Roundtable Session 1 – Table 9 - Life Cycle Management of CE Technology

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Scope

Life Cycle Management of CE Technology is a recurring, yet highly relevant and challenging topic for submitted release analytics of commercial pharmaceutical products.

While routine analytics of many products and companies are affected by technology modernization and replacement of outdated instruments, there is very little literature publicly available on how to implement such changes in a regulated environment.

The ongoing character of this topic as well as its high relevance point towards the question whether a good practice approach or even a standard procedure can be designed and publicly shared to facilitate and harmonize the handling of instrument modernizations in commercial release analytics.

Questions

1) What is the regulatory perspective on Life Cycle Management and what is the impact on analytical instrument replacements?
2) What are current common procedures a) publicly available and b) followed in different companies?
3) Can we set up a universal approach to meet instrument modernizations effectively and efficiently? Could a universal approach from our CE field set an example / be applicable to other analytical fields (such as chromatography…)?

Discussion notes:

- How to replace an object that was such an integral state in QC analytics. Important because of challenging. Many of us almost are affected by updates and changes. There is very little literature available on how to actually deal with the replacement of a new technology in QC analytics.
- How we can handle such situations, how we can find a way to actually to deal with it and make this become the most standardized procedure or a bit more into the direction. Once I realize I want to update the technology, I would do it, how do I do this best, and move into a direction where we're not all of us reinventing the wheel every time this is happening. So this is the guidelines for us is what we have to do. You need to be known as the regulatory perspective of that experience.
- The first thing is the new ICH guidelines. So Q2, R2 and Q14 go together. And there's much more emphasis on what we call performance characteristics.

- I think that's consistent with the idea that if you have a better instrument, or you've got better sensitivity or something like that, there shouldn't be a liability. What the most important is that you're looking at an attribute.
- You've got an analytical target profile. if those things are clear, then once you engage in the algorithm, that's the new ICH guidelines. So hopefully that's the direction that we're going to go.
- I echo that. We're working at the target profiles as well. This is part of lifecycle management, but like earlier filings, depending on how you file, that if you put specific instrumentation in your filings like ICE 3, so now you have to update.
- It's part of the filing strategy. The old ICH makes more difficult for us than the new one. In the past when you had such situations of making an update or including state of the art in your own site, was it so challenging that you actually had to change the way you were approaching it? Or was there some regulations that really made it difficult for you? Is there some problems that you should keep in mind?
- Specifications can come into play when you do transition technologies because if you go from one technology to the next one, if you're seeing slightly different results that your trends are different.
- That's one bucket that you'll have to cross and that's of course going to be filing updates as well, the authorities, the specifications might need to be updated.
- Have filing with the FDA, filing with the EU, and all those are going to a three-year roll-off plan. If it's a commercial product, it's probably going to be a three-year-ish exercise to get those BLAs and everything updated appropriately. So it's a pretty large lift if you're doing an update. A lot of our stuff is filed on ICE 3. We've got a transition to make sure that you're planning accordingly ahead of time to meet certain targets.
- Is the instrumentation actually called out by name?
- I think that comes down to the strategy. Some early files might have called out specific technology. You're withholding to that in the file line and then when you go to update it you have to you can't just change it outside of that final update.
- That's one strategy, is that you try to put as many people as possible in a library, but if the filing references those documents, you have that self-explanatory.
- I've probably spoken to 30 or 40 companies in the last year, and 99% of them, they're BLA's, have instrument-specific descriptions.
- Like a model or a technology?
- A model.
- It's the exception that someone puts in more of a descriptor than a specific model? Or an instrument name?
- As soon as you indicate an instrument name, it's a potential issue. So some people will say an instrument and then describe it in terms of performance as opposed to a model or a manufacturer. But it's rare that it's done. And more people are starting to look at it because it clearly becomes more flexible. As long as you can maintain the performance, then it's irrespective of the instrument that you've used to get it. It allows us to have leverage to do that, as long as you're meeting that performance, characteristics, you don't have to specify the instrumentation.
- The future strategy is to approach it based on methodology, not instrumentation
- There's different options of submitting amendments. Some companies say it's really quite simple. Other companies, it's a little bit more complicated. You're issuing amendments that

specifies the changes to the original filing. It's a lot of work. Some companies are registered in our products in 107 different countries.

- It's not to be taken lightly, but it's a memo if they can figure out how to do amendments, or addendums. And presumably that amendment is supported by putting in tons of documentation, and showing the improvement, whatever kind of bridging studies they're doing.
- The reality is most companies use a variety of techniques to do the bridging studies.
- A company places freedom races when i'm going through actively right now there's a lot even before getting to the filing updates. We have to determine the potential impact. We're still not there what sort of comparability package. We're gonna have to validate the race but we need to go into that validation and then that validation is going to support. Your company has done a great job at actually at least kicking off those initial comparability studies and there's going to be a difference between intra-company updates like iCE 3, Mauries or iCE 280. They‘re all the same product line that's being updated.
- We're still at the early phases. We don't have any qualified Mauries systems. That's kind of the first step before getting into the commercial space, is it has to be qualified. That's a left-up data integrity assessment and everything else to make sure that's going to stay.
- I operate more on the clinical side. We can operate with vendor IOQ to put numbers, commercial needs, qualified equipment. We're already starting to corporate the brace into our process flows. We need to plan the head across the portfolio. and that's going to be kind of how we determine what the path forward. The process is going to be a lot different than if you see some sort of qualitative or quantitative difference.
- So basically, if it's a technology that you're assuming, for example, two different models. you assume that the data is essentially going to be the same. So one approach that I've seen is essentially writing it into. Like intermediate precision assessment, validation. Those different methods, they are very generic, They are instrument-based. if everybody prepares the same thing and follows those methods, it doesn't matter which instrument you're using.
- We had the iCE first generation several years ago, now is iCE 3 of 2nd generation. How did you deal with that situation?
- Before my time joining, there was a program where the data produced was different. So it required a spec update. That was a much larger lift going from iCE 280 to iCE 3. And it wasn't something that was identified well up front, but it caused a lot of additional work on the backup. I think doing your due diligence up front is very important when you do any of these transitions between technology.
- I think it's going to be more on us than the vendor. It's our product. We need to understand our product and how it's going to work. It's our decision on purchase. We want the analytics. If you're seeing something different, I would definitely reach out the vendor. Maybe they have some insight that can help.
- We are seeing different profiles. but ultimately it is going to come down to us to make sure that we're making the appropriate decision for our product.
- In our company, for the current molecules, for the future molecules, we already started both conditions of both iCE 3 and Mauries in the method.
- They still add on another couple of years, and then a couple more years for the bridging and a couple more for the filing, and that's already up to eight years, so there's just a lot of moving pieces to get new technology into the lab space.
- How many filings are your team per site? In the case of iCE 3, it's across the board from our pipeline, we've got several approved products, so it's going to impact all those.

- That's a good question. It's not just pre-products. It's pending products, pending approvals for BLAs, plus BLAs that are being planned now quite often have iCE data.
- We would rather see how we are able to come up with a similar approach to evaluate the performance of a different instrument and provide an example, see how much we will do pretty well when it comes to such a different instrument. that is also valuable for other instruments?
- I think this is going to nicely, which is probably the best way to do it. is to really be comfortable with what differences you can actually make.
- You're saying that instrument A and instrument D, they're either exactly the same, or the globe is different?
- I'd like to use your imagination on those two. What kind of differences could you tolerate? What are your specifications? What are your challenges? What is your goal? What are your objectives? I can actually handle the two results.
- I think at the end of the day, the more data you have, the better, the more justification you get for it. Meeting your analytical target profile, but if you look at the samples at the head, if there's a difference between them, how do you judge?
- We just have GMP procedures in place to do this development in this case. Front-loading the data integrity requirements and that sort of thing. We have to do pre-data integrity assessments. That's something even before we purchase equipment now. We're trying to engage in vendors sooner to try and do those assessments.
- You can come up with just do an instrument comparability. But then there's also going to be a product-specific assessment that needs to be evaluated.
- We're working on a much closer collaboration. As the new product or the new iteration of that product, we've been working with customers during that process. you kind of already have expectations as the product developer, at least you know what you should be expecting at that time.
- Working with our scientists to figure out what we can provide as early as possible. if we knew exactly what was needed and what we can't share early on. You'd be able to go to the homepage and find all that information you need out in the game, instead of having to contact us because then you're already delayed.
- I think during the product development process, talking to customers, understanding what they need, what the expectations are, how we tie that to what we're able to share. But at the time of getting that information out as quickly as possible.