

Table 12: Global Filings, In-Country Testing Challenges and Solutions

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Scope:

Global alignment of filing requirements to enable one submission across the world would streamline the registration process and support expedited patient access. Despite ongoing efforts to drive standardization and develop reliance pathways amongst health authorities, companies still regularly navigate diverging requirements and must respond to unique country-specific requests.

In addition to global filing challenges, in-country lot release testing can be redundant, time consuming, resource constraining, and add to the complexity of releasing the product to the local market.

This roundtable will discuss specific challenges companies have faced conducting global filings, including in-country testing requirements, and associated solutions.

Questions for Discussion:

1. What strategies have been successful to streamline global filings and utilize a universal dossier?
2. Have companies recently leveraged reliance pathways? How did the process impact resourcing and filing strategy?
3. How have companies successfully supported method transfer for in-country testing? Have streamlined transfer strategies been utilized?
4. How are companies managing equivalent raw materials and reagents required for in-country testing given ongoing supply chain constraints?
5. How have companies managed divergence due to country-specific requirements that are added during review or as post-marketing commitments?

Discussion Notes:

1. What strategies have been successful to streamline global filings and utilize a universal dossier?
 - Comment practice: establishes a universal dossier within the company based on requirements for US or EU submission, utilizes the core dossier including additional information and data required for specific regions.
 - For example, additional method validation data have been requested by other countries, such as Japan, Russia, Argentina, China, etc.

- Better planning and early forecast of the company global regulatory submission timeline is important for CMC team, which allows CMC team to plan work ahead and gather data or information to fulfill regional requirements.

2. Have companies recently leveraged reliance pathways? How did the process impact resourcing and filing strategy?

- Reliance pathways have been leveraged with legacy products submission

3. How have companies successfully supported method transfer for in-country testing? Have streamlined transfer strategies been utilized?

- Establish strategic partnership with local/ regional testing laboratories
- Leverage master analytical method transfer protocol for in-country testing
- Justify waiving testing or subset of tests from release panel
- Method transfer needs to include stressed material to demonstrate the testing lab capable to detect protein degradation within shelf life, only use reference standard for method transfer is not sufficient
- The tests required for in-country testing may vary from country to country. Some countries can require additional test per country importation requirements, i.e. N-terminal sequencing, host cell DNA

4. How are companies managing equivalent raw materials and reagents required for in-country testing given ongoing supply chain constraints?

5. How have companies managed divergence due to country-specific requirements that are added during review or as post-marketing commitments?

- Product specification divergence can be managed with master specification document with regional acceptance criteria. Most stringent specifications are commonly applied for internal material release.
- Post marketing commitments regarding analytical method change is challenging. It may take up to 10 years to change a specific method across all regions.
- Leveraging approval by Stringent Regulatory Authorities (SRAs) in other jurisdictions can facilitate the rest of world approval process.