**Roundtable Session 1 – Table 7 – Is High Throughput Always Better**

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**Abstract:**

With the ever-increasing speed of pharmaceutical development, the need to generate data quickly has been a growing need. Tighter development timelines have required multiple projects to be balanced simultaneously and required more early development and screening samples to be run alongside each other. As such, multiple strategies are utilized to increase the throughput of early stage materials, and help facilitate pipeline progress or knowledge for the molecule of interest. Instrument platforms such as the GX Touch and the BioPhase 8800 present options for higher throughput analysis with shorter runtimes for assays or simultaneous data acquisition. Sample automation and the use of platform knowledge for modeling can also be leveraged to decrease the amount of lab work for an analyst. As useful as higher throughput methods are, they can also become a new pain point, echoing the usual problems of method development as well as adding the difficulty of new instrumentation to labs. Having a better understanding of how higher throughput methods fit into the analytical pipeline is key to utilizing them for their maximum benefit in pharmaceutical development. This Discussion will focus on where high throughput methods are appropriate to use, and how those methods can be leveraged to support pharmaceutical development.

**Discussion Questions:**

1. What high throughput techniques are currently utilized or being developed? Where is the data being used?
2. What problems have you encountered with using any of these techniques?
3. Where do you see high throughput techniques going in the future?

**Notes:**

**Q = Question**

**A = Answer**

**Q: What else outside instrumentation are you trying to do outside of instrumentation?**

**A:** Liquid handling robots like Hamiliton.

**A:** Liquid handlers like Hamiliton can be difficult to transfer to GMP. The liquid handlers are pretty consistent, but the systems are very flexible and open so hard to lock down for GMP.

**A:** Automation building with idea that people don't' need to go in and touch anything with Tecans for sample prep and robots with grippers to move plates. Analysts monitors from elsewhere. Automate though data analysis to where analysts review results.

**A:** Brick wall between early development and GMP release testing. Gold standard for GMP is reproducibility, accuracy and robustness. Throughput for GMP needs to be assessed. Samples for large batches can be limited. High throughput from the GMP space is not a lot of throughput for one sample, but running many different sample at once. Robots have a different set of parameters that an analyst doesn't do. Like prepping samples – typical CE sample might take 10 mins, but liquid handler could take a lot longer sitting at room temp or what your system is equipped for.

**A:** Right now, using for non-GMP, process development things. From method development for GMP are aimed at testing drug product/substance, not a wide range of additional conditions. HT methods can have different numerical results. Example iCIEF method, have one or two broad methods to test a wide range of samples, can get blobs for acidic, main and basic, for GMP they aim at getting better focusing and reproducible analysts to analysts. This can result in questions from other partners when the GMP results look different once the methods have been tailored.

**A:** Ideally having results with HT match GMP is the ideal state, but not reality right now.

**A:** BioPhase 8800 compares to GMP PA 800 Plus enough where something like LabChip to GMP will always have significant differences.

**Q: For the BioPhase 8800, has anyone done any work on it to see differences capillary to capillary.**

**A:** Yes, but minimal.

**Q: High throughput for product research where data processing was the top problem identified is this a pain point for most?**

**A:** If you don't have automatic integration parameters in place it is difficult. Using Empower or BioPhase software makes it easier to automate.

**A:** Often must manually integrate for CE-SDS. Build out processing methods, but there's always drift over time. Empower has an advantage due to cool data collection software solutions that will parse Empower results and report in a hub. Makes it easy to see what release testing labs have testing. Can pull it all together in a visual representation. Can quickly see data trending over time. Empower has a strong grip and this comes through from regulators with the question that is really aimed around Empower as the gold standard.

**A:** Big part of automation is the data handling.

**A:** When using Empower control if you take out capillary to clean then empower gives an error when you put it back, but if you hit run it just goes away.

**A:** With systems that pull data in bulk it feels like you lose granularity, you must be able to go back and find raw data easily. When you are running your iCIEF or CE-SDS yourself you have

high confidence and stand behind your data, but that is lost to an extent when you have so much data. Essential to be able to go back to raw data.

**Q: How often do you need to MS confirm peaks?**

**A:** Typically happens late phase during deeper characterization.

**Q: When you need clone screening do you need peak ID?**
**A:** One case their cell line screening is using CE-MS to do it, but not too many people say this too until later. If you can do it helps to have better product understanding and nice to have for IND, but hard to do with how many projects go through early phase.

**Q: Where's automation going in the future?**

**A:** Full GMP testing of samples with no-human involvement, but likely for GMP there will always be some involvement. Might run into specific challenges with reagents that must be prepared day of, but robots currently take too long.

**A:** Can run into trouble transferring to other countries that have their own requirements so need a human equivalent.

**A:** Classes of molecules… a lot of mAbs for higher throughput now but need for ADCs and new modalities. Method requirements can be different or novel technologies for CQAs that aren't used for a standard mAb. General feeling that current high throughput methods aren't going to work with current methods out of the box for ADCs.

**A:** Agilent has an Andrew Plus for DAR. It looks a robotic torose with 2 arms to do pipetting. Good for sample prep and ADCs when you want to limit exposure.

**Q: How often do you check bioreactor samples and what's the need for throughput?**

**A:** Starting to test for larger scale bioreactors for online screening. It's something that we want more of for product quality. Another response – don't' get too many requests to test bioreactor samples. Product like 908 Rebel can be used at line as a CE-MS system to monitor amino acid consumption.

**Q: How do you deal with differences in early dev and late dev?**

**A:** Save retains from early dev and test with GMP methods later. Correlate results if needed. Not saying this is what is always done which results in questions from process development groups questioning why results are different. Not sure if there is a perfect solution, but communication is key. Need to account for the lifetime of a product. Will get questions about a molecule developed in 1998. Very reluctant to update methods because that's a BLA update and can be dozens of countries. Ideally the late-stage method is it and it never changes. Have some ICE3 methods developed on ICE280 and from IEF gels. They live with these OG methods.

**A:** Do validation of automation and manual side by side so both are prepared, basically make the robot 'another analyst. Can mitigate differences in early stage.

**A:** Biggest wish is higher throughput for MS methods like peptide mapping…very slow to process the data. Need to review the automated peak ID and it takes a long time to review data.

**A:** One challenge with having higher throughput are internal partner expectations that they can get their results in x amount of time all the time. This can result in partners submitting late since they think the turnaround is on demand which can complicate planning. Can run the samples as fast as you want but need time to review the data.

**Q: If you remove the human element from sample prep and data collection will be lose insights into how to troubleshoot when issues occur?**

**A:** Open questions. Already an issue with lots of instrumentation today that operate more as a black box compared to older instrumentations.