CCQM Workshop on Particle Metrology

Breakout session 3
Particles in Biological Materials and Pharmaceuticals

12:20	Welcome and any further instructions	Jonathan Campbell (LGC)
12:25	NMI/DI perspectives and activities: **Characterisation of Nanomaterials in Complex Biological and Medical Samples: Advances and Challenges Imposed by Regulation**	Heidi Goenaga-Infante (LGC)
12:40	Invited presentations (15 min each, with questions deferred to discussion at the end of the breakout session) **Physicochemical Characterization of Nanomedicines: Characterization Considerations and Challenges** **One Size Does Not Fit All: Challenges of Particle Size Measurement in Pharmaceutical Applications** **Analytical Characterization of LNP-RNA Nanovaccines**	 Jeffrey Clogston (Leidos Biomedical Research) Xiaoming Xu (US FDA) Luigi Calzolai (JRC)
13:40	Break	
13:55	Discussion and formation of recommended actions	Jonathan Campbell (LGC)
14:40	Rejoin main session*	

*Participants from all three breakout rooms rejoin the main session

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- What are the relevant gaps that need to be addressed.

- Defining the measurand is considered critical and a very challenging task in this area. This is also linked to a particular product / application / area. In general, a step-by-step approach, building in measurand complexity in combination with state-of-the-art methods was held in favour.

- There was recognition that some of the more complex critical quality attributes are hard to measure. These can vary case by case, and again are compounded by complexity of the measurand. We should consider shifting attention into improving correlative measurements, rather than fixation on understanding CQAs.

- Classification and prioritization of studies by a nano-formulation route was emphasized, i.e. the example of liposomal products was given.

- The emergent/immature nature of regulation was recognized. How we follow this regulation is not always clear.

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- What are the relevant gaps that need to be addressed.

- In terms of method development, we should consider how we can improve comparability and ensure we can cross-validate where necessary. We need to carefully consider which RMs will be need in order to validate this framework.

- The lack of methods for surface chemical analysis was highlighted. At the NMI level we need to start developing methods that can quantitatively describe the surface of particles.

- Particle sizing was recognized as a more accessible form of measurement that other CQA linked measures, however we need to understand what properties of a particle size is measuring, and also to develop our understanding of the correlative functions that relate to size.

- Potency measurements were discussed. There are many critical issues, amongst them cell line selection, which will be application dependent. A well-defined surrogate method for potency testing was held as an interesting example of the direction of travel for these types of measurements linking physicochemical properties to efficacy.

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- What are the relevant gaps that need to be addressed.

- The need for more, and better RMs was generally emphasized. This links to multiple aspects,

- Sample preparation defines everything and particularly how you perform this in an uncontrolled (QC) environment.

- RMs are needed that are closer to the characteristics of products that are out on the market. Recognition that such products are beginning to become available with acceptable stabilities (an update on lipid encapsulated nanoparticles was given during the meeting by NRC Canada).

- Associated cost of development is a barrier

- Greater knowledge/understanding of what the community needs. RM producers need to coordinate these efforts - a recent JRC survey was given as a good approach.

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- What does the CCQM (or other CC's) need to do..

- **Improved communication and knowledge sharing. Knowledge management**
- In some cases, we need to strengthen communication between NMIs preparing studies for CCQM.
- Specific need for greater communication and knowledge sharing between NMIs and regulators
- Greater proficiency needed (from all stakeholders) in a wide range of disciplines ie. Research, metrology, regulatory, industry drivers, equipment/technical vendors. More effective knowledge sharing is required that raises the bar for all.
- There was a recognition that some good collaboration is already happening (ie. Standards fora, metrological research frameworks) but huge challenges remain in reaching the people we need to reach.
- Need for a more defined framework for the interaction of people and also the sharing of data (ie. Access to dosier), within the limits of what is possible ie, proprietary formulation etc.
- This platform should provide continuous engagement for stakeholders.

- **Mechanisms for participation by external stakeholders in CCQM comparisons** needs to be looked at. There is a lot of expertise outside the CCQM that could be drawn on. Good examples of parallel studies were highlighted.

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- What does the CCQM (or other CC's) need to do to address

- **Improved Harmonization and Documentary standards,**
- The general lack of, or need for, new standards preparation in this area was recognized.
- The successful transition of some well characterized methods and materials into documentary standards was highlighted and again, greater communication between stakeholders was recognized as important in facilitating this transition.
- Recognition that different organizations work differently (i.e. ASTM and ISO)
- Overcoming political hurdles and greater provision of national coordinating bodies.
- The (inevitable) delay between the emergence of advanced new materials and associated guidance for characterization was acknowledged. The field moves faster than what can be robustly tested (qualification) in many cases.