

# Speaker Abstracts of the Society of Quality Assurance 26th Annual Meeting, Cincinnati, Ohio, USA 25 – 30 April 2010

A-1

## A Risk-Based Approach to Auditing Laboratory Processes That Includes Electronic Systems

Guy Inman, Maria Samuel, Terri Cronin, Susan Meeker  
*Gilead Sciences, Inc., Durham, North Carolina, United States*

With the increasing number of data collection systems and computerized equipment in use, the Quality Assurance auditor will most likely encounter some type of electronic record and/or electronic system during their in-process inspection, facility inspection, system inspection, or data audit. It is important for the auditor to have a general overview of the process and how the electronic system is utilized within that process. Because every step of a process is typically not susceptible to error to the same degree, the quality audit should focus on the steps in the process where error is most likely to occur.

We have developed an auditing tool that assists the Quality Assurance auditor in preparing to conduct an audit of any process that includes an electronic system. The auditing tool guides the auditor in identifying the process steps, controls, types of records, and compliance concerns in order to risk-rank the process steps. The quality audit can then be focused on the higher risk process steps where errors are more likely to happen.

In this presentation, the approach to auditing processes that include electronic systems will be discussed, and then we will walk through this auditing approach using an example from a laboratory process.

**Keywords:** Quality Assurance, Auditing

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

A-2

## Towards Establishing Good Practice in the Use of Computer Prediction

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Recent developments in national and international legislation encourage the submission of computer predictions to support registration applications, in order to reduce dependency on animal experiments, but there are no formal, recommended procedures for using computer methods. Serious mistakes were made in the use of animal and *in vitro* study data for registration purposes before the introduction of Good Laboratory Practice (GLP). We need to develop procedures for good practice in the use of computer prediction and we should not wait until problems start to arise. The Organisation for Economic Cooperation and Development (OECD) has issued guidelines for evaluating prediction models which provide a good foundation. Procedures need to be developed to ensure that the OECD requirements are met, and to ensure that appropriate audit trails are in place. Proposals will be presented in the talk on what kinds of procedures might be used and how they might be developed and introduced in practical and political terms. The primary aim of the talk will be to stimulate debate and initiate ongoing action, rather than to present finished solutions.

**Keywords:** Computer Validation, Quality Standards, Computer Prediction

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

### B-1

#### Good Laboratory Practice Program Update from FDA's Center for Devices and Radiological Health

Chrissy Cochran (invited), Linda Godfrey  
*Food and Drug Administration, Center for Devices and Radiological Health, Silver Spring, Maryland, United States*

This presentation will provide an update to meeting attendees on the FDA's Center for Devices and Radiological Health (CDRH) good laboratory practice program. Discussion will focus on the current status of the program and where the program will be heading. Topics will include when inspections will be issued, the focus of inspections, current inspections, observations and lessons learned.

**Keywords:** Medical Devices, Good Laboratory Practice (GLP)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

### C-1

#### Thinking Outside the GLP 'Box' – Regulatory Concerns for Non-Standard Study Designs

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The FDA GLPs were written to define the regulatory requirements for conducting non-clinical research. The language in the regulations is

most easily understood in the context of standard toxicity studies. However, the regulations also apply to other types of non-clinical studies such as immunohistochemistry, tissue cross-reactivity, medical device, electron microscopy, and others where the requirements may not be easily translated into these study designs. These other types of studies require deep understanding of the regulations in order to assure compliance.

The goal of the presentation will be to discuss the potential regulatory concerns encompassing these various study designs and how those concerns might be adequately addressed in a GLP-compliant manner both prior to study initiation and throughout the course of study conduct (i.e. protocol requirements, facility requirements, SOPs, etc.). For example, in regard to tissue cross-reactivity studies, analysis of test and control article concentration and uniformity within the carrier is not conducted as specified under GLP regulations as no sufficient method has been determined which can accurately determine the concentration of the test and control articles under the conditions and carriers used in the assay. This particular regulatory requirement can be noted as an exception within the protocol and reiterated in the final report. An additional example may include a protocol requirement for digital imaging or histomorphometric analysis within a study. In this case, it's important to ensure that images are taken and any analysis is performed using validated systems and equipment.

Various study types will be addressed. As this presentation will allow the floor to be opened for discussion of experiences other auditors may have had in trying to get these and other 'outside the box' types of studies to fit the mold of GLP compliance, audience participation will be solicited.

**Keywords:** Preclinical Research (GLP), Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## D-1

**GCP Mock Inspections: Real Experiences of a Fake Inspector**

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*Verdandi AG, Zurich, Switzerland*

GCP inspections have become a reality for many companies and investigator sites. Over the years, the number and scope of inspections have increased considerably with many GCP inspectorates scrutinizing clinical trials at investigators, sponsors and CROs. To prepare for inspections, sponsors and CROs have developed inspection preparedness programs, many of which include GCP mock inspections.

Simulating a real inspection, such mock inspections are used to identify deficiencies and areas of weaknesses before being detected in a real regulatory inspection, to offer an opportunity to test the SOP on regulatory inspections, to train being interviewed by inspectors and to prepare and manage an inspection.

The presentation will discuss the experiences made as a GCP Mock Inspector for almost 10 years. Mock inspections were conducted at sponsors, CROs (across all functional areas) and investigator sites. The following questions will be answered:

- Behaving like an inspector: get real, but how much?
- Mock inspection process from announcement to report: what can go wrong?
- GCP systems audits vs. GCP mock inspections: only a semantic difference?
- Mock inspections as preparation for real inspections: what makes them successful?

And last but not least, the talk will finish with case studies from 'real mock inspections' and critically discuss the benefits and limits of GCP mock inspections.

**Keywords:** Clinical Research (GCP), Audit/Inspection

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## D-2

Abstract withdrawn by author.

## E-1

**Comparisons between Human and Animal GCP Auditing**

Marci Murphy, Kim Swisher, Paritosh Lamba  
*Boehringer Ingelheim, Saint Joseph, Missouri, United States*

What drives the requirements necessary for a GCP trial? Identifying these reasons highlights the differences and similarities that exist in Human and Animal GCP auditing. We start by looking back into the history of the FDA and regulations for clinical trials. Both human and animal drugs were regulated by the Pure Food and Drugs Act passed by Congress in 1906. In 1938 the Food, Drug and Cosmetic Act (the Act) was passed which required drugs (both human and animal) to be safe before marketing. Per Kefauver-Harris Amendments (1962) new drug could not be marketed without FDA approval based on convincing evidence of safety and efficacy. This law included the requirement to obtain an informed consent from the patients participating in clinical trials and reporting of adverse drug reactions to the FDA. Informed consent must be obtained both from subjects (human) and from owners (animal) before participating in a trial.

Since 1968, the Act has included provisions designed to ensure that animal drugs are safe and effective for their intended uses and do not result in unsafe residues in foods. Currently the FDA's Center for Veterinary Medicine (CVM) is responsible for ensuring these provisions.

In 1974 institutional review boards were instituted as a mechanism to ensure the protection of human subjects in research. In May 1980 the FDA regulations for human informed consent were codified in 21 CFR Part 50. In January 1981 the FDA regulations which set forth provisions for institutional review boards was codified in 21 CFR Part 56.

In 1985 the Improved Standards for Laboratory Animals Act was passed that mandated the establishment of Institutional Animal Care and Use Committees (IACUC) to oversee animal care and use (similar to IRB on human side).

As pharmaceutical industry became more global the need for harmonization of regulations to ensure the safety, quality and efficacy of medicines was identified. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) first met in April of 1990 and the International Corporation on Harmonization of Technical Requirements for Registration of Veterinary Medical Products (VICH) in April of 1996. The objectives of both groups are similar which bring together representatives from three regions (United States, Europe and Japan) to establish and implement common guidelines.

The regulations for clinical trials have evolved similarly for both human and animal drugs. The requirements diverge in the details. Clinical trials for humans have more regulations to protect their legal right which in turn creates more documentation to ensure that protection. The last half of the presentation we have set up a panel of GCP monitors experienced in both animal clinical trials and human clinical trials to discuss the similarities and differences in applying the regulations to auditing a study.

**Keywords:** Animal Health, Clinical Research (GCP), Good Clinical Practice (GCP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

F-1

#### Electronic Records – Perspectives from FDA and Industry

Monica J Cahilly<sup>1</sup>, Robert D Tollefsen<sup>2</sup> (invited)

<sup>1</sup>*Green Mountain Quality Assurance, LLC, Warren, Vermont, United States*, <sup>2</sup>*FDA, Division of Field Investigations, Bothell, Washington, United States*

The use of electronic records has become increasingly common in a variety of regulated research settings (e.g. human and animal clinical trials, non-clinical laboratory studies), but the degree to which they are incorporated into the conduct of a study varies widely from site to site. In this session, an experienced industry consultant and FDA representative (invited) will provide insights into new perspectives on 21 CFR Part 11, common findings during inspections, and guidance on ways to assure the integrity of electronic data and maintain compliance of computerized systems and automated operations in a variety of settings.

**Keywords:** 21 CFR Part 11, Electronic Data/Compliance

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

G-1

#### Starting from Scratch – Designing the Startup Quality System

Howard Cooper

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The opportunity to design a quality system from scratch offers great rewards in experiencing and understanding the functions of quality systems. For me, this ‘dream’ of building the ‘perfect quality system’ began during my early quality management days when I experienced quality system successes and failures. I learned from these experiences and thought, ‘If only I could set up my own system.’

Finally, the opportunity to design and implement a combination pharmaceutical and medical device quality system from scratch was given to me. Since this first experience, I have designed and implemented several quality systems (including virtual) that resulted in successful preapproval inspections. I have also revamped failing quality systems to make them compliant and more effective.

As you can imagine, starting from scratch and revamping failing systems is hard work, but the experience and knowledge gained is extremely valuable. The relationships built, both positive and negative, will last forever. I want to share these experiences with you so that you may gain insight about the hard work, expectations, pitfalls, and the rewards of starting a system from scratch.

1. Starting out – the first steps.
2. Staffing is key to success & training makes it happen.
3. Virtual? Brick & Mortar? Hybrid? ‘Green Field?’ ‘Building Modification?’
4. Working with outside contractors in designing the facility.
5. Establishing and managing the document change control system.
6. Coordinating activities with Regulatory Affairs in the approval process.
7. Importance of user requirements & specifications in equipment design.
8. Supplier/contractor qualification and materials control.
9. Do not forget the laboratory.
10. Commissioning & qualifying the facility.
11. Scaling up, and trial runs to Process Validation.
12. The pre-approval inspection.
13. Showstoppers.
14. The internal audit – maintaining and improving the system.

**Keywords:** Manufacturing (GMP), 21 CFR Part 11

**Level:** Advanced (In-depth review of topic).

G-2

### What is the Impact of Work Relationships in Your Company?

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It’s not just ‘touchy-feely stuff’ when poor working relationships delay batch record review, final product release, necessary equipment and facility changes or final approval of SOPs. How do you identify the most important characteristics in developing and maintaining productive relationships between QA, QC and Manufacturing in your company? What is the role of senior management in assuring these relationships are maintained? What practical and measurable steps can you take to overcome the hurdles to shorten approval, implementation and release times in an ethical and compliant manner? What can you implement that will support each group fulfilling their GMP responsibilities as required by 21 CFR 211?

You will learn what other QA, QC and Manufacturing managers and directors have found to be critical characteristics of the development and maintenance of productive relationships, such as consistency and open communication; steps to take to identify and overcome hurdles, such as answering the ‘Five Whys;’ how to identify and address priorities together by treating specific issues instead of generalities; how to avoid the erosion of these relationships; what to do if you find yourself in a toxic environment and how to understand the responsibilities of and challenges faced by each other’s work group with Team Building events.

**Keywords:** Manufacturing (GMP), Quality Assurance

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

H-1

### An Expatriate’s View of China

Jim Carignan

Carignan Consulting, LLC, Washington DC, United States

Have you have ever considered employment or business opportunities in China? If so, this

session will provide valuable insight from an American's perspective.

With the current trend of outsourcing pre-clinical work, Asian countries are being considered more than ever. Whether to accept employment or outsource work to one of those countries is a very important decision that should take into consideration many factors beyond the obvious regulatory issues.

This session will address the social and business climate in China from an expatriate's viewpoint. It will address the capabilities of companies in China to meeting global expectations for regulatory compliance. It will also introduce the attendees to the SFDA (China's FDA) GLP requirements from that same expatriate's perspective.

This intermediate level program will introduce the attendees to the Chinese GLP certification program and GLP requirements. It will provide a basic understanding of the regulatory environment as compared to the FDA GLPs and be a valuable tool for people or companies considering future endeavors in this rapidly developing 'preclinical' country.

**Keywords:** Preclinical Research (GLP), Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## H-2

**An Update on Health Canada's Initiative to Establish a GLP Monitoring Authority (GLP-MA)**  
Paul Sidney

*Charles River Laboratories Preclinical Services Montreal Inc, Senneville, Quebec, Canada*

Health Canada signed an agreement on June 22, 2009 with the Standards Council of Canada to act as their GLP-MA for Therapeutic Products. Health Canada's initiative to establish a GLP Monitoring Authority has been tabled in a Guidance document published August 2009. As an OECD member state,

Canada has an obligation to establish a Monitoring Authority to ensure non-clinical safety studies, conducted in compliance with the OECD GLP Principles, will be accepted internationally. This presentation will include a brief history of Health Canada's efforts to establish a GLP-MA, an overview of Canada's GLP programs, OECD Member state feedback on the status of Health Canada's OECD obligations, key organizations involved in the establishment of a GLP Monitoring Authority in 2009, a review of key items noted in the Guidance published by Health Canada on the Sponsors' obligations to conduct non-clinical safety studies in accordance with the OECD GLP Principles. A brief account of the implementation milestones of GLP monitoring program to date.

**Keywords:** Preclinical Research (GLP), Health Canada

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## I-1

**Transfer of Responsibility Does Not Mean Transfer of Accountability**

Celine Clive

*Polaris Compliance Consultants.com, Cary, North Carolina, United States*

Outsourced services are becoming common in numerous aspects of drug development. Many people are relying heavily on the companies they hire for critical aspects of their trials. Although some may perform vendor qualification audits, many are inappropriately confident in the skills of the vendors and neglect to be vigilant about following up on the actual conduct of the outsourced task. This presentation will look at the traditional model vs. virtual models of outsourcing; will provide examples of problems that can arise; and will offer suggestions for how the delegating company can prevent problems. The audience will gain an understanding that even though a Transfer of

Responsibility document is in place with vendors, that responsibility is not deferred and additional quality assurance is needed.

**Keywords:** Clinical Research (GCP), Quality Assurance, Outsourcing

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

I-2

### Who's in Charge? Managing Your Trial in the Outsourced World

Lisa Olson

*13, Cary, North Carolina, United States*

The conduct of clinical trials continues to make use of more and more outsourced services. This presentation will review the division of responsibilities between organizations involved in clinical research and the various vendors it may use. Considerations go beyond the vendor audit and must incorporate a collaborative working relationship before and during the trial, without leaving areas to chance. Examples will be drawn from vendors such as EDC (electronic data capture), clinical labs, IVRS (interactive voice response systems), imaging, drug suppliers and electronic patient diaries. The presentation will address areas such as:

- Definition and verification of study requirements.
- Interactions between sponsors, CROs, investigator sites, and other suppliers.
- Provision of authorized access to supplier systems.
- Provision of equipment.
- Verification of data 'movement' (data transfers).
- Ongoing support during the study.
- Changes during the trial.

**Supplier audits – when, why?** The audience will obtain an understanding of issues to consider when working with a vendor, to further the success of the trial. Although examples will be drawn from the clinical research world, the concepts are relevant to other GXP areas.

**Keywords:** Quality Assurance, Outsourcing

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

J-1

### Train the Trainer – Learn the Basics for Implementing an Effective 'Train the Trainer Program'

Cheryl McCarthy<sup>1</sup>, Michele Weitz<sup>2</sup>, Josephine Scrofani<sup>1</sup>

<sup>1</sup>*Clinical Solutions, Mansfield, Massachusetts, United States*, <sup>2</sup>*Independent Consultant, San Francisco, California, United States*

Members of the Beyond Compliance Specialty Section (BCSS) are presenting this session on presentation skills and 'Train the Trainer' concepts to highlight some of the soft skills needed to implement this type of program. Using the Speaking-Presenting-Teaching (SPT) model, we will discuss how you can become aware of your skills and learn how to organize and customize presentations to meet your audience's needs. This session will incorporate the SPT model by focusing on these concepts as follows: 1) Speaking – Know Yourself: Focuses on platform skills – including awareness of verbal and non-verbal behaviors 2) Presenting – Know Your Content: Discusses the content Roadmap – focusing on how to organize and internalize content in order to communicate it effectively to the learners and 3) Teaching – Know Your Audience: Reviews audience interaction – demonstrating ways to engage and 'read' the learners in order to ensure understanding.

This interactive session provides the foundation for understanding and implementing these concepts. Presenters have experience in adult learning theory, soft skill training and effective training methodologies that will be incorporated into this session.

**Keywords:** Personal Development/Training, Education/Training

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## K-1

**Animal Health Regulatory Update**

Elizabeth Luddy (invited)

*US Food and Drug Administration Center for Veterinary Medicine, Rockville, Maryland, United States*

All sponsor and CRO personnel involved in studies submitted to FDA in support of veterinary product approvals have an interest in seeing that the studies are properly designed, conducted, reported and submitted. In this session an experienced CVM reviewer will give their perspective on how to make quality submissions to CVM including: protocol reviews, technical section submissions and End Review Amendments. This session will also talk about common issues encountered by companion animal and large animal reviewers and biostatisticians at various stages of the review process and how you can help us achieve our goal of one-cycle review. This session will also provide a behind the scenes look at the review process in CVM, to include staff training, inspection requests, and communication with CVM staff.

**Keywords:** Animal Health, Submissions/Reviews

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## L-1

**Implementing Agile Software Development Methodology for Regulated Computerized Systems**

Patricia Miller

*SAS Institute, Cary, North Carolina, United States*

Agile Software Development methodology provides an efficient way to develop software solutions that is more intuitive to developers and testers than the traditional waterfall methodology, but it requires a different understanding of how to manage and document the development of the software product. This presenta-

tion presents the lessons learned when one group of R&D developers implemented agile development for potentially regulated systems.

**Keywords:** Computer Validation, Computer System

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## L-2

**Building an Effective Computer Systems Audit Program**

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Building an effective computer systems compliance audit function can be a challenge for a variety of reasons. On the one hand, the technical domain ranges widely from software design and development, to testing, to various elements of system administration (database to security). Obtaining even the most rudimentary expertise in all areas can be daunting. Layered on top of the technical domain are the rather nebulous regulatory expectations. While regulations are few (211.68, Part 11, 58.130e), guidelines are many. The domain of computer systems auditing within an FDA/EMEA regulated environment is characterized by few explicit regulations and a plethora of guidelines (both regulatory and industry). This disparity has led to a dissemination of interpretations that rivals the hermeneutics of biblical texts.

In this overview of computer system compliance, I describe the 'evolutionary' (or perhaps trial and error) process by which Genentech developed a computer system compliance program and share some tools and methods used to separate the compliance shaft from the wheat. I provide the audience with a brief overview of CS compliance history and a brief sampling of the various models that we have developed to make sense (i.e. structure) of this universe.

**Keywords:** Computer Validation, Computer System, Auditing

**Level:** Basic (Suitable for professionals with less than 2 years experience).

M-1

**Evaluation and Recommendations on Good Clinical Laboratory Practice (GCLP) Guidelines for Phase I–III HIV Vaccine Clinical Trials**

Marcella Sarzotti-Kelsoe<sup>1</sup>, Josephine Cox<sup>2</sup>, Naana Cleland<sup>3</sup>, Thomas Denny<sup>4</sup>, John Hural<sup>5</sup>, Leila K Needham<sup>1,4</sup>, Daniel Ozaki<sup>1</sup>, Isaac R Rodriguez-Chavez<sup>6</sup>, Gwynneth Stevens<sup>7</sup>, Timothy Stiles<sup>8</sup>, Tony Tarragona-Fiol<sup>9</sup>, Anita Simkins<sup>10</sup>

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The Global HIV Vaccine Enterprise created a worldwide alliance of independent organizations dedicated to the development of preventive HIV vaccines. Global clinical laboratory work performed under harmonized operations is a central component for the successful conduct of Phase I–III HIV vaccine clinical trials. In an effort to harmonize international laboratory operations, the British Association of

Research Quality Assurance produced GCLP guidelines. Subsequently, the Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health expanded the existing knowledge on GCLP standards by publishing guidelines on GCLP with increased implementation guidance. Although both of these GCLP approaches ensure that laboratory results from multiple clinical laboratories conducting safety, diagnostic and endpoint assays are reliable, repeatable, auditable, and comparable, they differ in the interpretation of few critical GCLP elements: training, auditing/accreditation, assay validation, and proficiency testing. These elements represent crucial stages in the conduct of GCLP-compliant studies performed by clinical laboratories: from the general set-up (training of personnel and assay validation) through assay conduction and laboratory oversight (audits, proficiency testing and accreditation). A Workshop was organized to bring together for the first time experts on GCLP to review and discuss the GCLP elements listed above and to harmonize the two main GCLP approaches into a single set of recommendations that can be followed by laboratories in the HIV field and in other scientific and medical fields. The authors reached general consensus on three out of the four GCLP elements described above, except for the issue of GCLP laboratory accreditation. GCLP accreditation remains controversial as currently there is not a public internationally available accrediting organization acceptable to all parties involved in clinical trials. The authors wish to raise awareness on the issue of GCLP accreditation and the need to establish a global accrediting body.

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of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract number HHSN272200800014C. The funders had no role in the decision to submit this work or in its preparation.

**Reference:** Sarzotti-Kelsoe M, Cox J, Cleland N, Denny T, Hural J, et al. (2009) Evaluation and Recommendations on Good Clinical Laboratory Practice Guidelines for Phase I–III Clinical Trials. *PLoS Med* 6(5): e1000067. doi:10.1371/journal.pmed.1000067

**Keywords:** University/Academic Research, Good Clinical Laboratory Practice (GCLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

M-2

### A University Case Study: Validate Our Digital Camera System? Say What?!

Sandy Hancock

*Virginia Tech, Blacksburg, Virginia, United States*

The typical university research laboratory now contains a variety of instruments and equipment with embedded, integrated or interfaced computers, which can range from simple spectrophotometers to complex state-of-the-art chromatographic systems. As the use of university scientific expertise in regulatory-compliant collaborations with industry rises, academia must begin to invest the resources necessary to understand and implement validation processes for computerized systems. Commercially available systems comprise the majority of computerized instrumentation and equipment used in the university laboratory, so a traditional system life cycle approach to validation may not be practical or cost-effective. The decision to validate a system and the extent of the validation must be carefully balanced in a university environment so that regulatory compliance requirements can be met and the timelines and

budgets of other active research efforts are not compromised.

For many years, the Laboratory for Neurotoxicity Studies (LNS) in the Virginia Tech College of Veterinary Medicine has had an active relationship with industry, performing specialized neuropathology that supports studies compliant with GLP regulations. And for many years, the laboratory has successfully managed to steer clear of the use of computerized systems in its regulatory-compliant work and avoided the uncertainty of the computer validation process. Even with the narrow technical scope of structural and ultrastructural neuropathology, it is impossible to remain on the cutting edge of research techniques without purchasing computer-interfaced equipment. With the purchase of a simple commercial digital camera system, the laboratory found it necessary to confront the validation process.

This presentation will describe the journey taken by LNS to bring a simple digital camera and its software into the validated state for use in GLP-compliant work. A comparison will be made between the routine university procedures for equipment procurement, implementation, use and maintenance and the rigorous processes and formal terminology that comprise a modified system life cycle approach to validation of a computerized system. Although equipment purchase at the university follows deliberate steps, with attention to cost, availability, space allocation, vendor reputation and on-site demonstrations, the process is often not well documented. Likewise, there is minimal recordkeeping for the installation of newly purchased equipment, training of operators or testing of equipment to ensure that operates correctly. For the validation process, LNS supplemented traditional university purchasing procedures and followed preplanned steps for the initiation, planning, requirements, testing and release phases of the digital camera system. The presentation will present concrete examples of those steps, including examples of test scripts, documentation guidelines and gaps in the process. As expected, this first effort of the

laboratory to carry out a planned and documented computerized system validation resulted in many 'lessons learned,' which will be highlighted in the presentation. It is hoped that presenting the results of our experience will diminish the learning curve for other university laboratories and demonstrate that it is possible and beneficial to introduce computerized system validation into academic research programs.

**Keywords:** University/Academic Research, Good Laboratory Practice (GLP)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

N-1

**Is It Time to 'Re-FOCUS' Our Audit Process?**  
MaryEllen Lander, Christopher Both, Cheryl Bissey-Black  
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Falcon Consulting Group has had the opportunity to perform numerous 'focused audits' at clinical investigator sites. Our clients developed their Audit Plans in a manner that required compiling information about specific data to be submitted in their New Drug Applications (NDAs). To gather that information we were required to go to the clinical sites with printed datasets to confirm.

There are many challenges when conducting focused audits. Challenges to be discussed in this presentation include learning the techniques for identifying the key areas of focus vs. standard auditing procedures, developing audit tools, adapting to the mindset required to focus on your audit plan objectives, fully understanding client expectations, and knowing when to deviate from the audit plan and dig deeper.

The lessons learned from conducting focused audits included an appreciation of the increased ability to quantify findings based on the larger sample size (generally 100% of subjects for defined dataset), recognition of the higher efficiency obtained when auditing

because of the focus on the key objectives of the clinical trial, insight into project management challenges, identification of essential training requirements and the necessity of consistency in reporting format.

**Keywords:** Clinical Research (GCP), Good Clinical Practice (GCP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

O-1

**GLP Test Substance Characterization: Are You Ready?**

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- Do you know the EPA regulatory requirements for characterization of test substances?
- Are you prepared for characterizing your materials by the GLPs if the FDA implements this requirement as part of its modernization initiative?
- Do you know the responsibilities of the testing facility management, study director, Quality Assurance Unit, and sponsor for test substance characterization?
- Do you know what types of analytical data are expected to be available for the characterization of test substances?
- Are you prepared for an EPA inspection on test substance characterization?
- Do you know what should be included on a Certificate of Analysis (CofA)?

The US EPA's Office of Enforcement and Compliance Assurance (OECA) is responsible for monitoring studies submitted to the Office of Pesticide Programs in support of pesticide

registrations as defined under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). All submitted studies are to be conducted according to the FIFRA US Good Laboratory Practice Standards (GLPs), which contain specific language concerning the characterization of test, control, and reference substances used in these studies.

When the EPA conducts an inspection of a facility and selected studies, the inspection letter clearly defines their expectations in regards to the characterization documentation to be available for any test, control, and reference substance that will be part of the inspection. Is a CoFA adequate? Is a characterization report and/or data needed? What if the sponsor has the records? These questions will be addressed during this session.

During this session we will expand on our Quality Assurance Journal publication (QAJ, 2007, Vol. 11, 196–207) by clarifying and offering problem-solving approaches to meet the GLP requirements and the EPA expectations for the characterization of test substances used during studies. Sponsor, Contract Research Organization, and Study Director Responsibilities will also be discussed.

**Keywords:** Test Article, Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## P-1

### The Regulation of Genetically Engineered Animals

Joseph Cormier (invited)

*US Food and Drug Administration Center for Veterinary Medicine, Rockville, Maryland, United States*

Animal biotechnology has long been an area of research interest. Recently, genetic engineering of animals has moved from theoretical discussions or limited laboratory utilization to

broader use and potential commercialization. To provide structure and guidance to the field as well as to protect the public health, the Food and Drug Administration (FDA) has recently released documents describing our scientific and regulatory approach for genetically engineered (GE) animals. Guidance for Industry #187, Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs, was released January 15, 2009 to clarify the agency's legal and regulatory authorities to regulate recombinant DNA constructs in GE animals, as well as to help industry understand their responsibilities and obligations under the Federal Food, Drug, and Cosmetic Act (FFDCA), and the National Environmental Policy Act (NEPA), as they apply to these animals. This presentation will outline FDA's regulatory approach for GE animals and briefly describe its legal and scientific underpinnings.

**Keywords:** Biotechnology, Transgenics

**Level:** Intermediate (Suitable for professionals with more than 2 years experience.)

## P-2

### Quality Review of Immunogenicity Data

Erica Henderson, Laura McCann, Sandra Fairbanks-McGlynn

*ICON Development Solutions, Whitesboro, New York, United States*

The emerging trend to treat disease by biologic means requires the need for pharmaceutical immunogenicity testing; also known as anti-drug antibody (ADA) testing. With this advancing technology, it has become imperative for pharmaceutical companies and contract research organizations (CRO) to adapt to the changes. Fulfilling government required regulations through Good Laboratory Practices (GLP) and providing a good quality review has become increasingly challenging. This new technology has no exact slot allotted within

the Food and Drug Administration (FDA) regulations and/or Organization for Economic Cooperation and Development (OECD) guidance's. Laboratories are left to implement their own quality policies and procedures by formulating the best fit from existing government guidance documents and regulations. Keeping all this in mind, the importance then lies on the overall procedures adapted by each individual laboratory conducting these types of assays.

I. This basic presentation will outline what is needed to achieve a good quality review of immunogenicity data. Given the complexity of immunogenicity testing and challenges that differ from conventional drug analyses, specific outlines for a quality review should be in place prior to analysis. Quality control procedures, the study protocol, standard operating procedures, validated methods and knowledge of industry standards all play a part in providing quality immunogenicity (ADA) data. Streamlining support systems such as sample tracking, reagents, characterized materials, instrumentation, equipment, and LIMS systems that relate to ADA studies can also be essential.

II. Development of a robust testing methodology for these antibodies requires many steps to verify a specific response characterization. Assay development complexities present a venue for result accuracy confirmation. It is essential that quality control procedures are rigorous and that the Quality Assurance Unit uses all the tools available when conducting an audit, such as, following the audit trail, potential risk assessments, and knowing how to interpret screening, confirmatory, and end point titer data. Quality system monitoring is critical to ensure competitiveness within the immunogenicity testing market.

Our goal is for all attendees to leave this presentation with enough knowledge to audit this emerging technology (immunogenicity) while maintaining a quality review within industry standards.

**Keywords:** Biotechnology, Audit/Inspection

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## Q-1

### **Effectively Auditing LC-MS/MS Raw Data and Understanding It**

Christopher Tudan

*BioAccurate Enterprises Inc., Vancouver, British Columbia, Canada*

The purpose of this presentation is to provide the QA person a scientific perspective using real examples in the interpretation of mass spectrometry-related chromatography, scans, spectra, response measures and method parameters that impact the data. The information is presented in a way that helps the audience understand the science associated with the details defined in the raw data. This will enable the QA inspector to not be overwhelmed but cognizant of the specifics to identify when reviewing MA raw data, including the identification and confirmation of ion transitions, appropriate chromatographic integration, consistent file naming, manual integration, and carryover identification, etc. Specific case studies and raw data examples are used to illustrate data interpretation and the successful implementation of validated method-associated mass spectrometric parameters and passing criteria. A layman's perspective on the science associated with mass spectrometry is also described that will allow the QA reviewer get the picture about what they are looking at. Finally, effective approaches to the technical review of raw data, including the acceptance and rejection of data, will be utilized towards the end of the presentation to cement the points considered earlier in the day.

**Keywords:** Bioanalysis, Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## R-1

**Critical Phase Inspections – How to Get the Most Bang for Your Buck**

Theresa Donegan

*Charles River, Shrewsbury, Massachusetts, United States*

The QAU is responsible for 'inspecting each study at intervals adequate to assure the quality and integrity of the study' but each facility and auditor may do this in a different way. How can you determine what is an appropriate number of critical phase audits for a study? How often do these need to be performed during the course of the study? How much time should be invested in each critical phase inspection: 20 minutes, 1 hour, more? During the inspection, do you need to view the entire procedure or is a portion enough? How do you ensure that a regulator or a sponsor will be in agreement with the approach taken when determining and conducting these? This presentation will discuss one approach for determining and scheduling critical phase inspections for non-clinical studies and subcontracted portions of those studies. It will also include approaches to maximize the quality of your inspection, and detect problems which could affect the quality and integrity of the study data. For more experienced auditors, it will provide tips to freshen up your auditing approach and get you out of the auditing rut that many auditors encounter after performing the same kind of inspections day in and day out.

**Keywords:** Preclinical Research (GLP), Audit/Inspection

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## R-2

**GLP Amendments, Deviations and Unforeseen Circumstances – The Good, the Bad and the Ugly**

Celeste Rose

*RoseTECH Consulting, Painesville, Ohio, United States*

Excursion from established GLP procedures is an area that continues to be problematic for both study personnel and the QA professional. Handling of amendments, deviations and unforeseen circumstances is an ongoing area of confusion, contention and concern. Procedural excursions and unexpected events can be nebulous in nature and many times go unnoticed or unacknowledged by the unwary. Proper documentation of excursions and unexpected events is crucial to the re-constructibility of a GLP study, as well as the quality and compliance of the study report. Improper handling and documentation of these occurrences can impact the integrity of the study. The impact of excursions and unexpected events may be minuscule or consequential, but without recognition and proper documentation thereof, assessment of impact may be impossible. Without awareness of the impact, the study results and conclusions may be flawed.

To complicate matters, there is an innate human aversion to 'uncomfortable' events. Many times there is a perceived association between these occurrences (deviations, excursions, unplanned events) and job performance or competence. The concern of reprimand and retribution is enough to subconsciously persuade an individual to fear attesting to the awareness of such an occurrence. The occurrences may be overlooked or disregarded intentionally or inadvertently, and therefore may not be effectively addressed.

Another quandary lies in the confusion over classification; the definition and distinction between what constitutes an amendment, a deviation or an unusual event or unforeseen circumstance. In order to be properly handled in the GLP study, the event must be appropriately categorized. Clear procedures must then be in place to guide individuals in the follow-up and documentation.

This session 'GLP Amendments, Deviations and Unforeseen Circumstances – The Good, the Bad and the Ugly' presents a practical approach to demystifying the subject and aims to convince study personnel, SD/PI, mgt, sponsors and QA professions of the positive aspects

of proper documentation. The terms Amendments, Deviations, and Unforeseen Circumstances are defined and similarities and differences are compared and contrasted. Strategies for the prevention and/or minimization of the potential for the occurrence of unnecessary excursions are presented. Effective tactics for enhancing proper GLP-compliant documentation and handling of excursions and events are discussed. Approaches to reducing the stigma of excursions are also covered. This session takes a practical approach to this topic by incorporating examples of “real life” instances and resolutions which allow the attendee of the session to immediately relate to the topic and rapidly assimilate the information covered.

**Keywords:** Preclinical Research (GLP), Documentation

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## S-1

### Clinical Regulatory Update

Jean Toth-Allen (invited)  
*US Food and Drug Administration, Rockville, Maryland, United States*

The speaker will provide an update on agency policies, expectations and inspection activities.

**Keywords:** Clinical Research (GCP), Food and Drug Administration, US (FDA)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## S-2

### FDA/EMEA GCP Initiative

Joseph Salewski (invited)  
*US Food and Drug Administration, Silver Spring, Maryland, United States*

During this session, updates on this pilot initiative will be provided.

**Keywords:** Clinical Research (GCP), Food and Drug Administration, US (FDA), Good Clinical Practice (GCP)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## T-1

### Demystifying RQAP

Patricia McFadden<sup>1</sup>, Barbara Randolph<sup>2</sup>, Michelle Holbrook<sup>3</sup>

<sup>1</sup>*The Dial Corporation, Scottsdale, Arizona, United States*, <sup>2</sup>*Biotechnical Services, Mead, Washington, United States*, <sup>3</sup>*Rho, Inc., Chapel Hill, North Carolina, United States*

Are you looking for a way to advance professionally? Join the select group of quality assurance professionals who have achieved the Registered Quality Assurance Professional (RQAP) credential. Let others in the industry know that pursuit of professional excellence is your priority.

Now, do you know what it takes to be an RQAP? Join the Council on Professional Registration (CPR) of the SQA to learn more about this credentialing process. Learn the history of the RQAP exams and the process of how the exams are developed. Learn about the reference lists and how best to prepare for the exams. Which exam is suitable, GLP or GCP? What references do you need to study to pass your exam of choice? The exams are currently offered on paper (limited offerings) and at computer testing centers twice per year; which one is best for you? All aspects of exam administration will be presented.

To those who have passed the RQAP-GLP and RQAP-GCP exams, congratulations!! Now, are you wondering what it takes to maintain your RQAP registration? We will answer questions and demystify the procedure for re-registration. Learn what options are open to

you and which activities can be used for re-registration units. Plenty of time will be devoted to answer questions from attendees.

Come explore the possibilities! Learn all about RQAP registration and get your questions answered!!

**Keyword:** Education/Training

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### U-1

##### EPA/GLP Update

Francisca Liem (invited)

*US Environmental Protection Agency, Washington DC, United States*

The speaker will provide an update on agency policies, expectations and inspection activities.

**Keywords:** Preclinical Research (GLP), Environmental Protection Agency, US (EPA)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### V-1

##### The Use of Electronic Communication in a GXP Environment—an Expert Panel Discussion Session

Richard Siconolfi

*Procter & Gamble Co., Mason, Ohio, United States*

Email correspondences, telephone calls, instant messaging, and maybe even social media sites are creeping into our regulated environment. As these forms of communications increase, their uses tend to blur the lines surrounding regulatory compliance for GLP and GCP studies, and the manufacture of regulated products. This session will attempt to discuss what are the current practices, what are the risks, and

how can we comply as the technology that surrounds us keeps on changing, and changing quickly.

**Keywords:** Computer Validation, Computer System

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### W-1

##### Approaches That Universities Can Use to Introduce Regulatory Compliance and Integrity Issues

Marilyn Marshall<sup>1</sup>, Marcella Sarzotti-Kelsoe<sup>2</sup>

<sup>1</sup>*University of Arizona, Tucson, Arizona, United States,* <sup>2</sup>*Duke University Medical Center, Durham, North Carolina, United States*

Details of the experiment that led to a UCLA's researcher's death have prompted evaluations of academic Safety Practices. A UCLA Report to the Chancellor on Laboratory Safety was released in July 2009. It is an excellent document that points to training, record keeping, laboratory inspections, job descriptions, and safety... sounds like Quality Assurance!! With other current news reports such as the Laboratory explosion at Texas Tech University, this may be an opportune time for University QA Units to assess how best to offer their talents and skills as University Safety committees rethink research procedures and good practices in the laboratory. This presentation will give examples of how several Universities are approaching laboratory safety, GXP issues and discussion of options for future QA interchange with University Administration. The new NIH and NFS requirement for formal instruction in responsible conduct of research specifically includes data acquisition and laboratory tools, again a chance for QA to be part of the team. This presentation should be helpful in raising awareness to the issue of Regulatory Compliance in academic environment.

**Keywords:** University/Academic Research, Good X Practice (GXP, multidisciplinary), University

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## W-2

### Promoting and Implementing GLPs within a University Environment

Raymond Anderson<sup>1</sup>, Sandy Hancock<sup>2</sup>

<sup>1</sup>*Cantrell Drug Company, Little Rock, Arkansas, United States*, <sup>2</sup>*Virginia Tech, Blacksburg, Virginia, United States*

Implementation of Good Laboratory Practice (GLP) within a university environment has been a challenge for many years. Workshops have been conducted and papers written to discuss the growing importance of GLPs in academia for over 15 years with SQA members playing a leading role. Universities have been limited in their ability to comply with GLPs because of a combination of inadequate funding, facilities, equipment or trained personnel. Establishing good documentation practices has also been a challenge. These factors have prevented institutions from providing industry with another venue for conducting research. Often those at the top of the academic organization chart are unaware of the requirements of the GLPs or are not convinced of their value in conducting research at their institutions or securing industry sponsored research.

The University Specialty Section (USS) has begun to define the core elements for promoting and establishing a GLP mindset at research institutions. Developing a quality assurance curriculum to teach QA principles and concepts is essential. Learning the language of the GLPs is critical to the development of a QA professional capable of conducting a study under GLPs. The importance of bridging the language gap between industry and academia should not be underestimated.

The opening speaker will present an overview of the project the USS has initiated to

determine and understand present conditions at universities relative to GLPs and also other GXP regulations. Other speakers will share their experiences with similar projects and lessons they learned.

The session will continue with a roundtable/open forum discussion where others will share their personal experiences in promoting GLPs and GXPs at their institutions including what worked well and what did not. A session moderator will facilitate focusing the discussion toward achieving the following outcomes:

- Determining the current role of QA in support of a university's mission of teaching, research and outreach.
- Evaluating communication tools for promoting GXPs.
- Defining the core elements of developing a QA program.
- Identifying key resources for implementing a QA program.
- Understanding and bridging the gap between industry and academia with respect to regulated research.
- Deciding how best to write and publish a white paper based on the USS project.

**Keywords:** University/Academic Research, Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## X-1

### How Effective is GCP Training, Really?

Cheryl Bissey-Black

*Falcon Consulting Group, LLC, Marietta, Georgia, United States*

As clinical QA professionals many of us have provided GCP training in one venue or another. The content doesn't change much regardless of audience or venue. Many clinical QA professionals experience first hand the lack of GCP knowledge while auditing investigational sites. And yet, certificates of GCP train-

ing can be provided as well as the content of GCP training provided at investigator's meetings as evidence of GCP training. Usually, the investigator and site staff have attended many investigators' meetings over the years.

Warning letters continue to be issued with the 'usual' findings. And you ask yourself, what was he/she thinking? How could that have happened? If the recipient of the warning letter is not a criminal or a sociopath, what went wrong? Surely they have received GCP training; were they not listening?!

This abstract will present the results of a survey of RQAP-GCP members and other Clinical QA professionals pertaining to understanding and application of GCPs by the investigational site, the effectiveness of GCP training, root cause of ineffectiveness and suggestions for improving training if it is determined to be required. Examples will be provided and conclusions discussed in an interactive session. The result of the session will be to determine what went wrong and what we, as Clinical QA professionals, can do to improve knowledge and understanding of GCPs and promote the safety and welfare of human subjects while promoting the principles of good clinical research.

**Keywords:** Clinical Research (GCP), Clinical Trials

**Level:** Advanced (In-depth review of topic).

X-2

### Quality Based Selection of Clinical Sites

Carol Bogner

*The Weinberg Group, Charlottesville, Virginia, United States*

The appropriate selection of clinical sites requires an experienced professional and often this paramount task is performed by an individual who has also been charged with choosing sites that will guarantee enrollment. There

is an inherent conflict of interest in qualifying a site for a clinical trial while concurrently striving to meet or exceed enrollment goals. Most investigator sites are selected during a pre-initiation site selection process conducted by monitors and sometimes this process occurs via teleconference. One solution to this dilemma would be for site selection to be conducted by qualified GCP auditors, experienced with identifying sites that are capable, competent and ready to meet all the requirements of executing a clinical trial. There are several distinct advantages to employing a proactive approach to site selection and having an experienced clinical GCP auditor perform this critical aspect of the clinical trial process. These advantages include the following: a nonbiased approach to the evaluation and one that is not based on enrollment statistics, a thorough report inclusive of risk and areas of weakness, and the opportunity for immediate onsite GCP-ICH training possibilities.

**Keywords:** Clinical Research (GCP), Risk Management

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

Y-1

### SQA-FDA Communication

Jim McCormack

*Charles River Laboratories, Frederick, Maryland, United States*

This presentation will provide members with a summary of recent outreach to FDA and possible opportunities for enhanced communication and interaction.

**Keywords:** Food and Drug Administration, US (FDA)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## Z-1

**Root Cause Analysis Tools and Guidelines**

Jo Ann Boyd

*Southwest Research Institute, San Antonio, Texas, United States*

An area of concern with GXP compliance resolutions consists of determining the proper root cause for trending root cause analysis. Root Cause analysis is a system of finding and correcting the most important reason for a performance problem and the risk significance. The key process depends on determining the underlying cause of the problem. There generally is only one root cause not multiple but a root cause that may create other problems magnify the issue. Organizations require root causes analysis categories that will provide the ability to trend compliance issues. Root cause tools and techniques will allow the organization to identify the proper category and provide investigation trends for improvements.

This presentation will provide topics such as purpose, definitions, processes, tools, and risk significance. The tools provided will allow the ability for GXP systems to reduce the risk issues in a timely manner and provide continuous improvement through process improvements. As in any process with failure analysis the key is to determine the root cause, provide potential solutions and alternative solutions to resolve the problems, implement the solutions and move to an alternative if the initial solution is not the root cause, and finally evaluate whether the solution provided the corrective action to the root cause. The presentation will help identify the tools needed to investigate the problem to its origin and determining the initial root cause effect.

Providing training and implementing simple problem solving tools to all staff involved in the process will expedite the reduction of risk analysis. Following the initial process the act of involving secondary support through quality and management allow for decisions to be determined and provide better than an 80–90% success rate. The tools and methods iden-

tified in this presentation will assist in evaluating the appropriate tool needed for the risk analysis.

**Keywords:** Multisite Studies, Root Analysis/Root Cause

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## Z-2

**Lean Six Sigma/Continuous Process Improvement Impacts on Quality Management Systems**David Asher<sup>1</sup>, Beth Galt<sup>2</sup>*<sup>1</sup>Asher Associates Inc., Double Oak, Texas, United States, <sup>2</sup>MPI Research, Mattawan, Michigan, United States*

Every regulated organization is concerned about creating solid and reliable processes to support quality outcomes. The move to quality management systems (QMS) has moved our thinking into improving processes rather than simply fire fighting individual issues which reoccur. The key to robust continuous process improvement (CPI) is the requirement of a good decision making methodology when understanding, focusing and identifying root causes associated with systemic quality issues. Lean Six Sigma has been used as the infrastructure to CPI programs throughout the Life Sciences industry: Pharma, Bio Tech, Med Device, CRO, and Clinical Delivery, over the last 6 years and is gaining continued acceptance as a way of doing business and insuring quality through improving processes and decision making. In order to understand the Lean Six Sigma Method as applied to continually improving processes, which drive quality systems to deliver quality outcomes, we must first understand the utility of the LSS methodology in CPI. This session will focus on understanding the LSS method, applications to the Life Sciences Industry, and how it relates to QMS.

**Keywords:** Six Sigma, Beyond Compliance

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### AA-1

##### **Electronic Data Capture in Clinical Investigations**

Joseph Salewski (invited)

*US Food and Drug Administration, Silver Spring, Maryland, United States*

During this session, attendees will learn how to effectively use EDC when conducting clinical investigation, as well as how to avoid common regulatory pitfalls.

**Keywords:** Clinical Research (GCP), Electronic Data Capture, Electronic Data Source

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### AA-2

##### **The Impact of Electronic Systems, eHRs and eData on Clinical Research**

Timothy Kuhn

*Celgene Corporation, Summit, New Jersey, United States*

Although the use of electronic data in the pharmaceutical industry is by no means a new phenomenon, its impact has evolved over time. Technology has revolutionized our lives in many ways; in the way we access information, in our entertainment, in the way we do business, and in the way we interact. This technological revolution has had very pronounced impacts on the GxP industries: eRecords, eData, eSignatures, Data Processing, Data Mining and the Regulatory Standards associated with them.

These impacts have been most apparent in the cGMP and GLP areas and there is a fair level of comfort with eData and Validation in those areas. Increasingly however, the impact of eData and the need for controls around its

use can be seen in the GCP area. Due to its large reliance on external sources of data, Clinical Research has some unique challenges. This session will cover:

I. Technology in Pharma and Validation Overview: a discussion of these concepts (which are widely felt to be cGMP artifacts) and relating them to the GCP area through analogies.

II. Centralized GCP Technology: The use of centralized eData and eSystems, primarily on the “sponsor side” has some unique challenges due to very short timelines and the external nature of clinical data inputs. Also the challenges of study-specific validation activities will be addressed.

III. De-Centralized GCP Technology – ‘Technology at the Clinic’: The advent of electronic Health Records (eHRs) has had a profound impact on Clinical Research and the way in which source data is handled; however the adoption of eHRs has been uneven, piecemeal, and largely independent of any research concerns. As a result, source data at clinical sites varies widely in format, from purely paper systems through purely electronic integrated source systems. However, a large and growing number of sites use a hybrid paper/electronic model with various sources of data, scans of source destroyed by hospital systems, paper notes, dictated notes, email notifications, and central sponsor data collection systems. Some ideas on how to address various hybrid source data scenarios will be presented.

**Keywords:** Clinical Research (GCP), Electronic Record

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### AA-3

##### **Maximizing Audit Efficiencies While Utilizing EDC**

Amy Hansen

*PAREXEL International, Waltham, Massachusetts, United States*

Discover how to become more effective as an auditor by building efficiencies when auditing studies that utilize EDC. Understanding the importance of being adequately trained on the system, the ability to filter data to evaluate trends and the significance of accessing real-time data will assist you with your auditing responsibilities.

**Keywords:** Clinical Research (GCP), Electronic Data Capture

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### BB-1

##### CVIC Regulatory Update

Robert D Tollefsen (invited)

*US Food and Drug Administration, Silver Spring, Maryland, United States*

Speaker will provide a regulatory update of computer validation issues, solutions, and topics to keep the quality assurance professional current with FDA's intentions on maintaining regulatory compliance to computerized systems and applications used in clinical, nonclinical, or manufacturing areas.

**Keyword:** Computer Validation

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### CC-1

##### SQA Mentoring Program Initiation: Shared Experiences Plus Updates for the Next Application Cycle

Janet Cunningham<sup>1</sup>, Melissa Eitzen<sup>2</sup>, Catherine Bens<sup>3</sup>, Jennifer Giles<sup>4</sup>, MaryEllen Lander<sup>5</sup>, Karen LoPresti<sup>6</sup>, Michele Weitz<sup>7</sup>

<sup>1</sup>*Eli Lilly and Company, Indianapolis, Indiana, United States*, <sup>2</sup>*University of Texas Medical Branch, Galveston, Texas, United States*,

<sup>3</sup>*Integrated Quality Management, Wellington, Colorado, United States*, <sup>4</sup>*Pfizer-Global Systems Compliance, Kalamazoo, Michigan, United States*, <sup>5</sup>*Falcon Consulting Group LLC, Rio Rancho, New Mexico, United States*, <sup>6</sup>*ChemGenex Pharmaceuticals, Menlo Park, California, United States*, <sup>7</sup>*GCP International LLC, San Francisco, California, United States*

The area of Quality Assurance is rapidly expanding. Some QA professionals have been lucky enough to find someone to look up to, someone to ask questions of, or someone who has been there and done that and is willing to share those experiences and their QA life lessons with them. This 'someone' served as their mentor. Rapid growth, however, means that more and more of us find ourselves in unfamiliar situations without the benefit of prior training. This is a rough road to walk for anyone. SQA members have expressed a desire for a mechanism to gain the necessary tools to perform new tasks without having to take a training course. And SQA has responded.

In an effort to meet the needs of these QA professionals, the Mentoring Program Committee (MPC) was formed and the Mentoring Program was developed. The Program covers GMP, GLP and GCP areas of Quality. The SQA Mentoring Program is a structured way for experienced QA professionals to share their expertise and knowledge with QA professionals that are just getting started or want to expand their knowledge into another area of QA. The Program matches an experienced professional (mentor), with a lesser experienced QA professional (mentee) in a partnership relationship. The SQA Mentoring Program also offers a pathway for two equally experienced QA professionals to support each other in a peer partnership. Partners work together via email, phone, and in person if possible to help expand the knowledge of both people.

The Program was launched shortly after the 2009 SQA Annual Meeting. Matching of partners occurred in July 2009 and partnerships were developed in August and September.

More than 30 matches were completed including mentor/mentee partnerships, peer partnerships, mentors with two mentees, one person who functioned as both a mentor and a mentee, and one person who functioned as both a mentor and a peer partner. These matches allowed for diverse partnerships. Evaluations at the end of the partnership period provided a mechanism for participant feedback and allowed the MPC to determine how well the program was functioning.

The members of the MPC will share the outcome of the first cycle of the mentoring program and improvements that have been or will be made based on the comments received from the evaluations. In addition, MPC members will share how the second cycle of the mentoring program will work in the hopes that many SQA members will be interested in applying as mentors, mentees or peer partners.

**Keywords:** Personal Development/Training, Mentoring

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### DD-1

##### **The Future of GLPs: Modernization and Globalization**

Connie Marvel

*Bristol-Myers Squibb, Mount Vernon, Indiana, United States*

Many scientific and technological advances have occurred since the Good Laboratory Practices (GLP) regulations became effective in 1979. These advances have resulted in dramatic changes to the way non-clinical studies are currently being conducted in our industry. In addition, historical interpretation of sections of the FDA GLP regulations has resulted in procedures that are often cumbersome and do not always add business value. A list of 15 items for consideration was presented to the FDA in November 2007 and has since gener-

ated much follow-up discussion with the FDA regarding feasibility of the changes and possible methods for implementation. The current status of GLP modernization will be discussed.

The GLPs have been a powerful tool in assuring the quality and integrity of nonclinical studies over the past 30 years. However, varying interpretations and enforcement of these requirements have brought confusion and inefficiency to the GLP environment, thus mandating the need for a unified GLP standard in order to facilitate the mutual acceptance of nonclinical data by regulatory authorities. An ICH guidance document for Good Laboratory Practice for Nonclinical Laboratory Studies would facilitate consistency in interpretation of the requirements. It would also provide assistance to countries that do not have their own GLP requirements, have only recently issued their own requirements, or have issued local requirements based upon existing GLP requirements. The ICH process will be highlighted as well as the proposed content of an ICH GLP Concept Paper.

**Keywords:** Preclinical Research (GLP), Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### DD-2

##### **China SFDA's 'International Workshop on GLP Inspection': A Presenter's Perspective**

Connie Marvel

*Bristol-Myers Squibb, Mount Vernon, Indiana, United States*

In early 2009, the State FDA (the regulatory authority in China) and the Pharmaceutical Research and Manufacturers of America (PhRMA) joined together to plan, prepare and present a four-day training event known as the 'International Workshop on GLP Inspection'. This workshop was held on September 10–13, 2009 in Hangzhou, China. The details of the

planning and delivery of the workshop will be discussed relative to the participants involved, logistics, overall content of the training, and feedback received.

**Keywords:** Preclinical Research (GLP), Education/Training

**Level:** Basic (Suitable for professionals with less than 2 years experience).

EE-1

### How Does Quality Risk Management Work in Practice?

Peter Schiemann

*F. Hoffmann – La Roche Ltd., Basel, Switzerland*

Clinical QA experts – be these auditors or regulatory authority inspectors – are getting more and more aware of the fact that audits and also inspections are not leading to a desired outcome that is giving assurance to all stakeholders involved, and especially to the public at large, that clinical trials, data obtained in these trials and medicines available to patients are safe.

It is obvious that we do not learn from our past mistakes, because findings have remained the same after audits and inspections; the ‘score board’ of findings from audits or inspections conducted over the last decades hasn’t changed. In this context there is a particular disturbing dilemma for inspectors mainly: when the outcome of inspection / auditing a trial reveals, for instance, one site is in compliance and at another major or even critical GCP and Safety findings were detected. This begs the question of whether the critical findings are an outlier or represent the real ‘face’ of that trial. The bottom line is that one does not get the required assurance on the level of quality and compliance from audits or inspections alone.

The solution to get you out of this dilemma is a Quality Risk Management (QRM) approach. The QRM approach monitors in a systematic manner a multitude of risk indicators that leverage data that is collected through

the routine clinical trial or pharmacovigilance processes. This allows companies and regulators to stay in control all the time and to maintain overview over many more entities than a regular size QA group can do with audits being their major tool. With this approach the importance and scope of audits changes and becomes a critical element in ensuring the QRM analyses are accurate and reliable.

In this session, you will learn the basics of QRM, what regulators expect from companies regarding QRM and how to build and apply QRM in your company. Information about tools and processes will be provided that will allow you to improve or even start your own Quality Risk Management approach in your company or institution.

**Keywords:** Clinical Research (GCP), Risk Management

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

FF-1

### Auditing Veterinary GCP Studies: A Trilogy

Debi Garvin<sup>1</sup>, Barb Stephenson<sup>2</sup>, Larry Thomas<sup>3</sup>

<sup>1</sup>*Pacific Rim Consulting/WCQTI, Mount Hood, Oregon, United States*, <sup>2</sup>*Pfizer Animal Health, Kalamazoo, Michigan, United States*, <sup>3</sup>*Bayer Animal Health, Shawnee, Kansas, United States*

VICH GL 9 is the global standard for veterinary GCP studies. According to this guideline, the Sponsor must ensure the quality and integrity of the data by implementing quality audits. Thus, the Sponsor’s quality assurance function and audits are of paramount importance to acceptable studies that support product approvals.

This presentation will cover three of the most common and challenging audits:

1. Companion Animal Field Study Sites
2. Food Animal Field Study Sites
3. Laboratories supporting a GCP Study

The three speakers will share information on the requirements and common findings of the audits. This will arm attendees with information useful for proactive enhancements of compliance. Also, best practices, tips, and similarities/differences will be highlighted. The session will address various phases of audits, including planning, execution, and reporting. Attendees will take away practical information to improve audits of veterinary GCP studies.

**Keywords:** Animal Health, Clinical Research (GCP), Audit/Inspection, Veterinary

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### GG-1

##### **Building a Better Way: The Evolution of eDC/ Clinical Database Validation Processes**

Timothy Kuhn, David Windsor, Mary Evanchick

*Celgene Corporation, Summit, New Jersey, United States*

The power and real-time feedback made possible by implementing 'eDC'/eCRF systems makes them indispensable to Clinical Research. However, the Data Management groups that typically own these systems often struggle with the appropriate way to implement and validate them; and then struggle in their attempts to appropriately validate the study-specific databases that they build within them. There are many reasons for this including: cGMP-centric concepts and terminology associated with validation, inflexible/inscalable validation methodologies, Data Management groups often being 'semi-technical' in expertise-level, the dual role Data Management has in terms of being both Developers and Users of the system, etc. By partnering with the right resources and using the right tools, a Data Management group can

move to a more dynamic validation paradigm with processes that make their validation more meaningful, their testing more robust, and their timelines shorter.

I. From the QA Perspective: This session will identify the challenges encountered in the implementation of eDC, the tools and ad hoc methodologies that were used, the processes that were developed, and the evolving role of QA moving from 'a police' role, to a 'partner' role, and ultimately to a fully independent role in which QA audits a process in which they are not involved day to day.

II. From the IT Validation Perspective: This session covers the challenges of providing validation services to a GCP-regulated area; the importance of understanding the more dynamic nature of Clinical Research as contrasted to the cGMP/GLP environments with which most Validation Engineers are familiar; methods for evaluating, adapting, and supplementing a vendor's 'canned scripts;' and the importance of managing external vendors who are conducting testing on behalf of the Validation Manager.

III. From the Data Management Perspective: This session explores the challenges experienced by a Data Management/Programming group while moving from a 'The Vendor builds our trials' model to a 'We build our own 'eDC' trials. We will share our journey through the frustration of finding that none of the Validation tools/templates that were available met the needs of our DM (and Client) groups, through working with our IT, Clin-Ops, and QA partners to build the tools we need, through reluctant skepticism regarding timelines, and ultimately to a point where the process is both improving our output and shortening our timelines.

**Keywords:** Computer Validation, Electronic Data Capture

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## GG-2

Abstract withdrawn by author.

## HH-1

### Current Status and Future Directions of Pathology Peer Review

Jack Snyder

*Cato Research Ltd., Rockville, Maryland, United States*

Histopathologists use light microscopes to study the structural manifestations of disease. Since the microscopic examination of tissue specimens is an evaluation of a 2-dimensional image of a complex 3-dimensional biological structure fixed in time, histopathology is considered a descriptive and interpretive discipline. Peer review of histopathology findings in safety assessment studies involving rodents and other animals seeks to ensure integrity of evaluation by microscopy. The fundamental need to satisfy regulatory demands for unbiased observations, however, is typically balanced by the need for sensitive and efficient evaluation of large amounts of visual (histological) information. Generally accepted results of pathology peer review (PPR) require consistent use of diagnostic criteria and common terminology, as well as continuing education for participants. Modern PPR may occur when a government agency sponsors a bioassay program, when a corporation sponsors 'in-house' or 'third-party' pre-clinical evaluations, or when a regulatory body suggests or requires individual or 'working group' assessments. The extent of PPR primarily depends on study results, but study size, duration, complexity, and purpose also influence the process. Essential elements of PPR include selection of tissues/lesions for review, selection of the reviewing pathologist(s), resolution of discrepancies, modification of data, and documentation of all aspects of the review process. US-EPA currently requires PPR on all submissions requesting re-consideration of carcinogenicity peer review decisions

based on changes in histopathologic diagnoses. PPR also is required for all carcinogenicity studies submitted to the European Agency for the Evaluation of Medicinal Products. Although FDA and other regulatory authorities do not yet require PPR, many of these bodies recognize that the reliability of pathology diagnoses can be greatly enhanced by comprehensive quality assurance and peer review. Looking to the future, as genomic technology to assess differential gene expression is increasingly used to predict morphological phenotypes such as apoptosis (cell suicide), necrosis (cell homicide), hyperplasia (cell proliferation), and neoplasia (tumor), PPR is challenged to provide uniform pathology phenotypes that can be correlated with changes in gene expression. This presentation will review types of PPR, stages of PPR, and best practice guidelines for PPR published in the US and UK. Strengths and weaknesses of current PPR, as well as examples of methods to resolve disputes among reviewing pathologists, also will be discussed. PPR can help ensure the integrity of pre-clinical toxicology studies used for important regulatory decisions involving the use of chemicals in our society.

**Keywords:** Preclinical Research (GLP), Pathology

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## HH-2

### Ensuring the Integrity of Your Samples during Global Transport

Michael Gordon

*World Courier, New Hyde Park, New York, United States*

Shipping cold chain samples has become more and more challenging as site locations become even more remote and timelines get tighter. In this session we will discuss the differences in logistic providers and how to overcome some global challenges and examine specific country

guidelines. Join us to discuss these and other import/export regulatory demands.

**Keywords:** Animal Health, Bioanalysis, Biotechnology, Preclinical Research (GLP), Clinical Research (GCP), Manufacturing (GMP), Medical Devices, Multisite Studies, University/Academic Research, Good X Practice (GXP, multidisciplinary)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## II-1

### GCP Requirements for Pharmaceutical and Medical Device Clinical Trials – How Do They Differ?

Katherine Cooper

*Cooper Quality Assurance, Maple Grove, Minnesota, United States*

Pharmaceutical and medical device clinical trials are governed by separate FDA regulations, 21 CFR Part 312 and 21 CFR Part 812, respectively. Although these regulations are very similar and include many of the same basic GCP requirements, there are some very distinct differences that need to be taken into account when conducting a clinical trial. This presentation will highlight the similarities and differences between these GCP requirements.

GCP requirements that are essentially the same for both pharmaceutical and medical device studies include:

- IRB oversight
- Informed consent
- Control of investigational product
- Selection of investigators
- Monitoring
- Compliance
- Documentation requirements
- Case histories
- Privacy (HIPAA)
- Financial disclosure

However, while most pharmaceutical and medical device GCP requirements are very similar, there are distinct differences that need to be

understood in order to run a compliant medical device trial. The most significant of these are in IRB and adverse event reporting that will be discussed along with other differing requirements.

This presentation will also include a discussion of the applicability of the following international standards:

- ICH GCP
- ISO 14155
- Clinical Trial Directive
- Medical Device Directive

The impact of recent changes in the Medical Device Directive on clinical trials will also be discussed.

**Keywords:** Clinical Research (GCP), Clinical Trials

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## II-2

### Dealing with an FDA Audit – What We Can Learn From Warning Letters and Audits

Michael Hamrell

*MORIAH Consultants, Yorba Linda, California, United States*

This session will describe the role of the FDA and the preparation of a site for an FDA audit. The presentations will cover the audit from different perspectives and focus on helpful hints and procedural issues regarding what to do in case they are chosen for an FDA audit. There will be a discussion on how to host the audit and how best to prepare for the actual audit. The audience will be taught some of the do's and don'ts of a successful audit and will learn some of the do's and don'ts of a successful audit from actual case examples and inspections.

**Keywords:** Clinical Research (GCP), Quality Assurance

**Level:** Basic (Suitable for professionals with less than 2 years experience).

JJ-1

**International GLPs: Use of OECD GLPs and Guidance 13 in the United States, and Comparison of the Practical GLP Interpretation among Tripartite Countries Coordinated by the Animal Health Specialty Section and the GLP Specialty Section**

Debi Garvin<sup>1</sup>, Greg Furrow<sup>2</sup>

<sup>1</sup>*Pacific Rim Consulting, Mt. Hood, Oregon, United States*, <sup>2</sup>*Charles River, Shrewsbury, Massachusetts, United States*

**Use of OECD GLPs and Guidance 13 in the United States** The United States operates primarily under two sets of Good Laboratory Practice regulations – 21CFR Part 58 (FDA) and 40CFR Part 160 (EPA), with TSCA GLPs used occasionally. Although facilities in the US have been conducting multi-site studies since the inception of GLP in the 1980's, there was confusion and lack of consistency in how these studies were handled. Early on (1980's to mid 1990's) it was common for the pharmaceutical companies to split out the bio-analytical and PK/TK portion of a study into a separate study altogether. Once EPA revised their GLPs in 1989, it became apparent that splitting a single study in two or more portions, each with their own Study Director was actually in violation of the GLPs. Although the violation was obvious, industry struggled with the nuances of conducting studies with components located at various facilities. Once the OECD GLPs and more especially Guidance 13 were finalized, clear direction was given regarding multi-site studies, including the roles of test sites and PIs, Quality Assurance and Study Director Responsibilities. These principles are widely used in the US as a framework for conducting multi-site and multi-discipline studies, but have created some new issues. In addition, due to the complexity of studies and the various disciplines and levels of expertise required an entire new set of problems have evolved which have not been adequately addressed.

**Comparison of the Practical GLP Interpretation among Tripartite Countries Q and A** In 2007 and 2008 the JSQA GLP Special Project Team, the SQA GLP Specialty Section and the BARQA GLP Committee cooperated on this International Project to explore and explain differences between GLP regulatory requirements in the United States, the United Kingdom and Japan. JSQA selected 66 Questions and Answers in the Pharmaceutical GLP Guide Books, translated these into English and submitted them to BARQA and SQA. BARQA and SQA independently provided JSQA with detailed answers to the questions with references to specific regulations or guidance documents in some cases. JSQA reviewed the responses and integrated them into the document titled 'Comparison of the Practical GLP Interpretation among Tripartite Countries Q and A.' The purpose of this presentation is to increase the awareness of this very interesting and valuable document (which is posted on the SQA website) by exploring a few of the questions that were addressed.

**Keywords:** Animal Health, Preclinical Research (GLP), Multisite Studies, Good Laboratory Practice (GLP)

**Level:** Advanced (In-depth review of topic).

KK-1

**How to be a Good Independent Contractor**

Celine Clive

*Polaris Compliance Consultants, Inc., Cary, North Carolina, United States*

With all of the downsizing and lay-offs in the pharmaceutical industry, many people are weighing whether or not to become Independent Contractors. This can be an exciting career change, but one must be fully aware of the responsibilities of a contractor before making the commitment. This program will address questions such as: What is involved in going independent? How do I get started?

What are the advantages and disadvantages? What would make a company want to do repeat business with me? Topics touched on will include: incorporating, insurance, time-sheets, invoices, expense reports, and continuing education responsibilities.

**Keywords:** Personal Development/Training, Independent Contractors

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### KK-2

##### **From Discovery to Market – Developing a Safe and Effective Quality Training Program**

Karen Waetjen, Mazz Whitaker

*Charles River, Horsham, Pennsylvania, United States*

Join us for an exciting journey from discovery, through development and to market of our final product – An Effective QAU Training Program!

We will answer the age-old questions, ‘Who has time for training?’, ‘Why aren’t the auditors consistent?’, ‘How do you set criteria for measurement of conceptual training?’ and ‘How can management use training as a tool?’ and address the common challenges for regulatory training. Our presentation will provide ways to determine if your current training program is effective. We will introduce our mentor/protégé program and discuss the differences between programs. Management representatives will discover our approach to tracking and trending of training progression, retraining techniques and development of individual auditor training designs.

**Keywords:** Personal Development/Training, Quality Assurance

**Level:** Basic (Suitable for professionals with less than 2 years experience).

#### KK-3

##### **Quality Circles: The Strength They Provide in a Total Quality Management Organization**

JoAnn Boyd

*Southwest Research Institute, San Antonio, Texas, United States*

This presentation will provide the definition for quality circles. The questions involved in this presentation will provide the history of quality circles and all the necessary information needed for success. The information to incorporate a quality improvement process through quality circles will identify the type of teams involved, the benefit of the teams, how to implement a team, the tools used to strengthen the team, and much more. By the end of the presentation the information provided will encourage use of quality circles in order to build and maintain a quality system that provides strength in continuous improvements. The presentation will encourage the user to evaluate and build teams in multiple uses as well as provide new information for an old quality tool. The presenter will answer the key question for a Quality Circle providing all the necessary information involved in the original and continuing purpose for the development of these teams. At the end of the presentation additional resources and information for additional training will be provided.

**Keywords:** Multisite Studies, Good X Practice (GXP, multidisciplinary)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### LL-1

##### **Increasing Value of the Bioanalytical Laboratory’s SOPs**

Irina Colligon

*Downingtown, Pennsylvania, United States*

The regulations that cover bioanalytical (BA) activities state that a BA lab must have SOPs. So, regardless of whether one believes SOPs have

a value in the bioanalytical (BA) lab, or is still in denial, the SOPs are being created. Much effort and time are usually put into this undertaking. This question whether the effort was worth it may be answered in many ways: (a) were the regulatory requirements met? (b) are staff using them? (c) has the quality of the work improved? Even if the answers to the above questions are positive, among the factors to consider when evaluating the value of the SOPs are: (1) the effort needed to develop and maintain the SOPs; and (2) the effort it takes to use the SOPs.

In looking at ways to maximize the value of SOPs, this presentation will examine the following topics:

- Approaches to developing SOPs for the BA laboratories and how these approaches answer the questions raised above;
- SOP topics and contents: must have, should have, nice to have, and need not have;
- Procedural documents vs. SOPs

In the course of the discussion, we will look into ways to reduce the effort associated with the SOPs while reducing the risk of non-compliance.

Looking at the SOPs from the QAU perspective, we will also consider the impact of their development and use on the activities of the Quality Assurance unit, including:

- Using SOPs to identify areas of increased error and/or non-compliance risk; and
- Cooperation between laboratory and QAU in developing processes that help improve effectiveness and efficiency of audits.

**Keywords:** Bioanalysis, Good X Practice (GXP, multidisciplinary)

**Level:** Advanced (In-depth review of topic).

## LL-2

### Auditing Chromatographic Electronic Data

Jennifer Bravo

*Agilux Laboratories, Worcester, Massachusetts, United States*

The FDA has provided ample evidence, in the form of warning letters and 483s, that in the case of data from chromatographic data systems

(CDS), the electronic data is the raw data. Gone are the days when a company could claim that only chromatographic printouts are the raw data. The expectation is that the content and meaning of the record is preserved regardless of the medium. For CDS this means that the electronic data and metadata, such as audit trails, should be reviewed by supervisory personnel and should be audited by QA. For QA professionals, this shift from paper to electronic data presents some interesting technical and cultural challenges. Besides having to be familiar with SOPs and applicable regulations, now the QA professional will be required to learn how to use and navigate through the menus of software such as Analyst or TotalChrom to audit data. Likewise, auditors will have to adapt longstanding auditing approaches developed for paper-based records to one that may require greater flexibility for electronic raw data.

- This presentation will provide an overview of the following topics:
- Common pitfalls identified in warning letters regarding chromatographic electronic data
- Controls necessary to ensure the data is 21 CFR part 11 compliant
- Discussion on how to audit chromatographic electronic data, with special emphasis on integrations and audit trails
- Examples of data integrity issues

**Keywords:** Bioanalysis, Preclinical Research (GLP), Electronic Record

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## LL-3

### The Odd Couple: A Successful Partnership between QA and IT in a Bioanalytical Environment

Abby Bousum, Laurel Branstrator

*AIT Laboratories, Indianapolis, Indiana, United States*

A successful partnership between Quality Assurance (QA) and Information Technology

(IT) in a bioanalytical environment is imperative. Unfortunately, the interactions between these two service groups are often tolerant at best. The regulations do not clearly define the role of IT, but in the bioanalytical world which calls for complex technology, the science cannot survive without IT support. QA techniques must match the sophistication of the science. As today's laboratory environment becomes 'paper-averse' and ever more dependent upon electronic systems, IT and QA must be proactively involved in developing process and vigilant to test and improve systems.

In an effort to improve this QA/IT relationship, AIT Bioscience is proposing an organizational structure that promotes synergy between QA and IT where the 'whole' is greater than the 'sum of its parts'. Both departments report through the same chain of command creating blended resources and valued liaisons to the laboratory. Validation efforts utilize resources from both departments.

In this presentation, we will examine QA and IT as the 'Odd Couple' that are tasked by Management to work together. Failure is not an option – mutual success is the stated goal. A case study of a software/hardware validation project that nearly went wrong but was successfully implemented with this QA/IT strategy will be examined.

**Keywords:** Bioanalysis, Computer Validation, QA/IT

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

**MM-1**

### **Facing the Challenges of Pharmacovigilance in Evolving Cultures of Safety**

Jack Snyder

*Cato Research Ltd., Rockville, Maryland, United States*

Global issues regarding safe use of medicinal products increasingly capture the attention of

lawmakers, regulators, journalists, policymakers, and the general public. Perceptions of unacceptable risk trigger remedial legislation, regulatory guidance, and judicial scrutiny. Sponsors recognize the urgent need to manage risk throughout a product's life cycle, but struggle to find the optimal mix of risk-minimizing methods and resources. This presentation will explain essential components, processes, tools, and business models for a modern proactive global pharmacovigilance (PhV) system. The goal is to enhance understanding of inputs required to efficiently obtain the minimum expected outputs of an acceptable safety program. Those outputs typically include case processing and reporting; periodic safety update reporting; database validation; risk management programs; literature monitoring; global compliance monitoring, and management of audits, inspections, product quality complaints, medical inquiries, and safety data exchange agreements. Delivery of minimum expected PhV outputs, however, is no longer sufficient to satisfy the demands of global product safety stakeholders. As medicinal product research moves from targets that ameliorate symptoms or reverse disease processes to targets that prolong and enhance normal functions and lifestyles, the safety expectations of healthy subjects most likely will exceed those of diseased patients. Consequently, this presentation also will explain newer PhV tools and approaches designed to further minimize risk at all stages of medicinal product development. Among those newer PhV outputs are risk evaluation and mitigation strategy (REMS) programs; pediatric investigation plans (PIPs); adaptive clinical trials; and enhanced signal detection processes (e.g., data mining, data pooling, e-DISH, and Sentinel Initiative). Finally, this presentation will address some of the information technology, training, and cost implications of the escalating global demand for medicinal product risk minimization. Specific topics to be covered include data migration; data consolidation; data and system interoperability standards; database hosting; dashboards; nature and scope of training requirements; and

relative cost advantages of 'in-house' vs. 'outsourcing' business models for PhV activities.

**Keywords:** Risk Management, Pharmacovigilance

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## MM-2

### Clinical Trial Oversight and Adverse Event Reporting

Ellen Kelso

*Goodwyn IRB, Cincinnati, Ohio, United States*

This session is about unanticipated risk and adverse event reporting during the conduct of a clinical trial. What should be reported to whom, the management of those reports and the actual responsibilities of those receiving them are of the most misunderstood aspects of clinical trial administration.

A key to protecting research subjects is monitoring the actual safety of ongoing research trials. Adverse event reports are central to this process. IRBs receive adverse event reports from investigators and sponsors but do not carry the responsibility for the safety monitoring of a research study. In effect the IRB's role comprehends much more: assuring the appropriateness of the research, its design, and that measures are in place for subject protections. It

is not necessary for the IRB to undertake data monitoring. It is, however, the IRB's responsibility to ensure that this function is carried out by an appropriate group, and that that group reports to the IRB on an appropriate schedule.

In support of this notion, the FDA and OHRP have each published guidelines that are intended to streamline the adverse event reporting process. These guidance's assign responsibility to the sponsors' and/or a data safety monitoring boards (DSMB) to triage all adverse event reports and report them to the IRB. The broader responsibility of the IRB to monitor unanticipated problems that occur during the course of the research is reflected in these recommendations.

The accreditation standards set by the Association for Accreditation of Human Research Protection Programs (AAHRPP) for reporting and IRB evaluation of unanticipated risks provide further support to researchers and IRBs, and support placement of the right responsibilities with the right expertise and assigned functions.

In this session, we will clarify the requirements and recommendations, and discuss options for management of adverse event reports that meet these standards.

**Keywords:** Clinical Research (GCP), Adverse Event

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

# Poster Abstracts of the Society of Quality Assurance 26th Annual Meeting, Cincinnati, Ohio, USA 25 – 30 April 2010

PP-1

## Start-Up of a Quality Assurance Department in a New Facility

Janice Lovullo, Jennifer Brault, Barbara Esser, Kevin Engholdt  
*Covance, Inc., Chandler, Arizona, United States*

Consistency and Quality are two important aspects of any Quality Assurance Unit. When starting up a new nonclinical testing facility there are many challenges each group faces especially when there are other well established Covance facilities that are doing the same work across the world.

Building good relationships between QA and operational groups helps facilitate ongoing communication. By organizing liaison groups between QA and the operational groups is pivotal in setting up relationships within a new facility.

Cross-site meetings between QA and operational groups lead to an improved internal customer view regarding auditing consistency and as a result has improved efficiency and confidence within QA.

This poster will outline the challenges and solutions that were put in place in QA when starting up a new nonclinical testing facility.

**Keywords:** Preclinical Research (GLP), Quality Assurance

**Level:** Basic (Suitable for professionals with less than 2 years experience).

PP-2

## Building GLP from the Ground Up in an Academic Health Research Setting

Joan Adamo<sup>1</sup>, Bruce Burnett<sup>2</sup>, Eric Rubinstein<sup>1</sup>  
<sup>1</sup>*University of Rochester Medical Center, Rochester, New York, United States,* <sup>2</sup>*Duke University School of Medicine, Durham, North Carolina, United States*

The ability of a research institution to perform both animal safety studies and to support initial clinical studies in humans in a GLP-compliant environment can be double edged sword for academic health centers. Performing GLP studies is attractive in terms of both translational research and for financial reasons, but it also opens up the university to considerable risk from a regulatory-compliance perspective. As such, several significant barriers exist to the implementation of GLP-compliant studies in the standard academic health research setting. At the University of Rochester, an institutional committee assessing infrastructure deficiencies identified GLP support as an asset to effectively compete for sponsored and contract research. We embarked on a formative process to identify the required elements to develop this capability. Using the University of Rochester and Medical Center as a model, we outline the development of a Quality Assurance Unit housed within an Office of Regulatory Support, the writing of Standard Operating Procedures, training of personnel and involvement of multiple levels of University administration. The Office of Regulatory Support was made possible through the Clinical and Translational Science Award, which has the vision to improve human health by transforming the research and training envi-

ronment to enhance the efficiency and quality of clinical and translational research. A GLP taskforce within the CTSA provided significant guidance and enhanced the development of a GLP-compliant program. Working within this taskforce provided the opportunity to identify infrastructure needs that can be generalized across multiple academic health centers.

Several characteristics of the academic setting present unique challenges for establishing GLP compliance – one of the most significant is the creation of and acceptance by researchers of a Quality System, including a substantial body of SOPs needed to govern research. While a Quality System is a natural component of any research laboratory in industry, it is not the central focus of university researchers and is often perceived as a barrier to the creative research process. Academic institutions are not typically structured to support SOP development, the training nor the oversight necessary to manage a Quality System. Even the transformation of an already SOP-driven animal facility into a GLP-compliant resource required a significant investment of both human and financial resources. In addition to Quality System management, other obstacles occurred in areas such as institutional sign-off, record-keeping and documentation, and the rigors of equipment validation.

**Keywords:** Preclinical Research (GLP), University/Academic Research, Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

PP-3

#### Designed to Exceed! Study Inspections and the GLPs

Anita Bosau, Deanna Talerico, Candace Brewer, Matthew Bruns, Lindsay McMichael, Krista Richardson

*Charles River, Spencerville, Ohio, United States*

‘The quality assurance unit shall inspect each nonclinical laboratory study at intervals ade-

quate to assure the integrity of the study’ (21 CFR 58.35).

**Challenge:** How does the QAU develop a program to accomplish and/or exceed the GLP requirements when it comes to inspectional strategy?

How does the QAU determine whether critical phase inspections, study system-based inspections or a combination thereof will accomplish this goal?

**Our Solution:** To exceed GLP expectations, decisions must be made concerning the type of inspections (critical phase or system-based) and the frequency of inspections for each phase/study.

- The QAU should determine which critical phases will be observed for every study and the types of system-based inspections that will be performed for each study type.
- Study-specific system-based inspections will be examined less frequently but will provide the opportunity to examine an entire method/process as well as all inter-related procedures, i.e., equipment, and documentation.

This poster will describe the selection and definition of critical phase and study system-based inspections, the frequency of the inspections chosen, and why the phases were chosen.

**Keywords:** Preclinical Research (GLP), Quality Assurance

**Level:** Basic (Suitable for professionals with less than 2 years experience).

PP-4

#### Requirements for Personnel in a GLP Facility

Shohei Maruno<sup>1</sup>, Shinichi Nakayama<sup>1</sup>, Motoko Hidaka<sup>1</sup>, Takumi Hamada<sup>1</sup>, Terumasa Hirai<sup>1</sup>, Yoshiyuki Yokoi<sup>2</sup>, Koichiro Fukuzaki<sup>1</sup>, Ryoichi Nagata<sup>1</sup>, Jodi Myers<sup>3</sup>

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*Pharmacokinetics and Bioanalysis Center, Wakayama, Japan, <sup>3</sup>SNBL USA, Ltd., Everett, Washington, United States*

It is critical for a GLP facility to effectively manage its personnel and organization; laboratory areas and equipment; SOPs, test articles and test systems. Effective management of these factors leads to quality GLP studies.

Personnel are a key factor in maintaining the facility and performing studies. The GLPs require that individuals engaged in or supervising the conduct of a nonclinical study have education, training and/or experience required to conduct experiments. However, since each department requires different skills, it is up to a department to define how much education, training, and level of experience required for each position, and to determine how these criteria are met. How should a GLP organization manage the personnel appropriately? We will consider the procedures required to ensure the effective training of personnel.

It is also necessary for an organization to build a training program that addresses continuing education and re-training. For example: Do individuals contributing to studies 10-years ago have the necessary skills for studies today? Or, will individuals contributing to studies today have the necessary skills required for studies in 10 years time? The answer, of course, is 'No', because ability, processes and knowledge will change with time. It is important to have clearly defined objectives so that supervisory personnel have a basis for evaluating competency and achievements.

This poster will address the procedures needed to ensure effective training of personnel. Use of this Training Cycle should lead to improved operations of the test facility and study conduct.

**Keywords:** Personal Development/Training, Education/Training

**Level:** Basic (Suitable for professionals with less than 2 years experience).

PP-5

### Checklists and Templates: Facility Audit Help or Hindrance?

Barbara Randolph, Melissa Hughes, Jason Plaxco

*Biotechnical Services, Inc., North Little Rock, Arkansas, United States*

Utilizing an Audit Template or Checklist to conduct a facility inspection has pros and cons. This poster will explore completing quality assurance work with a checklist in hand and suggest other tools and methods of inspection that may provide greater flexibility through a less restrictive approach.

Content on checklists or report templates may be written to achieve consistency between different audit staff members or to ensure that guideline or regulatory requirements are thoroughly addressed. At some point multi-page, step-by-step templates may be cumbersome and repetitive and lead to a loss of the big picture. Further, checklists may constrain the ability of experienced auditors to fully apply their skills.

This poster will contrast the value of checklists and the limitations they may impose. It will compare the use of checklists and templates with a variety of other methods or strategies for successfully completing a facility inspection. Suggestions of how to employ audit tools to effectively meet inspection objectives will be provided.

**Keywords:** Personal Development/Training, Audit/Inspection, Auditing Skills

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## PP-6

**Is the Whole (Comprehensive Examinations) Better Than the Sum of its Parts (Individual Examination)?**

Sandra Williams

*RTI International, Research Triangle Park, North Carolina, United States*

RTI International conducts non-clinical research for a variety of commercial, government and academic clients. These projects are supported by a single quality assurance unit. The quality assurance unit is responsible for monitoring each nonclinical laboratory facility according to FDA and EPA Good Laboratory Practice Regulations, 21 CFR 58, 21 CFR 210 and 211, EPA 40 CFR 160 and 40 CFR 792, respectively, and OECD Principles of Good Laboratory Practice, Section II.2.2 (1) (c). Facility inspections typically involve not one specific study but involve quality assurance oversight of the entire testing facility and more than one study. One approach we have used in the Regulatory and Quality Assurance group at RTI International is to comprehensively examine a research group's facility over a course of 1–4 days. For each research group an assessment was made of the systems being used and all systems in the facility were looked at. For one research group, training files, equipment and records, labeling, water systems, etc. would be inspected for compliance to the appropriate SOPs. In this approach, we had one QAU specialist look at most all the systems in a group.

A second approach was to prepare a list of each group's equipment. For instance, the first group may have balances, HPLC, water system, storage chambers, etc. The second group may only have balances, HPLC's and gas chromatographs. Then, it was decided typically based on the last date of inspection to schedule and assign inspections to different quality assurance specialists based on experience and availability. However, only a sampling of the non-unique equipment (approximately 10%) was inspected.

Both approaches involved scheduling, reading SOP requirements and regulations beforehand. Checklists are prepared or updated, the report is written and findings are reported to management. An evaluation of the two approaches for conducting facility inspections is described.

**Keywords:** Preclinical Research (GLP), Good Laboratory Practice (GLP)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

## PP-7

**Project In-Life Audit as Important Part of GLP System in Russia**

Maria Zaytseva

*Institute of Toxicology, St-Petersburg, Russian Federation*

The procedure for the planning, conduct and reporting Project In-Life Audit which shall assure that all preclinical projects are conducted in compliance with appropriate laws, guidelines, company policies and procedures in addition to written commitments to Sponsors. Quality Assurance Manager is responsible for the process initiation and conducting. Quality Assurance Manager contacts the Study director to audit agenda development. During the audit, Quality Assurance Manager discusses with the Study director and other relevant study team members issues related to project records and data. When the audit is assessing the trial master file, Quality Assurance Manager reviews all project filing to assess completeness, and internal consistency with standard operating procedures, reviews study organization chart, personnel files, training records, source documentation, inspect vivarium, investigational product storage zone, computer system. Quality Assurance Manager holds a closeout meeting to discuss the areas reviewed, request clarification of any outstanding issues and provide a verbal summary of the principal audit findings. All audits shall

be documented in audit reports prepared by the Quality Assurance Manager in order to report audit findings in consistent manner and ensure correct distribution. The Quality Assurance Manager shall issue an audit certificate once a satisfactory corrective action Plan is received, indicating all actions have been addressed. Issuance of the audit Certificate shall indicate that the audit is closed. These processes lead to quality improvement of pre-clinical studies.

**Keywords:** Preclinical Research (GLP), Audit/Inspection

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-8

##### **Establishment of a Quality Assurance Program for the Integrity of Peripheral Blood Mononuclear Cells Isolated for the Center for HIV/AIDS Vaccine Immunology (CHAVI) by Multiple International GCLP-Compliant Laboratories**

Leila K. Needham<sup>1,2</sup>, Eugene Urrutia<sup>3</sup>, Tania Garrelts<sup>3</sup>, Raul Louzao<sup>3</sup>, Thomas Denny<sup>2,3</sup>, Susan L. Stager<sup>4</sup>, Guido Ferrari<sup>4</sup>, Pauline Mokgotho<sup>5</sup>, David Mokgokolo<sup>5</sup>, Clive Gray<sup>5</sup>, Susan Fiscus<sup>6</sup>, Marcella Sarzotti-Kelsoe<sup>1,2</sup>

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The Center for HIV/AIDS Vaccine Immunology (CHAVI) is a major project under the Global HIV Vaccine Enterprise. The National Institute of Allergy and Infectious Diseases (NIAID) awarded the CHAVI grant to a consortium of investigators from academic research institutions, led by Dr. Barton Haynes of Duke University Medical Center. One of the key goals of the CHAVI is to use specimens obtained from Clinical Study Protocols established at multiple international sites to determine host immune responses during early acute HIV infection. These CHAVI Protocols require that the Site-Affiliated Laboratories (SALs) isolate and cryopreserve Peripheral Blood Mononuclear Cells (PBMC) in a process standardized by Central Standard Operating Procedures (SOPs) and in a Good Clinical Laboratory Practice (GCLP)-compliant manner. These PBMC specimens are shipped to CHAVI Repositories for long-term storage in liquid nitrogen freezers and redistributed from there to End User Laboratories for analysis.

A Quality Assurance program managed by the CHAVI Repositories and CHAVI Central Quality Assurance (QA) Unit was developed to monitor the quality of PBMC isolated and stored for CHAVI studies. This program was designed to monitor the integrity of the PBMC samples at each stage of this process including the PBMC isolation, cryopreservation, handling and shipment at the SALs and the handling, storage and shipment of PBMC at the Repositories.

Stage One: Monitoring of PBMC isolation, cryopreservation, handling and shipment at the SALs (located in the US, the UK and Africa), includes:

- Centralized training, qualification and annual competency assessment of the SAL operators using CHAVI Central SOPs for PBMC isolation.
- On-site monitoring and trending of the key Quality Control (QC) indicators of the initial PBMC processing (percent viability, PBMC yield per milliliter (ml) of processed blood, and time between blood collection and freeze of the isolated PBMC).

- Central Repository monitoring and trending of the key QC indicators of cryopreserved PBMC integrity (percent viability and total PBMC recovery upon the thaw of sampled cryopreserved PBMC after shipment from the SALs).

Stage Two: Monitoring the handling, storage, shipment and counting of PBMC at the Repositories (located in the US and South Africa) includes:

- The preparation of a large number of identical Control Sample (CS) vials from two HIV-negative leukapheresis donors by the Immunology Quality Assessment Center (IQAC). These CS vials are sent to each CHAVI Repository for storage in the liquid nitrogen freezers that house CHAVIPBMCs.
- Repository monitoring and trending, every quarter of the year, of the key QC indicators of cryopreserved CS integrity (percent viability and total PBMC recovery upon the thaw of sampled CS after storage).
- As an independent verification of shipment, stored CS integrity and cell counting, an exchange of CS specimens between the Repositories and the IQAC each quarter of the year and the IQAC's monitoring and trending of the key QC indicators of cryopreserved CS integrity.

Acceptance criteria were set for each QC indicator and investigations and corrective actions were implemented in the event of QC failure.

**Support by:** The Center for HIV/AIDS Vaccine Immunology grant AI067854.

**Keywords:** University/Academic Research, Good Clinical Laboratory Practice (GCLP)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

PP-9

**'Oh Yikes!!!! Now what do I do?' The Secrets to Event Investigations**

Tanja McAulay, Michel Kalpaklian, Louise McLean, Lise Dallaire

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Following the recent Crystal City III conference, and the published white papers<sup>1</sup>, interest in the industry on how to manage event investigations has peaked and this is now an expectation for any GLP laboratory submitting data to a regulatory agency. The investigation into unexpected events is however not a new concept in the regulations. The GLP regulations, 21 CFR part 58 states in section 58.185, that the report must include a description of all circumstances that may have affected the quality or integrity of the data. In addition, the GMP regulations have had event investigation guidelines 2 established since 1998 (draft) and finalized in 2006. Therefore, this phenomenon is nothing new, and it is obvious that anomalous data and/or circumstances must be investigated and not ignored. Recent FDA warning letters have cited failures to document and investigate repeated lack of conformance 3.

Types of events may be broad in scope and it is important to clarify, effectively evaluate, and judge the occurrence and scope of the event. Causes for events may range from laboratory equipment, reagents, training, procedure clarity, to data handling, stability or sample integrity issues. The possibilities are endless.

The timing of event investigations is crucial as key components must be fresh and available to conduct the investigation. Availability of reagents, equipment, and analyst's involvement will ensure that the key focus areas are investigated and resolved efficiently. Therefore, investigations must have a short initiation timeframe to ensure the event can be effectively managed. In addition, participation and cooperation of analysts, study directors, Management and QA will ensure effective documentation, follow up and corrective action/preventive action (CAPA) handling and resolution.

QA must be involved at all stages. QA should typically assign the event investigation number to effectively launch, document and track the investigation. QA is also involved during the investigation, and must audit the investigation, and CAPA. Management must be made aware of events and authorize additional testing, changes to procedures, and or CAPA and evaluate their efficacy.

The process to effectively investigate an event must be established and followed closely to ensure adherence and standardization of the sequence of verifications. These steps must be timely, efficient, scientifically sound, and defensible relative to the nature of the event. In addition, the details of the investigation, additional testing plans and results of the investigation must be well documented and submitted to a QA audit. An SOP or guidance document will help guide the event investigation.

Event investigations are effective learning tools to train employees, accountability and to prevent similar events from occurring in a repetitive manner. When events are investigated and documented properly, they tell a complete story of a circumstance, how it was handled and how it will be corrected and prevented in the future. Event investigations require the input of all levels of personnel in order to be effectively managed and should be seen as learning and training opportunity in addition to solidifying data integrity, and adequately documenting the circumstances affecting the quality of a GLP study.

**Keywords:** Bioanalysis, Preclinical Research (GLP), Clinical Research (GCP), Good Laboratory Practice (GLP)

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-10

##### **Systematic and Expanded Investigation of High and Unexpected Positive Deviation for QC Samples during GLP Incurred Samples Analysis by LC-MS/MS**

Georges El-Kadissi, Mireille Nohra, Natasha Savoie, Ericka Franco, Veronik Gill, Milton Furtado, Chantal Menard, Mary Carbone, Fabio Garofolo  
*Algorithme Pharma Inc., Laval, Quebec, Canada*

**Novel Aspect:** Importance of structured investigation by using multiple reference standards to explain the high deviation for quality control samples.

**Introduction:** Montelukast is used in the treatment of prophylaxis, chronic asthma and seasonal allergic rhinitis. A bioanalytical method was successfully validated in human plasma. During incurred sample analysis, high positive deviations for quality control samples were noticed. Consequently, an investigation was started. A preliminary investigation was conducted to eliminate all possible causes of this phenomenon due to error or oversight. Since no assignable cause could be identified following this preliminary investigation, an expanded investigation was started. Hypotheses were: 1) matrix effect causing response enhancement, 2) contamination of stock solutions, 3) solubility problems and impurities/alteration in reference standards. A series of confirmatory investigations were conducted.

**Methods:** Montelukast-d6 was used as internal standard (IS). The method employed protein precipitation extraction using MeOH:Acetone 50/50% v/v. The extracts were injected on a Agilent Technologies 1100 pump and autosampler coupled to a AB/Sciex API 3000 MS/MS equipped with heated nebulizer source in positive mode. During validation, the method showed an intraday precision range of 2.9% to 4.3% and an accuracy range of 96.1% to 112.5% and an interday precision range of 3.8% to 7.0% and accuracy range of 95.1% to 113.9%.

**Results:** Verification of the first hypothesis (matrix effect) yielded no significant enhancement from the matrix. Results from several tests suggested a problem with a particular stock solution used to prepare the quality control samples and/or the reference standard lot (B) used to prepare it. Tests were rigorously designed to investigate solubility and impurities/alteration in the reference standard. A new lot (C) of reference standard compared with reference standard lot A, used during method development and validation, and with reference standard lot B, used during sample analysis. Results demonstrated a solubility problem with reference standard lots B and C in MeOH:H<sub>2</sub>O 50/50% v/v for a period of time exceeding 2 days vs. reference standard lot A, which was perfectly soluble in this solvent. Reference standard lots B and C were more soluble in pure MeOH. After further investigation into the synthetic procedures used to prepare the different lots, it was discovered that the reference standard lot A went through an extra step of purification, explaining the differences in solubility with lots B and C. As a remedial action, stock solutions prepared in MeOH:H<sub>2</sub>O 50/50% v/v were only used between 0 and 2 days. However, as a long term corrective action, the solvent was changed to MeOH and the method went through a partial revalidation. In conclusion, rigorous tests, meticulous trend analysis and mainly investigating different lots of reference standard were able to reveal a severe and unusual analytical phenomenon that was not definitively apparent during method development and validation.

**Keywords:** Bioanalysis, Deviation Investigation

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

PP-11

**Current Regulatory Challenges in Bioanalysis**

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The drug development process relies on quality data at every step. Bioanalysis is one of the key aspects and is heavily engaged throughout the entire development process from discovery and early development to clinical trials. High quality data obtained through bioanalysis is a prerequisite for interpretation of toxicokinetic, pharmacokinetic and bioequivalence studies and is often included in regulatory filings. Data provided through bioanalysis not only depends on fast turnaround using state of the art instruments, it also requires innovative strategies looking to practical scenarios and problem solving for every new challenge, many of which are not well defined in regulatory guidance.

This poster demonstrates some of the regulatory challenges currently being discussed by bioanalytical community. These include innovative technology such as dried blood spots (DBS), bioanalytical strategies such as metabolite measurements (MIST), tissue bioanalysis, biomarkers, and currently regulatory thinking such as unexpected event investigations and incurred sample reanalysis (ISR). Many of these challenges are interlinked and careful analysis of each situation is needed, as will be illustrated in this poster.

**Keywords:** Bioanalysis, Regulatory Bioanalysis

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## PP-12

**Incurred Sample Re-Analysis; Considerations and Challenges for the Implementation of a Procedure on Incurred Sample Re-Analysis**

Joanne Tyas, Manal Hantash

*ITR Laboratories Canada Inc, Baie d Urfe Quebec, Canada*

ITR Laboratories Canada Inc. is a non-clinical contract research organisation located on the island of Montreal in Canada. Many of the toxicology studies conducted at ITR include a bioanalytical portion. ITR has a well established procedure for validation of bioanalytical methods; however, implementation of a procedure for incurred sample re-analysis into the validation process presented certain challenges for the company. The poster will present the considerations and the challenges.

**Keywords:** Bioanalysis, Incurred Sample Reanalysis

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

## PP-13

**Establishing GCLP Compliance in HIV Endpoint Assay Laboratories at the Duke University Medical Center – An Update after Seven Years**

Ella Bernstein, Marcella Sarzotti-Kelsoe, Daniel Ozaki, Christopher Todd, Leila Needham

*Duke University Medical Center, Durham, North Carolina, United States*

The Duke University Center for AIDS Research GCLP-compliant AIDS Program (CFAR-GAP) consists of a group of specialized laboratories that conduct endpoint immunological assays for Phase I-III clinical trials for human specimens. As a result of their participation in clinical trial research, the need for a quality assurance program is crucial.

The Duke Center for AIDS Research (CFAR) Quality Assurance Unit (QAU) at Duke University Medical Center was founded in 2003 in order to implement principles of GLP in the Duke HIV Vaccine Trials Network (HVTN) Endpoint Assay Laboratories based on a mandate from the sponsor, National Institutes of Health (NIH) / Division of AIDS (DAIDS). Since 2004, the NIH / DAIDS have required that HVTN laboratories transition from Good Laboratory Practices (GLP) to Good Clinical Laboratory Practices (GCLP).

Since its inception, the Duke CFAR QAU has been faced with several obstacles such as: lab operators having no formal training or experience in GLP/GCLP, initial resistance from Principal Investigators, very limited budget for QAU to establish compliance, and little external support for implementing GLP/GCLP in the academic setting.

Now, after seven years, the Duke CFAR QAU has significantly grown and consists of five members dedicated solely to quality and apart from the conduct the research. The Duke CFAR QAU has expanded to include the role of Central QAU for two additional international HIV vaccine networks: Center for HIV/AIDS Vaccine Immunology (CHAVI), funded by the NIH / Division of AIDS, and Collaboration for AIDS Vaccine Discovery / Comprehensive Antibody – Vaccine Immune Monitoring Consortium (CAVD/CA-VIMC), funded by the Bill and Melinda Gates Foundation. While the Duke CFAR QAU continues to administer and monitor the quality program within the Duke CFAR-GAP, they have also been instrumental in providing advice and assistance to other national and international academic research laboratories. The QAU routinely provides GCLP training and assistance in other quality activities such as proficiency testing, assay validation, computer system validation, SOP writing, and quality management.

**Keywords:** University/Academic Research, Good Clinical Laboratory Practices (GCLP)

**Level:** Basic (Suitable for professionals with less than 2 years experience).

PP-14

**Promoting Academic Research and Development Laboratories in the International Setting to Perform GCLP-compliant Studies for Human Clinical Trials: A Challenge for Assay Implementation and Re-Validation**

Daniel Ozaki, Christopher Todd, Kelli M. Greene, Hongmei Gao, David Montefiori, Marcella Sarzotti-Kelsoe

*Duke University Medical Center, Durham, North Carolina, United States*

One of the key challenges in university medical research involves the application of international standards and guidelines to the conduct of non-commercial clinical trial endpoint assays that were originally developed in academic basic research laboratories. In the absence of a single central laboratory to perform all assays for clinical trials, it is imperative that the data from multiple laboratories performing endpoint assays in support of clinical trials are accurate and reproducible. To date, there has been very little guidance available to academic research laboratories on how to comply with standards such as Good Laboratory Practice (GLP) and Good Clinical Laboratory Practice (GCLP). The Collaboration for AIDS Vaccine Discovery / Comprehensive Antibody – Vaccine Immune Monitoring Consortium (CAVD / CA-VIMC), supported by the Bill and Melinda Gates Foundation, is assisting an international network of historically academic research and development laboratories in developing countries to become compliant to GCLP Guidelines with the goal of adding quality to the conduct of endpoint assays for Human Immunodeficiency Virus (HIV) clinical trials. For the past four years, our CAVD / CA-VIMC Central Quality Assurance Unit has worked with seven international laboratories in

enhancing the quality systems for the implementation of a validated endpoint immunologic assay in each laboratory through training and routine monitoring. Each laboratory was required to undergo initial training at the Central Reference Laboratory in the US and then implement the immunologic assay on site through several stages that involved partial assay re-validation, competency/proficiency testing, and formal external audits. Furthermore, the development of an external proficiency testing program by our Consortium has allowed the international laboratories to assess the comparability of assay results at their site with the results of assays performed around the world. As a result, several of the international laboratories in our Consortium are now in the process of conducting or planning to conduct the immunologic assay in a GCLP-compliant manner for ongoing human clinical trials. Such standardization and validation allow for effective assessment and comparison of data for scientific evaluation used to base decisions on potential HIV vaccine candidates' advancement through the clinical trial phases.

**Keywords:** Multisite Studies, University/Academic Research, Good Clinical Laboratory Practice (GCLP), University Specialty Section

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

PP-15

**Development and Implementation of an International Proficiency Testing Program for the Neutralizing Antibody Assay for HIV-1 in TZM-bl Cells**

Christopher Todd<sup>1</sup>, Xuesong Yu<sup>2</sup>, Daniel Ozaki<sup>1</sup>, Kelli M Greene<sup>1</sup>, Hongmei Gao<sup>1</sup>, Blake Wood<sup>2</sup>, Maggie Wang<sup>2</sup>, Peter Gilbert<sup>2</sup>, David Montefiori<sup>1</sup>, Marcella Sarzotti-Kelsoe<sup>1</sup>

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Carolina, United States, <sup>2</sup>SCHARP, Fred Hutchinson Cancer Research Center, Seattle, Washington, United States

Recent advances in assay technology have led to major improvements in how HIV-1 neutralizing antibodies are measured. An assay has been optimized, and many performance parameters of this assay have been validated in compliance with Good Clinical Laboratory Practices. Without the presence of a single laboratory performing all of the neutralization assays for candidate HIV vaccines and given the fact that this assay has been adopted by multiple laboratories world-wide, an external proficiency testing program has been developed to qualify laboratories to perform GCLP-compliant neutralizing antibody assays for HIV-1 vaccine clinical trials.

The program was optimized by conducting three independent rounds of testing, with an increased level of stringency from the first to the third round. Results from the participating domestic and international laboratories improved after each round as factors that contributed to intra-laboratory and inter-laboratory variability were identified and minimized. Key contributors to increased agreement were increased levels of experience conducting the assay, standardization of key reagents and adherence to GCLP.

A Study Plan for the final program was written, and included a statistical plan and pass/fail criteria. Based on results from the three rounds of testing, standardized proficiency test kits were assembled at QBI, Inc under GCLP conditions. The kits were designed according to the statistical requirements set forth by the Statistical Center for HIV/AIDS Research and Prevention (SCHARP). Each kit consists of identical stocks of six virus isolates and five blinded serologic reagents. At the beginning of the proficiency testing program, five experienced reference laboratories utilized the kits, in three repeats, to derive acceptance intervals for each antibody-virus combination. The official program was launched in August 2009 under the

sponsorship of the Collaboration for AIDS Vaccine Discovery and the National Institute of Health with enrollment open to any laboratory running a pseudovirus based neutralization assay for HIV-1 in TZM-bl cells.

The recent announcement of an effective HIV vaccine, RV144 in Thailand, makes this Program particularly useful for the standardization of laboratories at multiple international sites, which will be testing samples from trial participants for neutralizing antibody responses.

**Keywords:** Multisite Studies, University/Academic Research, Good Clinical Laboratory Practice (GCLP), University Specialty Section

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-16

##### Quality Assurance Access to Biocontainment at the United States Army Medical Research Institute of Infectious Diseases: A Pathway to Compliance

Allison Schaefer<sup>1,2</sup>, J. Edward Brown<sup>1</sup>, Carolyn Mentzer<sup>1</sup>, Steven Orr<sup>1,3</sup>

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Advanced development of medical biodefense countermeasures requires FDA approval. Therefore, effective quality assurance (QA) auditing of lab studies is essential. In addition to FDA Good Laboratory Practices (GLP) regulations (21 CFR 58), laboratory studies at the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) employing select agents require compliance to federal regulations controlling use of those pathogens (7CFR331; 9CFR121; 42CFR73; AR 50-1). Effective management requires attention to

physical security of laboratories, inventory of select agent materials, and confidence that personnel are reliable and trustworthy. In addition, biological safety is a critical component. To protect laboratory workers and the general public, multiple protective layers, including extensive training, health and psychological screenings, vaccinations, and security investigations, must be completed before biocontainment access is granted. These additional regulations increase the complexity of QA monitoring of laboratory studies being conducted in compliance with FDA's GLP. Our experience indicates that full GLP compliance is attainable at biosafety level (BSL)-3 and BSL-4 with sufficient planning and senior management support. Our poster describes this process as implemented at USAMRIID.

**Keywords:** Preclinical Research (GLP), Biohazardous Agents, Biodefense

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-17

##### **Immunogenicity: New Technologies – Methodology and Quality Assurance**

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<sup>1</sup>*Pfizer, Andover, Massachusetts, United States,*  
<sup>2</sup>*Pioneer Hi-Bred International, Johnston, Iowa, United States,* <sup>3</sup>*Sedor Quality Associates, LLC, Marlton, New Jersey, United States*

Various new technologies are being implemented across the biotechnology industry to support preclinical testing for immunogenicity. A comparison of multiple technologies and integrated systems will be presented. The Enzyme Linked Immunosorbant Assay (ELISA) is a standard microtiter plate based bioanalytical method. Alternative technologies include bead based methods such as BioVeris or AlphaLISA utilizing electrochemiluminescence or chemiluminescence, respectively. Additionally Meso Scale Discovery (MSD) is a microtiter

plate based electrochemiluminescence method. Each technology has specific advantages with regard to sensitivity, drug tolerance, and higher throughput capability. The quality assurance and auditing perspective will include the systems vulnerability with each technology and areas of focus when conducting audits.

**Keywords:** Biotechnology, Quality Assurance, Immunogenicity

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-18

**Abstract withdrawn by author.**

#### PP-19

##### **Performing Vendor Audits for Better Quality Compliance**

Sudheendra Kulkarni

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Clinical Research Organizations conducting Bioavailability, Bioequivalence and Phase I clinical trials depend on the pharmaceutical industry [sponsor] for their business activity. The sponsor company who conducts these studies at the CRO should have the reassurance from the CRO that quality deliverables will be met by having vendors and suppliers who meet certain standard criteria set by the CRO to provide services/supplies, which will not compromise on the quality aspect during the conduct of these studies.

The vendors can be broadly classified into two distinct types – Suppliers and Service Providers. Suppliers include instrument/equipment, stationery supplies [paper, printed envelopes etc], laboratory consumables like vacutainer(s), RIA vials, urine containers, alcohol swab etc. Service Providers like Independent Ethics Committee, Third Party Archival of documents,

Catering, X-ray facilities, Biowaste Disposal, Emergency Care etc. Therefore, these vendors have to be audited/inspected from the CRO periodically, to ascertain that they have some type of quality management system in place to meet the selection and continual criteria as a vendor to the CRO. The Quality Assurance department ensures that all the vendors are audited/inspected on a yearly basis to meet the certain industry standards. The vendor's are updated on the requirements in terms of suggestions/observations for corrective action. A checklist for each type – namely supplier and service provider should be used for the assessment of the vendor. At the beginning of the year a vendor audit schedule should be drawn and the plan followed so that all the vendors are assessed routinely. The advantages of this vendor audit/inspection is that the CRO will assure the sponsor that they have the best vendors at their disposal and also at the same time vendors would be content of certain business.

Vendor audits play a very important role in the quality management systems by meeting the GXP standards. By developing a strong quality control and quality assurance a CRO can ensure it meets all the local and international regulatory compliance but also can conduct cost-effective quality research.

**Keywords:** Clinical Research (GCP), Quality Assurance

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-20

##### **Top 483 Observations (and Other Findings) for Clinical Investigators and Sponsor/CRO/Monitors in Veterinary Trials**

Fredda Shere-Valenti, Vernon Toelle  
*US Food and Drug Administration Center for Veterinary Medicine, Rockville, Maryland, United States*

It can be a challenge to assure appropriate FDA 483 observations are cited for clinical

investigators and sponsor/CRO/monitors in veterinary trials as they vary considerably from human drugs. Violations against 21 CFR 58 has been relatively easier to identify as this regulation is used by all of the centers for good laboratory practices. Until recently, applicable citations in TurboEIR weren't available for CVM BIMO inspections and sometimes field consumer safety officers incorrectly cited human regulations. Now that citations are available, the field consumer safety officer can now select an appropriate charge specifically for a violation against 21 CFR 511. But what happens to those observations that do not raise to the level of a violation under 21 CFR 511? These and the most common FDA 483 observations will be presented.

**Keywords:** Animal Health, Audit/Inspection

**Level:** Intermediate (Suitable for professionals with more than 2 years experience).

#### PP-21

##### **The Quality and Regulatory Product Lifecycle**

Howard Cooper

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This is a poster that discusses the regulatory and quality requirements needed to successfully develop and commercialize a product. This is based on Juran's concept of the 'Quality Loop' which is defined below. Juran, as you know, is one of the quality pioneers.

Juran was chief editor of the 'Quality Control Handbook.' The Quality Control Handbook is accepted by the courts and the FDA as a quality authority.

Quality Loop-Conceptual model of interacting activities that influence the quality of a product or service in the various stages ranging from the identification of needs to assessment of whether these needs have been satisfied-Juran.

This poster translates Juran's quality into the sequence of regulatory steps needed to commercialize a product. The poster contains a circle beginning with identification of need, discovery, development, GLP, GMP, GCP, submission, post market, and improvement. It will also briefly mention the product lifecycle discussed in ICH Q10.

**Keywords:** Good X Practice (GXP, multidisciplinary)

**Level:** Basic (Suitable for professionals with less than 2 years experience).