**Table 28: Quality Risk Management for Cross-Contamination in Multi-Product Facilities**

**Facilitator**: Helen Kumagai, *Genentech, A Member of the Roche Group*

**Scribe**: Pam Rood, Genentech, *A Member of the Roche Group*

**Key Words:**

Quality Risk Management, Cross-Contamination, Multi-Product Facilities

**Scope:**

Companies rely on the Quality Risk Management (QRM) program that is integrated into their PQS to conduct risk assessment and subsequent implementation of contamination control strategies (CCS) across the facility to ensure that the manufacture of multiple products within a given multi-product facility will pose minimal risk to product quality and patient safety. Appropriate risk assessment using robust and innovative tools as described in ICH Q9 and Q10 is critical in increasing process understanding and defining mitigation measures for the manufacturer's CCS. Advances in technology (single-use technologies, digital manufacturing and innovative facility design) and product modalities require manufacturers to challenge traditional paradigms.

The purpose of this roundtable will be to discuss, exchange ideas and share experiences in best practices or implementing and communicating risk assessments and controls for cross-contamination.

**Questions:**

1) How are we adapting the way the risk assessment is performed to keep up with emerging new technologies and modalities?

2) Recently EMA Annex I on the manufacture of sterile medicinal products guideline was revised to clarify how manufacturers can take advantage of new possibilities deriving from the application of an enhanced process understanding by using innovative tools as described in the ICH Q9 and Q10 guidelines.

- What are examples of adjustments to QRM and CCS based on this newly revised guideline?

- What is your company's preferred tool used for QRM?

3) As small volume manufacturing capabilities drive future personalized treatments:

- How have new innovations and approaches reshaped our thinking about risk assessment?

- Have you performed risk assessments for new approaches and technologies (ie SUT, Ballroom facility)?

- Are there new considerations for viral risks and controls for traditional/stainless steel facilities with multiple rooms vs SUT Ballroom (single room) facilities?

- How are manufacturing facilities that have viral and non-viral CGT products preventing contamination?

- Are facilities adopting isolators for open manipulation steps, or using isolators to achieve a closed system for CGT products?

4) What type of highly sensitive analytical methods are being used to detect cross contamination that are beyond engineering and operation controls?

**Notes:**

Companies are encountering more complexity when controlling cross-contamination

- Mixed use facilities for different product types and using different processes
- Use of ballroom areas instead of separate USP/DSP areas
- Shared spaces for multiproduct production
- Movement of products between buildings
- Many batches with small volume (e.g., ATMPs)
- Waste containment – convergence of multiple streams

Seeing a change in use of QRM as risk management matures. Using it for prevention instead of mitigation

Tools for risk management

- FMEA still commonly used
- Use of a Layers of Protection Analysis instead of FMEA. Used to ensure adequate, multiple independent and redundant layers of protection for overall risk reduction

Cross-contamination sources

- **People**
- Facility
- Equipment
- People

Cleanroom areas

- People considerations
    - Education and training are important, typically see high turnover (e.g., work 18 months for the experience and then move on), so need other tools to retain knowledge.
    - Include the why, not just how in the training. Most training doesn't promote critical thinking. An example was to involve manufacturing with the micro sampling and results along with impact to product discussions.
    - Use of color coding, labeling, error proofing, floor tape for mental barrier
    - Cross-training for engagement and back-ups
- Other considerations
    - Set up automation systems to tell you want is/is not working
    - ISO level requirements
    - Stop lights and sirens for air flow reminders
- CGT products
    - Real time microbial monitoring
    - Limited time and volume – requires tolerance for limited information

Facility location considerations (geographical)

- Earthquake proofing
- Water source environment

Cold room design

- 20% HEPA incoming
- Cost/contamination risk vs cost
- Need to justify location and need as well as the infrastructure/redundancy behind it