ANALYTICAL DEVELOPMENT CONSIDERATIONS

Some activities that might be considered to speed development activities include the following:

The four expedited programs were developed by FDA to minimize the time spent on the development and review of new drug and biological products that address unmet medical needs in the treatment of a serious or life-threatening condition. These programs help ensure that a therapy for a serious condition is approved and available to patients as soon as it has been proven to provide an adequate safety profile and clinically meaningful benefit.

- A focus on high priority assays, including but not limited to potency for biologics and content, impurities, and dissolution for small molecules to ensure suitability for control system
- Involving commercial quality control (QC) in assay design during development and co-validating, if possible
- Using qualified rather than fully validated methods for internal release and stability testing of qualification lots and completing validation before commercial release

-This approach presents a business risk, if problems arise in validating a method, and should be accompanied by a backup plan requiring retesting lots and/ or implementing alternative methods

- Launching from a clinical site with clinical QC release and transferring to commercial site post-launch

Analytical Methods

- Dialogue should encompass analytical methods.
- One of the complicating factors is the uncertainty around the power and reliability of the analytical methods on which the process rests.
- Regulators and industry should be/are turning their attention to how approaches can be applied to analytical methods and their development to help strengthen this link in the control chain.
- Start to think about the application of these concepts in other areas, the usefulness of this for analytical methods is fairly self-evident. these concepts all seem to apply to methods just like they do for process and product, and to have similar and significant benefits.

The effort involves changing the analytical paradigm. The traditional approach is “don’t look for things you don’t want to know. You already have the specification; the method is approved.” By contrast, this approach is to continue to improve the methods “in order to have a higher assurance of quality.”

Objectives in advancing methods early

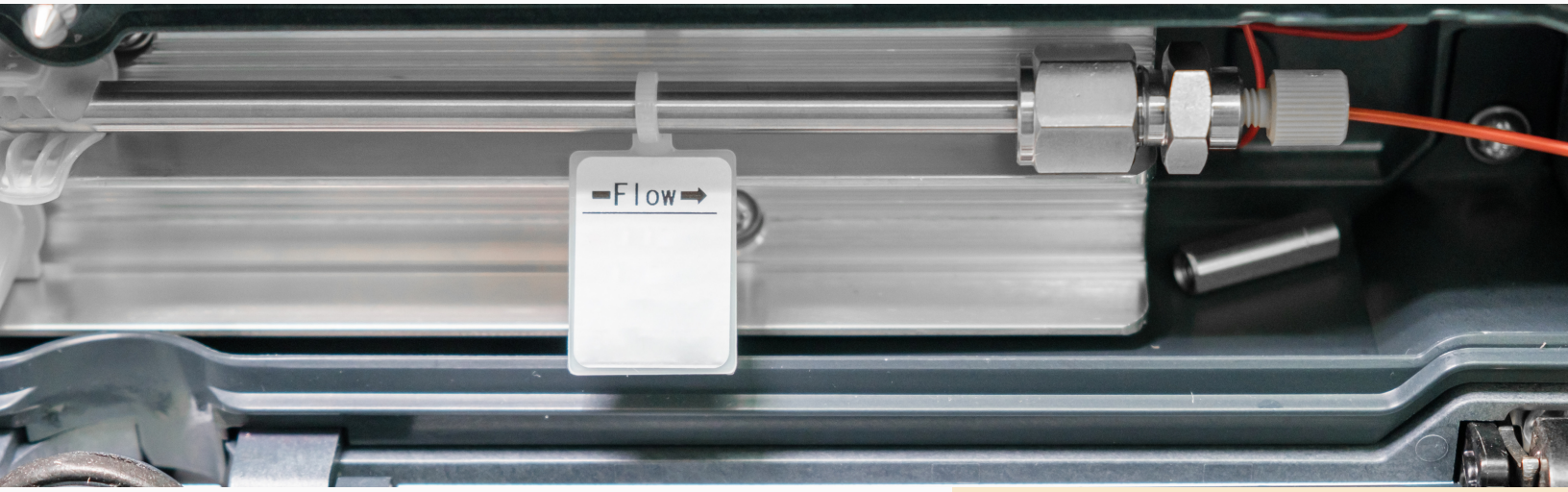
Short term

- Carry out a much more expanded version of robustness at the beginning of method development and carry that detailed information all the way through as you finalize and validate the method - so that you have in effect created the design space.
- Regulatory filings would then include greatly expanded ranges. Changes within this defined design space would/may not require approval.

Long term

- Identify the ‘critical method attributes’ and the ‘critical method parameters’ through the development process, and the supporting experimental data included in the applications. The critical method attributes would be the only regulatory commitment registered in an application. Continue to provide the specifics of the method and the target setpoint, but that wouldn’t be a regulatory commitment? While supporting continuous improvement and method optimization in principle, Q10 does not provide “clarity of how you are going to do that, so it would be firm to firm, product to product”. need “to provide some expectation of how these things will be done.”

-Eg. the method changes for development marketed products that now undergo regulatory review and approval...thousands of regulatory changes every year around the world, and about ~50% of those are due to analytical method changes. - imagine the reduction in workload that an approach like this would bring.



The principles and processes involved…

- (concept) Describe the 'analytical method target performance profile' (AMTPP?) – targets for each analytical method that must be met so that the data it produces is fit for the purpose it is being used.
- Behind concept, …the idea that before you actually develop the method, you should make very clear what you want with the method. In turn, a clear description of the performance profile essentially defines the method's design space.
- A system for analytical methods could be readily implemented - currently, alternative methods are 'annual reportable' and comparability protocols are in play.
- Analytical methods are 'an essential piece' so does not necessarily mean less analytical testing. It is the right analysis at the right time, based on science and risk.
- Can offer more flexibility, but it requires a higher degree of process, product, and analytical method understanding and a robust quality system.

Benefits from applying to analytical methods

- Facilitation of continuous improvement and technological innovation
- Enhanced method robustness
- More flexible regulatory approaches based upon data provided and acceptable quality systems at the Sponsor/3rd Party Analytical Testing Lab
- More effective utilization of industry and health authority resources

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