Roundtable Session 1 – Table 6: Regulatory Considerations and Experiences for Control Strategies in Different Regions - Focus on General Challenges with Divergence

Facilitator: Shermeen Abbas, Amgen

Scribe: Zachary Kaur, Zoetis

Abstract:

The harmonization of global control strategies for pharmaceutical products emerges as a necessity in the dynamic landscape of drug development and regulatory oversight. Harmonization of control strategy is important in fostering safety, enhancing access to innovative therapies, and streamlining global pharmaceutical processes.

Despite the available ICH standards, a benchmarking survey performed by IQ working group and published recently in the article, "Toward a single global control strategy: Industry Standard"[1], showed an overall <9% probability for all four established ICH markets to accept a single control strategy based on a study of 112 submissions. The data demonstrated local jurisdictional considerations present challenges and can potentially lead to drug shortage if material made and released for one region is unsuitable for a different jurisdiction.

Discussion Questions:

1. How can international collaboration be further enhanced to address and overcome existing regulatory variations among different regions?

2. Considering successful case studies, such as COVID-19 pandemic, what are the transferrable lessons for policymakers and stakeholders in different regions aiming to implement effective harmonization initiatives?

3. As stakeholders adopt more innovative manufacturing processes, what are some of the key considerations towards a harmonized control strategy?

4. What are some of the learnings from the recent implementation of ICH Q12 and how can that process be further improved?

Notes:

Shermeen introducing her experience on platforms and harmonization strategies.

IQ harmonization and giving an introduction with those numbers (<9% probability) was really eye opening.

Experience from one person BLA template exercise:

Plan ahead, they aren't seeing much difference for the other countries. They are the same after the go to the regulator

Challenges on IP and what to share to who for the submission but it's different for different regions.

Follow ICH guidance for the majors, US, Canada, Australia. They get the major package, other countries get less and just put in specification less control strategies.

Try to provide less and maybe get acceptance.

More countries are asking for more now that they are starting to cross talk with others. The expectation have now changed, Brazil is now Tier 1 vs 2 a few years ago.

Other countries are asking more and more now, Argentina.

Other countries are starting to talking to other countries… Brazil is talking to Argentina

Do you see convergence in the approaches, Amgen experience?

Discussion on Microbal testing

Review bias not necessary the agency, new reviewers new lens of scrutiny

We have seen boiler plate questions, but young reviewers are asking old questions,

Example of Canada asked for the scripts on programing for setting the spec.

They are talking to other organizations and know the baggage that a problem/difficult drug project already has.

Trade secrets are an issue so harmonization is less likely and documents are getting

How many flavors of the BLA are you going to have because some don't accept ICHQ12

Management is resistant to too many tamplates for submissions. Ends up sticking with old template.

Questions was asked by Sharmeen about the advantage of Cloud entry interface, do you have a platform on there.

Discussion around Obvase and another program for entering data for submissions

Some companies will enter in to have all 5 country access and some with only do a few.

Discussion moved to: Agencies are now sharing information among each other, but they can't get them to agree on the same specifications. Regulators will then ask questions that are from earlier submitted data and already answered.

The group seems to suggest this was for the "newer" reviewers to gain more knowledge

A question was raised that if we provide to much data, does it raise the Bar on what they will expect. There was some consensus on the questions are more for the review to gain more knowledge since the topic may be new to them.

The writers of the submissions are expected questions when their management would prefer to have no questions. Companies might feel that questions asked from regulators is challenging them when it is not intended to be.

The group move to discussing Terminology:

Terminology harmonization needs work and would help with submissions to various countries.

The questions came up for a smaller company employee that asked who QCs a translation when you are already using a CRO to do the translation for you. Another round table member suggested using another external company to check. Translation is very important.

Since not all countries follow the same guidance, the terminology does not work for all.

Discussion on adding into your template the definition of certain terminology. Example: Essential free from particulates. Put it in the template and define so it can be used for later submissions will remove questions on broad terms like the example above.

Did harmonization and work streams changes from Covid provide a usable learning experience?

One table member shared her experience on supply chain and validating different supplies of amino acids (raw materials). China did not allow them to use that amino acid supplier in the process (even though it was a qualified) if they have not released a lot of DP that was in the submission using that material. It was suggested to use many different lots of raw materials during the process development to allow more flexibility in raw material resourcing.

Discussion moved to harmonization of Specification in submission. A table member discussed how they keep their global specs wide and narrow when different countries require.

Shelf-life requirements vary greatly between countries because you won't the same real time data for each countries submission. The comment came up that the FDA emphasizes the importance of real time data verses extrapolation of stability data.

Question came up on how companies were handling stability data for drug+device.

> Others use comparability studies to support stability for drug and device combos. Focus on the CQAs.

Not much has changed for the submission format. The classic old way still seems to provide the faster path for BLA timing. Also, regulator seems to be most comfortable with it.

Since ICHQ12 is not accepted everywhere, not much incentive to implement it into the filings yet. Amgen is trying to take a more focused approach but they are not there yet.

Group ended on making sure your filing is telling a good story.