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T2 Management system of a BRC and quality of biological resources from human or micro-organism origin

T3

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Correspondence

At the time of publication, there were no international or European work documents dealing with the subject.

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QUALITY OF COLLECTIONS OF BIOLOGICAL RESOURCES **AFNOR S96R**

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Introduction

Biological resources are crucial to life sciences R&D and their applications. This makes it equally crucial to ensure that there is a system governing the conservation and provision of these biological resources.

This system should be based on infrastructures tasked with preserving and providing access to the biological material and related data.

The OECD, working in liaison with the international scientific community, developed a set of actions that were proposed to governments worldwide in order to promote the creation of biological resource centres (BRC). These actions were designed to:

— build up the existing collections, and create new collections where necessary;

— promote a quality-oriented approach;

— promote initiative to coordinate the BRCs by setting up an international network, founded on coordinated informatic systems and technological platforms;

— devise measures for harmonising the system governing how the BRCs were to operate, including on issues such as the accessibility, exchange and distribution of biological resources, in compliance with all applicable national and international legislation and conventions.

To drive the implementation of many of these actions and harmonise BRC practices, the OECD published general and specific guidelines in 2007. These guidelines were followed by further recommendations focussed on human healthcare and published by other national and international bodies, including the WHO, UNESCO, and the European Council.

In France, the ministries and institutions concerned opted to implement a standard-based certification initiative.

The scope of this standard founded on the OECD guidelines is limited to collections of human and microbial biological resources. Without detailing the content, it forms part of the prevailing legal and ethical framework at the heart of the activity of the infrastructures involved. The standard gives general legislative provisions of a quality management system that is designed to ensure that a Biological resource centre (BRC) is managed properly under the terms of a quality-oriented policy. The aim of this standard is to pave the way for quality conservation and exchanges of biological materials.

1 Scope

The present standard applies to entities whose core mission is to conserve and provide access to collections of biological human and (or) microbial resources, in particular for the purposes of research and analysis, and especially for diagnosis or prognosis, educational study and industrial value creation, in compliance with the applicable legislation. This standard does not, therefore, apply to therapeutic uses.

It states:

— the requirements concerning the quality management system for these entities;

— the requirements needed to ensure the quality of the collections compiled.

The present standard has been drafted through an approach that builds on and is compatible with existing document materials, and in particular the international ISO 9001 standard and the OECD Guidelines.

Help box 1:

This standard uses the term 'entity' to keep it consistent with the ISO 9000 series of international standards. The entity thus covers both the organisation and the system itself.

This document sets out general provisions governing how a Biological Resource Centre is to:

a) establish, document, implement and maintain its quality management system;

b) provide biological resources that comply with the regulatory requirements and with the requirements of the stakeholders;

c) obtain quality management system certification from an independent entity or carry out self-assessments on their conformity with the present standard.

NOTE This standard is a general standard that has been developed for collections of biological resources of human and microbial origin. It can equally serve as a working basis for other types of collections.

2 Normative references

The following reference documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references and where there is no reference to a version number, the latest edition of the reference document (including any amendments) applies.

NF EN ISO 9001:2000, *Systèmes de management de la qualité — Exigences (ISO 9001:2000).*

NF EN ISO 9000:2000, *Systèmes de management de la qualité — Principes essentiels et vocabulaire (ISO 9000:2000).*

NF EN ISO 9004:2000, *Systèmes de management de la qualité — Lignes directrices pour l'amélioration des performances (ISO 9004:2000).*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
biological resource centre (BRC)
a BRC is an entity whose under its core mission, leads it to at least conserve and provide collections of biological source material, in particular for the purposes of research and analysis, and especially for diagnosis or prognosis, educational study and industrial value creation, in compliance with the requirements set out in this standard

NOTE This term has been adopted for the entire international community under the OECD initiative. Other terms may also be applied, such as biobank, platform, tumour bank, etc.

The designation 'BRC' will be used for purposes of the present standard.

3.2
collection
a set of biological samples or materials compiled together according to shared characteristics for research, education, industrial value creation or analytical purposes, especially diagnosis and prognosis

3.3
biological resources
a generic term covering biological material and the related data (annotations)

NOTE Biological resources of human origin includes organs, tissues, cells, biologic fluids and their derivatives.

3.4
Annotations / related data
information associated with the biological material

3.5
user
person using the biological resources provided by the BRC

3.6
stakeholders
the stakeholders in a BRC are any person involved in the operations of a BRC

Help box 3.6:

A typical list of stakeholders would include:

— patients for and donors of human biological resources;

— suppliers of microbial biological resources;

— people or groups initiating the collections;

— people or groups consigning samples;

— users of biological resources;

— BRC staff;

— any individuals or groups, including the public sector, that have a specific interest in the BRC;

— the suppliers (of hardware and consumables, etc.) and their partners.

3.7
supplier
entity or person who procures a product or provides a service

3.8
catalogue
a document tool used to list the biological resources available

Part 1: Organisation and quality policy

4 Quality management system for BRCs

The quality management system is a set of processes and procedures established, implemented and monitored in order to apply the BRC's quality policy and achieve the target objectives.

4.1 General requirements

The BRC shall establish, document, implement and maintain a quality management system and continuously improve the efficiency of this system in compliance with the requirements of this standard.

The BRC shall:

a) identify the processes needed for the quality management system;

Help box 4.1 a):

There are three key processes that can be defined as necessary for meeting a majority of the requirements of this standard: these 3 processes, which are known as operational business deployment processes, are the **reception**, the **conservation**, and the **provision** of biological resources.

In scenarios where the BRC also conducts the **preparation** process, this process is added as a further operational process.

Furthermore, the BRC shall also define other organisation-specific processes, which are qualified as support processes.

The BRC shall outline its choices in the quality manual (4.2.2).

b) determine process sequences and process interactions;

c) monitor these processes, measure them and analyse them (6);

d) publish information on the development, deployment and updating of the quality management system (5.6);

e) regularly evaluate and update the BRC's quality management system whenever necessary, in order to guarantee that it reflects the entity's operations and incorporates the most up-to-date information (see 5.7);

f) implement a continuous improvement system (6.4).

Should a BRC opt to outsource any process liable to impact on the level of conformity of the service provided, the BRC shall guarantee the service is fully controlled. They will need to identify and document the management and control of the outsourced process or processes in the BRC's quality management system.

4.2 Documentation requirements

4.2.1 General

A document management system needs to be deployed that includes:

a) the management commitment;

b) the quality management manual;

c) all procedures and records;

d) the documents that the BRC needs to ensure the planning, operations and efficient control of its processes;

e) regulatory intelligence: texts referencing legislative and regulatory requirements;

f) records of stakeholders' requirements for a scientific project (5.2). These records have to be archived (see 4.2.4).

All of these documents must be implied and updated at regular intervals.

The document management system must also cover outsourced processes (4.1).

Help box 4.2.1:

Document requirements for the BRC may include:

— operating procedures;

— drawings, diagrams;

— job descriptions, proficiency records;

— schedules;

— user/customer satisfaction surveys.

The documentation itself may come in all sorts of formats on all kinds of media.

The range of documents filed may differ between BRCs depending on the specific features of individual infrastructures.

4.2.2 Quality manual

Help box 4.2.2:

The quality manual is the BRC's master document for implementing the requirements set out in the standard. It gives a precise outline of the scope covered under the quality management system the BRC opted to implement.

The BRC may well opt to follow the chapter structure of the present standard to make it easier to draft its quality manual. The manual will go on to detail the organisation-specific features of each individual CRB.

The BRC shall establish and regularly update a quality manual that includes:

a) the scope of the quality management system, which will specify:

— the biological resources handled;

— the target uses for the biological collections (earmarked for scientific projects, patrimonial rights for the collections concerned, etc.);

— the sites across which the quality management system is designed to apply;

— the processes covered by the quality management system;

b) general requirements (see 4.1);

c) rationales justifying any exclusions;

d) documented procedures drafted for the quality management system;

e) a description of the interactions between each process covered by the quality management system.

Help box 4.2.2:

a) in particular, the BRC shall specify those support processes that it wishes to include in its quality management approach (help box 4.1);

b) exclusions may concern certain collections of samples, or for multi-site BRCs, certain sites.

4.2.3 Document control

There needs to be full control over the documents required for the quality management system. Records are factored in as special documents that need to be controlled as stipulated under section 4.2.4.

There needs to be a documented procedure for:

a) approving documents before they are released;

b) revising, updating where necessary, and re-approving the documents;

c) ensuring that all document changes and version upgrades are clearly stated;

d) ensuring that current versions of all applicable documents are available at the place they are used;

e) ensuring that the documents remain readable and easily applicable;

f) ensuring that documents from outside sources are labelled as such, and that the release of these documents is controlled;

g) preventing any accidental use of outdated documents, and for properly identifying them if there is a reason why they are being held on to.

NOTE The term "documented" means that a document describing outlining the procedure has to be drafted, updated and filed.

4.2.4 Records control

Records need to be kept and archived as proof of conformity with the requirements and of the efficient running of the quality management system.

All records must remain readable, easily identifiable, and available.

A documented procedure needs to be drafted to ensure that the rules on records identification, storage, protection, availability, archiving period and deletion are applied.

Help box 4.2.4:

This procedure could be a table listing out the various records and how they need to be managed.

5 Management responsibility

Help box 5:

Two different types of management responsibility has been differentiated within the framework of BRC operations, and their roles can be defined as follows:

— institutional responsibility:

  — commitment to a quality-driven management policy;

  — commitment to provide the BRC with the support needed;

  — report on this commitment;

— operational responsibility, assigned to a director, a coordinating officer, or a leader:

  — provide governance for the BRC;

  — manage the BRC's resources;

  — shape development directions.

NOTE This standard uses the term 'management' to keep it consistent with the ISO 9000 series of international standards. The term 'management', in its use here, is defined as followed:

— a person or group of persons that directs and controls an entity at top level.

5.1 Management commitment

Top management shall provide evidence of its commitment to the development and implementation of the BRC quality management system and continually improving its effectiveness.

Help box 5.1:

Commitment and active involvement from top management are essential to developing and maintaining an efficient quality management system that creates benefits for the stakeholders.

This commitment is often expressed through a written document that is reproduced in the quality documentation (4.2.1).

Top management shall:

a) establish a quality policy governing how the BRC is to be organised (see 5.3) and make the policy available;

b) demonstrate that the organisational quality of the BRC is consistent with its operational objectives as well as its policy on accepting, conserving and providing biological resources;

c) communicate to the organisation the importance of meeting customer as well as legislative and regulatory requirements;

d) define, through a documented procedure, the conditions for accepting collections or biological resources;

e) define, through a documented procedure, the conditions for conserving collections or biological resources;

f) define, through a documented procedure, the conditions for providing collections or biological resources;

Help box 5.1 d), e) and f):

These conditions will need to take into account technical, scientific and ethical criteria as well as the requirements of the stakeholders and the quality policy governing the BRC. Top management may enrol the support of a third party, such as a technical committee, a scientific and ethics committee.

g) ensure that measurable quality objectives are established, tracked and analysed as part of a continuous improvement framework;

Help box 5.1 g):

Measurable objectives may deal with quality management and/or the quality of the biological resources.

h) lead management reviews (5.7);

i) make sure that appropriate resources are fully available (7).

5.2 Stakeholder needs and expectations

The success of the BRC hinges on understanding, integrating and meeting the present and future needs and expectations of current and potential stakeholders.

The BRC shall:

— identify its stakeholders (3.6);

— understand their needs and expectations;

— and identify those that the BRC is able to meet (4.2.1 f)).

5.3 The BRC's quality policy

The quality policy needs to be:

a) adapted to the entity's ultimate purpose;

b) conform to all legislative and regulatory requirements as well as the requirements defined in tandem with the stakeholders;

c) include the commitment to continuously improve the efficiency of the quality management system;

d) provide a framework for setting and reviewing quality objectives;

e) be implemented, maintained and communicated across all levels of the BRC;

f) be regularly reviewed to make sure it continually remains appropriately focused.

5.4 Planning of the quality management system

Operational management shall ensure that:

a) planning of the quality management system is carried out with the aim of meeting the requirements defined under article 4 as well as the BRC's quality objectives;

b) the quality management system will remain perfectly coherent when changes are scheduled and implemented.

Help box 5.4:

A quality system deployment timetable is considered a best practice.

Any changes scheduled at the BRC shall be analysed in terms of the potential impact on the QMS. For example: a new scientific project, a change in facilities, a process to be outsourced, etc.

If this analysis concludes that the QMS will be impacted, it will be necessary to check that measures are taken to maintain the efficiency of the QMS (5.7.2).

5.5 Responsibility and authority

5.5.1 General requirements

Top management shall ensure that responsibilities and authorities are clearly defined and communicated across the BRC in order to guarantee that the quality management system operates efficiently and continues to do so.

Help box 5.5:

Every staff member must have measurable objectives on specifically assigned tasks with clearly defined responsibilities.

A management organisation structure chart defining missions (who does what) and line management (who has decision-making authority and who needs to be reported to) may prove a useful tool.

5.5.2 BRC quality representative

Top management shall appoint a person tasked with coordinating quality management activities at the BRC. This person shall be trained in quality management. His/her knowledge and skills on quality-related issues shall be regularly revised and updated. His/her missions must be clearly defined and documented.

NOTE The person tasked with this quality management role shall be a member of the BRC who has other responsibilities at the entity.

The quality representative shall be given the responsibility and authority to:

a) ensure that the quality management system is established, implemented, kept up to date and made to improve, through cooperation with the BRC team;

b) issue independent opinions on quality policy directly to top management;

c) report to BRC top management on the efficiency and adequacy of the quality management system;

d) inform and give training on quality-related issues;

e) manage the implementation of measures for reviewing and updating the BRC's knowledge base on current legislation and regulations.

5.6 Communication

5.6.1 External communication

The BRC shall publish information:

— on the availability of its collections;

— on the conditions governing how these collections can be made available.

Help box 5.6:

The information published can equally well cover the quality system it implements and the biological resources it provides access to.

The BRC is advised to specify exactly which staff is tasked with this external communication mission and its respective responsibilities.

5.6.2 Internal communication

The BRC shall set up, implement and maintain efficient measures for communicating with the staff that have an influence on the BRC's organisational quality.

The person tasked with the BRC's quality management role shall guarantee that internal information is an integral part of quality management system updates.

Top management shall guarantee that pertinent information is integrated as inputs to the management review (5.7).

5.6.3 Confidentiality

The BRC staff is governed by the obligation of professional secrecy in order to safeguard the confidentiality of scientific research and, where necessary, to protect the anonymity of donors.

5.7 Management review

5.7.1 General

Top management shall review the quality management system at regular scheduled intervals in order to ensure that it remains well-focused, adequate and efficient.

This management review shall include an assessment of the opportunities for improving and readjusting the quality management system.

Records of the management reviews shall be kept and archived.

5.7.2 Inputs to the management review

The inputs to the management review must, among other things, contain information on the following points:

a) follow-up actions led in response to previous management reviews;

b) analysis of the results of operational process monitoring and of collection quality;

c) situations undergoing change and liable to impact on the quality management system;

d) the results of system improvement actions (preventive and corrective);

e) feedback from stakeholders;

f) audit reports.

These inputs are to be presented in such a way as to enable management to link them to the stated objectives.

5.7.3 Outputs from the management review

The outputs from the management review shall include decisions taken and actions launched on:

a) improving the efficiency of the quality management system;

b) improving the BRC's operations in relation to stakeholder requirements;

c) resource needs;

d) revisional adjustments to the quality policy and quality objectives.

6 Measurement, analysis and improvement

The BRC shall plan out and deploy all the monitoring, measurement, analysis and improvement processes necessary to:

a) guarantee the conformity the quality management system;

b) demonstrate that biological resources conform to the expected level of quality;

c) continually improve the efficiency of the quality management system.

This shall include determining applicable methods and their scope for deployment.

6.1 Monitoring and measurement

6.1.1 General

BRC management shall ensure that effective methods are deployed to identify areas requiring improvement in the performance of the biological resource quality management system. These methods include:

— stakeholder satisfaction surveys;

— internal audits;

— measures dealing with process analyses;

— measures dealing with the quality of the biological resources.

6.1.2 Stakeholder satisfaction

Management shall closely monitor all information that serves to assess stakeholder satisfaction levels.

Methods shall be determined for obtaining and using this information.

Help box 6.1.2:

These methods are founded on reviewing stakeholder-related data. This information can be either actively or passively obtained. Examples of sources of information on stakeholder satisfaction would include:

a) follow-up on customer claims;

b) implementing a satisfaction questionnaire and satisfaction surveys;

c) analysis of the responses obtained;

d) cross-sector study reports;

e) focus groups.

These elements are used to measure the drift between the level of quality expected by the customer and the level of quality experienced. This drift is named customer 'satisfaction performance'.

6.1.3 Internal audits

The BRC shall conduct internal audits at regularly scheduled intervals in order to determine whether the quality management system:

a) is conform to the operational processes defined, to the requirements of this standard, and the requirements self-set by the BRC;

b) is efficiently implemented and maintained.

An audit program is to be planned out, taking into account both the importance of the processes and areas audited and the results of the previous audits. Audit criteria, audit scope, frequency and methods must all be defined. Auditors must be selected and audits conducted in such a way as to guarantee that the audit process is objective and impartial.

Responsibilities and requirements for scheduling and leading the audits, reporting the audit results and archiving the audit records must all be defined in a documented procedure.

Internal audit report records shall all be archived.

6.1.4 Monitoring and measuring processes

The BRC shall use appropriate methods for process monitoring and measurement. These methods should prove the ability of the processes to achieve the planned results.

If the planned results are not achieved, then all appropriate corrections and corrective actions shall be undertaken to guarantee the conformity of the biological resources.

Help box 6.1.4:

A typical set of process performance measurements would cover:

— measurements of equipment performance drift;

— response times;

— effectiveness of the training programs;

— measurements of operating safety.

6.1.5 Monitoring and measuring biological resources

The BRC shall monitor and measure the characteristics of biological resources in order to double-check that all biological resource-related requirements are being met. Proof of conformity with acceptance criteria shall be archived.

This archiving procedure shall be carried out at appropriate steps in the product realisation process in compliance with the measures planned (9.2).

6.2 Control of nonconforming product

The BRC shall ensure that biological resources that do not conform to the requirements specified are identified and controlled in such a way that they cannot be accidentally used or made available. The product inspection system and the associated responsibilities and authorities enabling nonconformity issues to be handled must be defined in a documented procedure.

The entity shall deal with the nonconforming biological resource in one or more of the ways described below:

a) by triggering actions to eliminate the nonconformity detected;

b) by issuing a special concession, granted by the designated authority or possibly by the user, authorising the nonconforming biological resource to be used or made available;

c) by leading actions to prevent the nonconforming product from being used as it was originally intended.

All records on the type of nonconformity and on all later actions undertaken, including any later concessions issued, shall be archived.

When the biological resource nonconformity is corrected, the resource must be double-checked to demonstrate that is has been made requirement-compliant.

In cases where a nonconforming biological resource is detected after it has been delivered to the user, the BRC shall lead dedicated actions geared to stemming the real or potential effects of the nonconformity.

6.3 Data analysis

The BRC shall identify, compile and analyse the data suitable for demonstrating the appropriateness and efficiency of its quality management system and for assessing the possibilities for further improving the effectiveness of the system.

This data shall include data generated through monitoring and measurement activities and data from any other appropriate sources.

The data analysis is to generate information on:

— stakeholder satisfaction;

— compliance with the requirements related to biological resources;

— characteristics and trends in state-of-the-art practices.

6.4 Improvement

6.4.1 Continuous improvement

The BRC shall continually improve the efficiency of its quality management system through using the quality policy (5.3), quality objectives, audit results, data analysis (6.3), corrective actions (6.4.2) and preventive actions (6.4.3), and the management review (5.7) as tools.

6.4.2 Corrective action

The BRC shall lead actions to eliminate the causes of nonconformities so that they cannot be repeated. Corrective actions need to be geared to the effects of the nonconformity identified.

The BRC shall establish a documented procedure to specify the requirements for:

a) performing a review of nonconformities (including customer claims);

b) determining the root causes of nonconformity;

c) assessing the need to launch actions to prevent nonconformity issues from repeating;

d) identifying and implementing the necessary actions;

e) recording the results of the actions implemented;

f) performing the review of the corrective actions implemented.

6.4.3 Preventive action

The BRC shall identify actions for eliminating the causes of potential nonconformities to prevent them from occurring. Preventive actions need to be geared to the effects of the potential issues.

The BRC shall establish a documented procedure to specify the requirements for:

a) identifying potential nonconformity and its causes;

b) assessing the need to launch actions to prevent the occurrence of nonconformity issues;

c) identifying and implementing the necessary actions;

d) recordings the results of the actions implemented;

e) performing the review of the preventive actions implemented.

Part 2: Resources required for the BRC to operate

7 Resource management

The entity shall make sure that it commands the resources necessary (staff, facilities, lab equipment, supporting services and IT systems) for developing and implementing the BRC quality management system and for continually improving its efficiency.

7.1 Staff

All staff performing work that has an influence on the quality of the collections shall be competently skilled as proven through their initial and professional training, their know-how and their experience.

7.1.1 Competencies

a) each member of staff shall possess the competencies, qualifications and authorisations identified to be allowed to perform the missions they are tasked with;

b) these competencies, qualifications and authorisations shall be covered by document proof;

c) the delegation of responsibilities shall be clearly defined, implemented, and documented;

d) the level of safety training required shall be determined according to position-related requirements;

e) one person shall be nominated as Health and Safety officer. The Health and Safety officer is tasked with informing staff on the legislative and regulatory conditions governing hygiene and safety conditions and informing the operational manager on the implementation and application of these conditions.

Help box 7.1.1:

The guideline is to define the job descriptions that set out the missions for each position and the competencies needed for each mission.

A file for each member of staff shall be opened and kept up to date with information on their initial and professional training, their know-how and their experience.

7.1.2 Training

a) each member of staff shall be allowed to follow vocational training (internal or external) as and when they need it. An assessment shall be performed on the efficiency of the training program. All training courses followed are to be recorded;

b) all staff must be offered internal training (general technical training, training for specific tasks, tutoring, etc.). When they opt to follow in-house training, their course progress shall be logged and recorded;

c) all staff shall be made aware of the safety and quality issues "and have access to appropriate documentation".

Help box 7.1.2:

The BRC may opt to set up a new recruit integration policy.

Furthermore, it may be useful to give each member of staff a grounding in the importance of compliance with best practices, particularly the OECD best practice guidelines on biological safety (against infections, with vaccinations offered where possible), chemical safety (solvents, fixers), the use of appropriate equipment, and biosafety (safety of biological samples).

7.2 Facilities and workflow management

7.2.1 General requirements

The activities performed at the BRC will dictate how the facilities will be required to comply with various regulations and meet the safety standards governing not only the safety of the staff but also the safety of the biological resources and environmental safety.

The BRC is required to keep up-to-date information on the risks to persons, to equipment, and to biological resources (4.2.1).

Help box 7.2.1:

Every BRC shall focus specifically on how it will manage:

a) chemical risk control;

b) biological risk control;

c) fire safety;

d) control over risks stemming from the use of nitrogen.

7.2.2 Facilities

The facilities shall be fitted out to incorporate an access control system.

The facilities shall be designed to accommodate the equipment they contain.

Facilities maintenance and cleaning operations shall be performed on a regular basis and logged.

When facilities are being built or relocated, or during their use, the BRC is to define and indicate the various areas of the facilities according to the activities they house.

Help box 7.2.2:

The following facilities sectors could be clearly signed:

a) take-on/shipping of biological resources;

b) different preparation of samples according to activity focus (DNA extraction, cell culture, macroscopic analysis, etc.);

c) conservation of biological samples (for cabinets, freezers and nitrogen containers);

d) storage of annotations (related data);

e) document archiving.

The BRC is not obliged to assign one room per activity focus provided that each individual activity has its own clearly defined and indicated area.

Help box 7.2.2:

If the zone where biological samples are prepared is not dedicated exclusively to BRC activities, then best practice is to deploy the following measures:

a) signposting indicating risk of infection;

b) implementation of a level of confinement that is adapted to the biological samples being handled;

c) safeguarding asepsis (cleandown, disinfection, sterilisation) via a specific room maintenance procedure.

Conservation areas shall be designed in compliance with the currently applicable regulations. In particular, for the nitrogen-based conservation room:

a) the natural and forced-air ventilation systems shall be engineered and fitted, properly maintained, and regularly inspected;

b) the door shall be fitted with a peek-through hole;

c) a alarm signalling oxygen levels shall be fitted;

d) signposting shall be installed to warn of the risk of anoxia.

7.2.3 Workflow management

Individual zones shall be defined according to activity, and workflow diagrams shall be produced.

The workflows in each zone shall be identified in time and space and documented in order to:

a) safeguard sample quality;

b) guarantee biosafety;

c) minimise the risk of contamination;

d) control the use of multi-purpose areas where appropriate.

Help box 7.2.3:

The workflows concern for example:

— flows of staff;

— flows of biological samples;

— flows of consumables;

— waste disposal.

7.3 Laboratory equipment

For the purposes of this standard, the term 'laboratory equipment' covers equipment, consumables and instrumentation.

The requirements on laboratory equipment concern exclusively that material which has an impact on product quality and stakeholder satisfaction.

The activities performed at the BRC will dictate how the equipment will be required to meet the safety standards governing not only the safety of the staff but also the safety of the biological resources and environmental safety.

7.3.1 General requirements

All laboratory equipment must have the specific design characteristics required for its intended use. These specific design characteristics must be identified:

a) a person shall be tasked with monitoring equipment management and maintenance;

b) an equipment inventory shall be produced and updated at regular intervals;

c) equipment calibration and metrics shall be scheduled and documented. The resulting records shall be archived;

d) equipment servicing and maintenance shall be scheduled and documented. The resulting records shall be archived;

e) if a piece of equipment is revealed as noncompliant, the BRC shall evaluate and record the validity of the results of the measurements previously performed. In this scenario, the BRC shall take appropriate measures to act on the equipment or biological sample concerned.

7.3.2 Conservation equipment

The BRC shall set up a documented procedure to govern:

— temperature surveillance and real-time logging for all refrigerated facilities, plus alarm transfer and a standby plan;

— controls over nitrogen levels for all nitrogen containers;

— raising alarms in the event of overrun on predetermined thresholds;

— the course of action to protect and maintain sample quality in the event of a conservation equipment breakdown.

All resulting records shall be archived.

Help box 7.3.2:

The temperature and/or nitrogen levels alarms can be connected to a telephone line.

The BRC would be encouraged to set aside vacant areas, drawers, slide-in storage units, back-up freezers etc. to cope with the emergency transfer of biological samples following an equipment failure.

For replicable biological material, a back-up collection containing the same samples shall be built and stored in a different place.

7.4 Supporting services

Supporting services represent the resources provision activity required to perform operational processes such as logistics, communications, etc.

The BRC shall define the supporting services that play a role in the development and implementation of its quality management system.

For each supporting service identified:

a) a person shall be tasked with tracking relations with the suppliers of this service;

b) specifications specifying the BRC's requirements and expectations shall be drafted and forwarded;

c) the CRB shall evaluate the compliance of this service in relation to the requirements defined, and record the conclusions of this evaluation. In the event on noncompliance, the BRC shall take appropriate action.

7.5 IT system

For the purposes of this standard, the term 'IT system' covers computer hardware (7.5.1), software (7.5.2), and access to IT networks where appropriate (7.5.3).

The IT system installed at the BRC shall be geared to:

— data management;

— data security;

— data processing.

Data security shall be governed by a documented procedure produced to manage:

— access control;

— updates and maintenance;

— data backup and recovery;

— IT network access according to the applicable procedures.

Help box 7.5:

The procedure should indicate the following:

— the intervals for creating backups shall be specified, scheduled and documented;

— the media support for backups.

Backups shall be stashed away in a secure place, physically separated from the server or the disk containing the data related to the biological resources.

7.5.1 Computer hardware

The BRC shall deploy and maintain physical security measures. These measures shall be documented and forwarded to all of the staff concerned.

Help box 7.5.1:

These physical security measures would for example include uninterruptible power supplies, and a locked room.

7.5.2 Software

Software containing personal data shall comply with all applicable regulatory requirements.

Software that is used to manage data/annotations relating to the biological samples shall meet the needs and specificity requirements of the BRC.

In particular, the software shall:

a) enable data to be pooled and exchanged between different BRC actors;

b) enable multi-criteria searches;

c) enable a catalogue to be compiled;

d) enable data recovery in the event that the software manufacturer closes down without a buyer.

Software maintenance shall be performed and documented.

Help box 7.5.2:

Software maintenance covers software updates and both corrective and preventive maintenance.

7.5.3 Networks

Network supports shall be geared to needs.

The BRC shall deploy error detection procedures to improve the information system and preclude any network consistency issues.

The BRC shall take measures to prevent any unauthorised access to the services available through the network.

8 Procurements

The requirements governing procurements concern exclusively those procurements having an impact on biological resource quality and stakeholder satisfaction.

Help box 8:

Among other things, procurements include consumables, equipment, services such as transport, site cleaning, calibration, etc.).

8.1 Procurement process

The BRC shall ensure that all products or services procured conform to the specified requirements. In scenarios where the BRC uses a centralised procurement solution, the BRC communicates its requirements and evaluates the products purchased.

The stringency of the requirements will depend on how far the product or service procured impacts on the performance of BRC activities or on the quality of the biological resource.

The BRC shall assess and select suppliers according to their ability to provide a product or service in compliance with the specified requirements. The BRC shall set supplier assessment and selection criteria.

Records of the results of these assessments shall be kept and archived.

The BRC shall set up a document management system for its reagents, media and consumables in order to prevent stock shortages, cut down on end-of-use wastage, and avoid excessive stock-in.

8.2 Procurements-related information

The procurements-related information shall describe of the product or service to be procured, including, where appropriate:

a) requirements for approval of the product or service and the procedures, processes and equipment involved;

b) requirements for qualification of the product or service;

c) requirements for staff qualifications;

d) requirements stemming from the quality management system.

The BRC shall make sure that the procurement requirements specified are suitable before issuing them to the supplier.

8.3 Product checks

The BRC shall establish and implement all necessary inspections required to make sure that the products or services procured meet the specified requirements.

When the BRC opts to perform checks at the supplier's premises, the arrangements planned for these checks shall be stated by the BRC in its procurements-related information.

The BRC shall also detail the inspection and acceptance procedures for its product procurements.

Part 3: Handling biological resources

9 Operational processes

9.1 General requirements

The BRC shall identify:

a) type-specific requirements for the biological resources;

Help box 9.1 a):

Annex A cites the published documents describing the specific requirements governing biological resources of human origin and biological resources of microbial origin.

b) requirements specified by the stakeholders (5.2);

Help box 9.1 b):

The requirements specified by stakeholders may for example focus on the collection (conditions for providing access, conservation requirements, etc.), certain types of samples, the quantity of samples taken, etc.

These requirements shall be documented (4.2.1).

c) requirements not formulated by the stakeholders but nevertheless necessary for a specified usage or, where known, the intended usage;

d) currently applicable regulatory and legislative requirements;

e) any additional requirements set by the BRC;

f) the requirements set out in any available best practice guidelines issued by professional organisations.

Help box 9.1:

The requirements specified by stakeholders may for example focus on the collection (conditions for providing access, conservation requirements, etc.), certain types of samples, the quantity of samples taken, etc.

These requirements shall be documented (4.2.1).

9.2 Quality control

The BRC shall deploy a biological resource quality control system across all the processes according to the requirements defined under section 9.1.

The BRC shall identify all critical steps, quality control methods, and acceptance criteria.

The BRC shall implement a validation system covering the methods for identifying and characterising biological material

All results of quality controls shall be recorded.

The quality control system shall be documented and updated according to the state-of-the-art.

The results generated by this quality control system will also be used to meet the requirements set out in article 6 herein.

9.3 Traceability

It must be possible to quickly locate any given biological resource through an appropriate, documented traceability system.

The BRC must be able to communicate the characteristics of any sample:

— its origin and parentage,

— its characterisation;

— and if possible, the history log of accessible nonconformities.

Any item missing from any one of these characteristics shall result in the noncompliance procedure being triggered (6.2).

9.4 Reception of the biological resource

The reception process shall be governed by a documented procedure stating the acceptance criteria for biological resources and the quality control system applied at reception.

Help box 9.5:

Typical quality controls would include sample authentification, characterisation and identification, and data controls.

Reception shall take place in a clearly defined zone in compliance with the currently applicable rules on biosafety and biosecurity.

The biological resources shall be identified and recorded.

9.5 Preparation of biological samples

Each type of preparation shall be individually documented.

The delivery deadlines for critical preparations shall be specified and documented.

The methods used shall be documented.

9.6 Conservation of biological samples

The BRC shall define the place of sample conservation and conservation period for each collection.

The appropriate mode of conservation for each type of biological material and for each end-use shall be defined according to the state-of-the-art or according to specific, documented methods.

A sample identification system shall be deployed that is able to withstand the storage conditions.

9.7 Transportation

Transportation and packaging are to comply with currently applicable legislation.

The transport system used shall be documented.

9.8 Access to the biological resources

The principles governing access to and provision of biological resources shall be defined and published in order to ensure that they comply both with currently applicable legislation and with the contractual requirements established between the stakeholders, including in the event of competing interests.

The BRC shall draft a contractual document that includes the conditions governing the provision and use of biological resources. In particular, the quantity of biological material provided shall be compatible with the scheduled end-use. Any usage other than that scheduled shall be prohibited.

Help box 9.8:

This contractual document should specify the following points:

a) the person in charge of the research project and the contracting parties;

b) the title of the research project;

c) the nature, quantity, number and conservation period of the biological samples provided:

d) the results of quality controls;

e) the instructions for use;

f) the conditions and delivery deadlines for provision and use by third parties;

g) citing the BRC either in the acknowledgements or as a contributor;

h) authorisation or ban on transferring biological samples to a third party;

i) information and scientific results feedback to the BRC for sample annotation;

j) cost of provision;

k) the legal and regulatory provisions governing intellectual property.

When the samples are handed over, each one shall be accompanied with a document containing predefined information.

Records shall be made of every sample supplied.

9.9 Information system

The BRC's information system shall run the traceability of data on:

a) the collections and the biological resources;

b) the BRC's activities;

c) the stakeholders.

The information system shall enable data to be exchanged.

It shall manage the provision of all or part of the data content associated with the biological resources.

9.9.1 Data on the biological samples

Files containing data that directly or indirectly identifies biological samples shall comply with all applicable regulatory requirements.

The vocabulary used shall be the vocabulary used by recognised thesauri.

For all data associated with the samples, the BRC shall:

a) define a set of baseline data;

b) defined data required for each type of collection;

c) deploy error detection systems to screen for errors in all new data records as well as in previously recorded data;

d) ensure that all data are regularly updated.

Help box 9.9.1:

The baseline data for biological samples of both human origin and of micro-organism origin are described in the resource-specific documents listed in Annex A.

9.9.2 Data exchange

The BRC shall provide the stakeholders with access to a catalogue of available biological resources based on validated information.

Help box 9.9.2:

If the data is to be exchanged internationally, it is recommended that the catalogue be translated into English.

If exchangeable data if confidential, it shall be encrypted.

The BRC shall ensure the data publishing process maintains the integrity of the data.

9.9.3 Data storage

The BRC shall define data storage criteria (duration, place and archiving).

The BRC shall store all data associated with the biological resources for at least as long as the biological resources are in existence, and for as long as the data storage conditions are required for transferring the biological material.

If data is archived, the BRC shall be able to recover this information.

9.9.4 Data authenticity / match-up with the stocks of biological material

The BRC shall deploy a stock control system for checking the data validity and accuracy: information contained in the database shall be regularly cross-checked against the biological material in stock, according to a documented procedure.

The BRC shall hold proof of the data source (name of the depositors, scientific authority having validated the data on the sample).

The BRC shall set up data validation, modification and deletion channels as well as approval and traceability channels for these changes, thereby creating a log history of data changes.

A history of revisions and changes shall be available, indicating name and dates.

Annex A
(informative)

Requirements specific to biological resources

A.1 Requirements specific to biological resources of human origin

— HAS (French National Health Authority) recommendations on the conservation of resources of human origin (document awaiting validation);

— OECD best practice guidelines for biological resource centres, OECD, April 2007;

— Hospital tumour banks – Guidance on use by clinicians and research scientists, INCa, November 2006.

A.2 Requirements specific to biological resources of microbial origin

— OECD best practice guidelines for biological resource centres, OECD, April 2007.

Annex B
(informative)

Documentation system

The requirements governing the documentation system as a whole are set out under section 4.2.

Table B.1

Document name or document focus: names are given as an indication only and are not themselves requirements. Each BRC is free to name documents as they decide.	**Document type**	**Reference of the requirement in this standard**
Document control	Procedure	4.2.3
Records control	Procedure	4.2.4
Records list	List	4.2.1 c)
Procedures list	List	4.2.1 c)
Quality manual	Document	4.2.2
Process planning	Document	4.2.1 d)
Stakeholders' requirements as part of a scientific project	Record	4.2.1 f)
The management commitment statement	Document	5.1
Acceptance conditions for collections or biological resources	Procedure	5.1 d)
Conditions for conserving collections or biological resources	Procedure	5.1 e)
Conditions for the provision of collections or biological resources	Procedure	5.1 f)
Mission statement - quality manager	Document	5.5.1
Management reviews	Record	5.7.1
Satisfaction survey	Document	6.1.2
Internal audits	Procedure	6.1.3
Internal audit report	Record	6.1.3
Conformity of the characteristics of biological resources	Record	6.1.5
Control of nonconforming product	Procedure	6.2
Nonconformities	Record	6.2
Corrective actions	Procedure	6.4.2
Corrective actions	Record	6.4.2 e)
Preventive actions	Procedure	6.4.3
Preventive actions	Record	6.4.3 d)
Competencies, qualifications and clearances	Record	7.1.1 b)
Delegation of responsibilities	Record	7.1.1 c)
Assessment of training program efficiency	Document	7.1.2 a)

'continued'

Table B.1 *(end)*

Document name or document focus: names are given as an indication only and are not themselves requirements. Each BRC is free to name documents as they decide.	**Document type**	**Reference of the requirement in this standard**
Training	Record	7.1.2 a)
Course progress	Record	7.1.2
Upkeep and cleaning	Record	7.2.2
Risk-related information	Document?	7.2.3
Prevention measures	Document?	7.2.3
Equipment inventory	Document	7.3.1 b)
Workflow management? Identifying facilities layout	Document?	7.2.3
Calibration and metrics	Record	7.3.1
Servicing and maintenance	Record	7.3.1
Reassessment of the validity of measurements recorded prior to an NC	Record	7.3.1 e)
Conservation equipment	Procedure	7.3.2
Software maintenance	Record	7.3.3.2
Data backups	Procedure	7.3.3
Purchasing-related requirements	Record	8.1
Results of purchasing assessments	Record	8.1
Management of reagents, media and consumables	Record	8.1
General requirements	Document	9.1
Quality control results	Record	9.2
Quality control system	Document	9.2
Traceability system	Document	9.3
Reception	Procedure	9.4
Reception of biological resources	Record	9.4
Preparation	Operating procedure	9.5
Preparation delivery deadlines	Record	9.5
Methods	Record	9.5
In-house methods	Record	9.5
Transport conditions	Record	9.7
Criteria governing the provision of biological resources	Document	9.8
Service provision contract	Contract	9.8
Information supplied with the biological resource	Document	9.8
Provision	Record	9.8
Baseline data per collection	Record	9.9
Catalogue of available biological resources	List	9.9.2

Annex C
(informative)

Comparison between ISO 9001 and the BRC standard

Table C .1

ISO 9001:2000		BRC standard	
Introduction			Introduction
General	0.1		
Process approach	0.2		
Links with ISO 9004	0.3		
Compatibility with other management systems	0.4		
Scope	1	1	**Scope**
General	1.1		
Scope of application	1.2		
Normative Reference	**2**	**2**	**Normative Reference**
Terms and definitions	**3**	**3**	**Terms and definitions**
Quality management system	**4**	**4**	**Quality management system for BRCs**
General requirements	4.1	4.1	General requirements
Documentation requirements	4.2	4.2	Documentation requirements
General	4.2.1	4.2.1	General
Quality manual	4.2.2	4.2.2	Quality manual
Document control	4.2.3	4.2.3	Document control
Records control	4.2.4	4.2.4	Records control
Management responsibility	**5**	**5**	**Management responsibility**
Management commitment	5.1	5.1	Management commitment
Customer focus	5.2	5.2	Stakeholder needs and expectations
Quality policy	5.3	5.3	BRC quality policy
Planning	5.4		
Quality objectives	5.4.1		
Planning of the quality management system	5.4.2	5.4	Planning of the quality management system
Responsibility, authority and communication	5.5		
Responsibility and authority	5.5.1	5.5	Responsibility and authority
		5.5.1	General requirements
Management representative	5.5.2	5.5.2	Quality representative
		5.6	Communication
Internal communication	5.5.3	5.6.1	External communication
		5.6.2	Internal communication

'continued'

Table C.1 *(continued)*

ISO 9001:2000		BRC standard	
		5.6.3	Confidentiality
Management review	5.6	5.7	Management review
General	5.6.1	5.7.1	General
Inputs to the management review	5.6.2	5.7.2	Inputs to the management review
Outputs from the management review	5.6.3	5.7.3	Outputs from the management review
Resources management	**6**	**7**	**Resource management**
Provision of resources	6.1		
Human resources	6.2	7.1	Staff
General	6.2.1		
Competences, awareness and training	6.2.2	7.1.1	Competencies
		7.1.2	Training
Infrastructures	6.3	7.2	Facilities and workflow management
		7.2.1	General requirements
		7.2.2	Facilities
		7.2.3	Workflow management
Working environment	6.4		
		7.3	Laboratory equipment
		7.3.1	General requirements
		7.3.2	Conservation equipment
		7.4	Supporting services
		7.5	IT system
		7.5.1	Computer hardware
		7.5.2	Software
		7.5.3	Networks
Product realisation	**7**	**9**	**Operational processes**
Planning of product realisation	7.1	9.1	General requirements
Customer-related processes	7.2	9.2	Quality control
Determining product-related requirements	7.2.1	9.3	Traceability
Reviewing product-related requirements	7.2.2	9.4	Reception of biological resources
Customers communications	7.2.3	9.5	Preparation of biological samples
Design and development	7.3	9.6	Conservation of biological samples
Design and development planning	7.3.1	9.7	Transportation
Design and development inputs	7.3.2	9.8	Provision of biological resources
Design and development outputs	7.3.3	9.9	Information system
Design and development review	7.3.4	9.9.1	Data on the biological samples
Design and development checks	7.3.5	9.9.2	Data exchange
Design and development validation	7.3.6	9.9.3	Data storage

'continued'

Table C.1 *(end)*

ISO 9001:2000		BRC standard	
Control of design and development changes	7.3.7	9.9.4	Data authenticity / match-up with the stocks of biological material
Purchasing	7.4	**8**	**Procurements**
Purchasing process	7.4.1	8.1	Procurement process
Purchasing-related information	7.4.2	8.2	Procurements-related information
Checks on purchased products	7.4.3	8.3	Product checks
Production and service function	7.5		
Control of production and service provision	7.5.1		
Validation of processes for production and service function	7.5.2		
Identification and traceability	7.5.3		
Customer property	7.5.4		
Preservation of product	7.5.5		
Control of monitoring and measuring systems	7.6		
Measurement, analysis and improvement	**8**	**6**	**Measurement, analysis and improvement**
General	8.1		
Monitoring and measurement	8.2	6.1	Monitoring and measurement
		6.1.1	General
Customer satisfaction	8.2.1	6.1.2	Stakeholder satisfaction
Internal audit	8.2.2	6.1.3	Internal audit
Monitoring and measurement of processes	8.2.3	6.1.4	Monitoring and measurement of processes
Monitoring and measurement of product	8.2.4	6.1.5	Monitoring and measurement of biological resources
Control of nonconforming product	8.3	6.2	Control of nonconforming product
Data analysis	8.4	6.3	Data analysis
Improvement	8.5	6.4	Improvement
Continuous improvement	8.5.1	6.4.1	Continual improvement
Corrective action	8.5.2	6.4.2	Corrective action
Preventive action	8.5.3	6.4.3	Preventive action

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