Table 15: Viral Clearance- Analytical Strategies

Facilitator: Robert Kozak, *Bayer*

Scribe: Mark Paciga, *Merck & Co., Inc.*

SCOPE:

Cell Therapy and Gene Therapy (CTGT) are exciting rapidly advancing fields. Starting materials are a very important consideration when manufacturing CTGT products and should be assessed for viral safety and viral clearance as appropriate. Reagents and raw materials include viral vectors and their cell substrates which can benefit from viral clearance studies where feasible.

This round table will discuss what are the current trends raised by Health Authorities especially FDA when manufacturing vectors to ensure patient safety and avoid clinical holds.

QUESTIONS FOR DISCUSSION:

1. What viral vectors and substrates lend themselves to classical viral clearance studies?
2. What effective steps can be used and what precautions should be taken to avoid impact to the vectors themselves?
3. What trends have been raised by Health Authorities regarding viral clearance studies and final product testing?

DISCUSSION NOTES:

Common question with respect to viral clearance studies: what are the appropriate (or official) guidance documents?

- FDA guidance document (~2010 for viral vaccines
- ICG Q5A
- Harmonization efforts under way
- PDA / PDA Journal (PDA Technical Report 41 – being updated)

Another common question: what is the proper model virus to use in viral clearance studies?

- Parvovirus small size may pass through filter vs large virus (e.g. retrovirus) retained
- Key is to select the right model virus (relevant virus for relevant cell line)
- Not just CHO cells are used for manufacture of biotechnology products (i.e. test the relevant virus)
- Key is to design virus clearance study properly
- Understanding and identification of key effective virus clearance steps (e.g. pH, detergent, etc) in the manufacturing process

Current concerns regarding virus clearance are more challenging in cell & gene therapy (CGT)

- CGT concern with raw materials contamination
- Continuous filtration a path forward? ETT?
- Is there a relevant model virus for CGT?
- Information and knowledge exchange will be key

Virus clearance demonstration in platform manufacturing system vs full virus clearance study

- Need to show data that platform process is well controlled
- Need data for BLA showing the clearance capability of platform

Other topics

- Use of bacteriophage as a surrogate for small scale virus clearance study?