Roundtable Session 1 – Table 12: Regulatory Expectations and Challenges: Lessons Learned from Developing Countries

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Abstract:

Managing varying expectations across global regulatory health authorities can often be challenging for brands registered across numerous markets, including developing countries. In particular, differing and evolving local regulations in developing countries can lead to queries and/or market-specific requirements which then must be managed by the market authorization holder. The aim of this roundtable is to share experiences on the expectations, challenges, and lessons learned when navigating the complexity of initial registration and lifecycle management across global markets, particularly developing countries.

Discussion Questions:

1. What challenges have you faced when submitting variations to global health authorities, particularly in developing countries? How have you worked to address those challenges?
2. Are there areas or topics you have found to be of particular interest to health authorities in developing countries?
3. What have you learned from your past experience with global health authorities, specifically with those in developing countries? Were you able to leverage those lessons learned to proactively strengthen subsequent variations?
4. Have you experienced logistical challenges in submitting variations to developing countries?
5. What strategies have you used to successfully implement critical changes faster when review and approval timelines vary significantly across markets? Have you implemented critical changes at risk?
6. Have you noticed any recent changes in the expectations of health authorities in developing countries?
7. Is your company leveraging reliance for post-approval changes?
8. Are you adopting a single dossier format in developing countries?
9. Have you implemented any special training for employees related to managing regulatory activities in developing countries or have you taken a “learn as you go” approach?
10. Have you found it easier to manage regulatory activities in developing countries with internal resources or have you found it beneficial to contract out work to local specialists?
11. How are you managing changes with low/no product quality impact, especially in countries without specific guidance on timeframes for submission of these changes?

Notes:

- 5 participants *(including facilitator and scribe)*
- Opened with a reflection around the previous day's *Plenary Session 2* where WHO speaker discussed the cultural aspects around reliance and that it can sometimes be seen as weak
    - Most were surprised or had never thought about this perspective
    - Important that more established health authorities (HAs) promote reliance and play a role in education
- Discussion around the definition of "developing countries" as this terminology was thought to be controversial
    - Other terminology being utilized → most of world (MoW), rest of world (RoW), international)
    - Any country that is not a major or core market like US and EU
    - Small HAs that are not well established in terms of resources, infrastructure and regulations/experience
    - Countries that rely on approvals from a major market i.e. request copies of approval letters in order to complete their review process
- An inform that last year a draft IQ group position paper was prepared to align on requirements for CTA filings and now a BLA one is in progress

1. What challenges have you faced when submitting variations to global health authorities, particularly in developing countries? How have you worked to address those challenges?

- Country specific document requests like chromatograms for Mexico, China, Ecuador are always a pain point
- Stability data requirements i.e. full shelf life, DP data for DS changes → use of position papers
- Formalistic checklist type review procedures with no opportunity for scientific rationale/justification → can ICH M4Q help with this and more focus on overall control strategy?
- Lack of trust signals i.e. notarization/legalization of documents, stamp/signature on each page dossier sections, raw data
- Expectations to comply with pharmacopeias whether they are legally binding or not especially when not all are harmonized/aligned
- Change in supplier for raw materials → China requirements are more stringent
- Requests that don't make sense or have scientific basis → Russia asking for three ID test methods so now having to adapt internal strategies to validate three methods up front
- Demonstrating sameness of product when CPPs are issued with different supply chains
- Russia and Japan wanting additional system suitability criteria added to methods that have already been validated → sometimes successful in pushing back
- Transfer of cell based assay methods for in country testing in China and Russia → no success of waivers but getting better with physical and chemical tests

2. Are there areas or topics you have found to be of particular interest to health authorities in developing countries?

- China interested in new technologies and modalities

3. What have you learned from your past experience with global health authorities, specifically with those in developing countries? Were you able to leverage those lessons learned to proactively strengthen subsequent variations?

- COVID enabled improved collaboration between HAs → helped to push reliance forward but need industry to continue to engage in pilots and opportunities
- Most companies submit method summaries and not internal reports to avoid country specific requirements/adaptations being submitted globally

4. Have you experienced logistical challenges in submitting variations to developing countries?

- Ongoing use of paper dossiers and affiliates having to submit to HAs in person or by appointment
- No parallel submissions allowed so global implementation of changes can take a very long time with impact to supply chain

5. What strategies have you used to successfully implement critical changes faster when review and approval timelines vary significantly across markets? Have you implemented critical changes at risk?

- Some opportunities to accelerate approvals due to supply considerations
- Regular affiliate follow ups with HAs

6. Have you noticed any recent changes in the expectations of health authorities in developing countries?

- Requests for more core/major market dossier information

7. Is your company leveraging reliance for post-approval changes?

- ICMRA
- Project Orbis
- Access Consortium
- Worksharing agreement between MHRA and TGA → but need to manage expectations up front and really only beneficial when one round of questions is agreed to

8. Are you adopting a single dossier format in developing countries?

- Typical filing strategy occurring in 2-3 waves
- Some attempts for single dossier except for countries with intellectual property risks

9. Have you implemented any special training for employees related to managing regulatory activities in developing countries or have you taken a "learn as you go" approach?

- Databases for country specific requirements/documents which are resource intensive to maintain/keep updated
- Training and experts in certain countries and regions for better collaboration i.e. China partners

10. Have you found it easier to manage regulatory activities in developing countries with internal resources or have you found it beneficial to contract out work to local specialists?

- Most have internal experience with managing global markets
- Some have specialized regulatory intelligence/international operations groups

11. How are you managing changes with low/no product quality impact, especially in countries without specific guidance on timeframes for submission of these changes?

- Some experience with deferring changes and implementing at risk for low/no impact quality changes

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