ISO/DIS 20387
A draft ISO standard for general requirements in biobanking

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Design and Purpose

• Aims to be more suited to biobanking than ISO 9001
• “Horizontal” standard
  • Aims to apply across all types of biobanks/bioresources
    • Human, animal, plant, micro-organisms etc. in R&D
    • Specifies general requirements to ensure appropriate quality
    • “Vertical standards” will appear later for specific areas
• Not intended for
  • Food production
  • Therapeutic use
  • Biobanks solely for diagnosis → ISO 15189
• Terminology of Standard
  • Internationally-agreed
  • Conforms to CASCO when necessary
  • US spellings
  • Does not replace national law
General Requirements

• Procedures to address each type of biological resource held
  • Collecting/procuring, acquiring and receiving, tagging, accessioning/logging, cataloguing/classification, examination, processing, replicating, storing, data management, destroying, packaging, safeguarding, distributing, transporting, risk management, personnel
  • No big surprise for HTA-licensed biobanks

• Compliance with relevant ethical principles
  • No big surprise for any UK collection of human tissue
Impartiality and Confidentiality

• Your structure and management must safeguard impartiality
  • Be able to demonstrate impartiality not swayed by commercial or financial pressures
  • Reviewed assessment of risks to impartiality, and how minimised

• Protect confidential information and proprietary rights, via
  • Legally enforceable commitments (agreement, contract, licence)
  • When possible, inform providers in advance about communication of confidential information (consent, agreement, contract)
  • No surprises – required in UK by ethical approval, HT Act, DPA, other legislation
Structural Requirements I

- Be a legal entity, or be part of a legal entity, that is responsible for its actions
  - Have a course of action to address liabilities (insurance)
  - Meet the requirements of the Standard and stakeholders
- Document your structure and relationships
  - Organisational, managerial, technical, support
  - Responsibilities and authorities of personnel
Structural Requirements II

• Ensure you have personnel who, irrespective of other responsibilities, have the authority and resources needed to carry out their duties
  • Management systems, deviation, CAPA, reporting/improvement, validation
  • Doesn’t necessarily mean a dedicated QM

• Ensure you maintain the integrity of your management system
  • Change control
  • Communication of effectiveness (monitoring, trend analysis, feedback)
  • Personnel understand need to meet user/other requirements
General Resource Requirements

• Ensure you have everything you need to perform activities
  • Don’t offer what you can’t fully support
  • Have contingency planning (staff cover, back-up power, back-up freezers, database failure protocol)

• Document your strategy to safeguard continued financial viability for the expected lifetime of storage / handling activities
  • Self-funding, grants, contingency agreements
  • UK wishes to amend this wording
Personnel

• Few surprises to publicly-funded organisations, or large commercials, but...

• Must define and document the competence requirements
  • Based on appropriate education, training, demonstrated skills and/or experience necessary to perform duties
  • Defined by biobank
  • Documented on an ongoing basis
  • Includes Health & Safety training, as deemed appropriate by risk assessment
  • Must also include a formal induction and orientation
  • Personnel supervised until deemed competent
Infrastructure and Environment

• Your infrastructure must ensure conformity, biosafety, and biosecurity

• Where necessary, separate incompatible activities in neighbouring areas, e.g.
  • Take measures to avoid cross-contamination
  • Separate computer systems (NHS v Academic)
  • Put doors between areas
  • Use different swipe access for raised containment levels

• Measure, monitor, control, and record environmental conditions where quality and/or H&S involved
  • Already required for HTA licences and trials, e.g. freezers, radioactivity, CL3 pressures
Externally Provided Processes, Products and Services

• You determine procedures and requirements
  • To select external supplier, e.g. critical characteristics of product, ability to provide in timeframe, ISO 9001 certified
  • Assess their risk to your compliance

• You communicate your requirements to the external supplier
  • Retain evidence of communication

• You ensure their conformance
  • Monitor their performance, e.g. proof of formal acceptance against critical criteria
  • Review their performance at pre-defined intervals, reacting accordingly

• Use of external storage must be communicated to users
Externally Provided Preservation, Storage, and Authentication

• You need to ensure supplier’s processes are validated to ISO 20387
  • Intended to cover e.g. outsourced storage
  • Interpretation of e.g. “externally provided preservation” could include validating an NHS nurse drawing blood into an EDTA tube?

• You perform internal audit of outsourced service at least once a year
  • See also ISO 19011
Equipment and Software I

• You maintain register / database listing “critical” vs non-critical equipment
  • Intended to mean freezers, pipettes, scanners, etc. not pencils, paper
• You record performance, maintenance, verification / validation information for each item
  • Likely to include validation of critical custom software
  • Could be interpreted as meaning installation of OS by approved IT service
  • Not intended to mean validation of commercial OS (impossible), but could mean documented verification that it is required version/build
• You document processes to install, handle, transport, store, use, calibrate (if needed) equipment and software
Equipment and Software II

- You must record a minimum information set for critical equipment
- You must safeguard critical equipment from adjustment that would invalidate "output"
  - e.g. locks on centrifuge programs, or requirement to document verification of correct setting before each use
- You must ensure unbroken traceability of critical readings to an appropriate reference
  - e.g. thermometers, centrifuge speeds, micropipettor volumes
- Non-compliant equipment marked "out of service" until re-certified
  - Possible effects of non-compliance on previous biological resources examined and acted upon
Process Requirements I

• You define “lifecycle stages” which contribute to fitness for purpose
  • Example: collection, accession, identification, preservation, long-term storage, quality control, transport, disposal
  • Present as schematic, followed by detailed procedures
  • Make readily available to personnel

• Date-time for each relevant stage (to ISO 8601)
  • Does not mean timestamp for every stage – just every stage deemed “critical” by you/user, except...
  • Collection date-time mandatory
  • Difficult to achieve in current routine NHS environments; in theory less problematic for ISO 15189 Pathology Depts
Process Requirements II

• Collection information must also include basic data
  • Taxonomic information (default = human!)
  • Place and procedure of collection (e.g. Theatres, excision)
  • Any other information relevant to accomplish biobank objectives

• You must document pre-analytical steps used to assess fitness of material for purpose

• You must ensure collection is:
  • Planned by relevant qualified personnel/users according to your/user requirements
  • Performed by qualified personnel
  • When clinical assessment/diagnosis required, done under supervision of medically-qualified personnel
Shipping and Transport

• You must have documented shipping procedures
  • Intended to mean to/from biobank
  • Includes safety, packaging, organising, receipt
  • Critical transport conditions (if any) defined and monitored
  • You must track of chain of custody from shipper to receiver
  • Only trained personnel involved
  • Not incompatible with clinician-mediated transfer from NHS to Academic biobank

• You must have documented internal transport procedures
  • Intended to cover biobanks with >1 self-contained area (e.g. multi-floor in shared building, multi-building)
  • Very similar to shipping, except designated unattended “custody zones” may be defined
Reception

• You have documented procedures for
  • Material produced within the biobank, purchased, deposited, or consigned to biobank
  • Acceptance criteria, including biosafety, biosecurity, IPR
  • Segregation ("quarantine") in appropriate conditions until formally accepted
• You must obtain copies of available associated documented information
  • Note "available" – if consent copy is not permitted, it’s not available!
Traceability

• Must be across whole lifecycle, robust
• Tagging of material must be suitable for handling/storage conditions
• Must have linkage to information on permitted/restricted use
• Must have association with relevant versions of relevant procedures
  • Can be interpreted as “implicit by date” as well as “explicit by data entry”
• Annotation and query of any handling procedures must be possible, and deviations must be flaggable
  • Can be interpreted as “mixture of database and paper records” (not just “database only”)
• Location of material must be identifiable at all times
  • Includes act of distribution or destruction
• Disposal/transfer procedures must cater for emergencies and planned events
Preservation

• Means “stabilisation of desired properties”
  • EDTA tube for blood, refrigeration, fixation, freezing
• You define according to evidence-base or user-specifications
• You monitor and time-stamp each preservation step
• You time-stamp start of each intermediate *critical* step
• You have a disaster plan for storage failure
• Your storage locations must be precise, audited, and minimise risk of contamination/loss of quality
Quality Control 1

• Large section, due to wide diversity of “biobanks”
  • Combined diagnostic/research biobanks in several countries
  • Contributes to the interoperability of all biobanks

• Key phrases:
  • “The biobank shall define a minimum set of QC procedures to be performed on the biological resource”
  • “Exceptions can be justified for rare or legacy biological resources and QC procedures which lead to biological material elimination”
  • If none are possible, then document that none are possible
Quality Control II

• For QC Procedures
  • You pre-define the specifications
  • You perform QC at planned intervals
  • You analyse and trend
  • You use appropriate QC reference materials, e.g.
    • Certified reference materials
    • Previous samples
    • Material previously shared with other biobanks
    • Control material in EQA

• Data QC
  • You identify critical data
  • You perform random checks on regular basis for accuracy, completeness, consistency
Nonconforming Outputs

• If something is not right:
  • You quarantine
  • You perform fitness/risk assessment
  • You determine and perform CAPA, and/or authorise for release under concession, or initiate recall in a timely manner
  • You review effectiveness of PA
  • You communicate with affected users

• Nonconforming includes “legacy” material
  • Everything collected before first adoption of ISO standard
Validation and Verification

• Validation
  • “Confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled”

• Verification
  • “Confirmation, through the provision of objective evidence, that specified requirements have been fulfilled”

• You verify all standard methods

• You validate/verify all non-standard/modified/”own” methods to ensure material can meet its specification

• You document validation/verification and retain for a pre-defined period
  • ISO 21899 can be used to help
Complaints and Management Systems

• Biobanks should have a fully functional complaint system
• ISO 20387 provides the minimum requirements for a management system
• Alternatively, a management system meeting ISO 9001 – but used in a way to achieve the aims of ISO 20387 – should be acceptable
What Next?

• Talk to me 1:10pm – 2:00pm
• National comments discussed and addressed in November
  • If only editorial comments, the document will proceed to publication
  • If significant technical comments, document goes to Final Draft International Standard (FDIS)
    • Editorial comments only may be provided during 2-month FDIS ballot
• Publication phase to follow
• A “TR” (Technical Report) is being drafted
  • Interpretation guidance
  • Implementation guidance