Table 8: Can We Go Any Faster with CE Automation?

Facilitator: Morgan Stickney, *Amgen Inc., South San Francisco, CA, United States*

Scribe: Maria Eleanor Le, *Amgen Inc., Thousand Oaks, CA, United States*

Scope:

Consistency is key in every major process, including drug manufacturing. To achieve reliability, we turn to automation to help reduce human factor errors and relieve analysts of fatigue and burn-out. With automation in place, it helps streamline different processes and efficiently drives any company's output of success.

There are several automated systems currently available and widely used in CE sample preparations, such as the different liquid handlers ranging from small and simple volume transfer instruments, to complex end to end workflows in one huge equipment. With large batches of samples, automation comes in very practical in processing and providing considerable amounts of data, but time is of the essence. Current robotic platforms are not as fast as we have hoped for yet. Though automation provides dependable results, it still takes some time and effort to ensure that these machines operate accordingly and proficiently as expected.

Questions for Discussion:

1. What parts of the CE workflows are currently automated in terms of sample preparations and data analyses?
2. What automation platforms are currently available and widely utilized in the industry? Are these systems/processes in place qualified or validated?
3. How can automation improve the throughout in a lab? Is it beneficial to focus in RD vs. commercial manufacturing?
4. What are the challenges of implementing these automated systems in CROs/CMOs vs. big biotech/pharmaceutical companies?
5. Are there any disadvantages in automating CE? Is the cost of automation worth the investment?

Discussion Notes:

There were 9 scientists in the discussion. Most were from industry, many from pipeline or Instrument manufacturing. A lot of interest is placed on what people in industry want to be automated and how to do the automation properly.

1) What parts of the CE workflows are currently automated in terms of sample preparations and data analyses?

a. Sample prep = biomech from Beckman for start to finish – doesn't do buffer prep and samples at the same time, so these are done sequentially – automated system for CE-SDS

b. Data analysis = Empower + ELN, transferred from instrument to notebook

c. How do you do sample preparation automation? Use the biomech. When developing a method do you have the biomech fx or newer biomech system? Have older fx.

d. Do you write your own methods? Yes, Beckman helped set up original scripts, now they have a Tecan tech that helps write new scripts. Have to tell robot what tips to pick up and what plates to use, temp, etc. Had robotics team develop holders (customized a little) for both vials and plates. All sample info is pushed directly into empower. Once samples are prepared, they just need to place it in the instrument and hit run. But they don't have the robot arm yet to transfer samples between instruments. As it stands you have to manually open the door of the CE.

e. 32 karot(?) is another software that is useable. Older.

f. What is Tecan(?) doing? Tecan is a liquid handler. You can do sample prep on Tecan as well.

g. Use Hamilton for sample prep. Does plate format. Still have to manually transfer to Beckman. Have to manually cap samples. Can you use plates for the last step in the instrument? Yes.

h. New version of Empower has plate configuration. Amgen Massachusetts is evaluating that. Someone argues that vial is really tedious and plate is better.

i. Microlab Prep. Small benchtop instrument. Mainly for academia, mostly the software has limitations.

j. What prompted move towards automation? Human error, fatigue, and throughput. Also frees up time for analysts to do other things.

k. Volumes less than 1 uL, and viscous solutions cause problems for automation. Typically try to use at least 100 uL. Automation needs things to be scaled up. Special pipetting techniques can help with viscous and low volumes.

l. Has anybody done buffer exchange on automated platforms? No, not really. Trying to explore that. Unchained labs is working on it but their platform take ~1 hr at room temp which is unacceptable. Do you use a molecular weight filter for BE? Yes, 10k and 30k filters. Have you tried using a plate based molecular weight based filter? Haven't found one that works. What do you do right now? Use small tubes by hand. Is a rate limiting factor.

2) What automation platforms are currently available and widely utilized in the industry? Are these systems/processes in place qualified or validated?

a. Biomech, Tecan.

b. Maurice = IEF sample prep with 96 well plate. Will do IEF introduction onboard for you.

c. P800 gold standard for IEF at Amgen.

d. Do you use a lot of onboard mixing? Manual mixing is faster than automated onboard mixing.

3) How can automation improve the throughput in a lab? Is it beneficial to focus in RD vs. commercial manufacturing?

a. Do you have a lot of samples in QC? Yes – routine lab testing – 3-4 thousand samples a month on the CE & LC – 25-30 CE-Beckmans running nonstop

b. Commercial manufacturing has more hurdles b/c you have to rigorously validate the instrumentation

c. When you test using plates are the gel buffers also run in plates? Still use vials but Sciex just came up with a plate method for p800 and the Biomech.

d. Automation is focused on R&D, not QC? Yes, places are just starting to look into automation.

e. Do you prefer an internal team or for the vendors to develop automation methods for the front-end? Both, internal teams working with the vendors.

4) What are the challenges of implementing these automated systems in CROs/CMOs vs. big biotech/pharmaceutical companies?

a. Funding. Smaller companies don't often have the money. They often have older equipment.

b. Is the expectation that CRO/CMOs will use automation for outsourcing or tech transfer? Depends on the scope of the project. If the procedure is working without automation then there's no need to evaluate it.

c. How do you manage different individuals manually doing experiments? Both parties have to agree to developed procedures. And both parties have to agree that they have the expertise.

5) Are there any disadvantages in automating CE? Is the cost of automation worth the investment?

a. Automation isn't as fast as manual preparation. But, automation allows analysts to multi-task.

b. Does the technician also have to create the method? There are typically engineers/automation teams that write the methods/scripts.

c. Everyday use justifies the cost of the expensive equipment/instrument.

d. AssayMap Bravo saves time as an automated method for purification.

6) Misc.

a. Want buffer exchange automation.

b. Is there a reason why there isn't a standardized instrument/platform, as opposed to using a variation of different instruments from different manufacturers? Don't want to have only one system in case it breaks. Variation allows robustness. Also, we want to compare the instruments to determine the best for the job.

c. Is there a possibility of coupling the liquid handlers to the CEs? Customers are split on whether they want this. They are working on a platform that does this, but it's not ready yet.

d. Protein Simple ICE instrument has robotic arm capability – automated sample prep to ICE instrument integration (for IEF). How do you do that? It's a robotic arm that takes samples from prep and go right to ice 96 well plate slot – then onboard mixing of IEF component. Software recognizes incoming plate command.