Development of ISO Standards for Biotechnology & Biobanking – an update and discussion

8th September 2014

Newman House, Dublin

MMI hosted a meeting to discuss the new ISO standards (ISO/TC 276) being developed for biotechnology, including biobanking. Over 30 people attended the meeting, representing academia, industry, funding agencies and regulatory bodies. Presentations were given by Linda Hendy of the NSAI, Emma Snapes of the INFANT Centre in UCC, and Eoin Cotter of the UCD Clinical Research Centre (see attached at end). These were followed by a general discussion about why Ireland should actively participate in the standards development and how we should proceed in a timely manner to affect this. ISO/TC276 has already determined the scope of its working groups. In May 2014, Linda Hendy and Emma Snapes both attended a plenary session of ISO/TC276 in the DIN offices in Berlin to investigate the relevance of this ISO for Ireland and to determine if a need exists for Ireland to elevate its role from observer status to participatory status.

**Linda Hendy** gave an outline of the NSAI’s work and their role in standard development. She emphasised that the ISO meetings are an opportunity to influence and negotiate. She would like to set up a National Mirror Committee for the TC276 standards to include all stakeholders. These would normally meet about 3-4 times per year where a group of experts agree their input together to represent Ireland’s opinion. This group would “mirror” or follow the proceedings of the ISO technical group. Linda also explained that any ISO Member can propose a new work items for the ISO TC but this would need support from at least 5 other ISO members. As a mirror committee the group could suggest new work through NSAI.

**Emma Snapes** gave an excellent summary of biobanking guidelines that have been published to date. She noted that biobanks can cherry-pick elements of different guidelines and there is no clear single set of agreed internationally accepted standards for biobanks to seek accreditation for. She reminded the audience that we depend on patients and donors for contributions to biobanks and any issue created by one biobank that doesn’t follow best-practice guidelines could damage the reputation of biobanking as a science. She added that we need to ensure the confidence that is beginning to grow in Ireland is protected and encouraged, and that perceptions of value need to be promoted to the media and funders.

**Eoin Cotter** described the core activities of the UCD Clinical Research Centre (CRC) at the Mater and St Vincent’s Hospital, explaining they provide a range of service from hosting a freezer to full design of a study. They have implemented standardised training and standard operating procedures across both hospital sites, using patient kit models for all studies. They have developed a “biocollections handbook” as well as standardised logs and a labelling system. They redrafted all their SOPs in 2013.

**Discussion:**
It was generally upheld by all that Ireland should be engaging and participating in the development of these standards. It was pointed out that Ireland is well-recognised internationally and is often over-represented for our size in European forums. Our pharma and biotech industry here helps us to be taken more seriously. In addition, Ireland’s vote on the working groups of the ISO276 representing 4.5 million people would carry the same
weight as the US vote for instance should Ireland declare its desire to be a participant rather than an observer.

Although any resulting standards to be created would most likely be voluntary, once they are created there will be an increased drive to apply them in order to demonstrate Irish biobanks operate to those standards. Therefore if Ireland chooses not to engage now, we will have no further opportunity to contribute to standards that will be imposed on biobanking in the future.

Having an international standard mark would be a positive thing to help new and existing biobanks to have a mark of quality and efficiency. It can be difficult to convince regulatory bodies, funders and our own institutions to understand how Irish biobanks compare internationally when there are no actual standards, rather 9 or 10 sets of different guidelines.

It was suggested that in the interim period we could update the MMI Biobanking Guidelines to include quality standards. Linda Hendy added that if we were part of the technical committee, we would get a "heads up" on what is coming down the line.

The ISO technical group will listen to contributions from all participants; therefore we need apply to be participating in the relevant working groups now. We need to identify relevant experts to go and represent the agreed desires and needs of the biotechnology and biobanking community in Ireland.

It was agreed that an outcome from this meeting should be the formation of a national forum of stakeholders. It was suggested we could set up a Biobanking Association, similar to that set up for the Clinical Research Providers of Ireland (CRPI), where we would charge a small annual fee of about €30 and hold an annual meeting with a charge of €20-30. The funds could go towards funding bursaries for members to attend meetings abroad. We could also seek funds from industry. Orlaith Gavin, representing Pfizer Oncology explained how they are often asked to fund individual biobanks but they focus on national, all-encompassing biobanks that are accredited. She believed they would be interested in funding a national initiative.

There was a general consensus that this group could be set up informally at first but become the National Mirror Group with the NSAI. This would be a medium of expertise and experience, rather than just a focus on the physical biobanks.

The suggested stakeholders are: regulators, industry, academics (including a pathologist), and funders, as well as potentially someone from the Dept of Health or Trade.

**Action points:**

- Seek volunteers/nominees to be on our stakeholder group/national mirror committee.
- Next working-groups: the work groups are convening in Berlin in December, we should have participating representation at this meeting.
- Investigate the possibility of submitting MMI Guidelines as a relevant reference for WG2 in the upcoming Ballot.
Standards in Biotechnology & Research

Molecular Medicine Ireland meeting – 8th Sept, 2014
Linda Hendy.
National Standards Authority of Ireland

• National Standards Body (NSB) of Ireland

• Standards, Certification, Agrément, Legal Metrology, National metrology lab

• Provide infrastructure to assist trade of goods and services
Principles of standardization

- Transparency
- Openness
- Impartiality and Consensus
- Effectiveness and relevance
- Coherence
- Development Dimension
- Viability and Stability
Standardization towards the global level

International level: ISO, IEC, ITU

European level: CEN, CENELEC, ETSI

National level: NSAI (ETCI for Electro-Technical)

Industry and other stakeholders
NSAI and international work
ISO TC 276 - Biotechnology

• New area of standard development - 2013
• **Scope:**
  • Standardization in the field of biotechnology processes that includes the following topics:
    • Terms and definitions;
    • biobanks and bioresources;
    • analytical methods;
    • bioprocessing;
    • data processing including annotation, analysis, validation, comparability and integration;
    • metrology.
ISO TC 276 Working groups

• WG1 – Terms & definitions
• WG2 – Biobanks & bioresources
• WG3 – Analytical methods
• WG4 - Bioprocessing
Further information

• ISO Website – ISO TC 276
• Developing ISO standards
• ISO Free publications
  • ISO in Brief
  • My ISO Job
Thank you

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What Ireland Can Gain from Participation in ISO Development

8th September 2014
Emma Snapes
Biobanking in INFANT

SCOPE: SCreening fOr Pregnancy Endpoints

Pre-eclampsia is a complex disorder that requires a personalised medicine approach. The main goal of IMPROVED is to develop a clinically robust predictive blood test for pre-eclampsia, using innovative technologies and utilizing novel metabolite and protein biomarkers.

UCC BIOBANK INITIATIVE
Biobanking Guidelines

Development, publication and updating of guidelines and quality metrics has established biobanking as an independent scientific and professional entity.

March 2009 Biobanks: Saving Your Parts
Guidelines- are they sufficient?

Recommended, non-mandatory controls
- help support standards
- serve as a reference when no applicable standard is in place.

• Guidelines should be viewed as best practices that are not usually requirements, but are strongly recommended.
• They could consist of additional recommended controls that support a standard, or help fill in the gaps where no specific standard applies.
ISOTC276 Timeline Thus Far

- Creation of ISO/TC Biotech by DIN Approved Feb 2013
- Foundation meeting 50 experts/ 15 countries Jan 2014
- “Int Standards for Biology WS” Oct 2011
- Biotech - area of potential for standardisation - ISO Biology Task Force
- Discussed initial topics for standardization and deliberated the possibility of setting up ISO/TC Biotechnology
- 2 d WG meeting, 1 d plenum Business plan & WG SCOPEs presented May 2014
- Individual WG meetings Jun/Jul 2014
- Vote Sept 2014

- Oct 2011 - Approval of “Int Standards for Biology WS”
- Jan 2014 - Foundation meeting with 50 experts from 15 countries
ISO Technical Committee 276

WG1

Terminology - Inventory development of existing standards, guidelines and other relevant documents as well as terminology related to ISO/TC 276

1. Biobanks, Biological resources centers and specimen repositories
2. Collection, processing, storage and transportation technology criteria for animal germplasm
3. Collection, processing, conserving and transportation criteria for Human Genetic Resources
4. Technical Specifications for Human Biobanks & Human Bioresources in Research & Development

WG2

1. Methods to determine a relative accuracy for cell counting approaches
2. Quality considerations for targeted nucleic acid quantification methods
3. Methods to determine the concentration of total nucleic acids
4. Methods to evaluate the quality of the massive sequencing data

WG3

1. Methods to control bioreactor processes for cell culturing
2. Raw materials control for bioprocessing
3. Best practice in raw materials selection in the design of human cell therapy manufacturing processes

WG4

1. Biobanks, Biological resources centers and specimen repositories
2. Collection, processing, storage and transportation technology criteria for animal germplasm
3. Collection, processing, conserving and transportation criteria for Human Genetic Resources
4. Technical Specifications for Human Biobanks & Human Bioresources in Research & Development

Infant
Irish Centre for Fetal and Neonatal Translational Research
Why Participate?

• Standards being put in place in different organisations/locations can differ and sometimes the quality efforts are not sufficient
  – In time this could lead to a well poisoning scenario

• Ensure that the Irish engagement in this realm is practical and pragmatic so that meaningful standards are set but without creating unnecessary costs, burdens or hurdles for biobanks and researchers
Stakeholders

- **Patients/Donors & families**: Build Confidence in Biobanking as a new science
- **Media**: Promote perceptions of value
- **Funders**: Integration of biobank resource infrastructures in scientific road map
- **Biobanking Community**: Clear sign of Irish Commitment to Creation of a strong networked RI base in Ireland
- **End users/Biobank Clients**: Assurance of Sample Quality, Enable comparative analysis & interoperability
- **Health Products Regulatory Authority-Submissions**: Cert of Conformity
- **Public Bodies, Registration Agencies/Ethics Committees/Data Inspectorate**: Statement of Compliance-lends authority
- **Institutions/Owners e.g. HSE**: Reference Resource For set up of new biobanks

ISO276 contribution
Active Stakeholder participation

- Allow biotech sector in Ireland to provide insight & information pertaining to the WGs
- Inclusive of
  - those researchers, industry & academia, regulatory bodies with authority & ability
  - All interested Biobanks in Ireland
- Quality stakeholders need to publically & privately support quality
  - Ease liaising with other biobanking/biotech efforts for validation purposes
  - Increase the profile of Irish contribution to science standards internationally
- Ensure needs/opinions of Irish stakeholders are represented in international final mark
Impact

**Scientific:** Enhance reproducibility, validation
Ease acceptance of publications, regulatory submissions etc.
advancement of the state of the art, and one way to measure such advancement would be thru the contribution to, or the generation of, new standards

**Economic:** reduce errors, increase efficiencies

**Societal:** demonstrate Ireland’s dedication to really valuing donor contributions

Demonstrate Irish commitment to biobank – willing to participate in development of scientific excellence with scientific and economic impact.
In Summary

The Irish biotech/biobanking community now have a unique opportunity to **work together** play a **significant role** in the development of appropriate standards to address a worldwide need for a commonly recognised resource.

Travel resource funding mechanism

We just need to say **YES!**
Biobanking at The UCD Clinical Research Centre

Dr. EJ Cotter

Senior Scientist CRC
The UCD CRC

• State-of-the-art facilities for high quality clinical research
• An attractive environment for patient participation in research
• A cohort of professional and experienced research scientists and nurses that are available for deployment on individual projects as required
• A supportive environment for hospital-based clinicians to engage in research that will drive high quality clinical care
• Opportunity for collaboration between clinical and biomedical researchers to advance programmes that will benefit patients, their families and wider society
• Facilities at both SVUH and MMUH
Support a wide range of studies

• Clinical trial (phase iii, iib, etc)
• Preclinical/basic science
• Investigator initiated clinical trials
• Clinical studies (academic and industry sponsored)
• Biobanking and registry studies
Biobanking at the CRC

• Some ‘pure’ biobanking projects undertaken
• Some biobanking occurring as an adjunct to other studies
• Some freezers ‘hosted’ for other research groups – service provision model
- The CRC has significant biobank facilities across both sites
  - LN2 cryostorage facilities
  - over 20 freezers hosted
-collections from a wide variety of disease groups
Prof. M Keane

Prof. P McLoughlin

Dr. Kate O’ Reilly

SVUH
- Radiology
- Endoscopy
- Surgery

SVUH Clinics

MMUH
- Tx Surgery

EBUS Needle Biopsies
- BAL
- Control and Cancer Lung Tissue

Primary Lung Fibroblasts (IPF and normal)
- Cryopreserved Tissue + EBUS
- PBMC
- Serum
- Cells extracted from BAL

CRC biobank
Clinical Data Management

• Clinical Database software – distillar
• Licence covers both sites
• Secure Access to single studies from either site (VPN tunnel)
• Complies with data protection standards
Relevance of and Roadblocks to standardisation

• By definition we don’t operate a ‘gatekeeper’ model of biobanking
• We provide essentially a range of services to a wide variety of different studies trials etc
• Biobank is an adjunct of the general laboratory (no specific biobank resource)
Focus is on

• Standardised training across all sites
• Procedures based on international best practise
• Encourage use of patient kit model for all studies and provide support for same.
• Research Laboratory IMB accredited
• Hospital laboratories we work with obviously suitably accredited.
Standardisation of laboratory/biobanking processes

- IMB audit (2011)
- Development of ‘biocollections handbook’, standardised logs, labelling systems etc (2012/2013)
- Redrafted SOPs 2013
Usefulness of universal standardisation

• Much of laboratory and quality management standardisation already codified

• Standards will be useful if they focus on:
  • Harmonisation of processes
  • Harmonisation of QC metrics
  • Harmonisation of data handling/transfer

• But ideally must allow for difference between biobank
  • Types ie research vs commercial, hospital based vs standalone
  • Size
  • Study types covered.

• Local peer derived standard generation?