Roundtable Session 1 – Table 4 – Moving Away from Animal Testing and Animal Derived Components Including Alternate Endotoxin Test

Facilitator: John Amery, *Pfizer, Inc.*

Scribe: Joshua Bunger, *AstraZeneca*

Abstract:

The use of animals and animal derived materials has a long history in the manufacture and testing of biologic products. While great effort has been made to minimize and eliminate the animal components, there are still many instances where they are used. For some products, the use of animals and animal derived materials result in a superior quality product or results when compared to non-animal derived. As a manufacturing industry and regulatory authority, how should we balance the tradeoffs between reducing the use of animals and animal derived materials with the requirement to make high quality product and test with the highly resolving techniques?

Discussion Questions:

1. Why are we wanting to move away from Animal Testing and Animal Derived components? Is this a scientific reason or a moral reason?

2. Do all countries have the same (or similar) stance on animal testing & components? How do we accommodate different country requirements for international products?

3. If the use of animal testing & components results in a higher quality product (or greater assurance of the product quality) why wouldn't we choose this option?

4. If a manufacturer desires to move away from animal testing & components, what challenges exist that may make it not worth the effort?

Notes:

Start typing notes here. Be sure to leave out the names and organizations of attendees at the table in order to promote a more free flowing discussion.

- LAL reagent to recombinant material – why move away?

Sourced from a wild animal is unique compared to other sources of animals, inherent variability. Better control from a recombinant source vs wild sources.

Population impacts on horseshoe crabs – population is flat or going down, future could include the absence of horseshoe crabs.

- FBS?

FBS control has always been a problem. rFC and recombinants have fewer issues in control for biotech product vs wild animal product

Sourcing issues - only FBS from NZ was allowable due to TSE/BSE concerns, but limited resource due to farmed animal/single source.

Testing for adventitious viruses in FBS is limited by being able to only test for what you know. Risk of FBS is high due to adventitious viruses.

Animal products induce more risk, but fully synthetic may not always act/be the same

- Comparability?

Observed comparisons between recombinant are comparable to wild sourced

Evaluation of individuals compounds, sometime show disparate results between recombinant vs wild (multiple lots)

How do you justify if individual compounds are of less quality? How do you justify change is equal or acceptable?

Continue to develop method if clinical

For marketed – still need method dev, continue to trying a new/appropriate method.

For FDA – very mature to assess changes; how about smaller HAs?

WHO has a draft guideline on moving away from animal products.

Endotoxin is lower risk – move to recombinant

- Animal testing – potency testing for vaccines, how do we measure without using the animals?

In vitro test; critical tests for conformational structure; however, only way to assess higher order/immune response, in vivo is considered necessary

Understand what are the CQAs and what is the potency readout in mice mean and how can you link in vitro equivalency to in vivo. Show non-inferiority. Moved to cell-based assay

CQA is potency, need to agree on what is necessary to define for biologics

In silico models? Potentially useful for safety, CRISPR guide-strands as an example

- Opportunities to reduce animal use?

Cell bank testing. Moved away from all animal testing for MCB and WCB, pre-MCB testing will move that way as well (but currently internal under non-GMP)

In vivo assays can have false positives, so hopefully moving away will be better.

GMP NGS for cell banks (CHO), for adventitious agent testing.

Prior knowledge may be applied. Unknown if it will be accepted

Change IPC to in vitro NGS testing

A difficulty in transitioning from in vivo to NGS, what if NGS is more sensitive and find something that you weren't expecting

Example, A cell line will turn positive for AAV, but needed to include in viral clearance to show it could be cleared (AAV did not replicate, but was detectable)

- Cost/Benefit, Coral snake antivenom product example

Antivenom generated in horses. FDA approval of antivenom. Recombinant could be made – but what would be the justification vs the cost and benefit (based on number of cases)

Similar concern with HCP reagents

- Concluding thoughts

Next generation students are encouraged to move away from animal use

Animal health companies have a conundrum as well in moving away from animal products