

Alturas Advisor

FALL WINTER 2015-16

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Crystal City VI: Assay Criteria and Level of Validation Required for Biomarkers Will Depend Upon the Intended Purpose of the Assay

By Jennifer Zimmer, Ph.D.

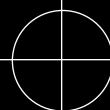
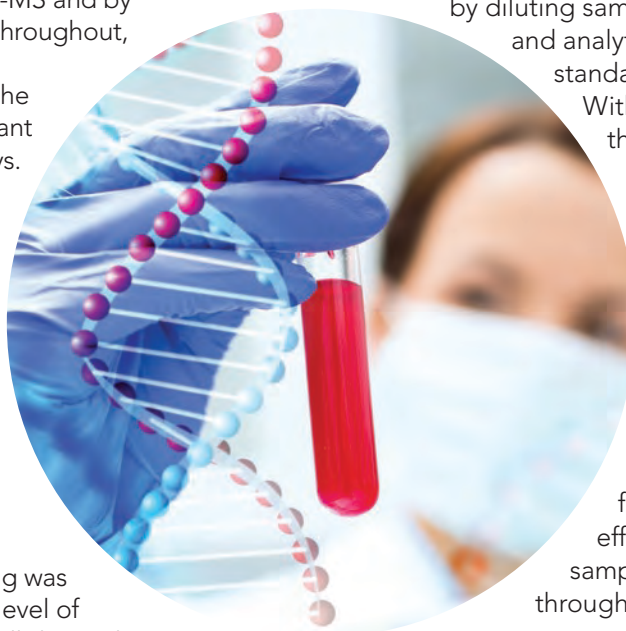
At the AAPS-FDA Crystal City VI meeting, regulators and industry gathered to discuss the draft bioanalytical method validation guidance and how it relates to the assay of biomarkers, both by LC-MS and by immunoassay. One thing was clear throughout, biomarker assays are not PK assays; however, some of the tests used in the validation of PK assays are still relevant for the validation of biomarker assays. In addition, there is a wealth of knowledge that has been gathered over the last 25 years by the clinical chemistry community who operate under CLIA guidelines. While CLIA may not be entirely applicable to the bioanalytical validation of biomarker assays, there are portions of the CLIA regulations that can be adapted for use in this purpose.

The overall consensus at the meeting was that the assay criteria as well as the level of validation required for biomarkers will depend upon the intended purpose of the assay. The acceptance criteria for biomarker assays will not be as prescriptive as the criteria for PK assays and should take into account the biology of the biomarker, ensuring the assay can measure with precision any biologically relevant changes between disease and normal and/or between treatment groups.

In order to demonstrate assay performance, the following should be evaluated: precision, sensitivity, assay range, relative (or absolute, if possible) accuracy, parallelism and sample stability. The measurement of precision, sensitivity and assay range for biomarker assays does not vary much from the measurement of these parameters in the PK realm. As absolute accuracy is not possible without a true reference standard, most biomarker assays will rely upon relative accuracy. Parallelism is imperative to understanding the performance of your biomarker assay. In order to demonstrate parallelism, the response curve generated by diluting samples of the endogenous matrix and analyte should be parallel to the standard concentration response curve.

Without a true reference standard that allows the creation of spiked standards that represent incurred samples, determining short-term and long-term stability becomes more challenging because there is no nominal concentration against which to measure. In addition, measuring a true $t=0$ timepoint presents a challenge when there is limited availability of fresh samples; regardless, best efforts must be made to assess sample stability from collection through analysis.

Once the biomarker assay has been sufficiently validated, the validation reports should go into much more descriptive detail than a typical PK validation report in order to allow the FDA reviewer to verify that the assay performance allows the validated assay to measure relevant changes in the disease biomarker.





STAFF PROFILE:

Ryan Collins

Congratulate Ryan Collins on his promotion to Senior Scientist at Alturas Analytics! Ryan's degree from the University of Idaho in Chemistry, with a Minor in English, Writing Emphasis, and his clear communications and professional demeanor landed him a position as Technical Writer with Alturas Analytics in 2008. He has been a valuable member of the team ever since. In 2009 Ryan joined the laboratory operations team first as Archivist then Sample Custodian, before advancing through Scientist positions of increasing responsibility, gaining valuable technical skills. Having held a variety of positions in the company gives him insights and the experience necessary for interfacing with clients on all technical aspects of a study as Study Director and Principal Investigator.

Ryan's acquired skills in the operation of LC-MS/MS and GC-MS/MS systems have contributed greatly to overall productivity of regulated analysis as well as to rapid development of complicated methods. He has a knack for instrumentation, understands compliance and the importance of timelines, and has the respect among peers and the scientists on his team. Ryan's commitment to scientific integrity and his attention to detail is a great match with the Alturas Way and key to his sustained success with the company. As his experience deepens with new responsibility, so will his influence on the direction of Alturas to meet company goals into the next decade.

From Boise, Idaho, Ryan enjoys backpacking, whitewater rafting, and fly fishing; basically reveling in northern Idaho's beauty in any way he can. He is also a huge baseball fan and an avid supporter of the Seattle Mariners. We hope you have the distinctly delightful experience of meeting and working with Ryan Collins if you have not had the opportunity to do so.

Biomarkers and Personalized Medicine in the Palm of Your Hand

By Shane Needham, Ph.D.

Recently, Shane Needham, Ph.D., Co-founder and Laboratory Director at Alturas Analytics, Inc. gave a plenary lecture at CPSA Brasil entitled, "Analytical Technology: From the Analytical Chemistry Bench Straight Results to Patients: Is This Really True?" The presentation focused on the development of analytical devices to measure biomarkers for diagnostic and maintenance phase of disease. Although biomarkers are important diagnostic tests, history shows us that giving the patient tools to monitor biomarkers real-time produces the best outcomes for personalized health management.

A role of the analytical chemist is to develop instruments and assays that will allow real-time monitoring of biomarkers. Examples of real-time monitoring devices developed by analytical chemists include pulse oximeters

(continued on next page)

Outreach 2015-16

Clinical & Pharmaceutical Solutions through Analysis (CPSA) Brasil

Plenary Speaker: Shane Needham, Ph.D.

Co-founder & Laboratory Director

"Analytical Technology: From the Analytical Chemistry Bench Straight Results to Physicians: Is This Really True?"

August 3 - 5, 2015

São Paulo, Brasil

11th Annual Applied Pharmaceutical Analysis (APA)

Silver Sponsor

September 14 - 16

Cambridge, MA

AAPS Workshop on Crystal City VI:

BMV for Biomarkers

Attending

September 28 - 29, 2015

Baltimore, MD

Clinical & Pharmaceutical Solutions through Analysis (CPSA) USA

Symposium Sponsor

Getting Medicines to Patients Faster by Eliminating the Bottlenecks in Drug Discovery and Development

October 5 - 8, 2015

Sheraton Bucks County Hotel, Langhorne, PA

and blood glucose meters. The pulse oximeter is a spectrophotometer device that fits on the tip of your finger and is commonly used in the ER and now by pilots, asthmatics and athletes to determine oxygen levels in their blood. Blood glucose meters are hand-held electrochemical measurement instruments to determine the levels of glucose in blood. These devices are commonly used by Type I and Type II diabetics to ensure healthy levels of glucose in their system. Athletes are now using blood glucose meters to correlate performance and blood glucose levels. Both of these devices are widely available without a prescription for <\$50.

As the population has seen the expansive use of hand-held devices to measure biomarkers in real-time by the patient: scientists, researchers, athletes, coaches et. al. also see the potential for hand-held devices that would monitor other biomarkers or therapeutics in real-time. Major sports franchises are looking at measurement of biomarkers to determine when to rest, feed and play an athlete. Can major injuries be minimized if biomarkers exist to know how many pitches a pitcher can throw before they may be "overtraining"? Is there a real-time biomarker available for coaches, to determine if an

athlete has suffered a concussion? Are there biomarkers to measure if an athlete is more prone to broken bones, ACL tears or muscle sprains? Of course, once tools are developed for a special population (i.e. athletes), the devices are generally mass produced and marketed to the general population.

Imagine a hand-held device that could measure a patient's thyroid hormone levels real-time as they are treated for hyperthyroidism or hypothyroidism instead of having to go to a clinic for a blood draw or send in a dried blood sample. Imagine a hand-held device that could monitor a patient's liver function during long-term treatment with statin drugs without having to go to a clinic for testing every 3-6 months. Imagine a hand-held device that could test a patient's renal function while under sustained treatment for a chronic fungus. Now imagine this device being your smart phone and being able to test for all of the above biomarkers and others with just the update of an App. We call this device, "Smart Phone Analytics", and its development is closer than you think.

Stay tuned for our next article of "Smart Phone Analytics: The Hand Held Device for Personalized Medicine".

International Society for the Study of Xenobiotics (ISSX) 2015 North American Annual Meeting

Exhibiting- Booth #502

Poster: "Performance of a Selective Method for Quantitation of Midazolam & its Metabolite, Developed to Monitor Drug-Drug Interactions In the Presence of Coadministered Drugs"

Presented by Sarah Vukelich, Associate Scientist

October 18 - 22, 2015

Hilton Orlando Bonnet Creek Resort, Orlando, FL

6th Annual World ADC

Panelist: Shane Needham, Ph.D.

Co-founder & Laboratory Director

Workshop Thursday, 1:00 – 4:00

"Preclinical & Clinical Assay Development for Improving ADC Understanding"

October 19 - 22, 2015

Sheraton San Diego Hotel & Marina, San Diego, CA

American Association of Pharmaceutical Scientists (AAPS) Annual Meeting & Exposition

Exhibiting - Booth #1155

October 25 - 29, 2015

Orlando Convention Center, Orlando, FL

American College of Toxicology (ACTox) Annual Meeting

Silver Sponsor

Symposium Session, Tuesday 2:00 - 5:00

"Applied Toxicology Workshop: GLP Issues"

November 8 - 11, 2015

Red Rock Resort, Summerlin, NV

American Society for Clinical Pharmacology and Therapeutics (ASCPT)

Attending

March 8 - 12, 2016

Hilton Bayfront, San Diego, CA

10th Workshop on Recent Issues in Bioanalysis (WRIB)

Silver Sponsor

April 18 - 22, 2016

Hilton Orlando Lake Buena Vista, Orlando, FL

2016 AAPS National Biotechnology Conference (NBC)

Exhibiting

May 16 - 18, 2016

Sheraton Boston Hotel, Boston, MA

64th ASMS Conference on Mass Spectrometry and Allied Topics

Presenting

June 5 - 9, 2016

Henry B. González Convention Center, San Antonio, TX

A MESSAGE FROM THE FOUNDERS

When Robin and I started Alturas Analytics, we wanted to push the boundaries of bioanalytical methods and applications in MS/MS. We had a vision of building an enduring company that would help pharmaceutical companies get their life-saving breakthrough therapeutics to market sooner. We had a vision to create a company that would be responsive and innovative, with a commitment to unmatched, quality science and scientific research, while delivering an excellent client experience. Now, fifteen years later, I look at the outstanding company we have created and I feel grateful. To all the sponsors we have collaborated with, and to all future sponsors, I'm pleased to say we are still pushing boundaries, accelerating breakthroughs, contributing to quality research, and delivering an excellent client experience. I sincerely appreciate every opportunity to work with our sponsors to ultimately cure disease and enhance life.

Sincerely,



Shane Needham, Ph.D., Co-Founder



Alturas Analytics is growing! Our commitment to push boundaries and deliver an excellent customer experience has yielded strong, well-managed growth. We are constantly enhancing our business model so we can continue to do what we do best: provide personalized service and quality MS/MS bioanalysis to help cure disease and enhance life. We have made improvements to our systems and processes to allow for expansion and meet long-term goals while maintaining focus on overall quality. In 2015, we have enlarged our laboratory space and facilities, hired additional staff, and created positions such as dedicated Project Coordinators to manage timelines and monitor efficiency in our workflow.

Unlike public companies whose primary responsibility is to their shareholders, our priority is to our sponsors, building rapport that encourages collaborative partnerships and mutual loyalty. Being privately-owned also allows us the freedom to embrace innovation in our approach to scientific challenges. I am proud to say we will continue to uphold our high standards to provide you with reliable scientific data to support your programs well into the future.

Thank you for choosing Alturas Analytics.

Deepest Regards,



Robin Woods, President, Co-Founder

The LC/MS Experts™

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