Table 27: Shipping and Cold Chain Management

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SCOPE:

Expectations for shipping studies and cold chain management has evolved over the past decade and regulatory agencies are requiring more information on shipping and cold chain management. The US and ROW countries such as Brazil require submission of validation data for shipping or, at minimum, a shipping validation protocol. This Table will discuss the challenges and considerations from an industry and regulatory perspective for the validation of global shipping and cold chain management.

QUESTIONS FOR DISCUSSION:

1. What are the Table’s experience with shipping validations?
2. Does your company use platform information to support shipping validations?
3. What are some of the testing strategies (laboratory vs field vs both) that are being used?
4. How are the majority of your products being shipped (e.g., planes, trains or ships)?
5. Has your company received feedback about your shipping studies? If so, could you share at a high level?
6. Does your company test shipping temperature outside the label claim? If so, do you submit this information or have it for internal use only?
7. How does your company support “time out refrigeration” or “thermal stability budget” i.e., all of the time the product is exposed to room temperature conditions from manufacturing through cold chain to the patient?
8. What are the temperature ranges that are generally used for global shipments?
9. What standards does your company use when creating a shipping validation, ASTM, ISTA etc?

NOTES:

- Multiple companies use the following: trucks, planes and container ships. Ships cheaper than planes and no vibrations. There is also none of the of pressure changes associated with air shipment.
- Active shippers such as biotainer are commonly used and even if unplugged, can keep cold for certain amount of time. They typically get validated once to show how long to shipping can occur for.
- Passive shipping gets validated and is cheaper.
- Liquids, lyophilized and other dried dosage forms can have different approaches.
- Reducing (and the expense) of shipping large amounts of water is a common challenge for DS and DP.
- Some companies are moving towards global validation and conservative conditions for validation.
- It was mentioned that it is a good practice to use Brazil shipments as guidance as hits summer and winter if shipping from South to North Hemisphere.
• Validation of shipping to show okay for a certain amount of time. Lab data can be used with formal stability data to approve excursions. Agitation data from lab experiments can be used. Some sponsors submit lab data to show shipment okay. Temperature excursion can be supported by development and formal data.
• CQA such as aggregates or others CQA are considered in setting acceptance criteria.
• The shipping validation is to look at the actual maintenance of temperature. The formal data is used for actual temp excursions. Lab scale assess before and after but often not against spec.
• In manufacturing, the excursions controlled using temperature hold studies.
• Temptales are commonly used. Temperature cycling studies and forced degradation allow some flexibility. Thermal cycling study allow product to see high and then low. Other shipping conditions: 1-30 deg C often used.
• Formulation changes can enable -20 use instead of -70 deg C.
• ISO and ASTM have shipping standards that companies inform on how to do shipping studies. The regulators will want to know more about the ASTM, etc.
• Some formal stability programs do some sort of excursion and beginning (high or low) and then do the full ICH stability.
• FDA will look at it from a supply to patient perspective. For example, if the patient cannot get his/her medicine supply.
• FDA expects clear shipping studies. This topic can also be inspected by FDA at a site.
• Big challenge is cumulative temp excursion time. Shipping, manufacturing, patient use, etc. Good to do extensive cumulative hold times during PPQ.
• Generally, the group felt that Industry attendees aligned with FDA expectations.