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Innovations in cryoconservation of animal genetic resources

Practical guide

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SECTION 2

Quality management for improved organization and implementation

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2.1 INTRODUCTION

Development and implementation of a formal livestock gene banking strategy is a critical step in ensuring that a country's cryoconservation programme can address the needs of multiple stakeholders involved in the management of animal genetic resources (AnGR) for food and agriculture. However, it is important for the strategy to have flexibility to accommodate the vagaries of the real world. Once the implementation of the strategy starts, complementary actions should be undertaken to establish an enabling environment for achieving the strategy, to ensure that the strategy is being implemented as planned, and to document progress toward the achievement of the strategy's goals.

Implementing a quality management system (QMS) is a useful approach for a gene bank to deal with the complexity and wide range of management and technical implementation issues. A QMS may be useful to both stakeholders and gene bank management. A QMS oriented towards user satisfaction will build trust with stakeholders, and help the gene bank to implement its strategy. Globally, several gene banks have chosen to adopt some form and/or elements of a QMS (Zomerdijk *et al.*, 2020; IMAGE, 2020).

2.1.1 What is a Quality Management System?

A QMS is a formalized set of policies, processes, procedures, protocols and responsibilities to be undertaken to achieve an organization's goals, with an emphasis on satisfying the demands of the organization's clients and/or stakeholders, while identifying and mitigating the key sources of risk.

The core elements of a QMS can include (Kelderman, 2021):

1. **Quality policy and objectives.** The gene bank should write a quality policy that defines what *quality* means to the gene bank and establish goals that reflect improvements in the services it provides to stakeholders. Objectives should include an expected date of achievement and a framework for assessing progress in achievement.
2. **Quality manual.** The quality manual is the first document to be prepared for a QMS. It should explain the quality objectives, outline the scope of the QMS, indicate

any formal quality standard being followed (e.g. ISO 9001), and refer to quality control procedures and policies being followed.

3. **Organizational structure and responsibilities.** An organigramme should be drafted, that illustrates the organizational structure including personnel and governing bodies, and explains the responsibilities of each. Flowcharts or other visual aids may be used to demonstrate specific roles, such as showing what each person does when processing a sample of materials to be gene banked.
4. **Data management.** Organizations must outline how the information associated with establishing and implementing a QMS is prepared, stored and routinely utilized.
5. **Key processes.** All activities, procedures and equipment associated with optimal operation of the gene bank must be documented.
6. **Stakeholder satisfaction**. Measuring stakeholder satisfaction with the service received from the gene bank is an important indicator, helping to ensure that the gene bank is having the desired result and to identify opportunities for improvement.
7. **Opportunities for continuous improvement.** Approaches to address the shortcomings noted in customer satisfaction must be documented, and possible solutions must be proposed.
8. **Instruments for measuring quality.** Any tools being used to monitor quality must be identified, and plans for regular control and calibration must be specified.
9. **Document archiving.** All documentation showing evidence of quality management, including communication with stakeholders must be maintained in an organized manner.

The most important elements of QMS for livestock gene banks will be described in this section.

2.1.2 Benefits of a QMS for livestock gene banks

Gene banking is a complex and long-term endeavour. For example, samples acquired in 2000 may be of utility in 2050, whereas many gene bank staff will have come and gone, and new equipment and processes will have emerged in the interim. Ensuring that those early samples remain in the bank and are still viable is crucially important. A QMS helps ensure and document the integrity of samples maintained in the bank, as well as the standing of the bank itself to its many stakeholders.

Livestock gene banks are generally responsible to an array of stakeholders, the most immediate being the government and the livestock sector. Therefore, it is important to demonstrate that the gene bank is effectively and efficiently operated, and has a positive impact on the conservation and sustainable use of AnGR. This in turn may result in greater willingness by the government and other stakeholders to maintain or increase financial or in-kind support for the gene bank.

A QMS should yield direct benefits to the gene bank. These benefits may include the following:

- increased efficiency- and cost-effectiveness;
- prevention of errors that may result in loss of material or decreased viability;
- continual improvement of expertise, both technical and organizational;
- greater staff safety;

- improved risk management;
- increased job satisfaction and performance of staff;
- enhanced identification of staff development needs and opportunities; and
- improved communication both internally and with stakeholders.

2.1.3 Trends in QMS among livestock gene banks and other biobanks

Countri22 and gene bank managers around the world have recognized the benefits offered by Development of an international standard for biobankseither implementing or developing QMS or adopting some of its elements.

In 2019, FAO undertook a global survey of quality management procedures and plans among livestock gene banks (Zomerdijk *et al.*, 2020). Ninety gene banks responded, representing 62 countries. Approximately 30 percent of these banks reported having a QMS. Around 60 percent of the remaining banks were in the process of developing a QMS. In other words, more than 70 percent were at some stage in adoption of QMS. In particular, the gene banks were concerned with quality management of processes associated with technical aspects of cryoconservation such as processing and freezing of genetic material. Less emphasis was placed on interaction with non-governmental stakeholders (IMAGE, 2020).

The global interest in quality management for gene banks and other types of biobanks has led to the development of formal standards for evaluating the competence of biobanks (see Box 2.1).

As noted in Section 1, gene banks can support research activities. Therefore, gene banks (and other biobanks) can be considered part of a country's overall research infrastructure. In Europe, the concept of a research infrastructure has been formalized, and adoption of QMS is a recommended process within this formal structure (see Box 2.2).

BOX 2.1

Development of an international standard for biobanks

In 2014, the International Organization for Standardization (ISO) Technical Committee for Biotechnology (TC276) initiated a working group on biobanking in general. This working group developed a new ISO standard for biobanking activities, covering all biological domains including animals, humans, plants, and microorganisms. The standard thus recognizes the common processes underlying any biobanking activities, including animal gene banks. The document is targeted toward gene bank managers, users, regulatory authorities and accreditation bodies. The new standard, ISO 20387[1] is now considered the international reference document for quality management of gene banks. The standard covers the various gene banking processes from collection or reception, preparation and preservation, storage and validation. Technical and human resource requirements are addressed, as well as the requirements for QMS.

[1] **International Organization for Standardization (ISO).** 2018. *ISO 20387: 2018 Biotechnology – Biobanking – General requirements for biobanking*. Geneva. Cited 20 January 2021. www.iso.org/standard/67888.html

BOX 2.2

Gene banks, biobanks and QMS within the European Union's research infrastructure framework

The European Commission[1] defines a national research infrastructure as "facilities that provide resources and services for research communities to conduct research and foster innovation." This definition includes research equipment and instruments, collections of material and data (e.g. gene and biobanks), and computing systems and communication networks. The European Strategic Forum for Research Infrastructures (ESFRI) has developed a roadmap that includes a list of European Union and cooperating research infrastructures and the strategy for their utilization, and has encouraged European Union member states to develop national roadmaps. Inclusion within these roadmaps is based on various recommended criteria, including the presence of a QMS. The ESFRI roadmap includes biobanking infrastructures for medical research (BBMRI), marine research (EMBRC) and microbial research (MIRRI), thus recognizing the importance of gene and biobanks for research (European Commission, 2020).

[1] **European Commission.** 2020. *European Research Infrastructures.* Brussels. Cited 20 December 2020. ec.europa.eu/info/research-and-innovation/strategy/european-research-infrastructures_en

2.2 QUALITY MANAGEMENT FOR GENE BANKING

2.2.1 Defining the quality policy

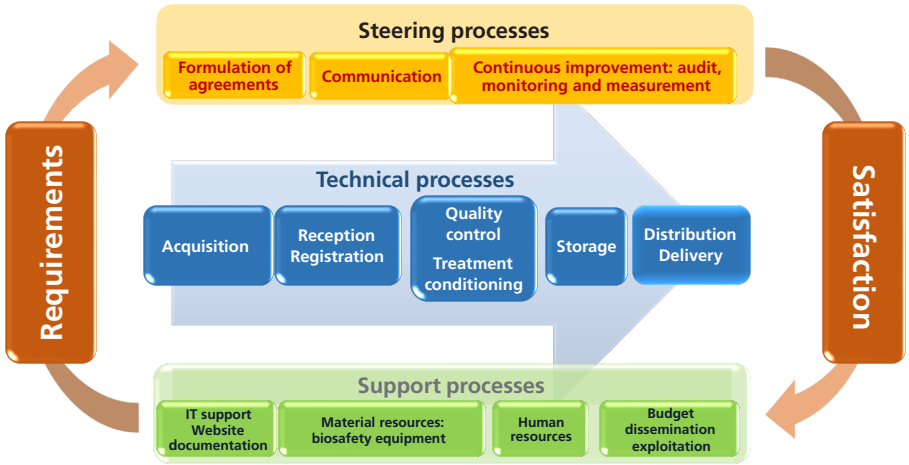
As a foundation for its QMS, a gene bank shall compile in a single document its main objectives, commitments and plans to reach its objectives, addressing issues described in Section 1. This quality policy document should be brief, formally institutionalized and made freely available to the public. Commitment of the leadership is particularly important to support the implementation of the strategy. The quality policy, once completed and approved, is a reference document for the gene bank that needs to be regularly updated.

2.2.2 Mapping key processes

The gene bank will map the different key processes supporting its strategy. In general, there are three main types of processes: (i) steering and management (decision-making, communication, monitoring), (ii) support (human resources, informatics, equipment), and (iii) technical (collection, processing, documentation, storage, distribution). Figure 2.1 provides an example of a map of key processes for an animal gene bank.

The gene bank will at the same time identify and refer to the relevant public policies and regulations for the type of biological material to be collected, stored, and distributed. These policies and regulations are discussed in more detail in Section 9, and may include the *Global Plan of Action for Animal Genetic Resources* (FAO, 2007) and the national strategy and action plan, sanitary regulations, animal breeding regulations, access and benefit sharing, intellectual property, at the national and international level.

FIGURE 2.1
Mapping the processes of a gene bank quality management system (QMS)



Source: Authors' own elaboration.

2.2.3 Stakeholder involvement

As shown in Section 1, the gene bank will cooperate with a range of stakeholders. The steering process of a gene bank should prepare a document that identifies all stakeholders, sometimes called "interested parties" in QMS terminology, list their expectations, match these to the strategic objectives of the gene bank, and identify the pathway to fulfil these expectations. To this end, the gene bank may set up one or several committees to support stakeholder involvement. The document should describe the operating rules of the committees and the calendar of their activities. Organizing interactions with stakeholders is the best method to reach consensus, maintain trust in the gene bank, and analyse trends across time. Ideally, the gene bank will have a decision-making body and one or several advisory committees, such as a users' committee, a scientific advisory board, or a strategic steering committee.

The general public may be engaged in many ways, but one of the most effective is through the popular press (e.g. newspapers, television, and/or documentaries produced by government). This activity must not be overlooked since the support by the general public is important for policymakers.

2.2.4 Risk assessment

Risk assessment and preventing risks associated with the gene bank collections and operations are central elements to its management. Table 2.1 shows the main risks and mitigation measures according to the main components of the gene bank activities.

TABLE 2.1
Sources of risk to gene bank operations and possible preventive measures

Component	Risks	Preventive measures
equipment	failure or breakdown leading to loss of material	alarms; maintenance of equipment; secured access; electricity supply; duplicate storage
human resources	insufficient manpower or lack of expertise leading to mistakes and degradation of resources	human resources management plan; replacement policy; training programme; cross-training in the staff
malpractice	intentional damage to collection	security clearances for personnel; logs monitoring date collection accessed and by whom
hygiene and safety	staff injury or death; release of potentially dangerous material or chemicals in the environment; specific animal health risks	adapt organization to prevent accidents; safety plan; controlling sanitary status of animal material; waste management plan
biological material	insufficient quality	perform regular quality control; request quality test results before entry into collection
information system	loss of data	backup system
budget	suspension or discontinuation due to lack of funds	regular budget monitoring; monitoring and allocating funds derived from fees or extraordinary funding sources
catastrophic events (e.g. floods, earthquakes, fire, internal disease transmission)	destruction of or damage to facilities, resulting in loss of collections	backup or duplicate collections; selection of storage sites
customer relations	dissatisfaction of users or stakeholders	establish a multiactor board; satisfaction scores and complaints; corrective measures in case of complaints

Source: Authors' own elaboration.

2.2.5 Evaluation framework

A gene bank must regularly undergo evaluation to confirm if quality control measures are up to standard. Three approaches can be taken: (i) self-evaluation; (ii) external assessment within the field of activity; and (iii) external audit by an accredited body.

2.2.5.1 Self-evaluation

The gene bank can start by implementing a self-evaluation test with the following actions:

- establish a strengths, weaknesses, opportunities and threats (SWOT) analysis for all or part of its activities, particularly those considered critical, and update the SWOT at regular intervals. The strengths and weaknesses are internal, whereas the opportunities and threats come from external origin;
- use an external reference document such as ISO 9001 or ISO 20387 (ISO, 2018), and check whether the operations of the gene bank comply with the requirements of these documents; and/or
- use a self-diagnostic tool like the one developed by the Horizon 2020 European Union project Innovative Management of Animal Genetic Resources (IMAGE, 2020) to help gene banks in the development of their QMS (see Annex 2.1).

2.2.5.2 External assessment

Then, an external assessment can be used with the following actions:

- perform regular surveys to check satisfaction of its users and analyse the general trends as well as potential specific messages, this can be done periodically as deemed necessary; and/or
- use cross-evaluation among a set of other gene banks, which could include a peer review system.

2.2.5.3 External audit

Finally, independent evaluation with an external audit (also called third-party evaluation) is recommended to get an external and impartial analysis of the internal operations of the gene bank. This independent evaluation is a requirement of most official certification processes. This action can be performed by persons accredited with audit standards, who preferably have technical expertise in gene banking. Their report can then be used to strengthen gene banking processes, and to make higher level administration aware of current and future gene banking needs.

These approaches have comparative advantages and disadvantages. The self-review can usually be expected to be the simplest and lowest cost option, but is also the least impartial and has only internal value. The independent review is usually the most complex and expensive, but will be impartial and may be of value for external certification purposes if such certification is needed or desired. The independent evaluation is also likely to be more effective for building trust with potential new users or stakeholders that are familiar with the evaluation procedures.

2.3 KEY PROCESSES

The QMS shall include the preparation and maintenance of a library of documents, that list and describe the key processes involved in successful operation of the gene bank.

2.3.1 Management

Gene bank management has a unique responsibility. It not only oversees the day-to-day operation of the gene bank; in many countries, management is the interface between the gene bank and its stakeholders. The QMS documentation should include a description of the roles and responsibilities of management. The following is an exemplary list of external and internal roles of gene bank managers.

Externally, gene bank managers may be responsible for the following:

- organizing and conducting meetings with funding bodies and advisory groups;
- raising awareness among stakeholder groups such as breed associations or companies, of gene bank activities, interests, needs and concerns;
- informing upper administration of the institution hosting the gene bank about the status and goals of the gene bank, and stakeholder response to gene bank activities;
- securing long term support for gene bank operations;
- providing stakeholders with information about the collection, tailored to their species and/or breed; and
- implementing a technological watch and monitoring relevant regulatory developments.

Internally, gene bank managers are usually responsible for the following:

- establishing and adhering to all factors impacting collection security and operational safety (see Box 2.3);
- ensuring implementation and overseeing day-to-day operation of the gene bank, including incoming and outgoing shipments of germplasm and tissue, processing and cryopreserving samples, checking data entry, evaluating genetic diversity acquired from various breeds;
- performing gap analysis for the various species and breed collections;

BOX 2.3

Maintaining operational safety in gene banks

As noted in Table 2.1, factors that may compromise hygiene and safety are among the important sources of risk to staff and to regular gene bank operations. A QMS must consider specific sources of risk and measures to control them. The two most important hazards to staff involve their interaction with donor animals and liquid nitrogen.

Interaction with animals (and their tissues) is associated with two potential dangers: (i) injury during animal handling; and (ii) transmission of zoonotic disease. For both cases, the most effective measure is to ensure that all staff are sufficiently trained and/or experienced. For animal handling, additional prevention measures include appropriately designed and maintained animal housing and material collection facilities. Actions to improve staff safety will also tend to maximize animal welfare. With regard to zoonotic disease transmission, a first step is to ensure that donor animals are healthy and that their source herds are free from disease (by veterinary inspection and/or testing) before bringing them to the collection facility or performing collection in the field. Upon arrival at the collection facility, animals may be additionally subject to quarantine. Then, high sanitary standards must be applied for collection, and all persons handling the collected material must be properly clothed with proper personal protective equipment. All safety measures associated with handling of animals and their biological materials must be recorded in the QMS documentation. In addition, whenever facilities and equipment are inspected, the results should be recorded for the QMS.

Liquid nitrogen vaporizes at -196 °C and therefore poses two major safety risks: (i) freezing or "burning" of skin upon contact; and (ii) hypoxia (lack of oxygen) and respiratory distress. Prevention of contact injury is achieved by using protective clothing, including specifically designed gloves, lab coats, closed shoes and safety goggles. Both the liquid nitrogen itself and the stored materials and associate storage vessels must only be handled with equipment that is designed to resist extreme cold. The risk of hypoxia can usually be avoided by ensuring that the material storage rooms are well-ventilated, and outfitted with an oxygen monitoring system with alarms that are activated when the oxygen level falls below a certain threshold (e.g. 19.5 percent). As with animal handling, all safety measures associated with liquid nitrogen must be fully described in the QMS documentation, including maintenance and inspection routines and their results.

- managing human resources by providing direction for operations and hiring competent staff; and
- managing financial resources, in particular, funds needed to execute collection objectives.

2.3.2 Gene bank equipment

The QMS will include a support process to record mandatory information about equipment. As a minimum, this information usually includes the following: (i) manufacturer and commercial model; (ii) date of purchase; (iii) value at purchase; (iv) location in the facility; (v) maintenance operations, including calibration; and (vi) records of failure and repair. Records of both maintenance and calibration are needed as a cross reference when comparing various measurements over time.

Gene bank managers need to be aware that new equipment purchased to replace equipment that is becoming outdated may perform differently due to manufacturer improvements. As a result, historic data may not correspond with measurements taken with the new equipment. To document such differences the old and new equipment must be tested using the same set of samples. If differences exist, conversion equations, such as by linear regression, can be developed to enable the utilization of old and new data.

The intended size of the germplasm collection will govern the scope of equipment and physical space. Equipment can be partitioned into various gene bank functions. How many samples and from what species might be processed will need to be assessed so that equipment purchases will match the maximum number of samples to be processed in a single day.

2.3.3 Gene bank personnel

The QMS will include a support process dedicated to human resources that records mandatory information about each staff position. This information will usually include: (i) job description; (ii) training programmes; and (iii) expertise on technical processes. The gene bank may want at least two persons trained for each critical activity, to avoid interruption of those activities.

Fully functional gene banks require combining the disciplines of genetics, cryobiology and information systems. Like gene bank equipment, gene bank personnel can be scaled to match the size and requirements of the gene bank. At a minimum, a gene bank manager and a technician are required, and these may be part-time roles. Under sparse staffing conditions, gene bank managers may seek outside support from other branches of government or academia to fulfil short-term needs as well as to establish long-term collaboration with scientists. At the other end of the spectrum, gene banks may employ full-time scientists and technical support for each of the disciplinary areas mentioned above. If countries should choose to have a distributed gene banking system, with more than one location, the various sites should each harbour the core set of expertise for gene banking (i.e. manager and technician), while sharing staff with expertise in a specific discipline. Close coordination among sites will be critical for maximum efficacy and efficiency.

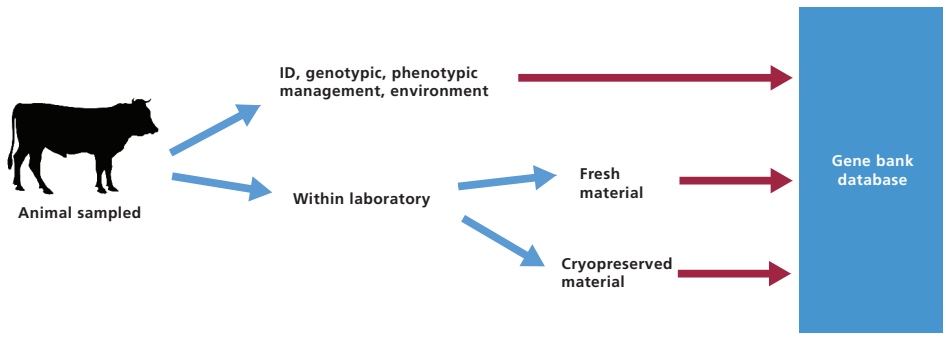
2.3.4 Genetic material database

Section 8 details the issues related to data management, but the following issues are critical for quality management:

- Databases are indispensable infrastructure for efficient operation of the gene bank.
- The gene bank's database shall make publicly available a set of data defined in agreement with material providers and complying with regulations. This means they need to be accessible via the internet, according to FAIR principles (where applicable, see Section 8). The database will generally also have a private section to keep information needed for internal use, such as sample storage in a specific tank location, or privacy-sensitive information.
- Spreadsheets are not sufficient to efficiently and reliably run gene banks, i.e. they are not a substitute for a formal database.
- Security of data is a critical issue that merits maximum attention. One or more levels of redundancy should be maintained on machines in different physical locations or units of cloud storage. If a country has multiple gene banks, all locations must be connected to a common portal or utilize the same database, to facilitate data sharing.
- The QMS documentation should describe all of the pertinent features of the database, including software utilized, data fields stored, security procedures and access rights.

Information about the samples is as important as the samples themselves (see also Section 8). There are two data streams per sample that gene banks should be acquiring (see Figure 2.2 below). From outside the gene bank, information such as species, breed, breeder, animal ID (which should follow a standard as much as possible, since there may be more than one ID), date of birth, pedigree, date of sampling, sampling protocol, phenotypic measurements, genotypic information, environmental descriptors or potentially the geographic information system (GIS) coordinates for where the animal was born, and management system (extensive, mixed crop-livestock, or intensive) the animal was produced.

FIGURE 2.2
Data stream of information captured by a gene bank



Source: Authors' own elaboration.

Within the gene bank the data stream focuses upon various processes associated with sample handling. For example, date of arrival, sender name and address, state of arrival (fresh or cryopreserved), the temperature, pH, and sperm movement analysis of fresh semen at arrival. For samples already cryopreserved, information includes data on the straw itself, noting if there were any peculiarities about the shipment, etc. Once samples are frozen, the storage location will also need documenting. This usually includes a hierarchy from the largest storage space to the smallest. For example, tank number, pie within a tank, canister, goblet and cane/visotube (the level where no individual animal samples are mixed).

2.3.5 Genetic material acquisition

The QMS documentation should describe the process of acquisition, and specify the conformity criteria applied for collection and acceptance of the material. The conformity criteria will include both strategic (such as prioritization) and technical elements. These criteria should address standards for collecting material of a particular donor animal of a certain breed, as well as for individual samples of material and related data. Following the decision to acquire genetic material, a system must be in place to trace the acquisition between the provider and the gene bank. Generally, an agreement between animal owner and gene bank will be signed, and will serve as the chain of custody as the sample moves from the farm or collection centre to the gene bank (see Section 9).

Within and among countries there is no "one size/approach fits all" scenario. The acquisition of germplasm and tissue is highly variable based upon the species and how functional technologies are for a species. Many gene banks have demonstrated that acquiring cryopreserved semen from industry sources is an efficient mechanism to capture a wide range of breeds and animals within breed. In addition, acquiring already cryopreserved samples can be a mechanism for obtaining biological samples that have been cryopreserved for a long period (> 40 years), particularly in the case of beef and dairy cattle. Movement of these samples can be relatively easy with commercially available courier services and using liquid nitrogen shipping tanks. All acquisition options that are utilized must be recorded in the QMS documentation.

For some species cryopreserved semen is not typically used. For example, the swine industry mainly uses fresh semen in their artificial insemination programmes, relying on semen extenders that maintain the semen viable for as long as a week. Extended semen can thus be shipped to the gene bank, where it can be processed and cryopreserved in the gene bank's laboratory. Such innovative approaches have not been implemented in the poultry industry, where frozen semen almost never is utilized commercially as rooster sperm needs to be cryopreserved within a short time after collection (see Section 3).

Gene banks often acquire cryopreserved material that has already been fully processed by a third party. The gene bank must therefore define and document criteria for acceptance or rejection, be it at the level of quantity, quality or documentation. The receiving bank must obtain a technical description of the cryopreservation procedure used, which will not only help confirm the quality of the material, but also define how the material can be eventually utilized. To better control external processes, the biobank may include in its QMS a list of recommended material processing and cryopreservation protocols to be used by all providers of genetic resources.

In the case of frozen semen, the monitoring of the cold chain is critical, and the gene bank must define a threshold temperature above which it should not accept frozen semen for future reproductive use. In case of any doubt, the gene bank may use an aliquot for quality assessment, for instance, by thawing semen and measuring the proportion of live sperm cells and their motility (see Section 3).

2.3.6 Material collection

As will be seen in Section 3, animal germplasm may be collected and cryopreserved in various ways that are dependent upon technical expertise and on access to donor animals for collection. The gene bank should identify the anticipated use of a biological material (i.e. for reproduction, molecular studies or health monitoring) in order to choose a collection procedure that will ensure fitness for purpose of the material collected. Also, prior to collection, the gene bank needs to have developed a unique identification system to ensure traceability of samples acquired. At the same time, the gene bank will define the information to be collected at sampling, also referred to as "the minimum data set," to properly document the material at the time of entry into the collection.

The gene bank must list the technical steps to be followed by the collection procedure, in order to control the risk of degradation of the biological material at sampling. The gene bank should collaborate with researchers for the development of new methods or to remain informed of the latest technological progress. Before starting the collection, the gene bank should ensure it is complying with existing regulations, in particular, with regard to animal care, animal health, and access and benefit-sharing issues (see Section 9).

When collecting germplasm and tissue on farm, gene banks can either send staff or use commercial vendors. The samples collected on farm can be cryopreserved in the field, or as mentioned above, be shipped fresh and extended to the laboratory for processing. Gene banks should also take blood samples from the donor animals, and perform a series of health tests to ensure the animal is free of any diseases transmitted via the germplasm (see Section 7 for further discussion). Depending upon national regulations gene banks may need to store material that has different health status separately. Standard operating procedures for on farm collection, including both technical and administrative actions, should be documented in the QMS.

Germplasm can also be collected at commercial AI or animal reproduction centres. Such centres have a controlled collection environment, including quarantine and health testing, as well as high levels of technical expertise. This may be the preferred route for semen collection, especially when the bank is acquiring material from an animal that the centre had already intended to collect. In such cases, the cost of obtaining a few extra samples may be low. On the other hand, if this scenario involves animals in which the centre has no direct interest, the costs of the services provided may be quite high.

2.3.7 Material processing

As discussed in Section 3, there are a wide range of cryopreservation protocols that can be used for each species. The QMS documentation should clearly outline the protocols being applied. In many countries, there are professional organizations that establish standards and practices considering a wide range of protocols. When such protocols are used, the

QMS should refer to these organizations and protocols. Details on material processing are in Section 6.

The gene bank's primary concern is to ensure viability of the stored material, i.e. to obtain pregnancy or a fertilized egg when needed. Procedures for monitoring cell damage through the preservation stages and performing post-thaw analysis on cryopreserved samples can be parts of material processing and listed in QMS documentation. Criteria for acceptable levels of success in processing biological material may be based upon literature values or experimentation by the gene bank (see Section 6 for more detailed information about different types of biological material and associated criteria).

While recommendations from research and industry organizations, as mentioned above, may be useful, gene banks still need to formalize processes and testing procedures performed in-house. These processes and procedures need periodic review, and in the case of cryopreserved semen samples, to routinely withdraw a specified number of males from the gene bank and perform test-matings to ascertain the level of fertility that can be achieved. If samples were collected and cryopreserved at a commercial AI centre, such a test may not be necessary, because that entity will be selling samples from the same animal and any fertility problems will be known.

Often, gene banks will be confronted with the challenge of dealing with poor quality semen samples from rare breeds. In these situations, gene bank standards for collection and post-thaw quality may have to be relaxed, while knowing that additional animals and samples will need to be collected for reaching collection goals.

2.3.8 Material storage

The key factors to consider for storage are traceability and safety. Each storage unit should be uniquely identified (such as with a barcode label, a printed unique identification number or a colour code for semen visotubes) so that the identity and location of the biological material are unambiguously known and entered in the gene bank information system.

Duplicate storage is recommended. In addition, an empty storage capacity should remain available to rescue material in the case of failure of storage equipment.

Systems for continuous temperature control and control of access to the storage room must be implemented. The systems should record all fluctuations in temperature and entries of personnel into the room. These data are to be entered into the gene bank database so that long-term trends can be documented during gene bank reviews.

2.3.9 Material distribution

The gene bank should establish in its strategy and QMS the procedure for stakeholders to request material. Mandatory information to be provided by the applicant must be established, and the decision-making process for access to gene bank material must be agreed with the governing board. Criteria to consider may include: (i) the consistency of the request to the strategic objectives of the gene bank; (ii) the soundness of the request regarding to its objective (such as the number of semen samples requested considering the mean fertility of frozen semen in the species); (iii) the technical feasibility of the intended use; (iv) the quantity of material available, so as to maintain the minimal quantity of material the gene bank is committed to keep; and (v) opportunity to obtain the material from other sources.

From a technical viewpoint, distribution must be performed in such a way that quality of the material is preserved for the intended use. The gene bank should prepare a standard shipment procedure, and identify reliable third parties in charge of transportation. Traceability of the shipment throughout the process is mandatory. The gene bank shall record all distribution events and update its database accordingly.

2.4 IMPLEMENTATION AND CONTINUOUS IMPROVEMENT OF QUALITY MANAGEMENT SYSTEMS

2.4.1 Reviewing indicators

Each process of a QMS must define its targets and establish indicators to monitor the achievement of the targets. For instance, regarding human resources, a target may be sufficient capacity for a given procedure, so a logical indicator would be the number of trained staff in that technique or the number of training events offered in a given period. Regarding storage, the target may be capacity to avoid loss due to equipment failure, and the indicator may be the number of rescue tanks available or the rate of duplicated storage.

Indicators for the management process are usually related to risk control or to satisfaction of users, but can also include more specific elements related to the gene bank strategy. An example is the percentage of endangered breeds for a given species with stored material in sufficient quantity according to SDG Indicator 2.5.1b. For user satisfaction, the gene bank may, for example, organize a survey among its stakeholders to check if their expectations are fulfilled.

Each process should regularly be reviewed to check indicators, confirm or revise objectives, update the SWOT, and identify the need to update procedures or to add new procedures. Once a year, the management review of the gene bank will examine each process and its indicators; check for adequacy, effectiveness and alignment with the objectives; identify priorities for actions, including any need for changes in the QMS; in order to establish an action plan for continuous improvement.

The action plan will include the organization of internal and/or external audits as deemed necessary by the decision-making board. The audits are aimed at checking if the QMS: (i) is effectively supporting the objectives of the gene bank; (ii) complies with the requirements set by the gene bank; and (iii) is effectively implemented and maintained. The gene bank shall retain all information collected during the audit.

2.4.2 Recording operations

Recording all steps, both in management and technical procedures, is mandatory. A QMS can be summarized as "writing what is done and doing what is written". Gene banks should record and be able to trace any action associated with an objective of the gene bank. For instance, agreements signed between the gene bank and the provider of biological material are a key record for tracing the entry of resources, documenting its purpose and legal status, and identifying a contact person for any future needs. Another example is monitoring equipment, date of purchase and date of maintenance or repair.

2.4.3 Non-conformity assessments

Any deviation from normal operations or from achievement of the objectives, or any complaint from users, must be reported and classified according to its impact on gene bank operations. Impact can be minor, moderate or critical. Critical non-conformities are those that prevent the gene bank from performing its operations. Examples include: (i) long-term electricity blackouts without a safety generator; (ii) interruption of liquid nitrogen provision; and (iii) computer failure preventing access to the database and blocking material distribution. Minor non-conformities are those that can disrupt an operation but not block it completely, or those that do not affect technical quality of the material. Moderate non-conformities fall in between, such as those that may reduce technical quality of material but not cause it to be inviable, or that may block some operations for only a very short period. The impact classification of a non-conformity should be reviewed to inform the establishment of necessary corrective and/or preventive measures.

Any non-conformity must be analysed by considering the possible causes involved. The potential causes are human resources, equipment, method, biological material and management or a combination of these. Then, the gene bank must evaluate the need for action to eliminate the cause(s) of the non-conformity, and to ensure it does not recur or occur elsewhere. It may update its risk assessment and mitigation plan to account for observed deviations or complaints.

2.4.4 Corrective and preventive measures

Corrections are actions taken to mitigate the risks and attenuate the impact of a non-conformity. They may consist of repairing an equipment, providing additional training to an employee, or adding a step in the monitoring process of an activity.

Preventive actions are steps to avoid that a non-conformity occurs. They may consist of replacing an equipment before it breaks down, hiring new staff, implementing a new protocol, or modifying a given decision-making process.

Corrective and preventive actions are examined at each process review and at the management review.

2.5 REFERENCES

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