Table 38: Between Shipping and Administration: What is the Product Quality of the Drug Patients Actually Receive?

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SCOPE:

Biological products are susceptible to stresses (such as exposure to temperature, agitation, etc.) that occur during routine handling as part of delivering the medicine to patients. Biological product developers design formulations that aim to enhance product stability to support safe and efficacious administered medicines. Additionally, instructions for product handling are provided in the prescribing information that health care providers, including pharmacists and patients are expected to follow. We will discuss how the healthcare ecosystem handles biological products in a manner that ensures that patients receive safe and efficacious product.

QUESTIONS FOR DISCUSSION:

1. What type of market research or other activities do biologics developers undertake as part of understanding the “last mile” of the “product journey” (i.e., how the product is handled all the way to administration) and how that may impact the safety or efficacy of the administered product?

2. What types of studies do biologics developers perform as part of product commercialization (e.g., formulation development, stability studies, stressed stability studies, transportation qualification) to support use by health care providers and patients?

3. Are healthcare providers (doctors, nurses, pharmacists, etc.) effectively communicated to and understand the sensitivities of biological products?

4. What are the best practices in providing healthcare providers with product handling information to ensure safe and efficacious product administration?

5. Are there gaps, and if so, what opportunities exist to enhance the education and adherence/compliance to instructions for handling biologics through the product delivery ecosystem to ensure patients are administered safe and efficacious medicines as intended by the developers and approved by the regulators?

6. What mechanisms exist to enable potential adverse events to be traced to improper product handling? i.e., how are adverse events investigated as they relate to potential for contributions from improper product handling to impact on product quality which in turn results in the adverse event?
7. Who owns, or is responsible, for the product once it is outside the control of the manufacturer and what responsibilities do all parties have to ensure safe and efficacious product is administered to the patients?

NOTES:

1. What type of market research or other activities do biologics developers undertake as part of understanding the “last mile” of the “product journey” (i.e., how the product is handled all the way to administration) and how that may impact the safety or efficacy of the administered product?

Dialog Points:

- The Product journey in the context of product handling and use is a relatively use concept. Not enough has been done in industry to capture and evaluate all the potential ways products may be handled in the clinical, home, or pharmacy setting.

- Much of industry’s experience and knowledge has come from product complaint investigations where the results leave the firm with this ‘Who would think the product could be used or handled!!!’ in a manner clearly not described on the label/PI and not contemplated by the developer.

- With the diversity of HCP settings for biologics use increasing (from academic hospital to clinics and home infusion), there is also a diversity in handling practices (e.g., centralized pharmacy supplying for multi-admin sites, compounding pharmacies, IV bags vs. transportation within a building).

- The participants agreed Bio-Pharma must do more to understand these product handling scenarios expected in the real world.

2. What types of studies do biologics developers perform as part of product commercialization (e.g., formulation development, stability studies, stressed stability studies, transportation qualification) to support use by health care providers and patients?

Dialog Points:

- Several stability and handling studies are conducted during development and they tend to be quite harsh (e.g., distribution, temperature, etc.) to enable setting conservative limits (e.g., room temperature storage).

- Requirements are provided by the clinical and commercial teams.

- Packaging is designed to protect product from these conditions.

3. Are healthcare providers (doctors, nurses, pharmacists, etc.) effectively communicated to and understand the sensitivities of biological products?

Dialog Points:
• The panel was clear that HCPs are not where they need to be in the sensitivities of biological products.
• PIs are required by regulations, however it is clear from clinical/field experience that they are rarely read and usually discarded without review to assure proper product handling

4. What are the best practices in providing healthcare providers with product handling information to ensure safe and efficacious product administration?

Dialog Points:
• The panel was unable to point to clear education avenues to HCPs on the sensitivities of biological products.
• Pharmacists and nurses do not have robust training on handling biologics
• Labeling text is complex and PILs could provide a simple summary to patients that facilitate/highlight product handling considerations for biologics
• Panel suggested the development of universal standardized symbols that could be put on product cartons to communicate key sensitives. (e.g. do not microwave, do not expose to light, compounding more than X vials/doses is not recommended)
• Focus on the ‘real world’ use of our biologics - understanding globally, how clinical/dosing methods and apply in formulation dev./stability. Glean from the clinical experience and use clinical site initiation sessions as learnings
• Formulation developers go to the hospital/clinics along with marketing to understand product use and handling.
• Observe human factor experiments and incorporate in studies.
• Packaging design studies for robust use by the end of chain consumer

5. Are there gaps, and if so, what opportunities exist to enhance the education and adherence/compliance to instructions for handling biologics through the product delivery ecosystem to ensure patients are administered safe and efficacious medicines as intended by the developers and approved by the regulators?

Dialog Points:
• Pharmacists and nurses do not have robust training on handling biologics
• Support training systems on biologics handling and dosing in nursing seminars
• Evaluate Pharmacist training and find ways to influence biologics specialty
• Educate and assess use/handling in the clinical trial setting. Follow-up by Clinical Ops in initial clinical site visits.
• It was suggested Bio-Manufacturers attend APAJ – American Pharmacists society meetings/forums/continuing education to advocate training on biologics and differences compared to small molecule therapies.
6. What mechanisms exist to enable potential adverse events to be traced to improper product handling? i.e., how are adverse events investigated as they relate to potential for contributions from improper product handling to impact on product quality which in turn results in the adverse event? Panel did not address this question.

7. Who owns, or is responsible, for the product once it is outside the control of the manufacturer and what responsibilities do all parties have to ensure safe and efficacious product is administered to the patients?

Dialog Points:

While from legal perspective there is a clear delineation of product ownership/title changes as defined by contract agreements, in reality any issue arising out of product mishandling reflects directly on the developer/manufacturer – therefore firms need to do all they can to not only ensure patients get safe and efficacious product but also to protect any reputation harm that may arise from these issues. In some countries (e.g. Australia), the regulators are holding the MA holder accountable for product al