional and national reference laboratories, vaccine banks, and national, regional, international authorities or organisations should be encouraged as well as mechanisms for consultation with vaccine manufacturers. Risk assessment studies, preferably conducted at a country or regional level, should be used to determine the antigen or vaccine to be stored with a suitable priority level. Close liaison with national and international reference laboratories is therefore recommended. Competent Authorities may consider restricting information relating to the storage of antigens or vaccines.

D. QUANTITIES OF VACCINE REQUIRED IN A BANK

The decision as to how many doses of vaccine are required is complex, embracing questions of epidemiology, vaccinology, logistics and resources (human, technical and financial).

Factors bearing on the decision include:

- i) the nature of the disease in question (serotypes, strains, pathogenesis, routes and rapidity of spread, presence and competence of vectors, etc.);
- ii) the characteristics of the available vaccines (serotypes, strains, monovalent or polyvalent types of formulation, DIVA vaccines (detection of infection in vaccinated animals), potency of the vaccines;
- iii) the number, species, location and density of the animals to be protected;
- iv) the types of emergency vaccination likely to be applied, and whether vaccination is with or without booster;
- v) logistical requirements (the availability of trained personnel, storage facilities, maintenance of the cold chain, transport, vaccination equipment, consumables, etc.);
- vi) the current and predicted global, regional and national epidemiology of the disease;
- vii) patterns of animal production, movement and trade;
- viii) analysis of the risk of the introduction and spread of the disease in question (which may include epidemiological modelling);
- ix) application of contingency planning (including risk–benefit and cost–benefit analysis and the construction of decision trees, awareness and acceptance by stakeholders).

Decisions on the quantity of the product inevitably involve a compromise between the potential economic impact of the disease, fixed cost of the maintenance of the vaccine bank, cost of purchase, storage and replacement, cold chain capacities of the beneficiaries and the likely number of doses required. The post-vaccination disease control and surveillance strategy further impacts the decision on the number of vaccine doses required.

The minimum vaccine requirement should be based on a country's planned vaccination strategy. The procurement of additional supplies of vaccine, either from other banks or from commercial sources, is likely to take considerable time. It would be beneficial in terms of cost, time and volume, for different national or regional vaccine banks to cooperate, or to consider setting up regional or international vaccine banks.

When relevant, the proportion of antigens (core strains and optional strains), and ready-to-use formulated vaccines (for rapid deliveries) can also be balanced.

E. REGULATORY CONSIDERATIONS

It is important to note that the regulatory principles of vaccine production apply to antigens and ready-to-use formulated vaccines procured for vaccine banks, in accordance with the requirements laid down in the general

(e.g. as defined chapter 1.1.8) and disease-specific OIE standards (e.g. chapter 2.1.8 *Foot and mouth disease*). In some regulatory environments vaccines are considered to be veterinary medicinal products and additional regulatory requirements may apply, in particular for food-producing animals.

For vaccine banks the following additional considerations apply, with more detail developed throughout this chapter, as relevant:

- i) storage conditions:
 - a) facilities,
 - b) containment of stored antigen or vaccine,
 - c) labelling of stored antigen or vaccine;
- ii) monitoring of stored concentrated antigen;
- iii) transport to storage facilities;
- iv) transport for deployment:
 - a) transport of antigen for reformulation,
 - b) transport of vaccines for use.

Countries requesting vaccines from a vaccine bank also need to consider import permits and customs clearance, where appropriate.

F. ACQUISITION OF ANTIGENS OR VACCINES FOR A BANK

According to the type of bank and the disease concerned, the acquisition of the appropriate vaccine(s) or antigen(s) will depend on whether they are available from the commercial sector, government institutions or other production facilities. All production facilities should be appropriately licensed. Appropriately licensed manufacturers should comply with the relevant OIE standards (e.g. as defined in chapter 1.1.8). Vaccines also should be appropriately licensed according to national veterinary legislation, in consideration of OIE standards such as the OIE *Terrestrial Code* chapter on veterinary legislation.

Competent Authorities should consider the option of direct procurement or procurement through international calls for tender for antigens or vaccines, particularly where regulatory considerations are of paramount importance. They may wish to seek advice from appropriate official licensing authorities on the necessary standards required for the technical specifications for the procurement. Requests for tenders can then ensure not only a competitive price, but also a veterinary medicinal product manufactured to an acceptable level of quality, the standards being those set out in this OIE *Terrestrial Manual*. For diseases where there is official OIE recognition of disease status, vaccines used in the Member Countries concerned must comply with the standards in the OIE *Terrestrial Manual*. It is recommended that the process of selecting suppliers not focus solely on the lowest bidder principle but also take into consideration technical and quality criteria as well as delivery capacities. This could be achieved by a stepwise process, first assessing the technical proposal responding to the technical specifications, followed by an evaluation of the commercial bid of the eligible candidate suppliers. The technical specification should establish that suppliers can produce the desired vaccines or antigens and dose amounts within a specified time period that meet necessary or mandatory tests of compliance such as sterility, safety, and potency.

G. STORAGE OF VACCINES OR ANTIGENS IN A BANK

It is important that the areas of storage for vaccine banks comply with recognised quality standards (e.g. chapter 1.1.8), which also address security of the premises (e.g. restricted access to premises, logbooks, continuity of access to electric power). Storage areas for vaccine banks should be regularly inspected by the Competent Authorities to ensure continual compliance.

If the vaccine bank is co-located with a laboratory or other facility where pathogens are handled, the bank storage facilities should be completely independent and be protected by positive air pressure with high efficiency particulate air (HEPA) filtration at the air inlets. Maintenance and monitoring personnel should, where they have had possible exposure to relevant infection, obey a quarantine procedure before entering the bank.

Storage of antigens or vaccines in a bank should be appropriate to the product. The antigen may be a chemically inactivated or killed organism, or it may be an attenuated, live vaccine. Antigens may be concentrated in frozen liquid form held at temperatures below -70°C in appropriate containers appropriately labelled (see e.g. chapter

2.1.8, Section C.6). Freeze-dried vaccines and their diluents should be stored in accordance with the manufacturer's specification, typically at +4°C or –20°C, or as appropriate. Backup storage, equipment and contingency power supplies should be in place. For all methods of storage it is vitally important that vaccines or antigens are optimally maintained and routinely monitored, and that their storage is properly documented, in order to have assurance that they will be fit for use when needed. Managers of vaccine banks should therefore ensure that the necessary arrangements are in place to monitor their reserves on a routine basis and to include, where necessary and at appropriate time intervals, a testing regime to ensure integrity of the antigen component or acceptable potency of the final product. For example, storage facilities should be equipped with continuous temperature recording and alarm systems to detect divergence outside the required range; periodic inspection should also be carried out of the antigen containers for cracks or leakage. In this context, managers may wish to also consider the possibility of independent testing, or of greater reliance on overseeing or auditing of the manufacturer's test procedures.

In the case of antigen-containing banks, there is a need for routine stability testing of stocks. Sufficient samples that are representative of the larger stock are necessary for such purposes and should be stored side by side with the bulk antigen.

Where the requirement is to hold antigens or vaccines at a site other than at the principal site of manufacture, Competent Authorities should accept them only after they have been shown to have passed the necessary acceptance testing procedures. Alternatively, if the antigen or vaccine has to be located in the bank prior to completion of any acceptance testing, then the antigen or vaccine should be stored separately and identified as quarantined material until the testing shows full compliance with the vaccine banks requirements.

H. DEPLOYMENT PLANNING

Deployment planning addresses all aspects of the release of antigen for formulation into the final product, and the release and delivery of the ready-to-use formulated vaccine to the destination.

The request to deploy should be made by the Competent Authority(ies) of the requesting country or region, the decision for deployment being taken in agreement with the governance and management of the vaccine bank.

For the optimal use of a vaccine bank, the order for deployment should be informed, where appropriate, by results from a diagnostic laboratory (preferably a reference laboratory) with the ability to characterise the agent causing the disease and match the field strain with the available stored antigens or the ready-to-use formulated vaccines.

Competent Authorities should have emergency plans to ensure that the stored vaccine is distributed and administered to meet disease control goals. In an outbreak situation, the speed of the implementation of the vaccination programme is critical in reducing the number of infected premises, the duration of the epidemic and, for certain diseases, the number of animals that need to be culled. The Competent Authorities should ensure that the necessary cold-chain facilities for vaccines and diluents, if appropriate, are available, that vaccination protocols are defined in advance, that vaccination teams are established and trained appropriately, that all the other necessary documentation, equipment, reagents and clothing are stored at sufficient levels to support any potential vaccination campaign, and that stakeholders are aware of the need for such a campaign (see OIE *Terrestrial Code* Chapter 3.3 *Communication*). Performing periodic exercises and simulations should be considered.

I. CONSIDERATIONS FOR VACCINE BANKS MANAGED BY INTERGOVERNMENTAL ORGANISATIONS

Vaccine banks managed by intergovernmental organisations, such as the OIE, may rely on specific funds for financing, to achieve prevention and control of specific diseases. Such mechanisms have been used to establish vaccine banks for FMD, peste des petits ruminants, avian influenza, and rabies for dog vaccination, and may be considered for other animal diseases in the future.

With the financial support of donors, in the context of international aid or with the use of other financial mechanisms such as trust funds or complementary funding, an intergovernmental organisation (regional or global) may manage regional or global vaccine banks retained by the manufacturers selected through specific international calls for tender. Multiple donor funding mechanisms allow for cost sharing (establishment or replenishment), and for the management of donor-specific requirements.

Eligibility criteria are defined for countries that have access to such vaccine banks as well as guidelines on the use of regional and global vaccine banks. Depending on the diseases, these banks may include vaccines produced and delivered on demand (planned deliveries), or specific replenishment mechanisms for rolling stocks.

The benefits of regional (or global) vaccine banks are numerous:

- i) save costs (economies of scale);
- ii) facilitate the delivery of determined quantities of high quality vaccines complying with OIE standards;
- iii) deliver more doses at a lower cost with access to more vaccine strains;
- iv) reduce the risks associated with the storage of vaccines;
- v) facilitate the harmonised implementation of regional or global disease control strategies;
- vi) create incentives for the implementation of disease control programmes;
- vii) reduce the number of procurement procedures;
- viii) facilitate compliance with OIE quality standards.

Specific financial mechanisms can also allow countries or intergovernmental organisations to purchase directly from such banks.

Collaboration between vaccine banks (including those managed by intergovernmental organisations) and regional organisations is an economical way of increasing the amount of emergency vaccines available. Care is required to ensure that collaborating vaccine banks and regional organisations operate to the same standards. Drawing rights should be clearly defined, and regular contact should be maintained between vaccine banks and regional organisations to confirm the quality of the vaccines. In the case of shared banks, regulatory compliance needs to be addressed at an early stage to ensure that vaccine produced from the bank can be safely used in recipient countries.

Some vaccine banks also rely on service contracts with selected providers that may include replenishment mechanisms and production on demand for non-urgent or planned deliveries, and buy-back schemes. While vaccine banks often hold physical stocks of antigens or vaccines, it is also possible to establish virtual vaccine banks with reduced physical stock. Specific service contracts between the bank holder and the manufacturers operating any of the above solutions should set out clear obligations, pricing specifications, maximum delays for delivery and contractual penalties in case of failure to meet the conditions of the service contract.

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