Interview with Anne Carter, Quality Manager of BBMRI.uk

Anne Carter is the Director of the UK Clinical Research Collaboration's Tissue Directory and Coordination Centre at University College London. This role builds on her previous experience and expands her remit to cover all types of biobanks, including disease-focussed biobanks, population studies, diagnostic archives and clinical-trial associated collections. She was nominated as the UK's National Node Director for BBMRI-ERIC when the UK joined the Consortium at the end of April 2015.

Anne has a master's degree in Biomedical Science, is a member of ISBER, ESBB and the Marble Arch Working Group on International Biobanking, and represents the UK at ISO/TC276 WG2, developing quality standards for biobanking.

Interviewed by Andrea Wutte

A: Anne, you are the National Node Director of BBMRI.uk, and you represent the Quality Manager as well, how did your experience lead to these positions?

Anne: I began my career in a hospital diagnostic laboratory where I was specialised in Bacteriology. After 21 years of experience I have seen many changes as my job description progressed from bench to management. My next role was at the UK's National Institute for Biological Standards and Control (NIBSC), where I was Quality Manager for eight years between 1998 and 2006. This was an exciting time for quality systems related to medicines control; I worked with the European Directorate for the Quality of Medicines' network of Official Medicine Control Laboratories (OMCLs) in the development and adoption of quality standards and quality systems for network members across Europe, helping develop and deliver training and a peer-based audit programme. At the same time the World Health Organisation was developing national medicines control systems around the world and I was delighted to get involved in delivering the laboratory quality systems aspects of this programme.

My involvement in biobanking began in 2002 when NIBSC set up the UK Stem Cell Bank. As Quality Manager, I provided guidance in the development of quality systems for the new bank which planned to store cell lines for research and for clinical use. This experience proved very useful in 2006 when I joined the newly-formed onCore UK as Head of Quality. onCore UK was set up as the UK's national cancer tissue bank, with an additional remit to engage with other biobanks in the UK. As a member of a small team, I was able to influence all aspects of the operation of the organisation and developed a deep understanding of biobanking issues. onCore UK set up a network of established biobanks, which became the Confederation of Cancer Biobanks, and I led in the development of harmonised standards for the biobanking community in the UK.

A: Congratulations on your career in terms of Quality Management in biobanking. Tell me about the UKCRC Tissue Directory and Coordination Centre!

Anne: The UK Clinical Research Collaboration (UKCRC) Tissue Directory and Coordination Centre (the

Centre) was set up to support the UKCRC Experimental Medicine Funders Group in achieving their Vision for Human Tissue Resources. The Centre is funded for three years, from December 2014, and aims to optimise the use of human tissue collections and associated clinical and sample handling data whilst minimising duplication of effort.

The Centre is based in the School of Life and Medical Sciences at University College London (UCL) and is a collaboration between UCL (led by Professor Brian Davidson, the grant's PI) and the University of Nottingham's Advanced Data Analysis Centre (ADAC, led by Professor Jon Garibaldi). Although the Centre is based at UCL, its role covers the whole of the UK and all types of biobanks and biomedical resources for research, including disease-based collections, cohort studies, clinical trials collections and pathology archives.

The work of the Centre is organized into three workstreams:

- Informatics: based at ADAC and tasked to deliver a tissue directory. In the first instance this will be a searchable directory of biobanks and tissue collections, using metadata to describe the samples available. By the end of the grant period an example of a more comprehensive directory, providing links to clinical data for individual samples, will be created using hepatitis C virus collections to demonstrate feasibility.
- Harmonisation: building on the work of the National Cancer Research Institute's Confederation of Cancer Biobanks in this area. This work stream will review standards, set up voluntary self-assessment and peer review audit programmes, produce a biobanking toolkit and highlight good biospecimen science.
- Communication and engagement: this work seeks to engage all types of biobank stakeholders in helping to direct the Centre and to ensure that the deliverables from the Centre are based on stakeholders' needs. An annual biobanking meeting is part of the remit of this work stream, as is public engagement.

The Centre was set up with an additional remit to monitor developments in biobanking internationally, and report to stakeholders. On 27 April 2015 the United Kingdom joined the BBMRI-ERIC. The Medical Research Council represents the UK at the Assembly of Members; the Centre was nominated as the UK's National Node and the Centre's Director as the UK's National Node Director and National Coordinator.

A: You are the National Node Director of UK, the work streams of Centre harmonize very well with the common goals of BBMRI-ERIC, we are happy to have you on board!

How is biobanking regulated in the UK?

Anne: It is complicated! The way in which biobanking is regulated is different in the different countries of the United Kingdom. The Human Tissue Act (HTAct) came into force in 2004. This Act makes provision for licensing of establishments storing tissue for research and has requirements for:

- consent, which must be taken by appropriately trained personnel and be recorded;
- confidentiality, which must be maintained;
- the environment tissue is stored in, which must be suitable;
- security measures, which must prevent unauthorised access to the tissue; and
- traceability, from the donor through processing and storage to eventual use or disposal.

You can get more information from their website.

All of the provisions of the HTAct apply to England, Wales and Northern Ireland, whereas only the regulations

specific to DNA apply in Scotland. The Human Tissue (Scotland) Act (2006) (HT(S)Act) applies to both tissue and fluids, but only if they come from the deceased, whereas the HTAct applies to material from the living and the deceased. The consent requirements of the HTAct apply to storage of all types of human tissue, fluids and derivatives but the need for a licence applies only if the material stored contains cells.

A: How about quality systems?

Anne: Also complicated! The HTAct has some requirements for elements of quality systems to be in place, and the Human Tissue Authority audits biobanks (in England, Wales and Northern Ireland) against these requirements as a condition of their gaining and maintaining a licence.
In Scotland, an accreditation scheme for research biobanks has been developed by Healthcare Improvement Scotland and the Scottish Government to focus on four main areas:

- governance;
- access;
- the data/audit trail; and
- consent.

The purpose of this accreditation scheme is to demonstrate that research biobanks in Scotland perform to standards equivalent to those imposed by licensing in the rest of the UK. The accreditation scheme focusses on the four lead NHS Research Scotland (NRS) Health Boards (Grampian, Greater Glasgow & Clyde, Lothian and Tayside), which have partnered with biobanks in their region in a "hub and spoke" model. Each individual collection does not receive its own accreditation. Instead, accreditation concentrates on the 4 "hub" Boards but includes their partner "spokes", which are expected to meet national standards. Biobanks which are not linked to one of these hubs cannot achieve accreditation.

A: What about the CCB's quality standards?

Anne: The Confederation of Cancer Biobanks (CCB) is a is a network of clinical biobanks and biosample collections based in the UK, established in 2006 to encourage greater coordination and promote harmonisation between biobanks – enabling them to share best practice and raise awareness of their collections with researchers. There are now over 30 member biobanks and the CCB assists biobank development by providing advice and mutual support. Full members must comply with the CCB Guiding Principles, which state:

- biobanks are for the public benefit
- biobanks should be based on donation with consent
- biobanks should protect public trust
- biobanks are integral to the provision of healthcare, although often secondary to the primary healthcare of the donors
- the operators of biobanks act as custodians
- biobanks exist to provide a quality service
- human biobanks should be purposeful
- biosamples should not be traded as commodities.

Further information about the Guiding Principles is available on the CCB website.
The CCB members have developed two standards to help biobanks interact with one another and to give researchers, funders and donors confidence in the way the biobanks operate. These are the Biobank Quality Standard and the Biobank Data Standard (Standards).
The standards were created in light of the legal and regulatory environment governing the use of human tissue and data for research in the UK. They are designed to be pragmatic and achievable, while at the same time assuring the quality of the samples and data held. Both standards consist of "requirements" and "best

practices" for the management of quality in a biobank. They do not mandate *how* the standards are to be achieved so that they are applicable to all disease areas and biobanks of different sizes with different business models.
The CCB's quality and data standards were developed by a wide range of biobanking stakeholders, including scientists, researchers, pathologists, patients, funders and regulators, from healthcare, charities, academia and pharma. The aim from the beginning of the project was to take account of currently available standards and best practices, adopt them where they existed and were suitable, and to develop new standards when suitable ones were not available. Hence the data standard adopted many of the requirements of the MIABIS standard, but developed extra requirements relating to descriptions of the donor's diagnosis and the type of tissue.
Once the drafting committee was satisfied with the final draft of the CCB standards, they were made available for comment to the wider community. We were surprised and delighted at the number of responses received, including comments from biobankers in France, Germany and the Netherlands, allowing the standards to be improved and finally published.

A: What happened next?

Anne: Well, once you have a standard, it is possible to assess compliance! A self-assessment questionnaire was developed and made available to biobanks. Then a voluntary peer-review audit scheme was developed and trialled. The biobanks who volunteered to be audited came from within the NHS, universities and even from pharma! I think we all benefitted; the biobanks from hearing how well they complied and how they could improve, the peer auditors from seeing how other biobanks do things and from sharing ideas, and the audit system itself from finding out what worked best and amending the audit systems.

A: How will the UK take this forward?

Anne: The Centre is tasked with taking on the CCB's harmonisation work and applying it to other disease areas and to other types of biobanks. In the meantime, ISO TC 276 has been set up and has work streams looking at developing ISO standards for biobanks. It is my task to represent the UK on TC 276 WG2 (Biobanking) and will make sure that the developments at ISO are compatible with UK standards for biobanks.

There are a set of nine technical standards for pre-analytical factors, developed through the SPIDIA project and adopted by the European standards agency (CEN), which will be brought to the attention of biobanks in the UK. Development of technical standards is very exciting; so far the evidence to show that one method is better than another has been limited, and methods have been chosen based on personal experience and preference. The move towards biospecimen science provides published experimental evidence of the effects of sample collection, processing, storage and transport on sample stability and research results. This will allow biobankers and researchers to ensure that the samples and techniques they use are suitable for the research questions posed.

A: That is right and the BBRMI-ERIC family is going to develop a common Self-Assessment-Tool for this specific need for common use. The valuable input of BBRMI.uk is highly appreciated!

Anne, is it difficult to cooperate with UK's biobanks seen from the perspective of the biobanks of the continent, in terms of material and knowledge transfer for scientific purposes? What is your experience?

Anne: Well, I have only had good experiences when working in a biobank in the UK! There are no "unusual" rules in place that would stop biobanks in the UK working with colleagues and researchers in the rest of Europe and indeed many biobanks do so.

I do think some biobanks have a somewhat insular view, and do not make efforts to look outside their local area for collaborations, even within the rest of the UK. Sometimes it is seen as unnecessary effort, if the biobank is well used by local researchers and those researchers are satisfied with the quality of the samples and data supplied. We will be challenging this view, especially as the biobank funders in the UK are keen to increase harmonisation and quality. I know from past experience that, even when certification or accreditation is not mandated, there will be biobanking thought leaders who consider quality carefully and seek to gain recognition of their efforts. Over time, as it becomes accepted that it brings benefits in funding and collaborations, more and more biobanks seek such recognition. This brings an overall increase in good practice (and all quality managers are happy).

A: What next for the Centre?

Anne: The Centre is developing a system to engage with biobanks in the UK and is in the process of identifying biobanks and other tissue collections. There are at least 250 ethically approved Research Tissue Banks in the UK. This is the lowest estimate of numbers of biobanks, since ethical approval of a research tissue bank is optional - a bank can choose whether or not to seek ethical approval. However, biobank ethical approval is seen as best practice – an example of the community raising standards as described in the previous answer! The advantage of seeking ethical approval of the biobank is that, under predetermined circumstances, the biobank is able to release tissue for research without the researcher needing to seek separate ethical approval for their research project – initially extra work for the biobank, but saving significant time and effort for the researcher.

Systems for engaging with the biobanking community are being developed. The BBMRI-ERIC Partner Charter will be vital in setting up the "hub and spoke" network of biobanks in the UK. In addition, partner biobanks will be asked to commit to a set of guiding principles, based on those developed by the CCB and those published recently by Mascalzone et al in the European Journal of Human Genetics (EJHG (2015) 23, 721-728). These are under development alongside the review of the CCB's quality standards and audit procedure. It is an exciting time for development of quality systems for biobanks in the UK.

A: Dear Anne, it is really a pleasure to have you in the BBMRI-ERIC family, and thanks you took over the function as Quality Manager as well, you are definitely an enrichment for us. Thank you for the interview!

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Biobanking and BioMolecular resources Research Infrastructure United Kingdom

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FACTS of BBMRI.uk

National Node		**UKCRC Tissue Directory and Coordination Centre, BBMRI.uk**
National Node Director		**Anne Carter, MSc.**
QM Coordinator, BBMRI.uk		**Anne Carter, MSc.**
QM Coordinator, local		**Anne Carter, MSc.**
Number of biobanks	**250**	**There are at least 250 different ethically - approved research tissue banks in the UK.**
Partners		**Currently biobanks are being recruited as partners in the BBMRI.uk network.**
Type of biobanks		**Disease oriented biobanks** **Population biobanks** **Archive tissue biobanks** **Clinical studies associated biobanks** **Virtual biobanks**
Catalogue		**Currently using the NCRI's Biosample Directory.** **The national directory is being developed and will be connected to BBMRI-ERIC.**
Number of certifications		**This information will be sought as part of the partner recruitment process**
Number of certification in progress		**This information will be sought as part of the partner recruitment process**
Number of accreditation of associated medical laboratories		**ISO 15189: 47 medical laboratories currently.** **Clinical Pathology Accreditation (gradually transitioning to 15189): 840 medical laboratories.** **It is not known yet how many of these are directly linked with a biobank.**