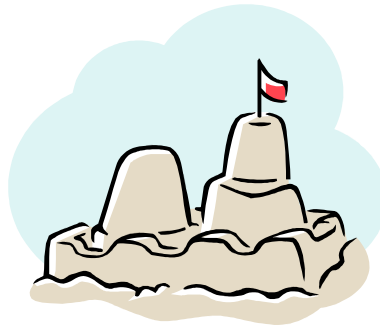




“News from the Heartland”
Mid West Society of Quality Assurance Newsletter
September 2007



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Please submit articles for the next newsletter by **Nov. 15th** to editor@mwsqa.org



Midwest Regional Chapter, Society of Quality Assurance Summer Meeting

Barbara Stephenson
MWSQA, Vice President
& Planning Committee Chair

The annual summer meeting for the Midwest Society of Quality Assurance was held on 17-18 July 2007 in Kalamazoo, Michigan at the Radisson Plaza Hotel & Suites. The Corporate Sponsor and Host for the meeting was MPI Research.

The meeting consisted of two half day pre-conference workshops: The first workshop was presented by Deb Garvin, of WCQTI/Pacific Rim Consulting, Inc, US and OECD GLPs and Managing Multi-Site Studies. The second workshop, GXP: Good, eXtreme Practice for Validation of Computer Systems was co-presented by Bob Herr, Tom Klomprens and Brenda Kolkman of Pfizer, Inc. Both workshops were well received.

Our Keynote speaker, Bill Harrison of MPI Research, emphasized the importance of mentoring in the development of Quality Professionals. Other presentations covered a wide range of topics, including responsible approach to computer validation, bioethics in research, GLP training of animal technicians, risk assessment and dose formulation analysis.

The networking event on Tuesday evening, sponsored by MPI Research, was held at the Gilmore Car Museum which included live musicians, beer and wine tasting combined with a terrific menu. For those of us who are old enough to have a license and know how to drive a stick shift, vintage cars were available to drive. There were many smiling faces that evening as we drove or rode along the private roads at the museum.

Our attendance was excellent with one hundred attendees and eleven speakers.

I would like to thank our Vendors, Sponsors, the Planning Committee and each and every attendee at the meeting for making the 2007 Summer Meeting a meaningful and fun experience.



Minutes from MWSQA Business Meeting

Jon Krueger
Covance

Date of Meeting: 18 July 2007

Discussion Items:

MWSQA BoD is considering offering only one meeting per year instead of two/year as done in the past. The general consensus of the group was that one/year is preferred. Since there are now many choices of meetings that people can go to (SQA annual meeting, EdComm, MWSQA meetings) and people are generally only permitted by employers to attend one meeting it would be better to only offer one/year. We can then offer more in one meeting than splitting resources (e.g., speakers, costs, etc) for two meetings/year. Attendance is generally larger for once/year meetings.

Brian Mitchell stated that we need to find a sponsor for next years meeting and asked attendees to consider asking their companies if they may be interested in sponsoring the 2008 MWSQA meeting.

SQA Update □ Brian Mitchell provided a brief summary of the transitions which have taken place over the past several months and will be continuing. SQA Head Quarters is planning a key role – assisting with membership lists, sending out notices/reminder notices, receiving dues and payments for conference meeting, etc.

MWSQA membership has significantly grown this year to an all time high of 325 members. This appears to be a result of the resources, which have been available to us from SQA Head Quarters.

Membership directories are targeted to go out to members around August 7.

Many accounting tasks have also been transferred by SQA Head Quarters. Our current treasury is just under \$55,000 prior to paying bills for the July conference. Brian Mitchell explained the advantage that we now have combining our savings with Head Quarters in that we can earn a higher interest rate on MWSQA savings account.

Website has not yet been transitioned to SQA Head Quarters but is planned to be transitioned in the near future. Plans are to have a member only page with member login username and password similar to the SQA website. Newsletter update

Newsletter articles are due July 27 and should be submitted to Celeste Rose or Paula Wehmeyer.

Closing Summary: MWSQA is currently in a positive position and is financially strong with strong membership.



23rd Annual SQA Meeting – A Success Story

John L. Decker, RQAP-GLP
MPI Research

The 23rd SQA Annual Meeting held in Austin, Texas, was a great experience for all who attended. I was fortunate to be awarded a scholarship by the Midwest Regional Chapter of SQA to attend this informative conference. This was the first opportunity for me to partake in the conference as an auditor, and as an active member of the MWSQA and SQA.

Highlights from the conference included numerous opportunities to network with auditors from many different companies, participate in pre-conference trainings, attend informative sessions, and learn of regulatory updates by representatives from the respective agencies.

The networking opportunities provided auditors the chance to communicate issues occurring within their own companies and consulting groups. Issues that have not been resolved within their own groups are now being discussed in open forums and new and fresh ideas are being shared. These ideas are now being taken back to companies and applied to those issues and problems and the situations are resolved, which increases auditing efficiencies and compliance within those groups.

The conference also provided numerous sessions with many informative lectures pertaining to training styles and techniques, regulatory agency updates, new information on developing product lines (i.e. *In vitro* toxicology), and issues associated with multi-site studies. These are a few of the topics discussed at the Austin, Texas meeting and the topics that benefited me as a trainer and auditor.

Finally, the regulatory updates provided by agency officials were particularly interesting. These sessions provided all in attendance an idea of the scope of future inspections conducted by the regulatory agencies. The final session of the conference included regulatory agency officials who addressed pre-submitted questions and scenarios.

Overall, I was very thankful for the opportunity presented to me by the MWSQA regional chapter. The ideas and training received through the 23rd SQA Annual Meeting were very beneficial to me as an auditor and trainer. I would like to thank the Board of Directors for this opportunity and look forward to using the knowledge I gained to promote the goals and objectives of the SQA.





MWSQA Seeks Candidates for Office

Andrea Steed
Eli Lilly

The Midwest Regional Chapter of the Society of Quality Assurance's (MWSQA) Nominations Director is seeking candidates for the upcoming elections in November!

The positions needed are:

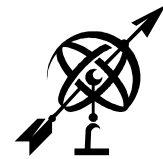
- Vice President (3 year commitment),
- two Directors (2 year commitment), and
- Treasurer (2 year commitment).

To view the position descriptions, go to the MWSQA website at mwsqa.org and click on the "officers" link.

This is a great way to get involved and make a difference in where the chapter is headed in the future! For more information or to put your name on the ballot for a position, please contact Andrea K. Steed at aksteed@lilly.com or (317)655-9131.

MWSQA Needs You!





Part 58 Data – The Principals of Compliance

Mark Sullivan
Covance

The evaluation of compliance in a GLP laboratory is a daily struggle. Interpretations seem to swing back and forth over the years making it difficult to assess what is most compliant. If this is happening in your laboratory, then it is time to assess how these interpretations are made. The beauty of Part 58 is its simplicity and elegance. If there is variation in interpretation, then it indicates that compliance decisions are not reflecting directly back to the regulations. The regulations do not change. For example, it is easier to train someone to record all items in a protocol than to train them to evaluate what is actually necessary. Unfortunately there is a continuum of increasing detail ranging from SOPs to sequentially recording all observations. All these methods of data production are compliant, so it is the Study Director, and no one else, who determines the best data structure to support any conclusions. Today, so many simplifications have become traditional they are difficult to see beyond. A proper compliance discussion should involve what is the most appropriate regulatory citation, and how can the underlying principles in the regulations be applied to the work, and not what has always been done,

The following literal interpretations may give you an opportunity to reflect whether the regulations conflict with how things are done at your laboratory.

Part 58 data requirements are actually rather simple. The Study Director is responsible for all data recording, verification, analysis, and reporting. (58.33)

All data generated shall be recorded directly promptly and legibly in ink.

All data entries shall be dated on the date of entry and signed or initialed by the person entering the data. The principle that all data entries must indicate by whom and when they were created is called attribution. Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change. Part 11 follows these principles for electronic data with the refinement that the electronic signal is the raw data. In summary, compliant data is legible, directly associated with the original observation, and has attribution. (58.130 (e))

Raw data, which is a subset of Data, is defined as any laboratory worksheets, records, memoranda, notes, or exact copies thereof that are the result of original observations and activities of a non-clinical laboratory study and are necessary for the reconstruction and evaluation of the report of that study. (58.3 (k))

Each GLP laboratory is required to enact a set of Standard Operating Procedures which are approved by Management. The Quality Assurance Unit is then responsible to assure that the final report accurately describes these procedures and methods, and that the reported results accurately reflect the raw data of the non-clinical laboratory study. (58.81)

The objective of GLP compliant data is to provide a robust body of information which is then represented in the final report.

Since raw data is composed of original observations, it is not possible to go back in time and do any study activity over. Therefore whatever is recorded is what there is, and raw data cannot be "fixed." This principle is "The data stands."

A GLP study initiates when the protocol is signed, and ends when the final report is signed. (58.3 (o) (p)) Within this interval, study activities such as data clarification may occur. The regulations do not have any limitations on the recording of information as long as that information is recorded in ink, and who and when the information is recorded is clear. Therefore clarifications can be made at any time within the interval of a study, but a clarification cannot "fix" a compliance deviation. A clarification can become raw data because it may be necessary for the interpretation of the overall data, regardless of when in the study the clarification is created. The principle here is that it is possible, and often desirable, to make and record an original observation of the raw data as it stands.

The regulations clearly require each GLP laboratory to institute and maintain a set of Standard Operating Procedures. (58.81) The purpose of Standard Operating Procedures is to regularize laboratory processes and to simplify data recording. Since the final report must accurately describe methods and procedures, there is no doubt that SOPs may support a final report. (58.35 (b) (6)) The principle here is that it is not necessary to duplicate a Standard Operating Procedure in the raw data. But if the SOP is not clear, or contains options, then whatever is done must be recorded.

The existence of Standard Operating Procedures has another profound result. At no time can an original observation be recreated after the fact, but a Standard Operating Procedure exists until it is deactivated by management. Therefore at any time during the interval of the study, a procedure can be described in the data as long as that procedure is in effect. Often a process is completely reconstructable from the Standard Operating Procedure, but the product of that process may be lost or unclear. The principle here is "differentiate process and product."

The Study Director is the single point of control, and responsible for all data recording, verification, interpretation and reporting. (58.33) Therefore it is a principle that all data is recorded at the pleasure of and for the convenience of the Study Director. Exact copies may be made of raw data, (58.3 (k)), and used as raw data, but there is absolutely no requirement to make multiple records for the convenience of anyone. Likewise there is no differentiation in the regulations between "study data" and "facility data". The regulations clearly indicate "all data generated" (58.130 (e)) The reason for this is that no matter how carefully a study is planned, there will be unforeseen events. It is not until the data as a whole is evaluated, that it will be known what data is necessary for the reconstruction and evaluation of a non-clinical study. All data should be considered raw data.

Since Standard Operating Procedures have the function of regularizing study activities, it has been an assumption that data must be consistent. In fact, the regulations do not ever mention consistency, but actually indicate that unforeseen events must be recorded in the data.

Presently it is traditional to format all clarifications and additions to data as footnotes. Nowhere in the regulations does it actually address the use of footnotes. Other formats could be used as long as they do not obscure the original entry and clearly indicate by whom and when the entry was made. (58.130 (e))

Data can always be better, and it can always be worse. Positive documentation is a concept that is prevalent today. Nowhere in the regulations does the term "positive documentation" occur. This concept exists to facilitate training. If all study personnel are taught that each item in a protocol must be written down, and then that item is described in the report, it simplifies the whole process into a chain of events. But there is no requirement to duplicate the regulations or SOPs in the data or the protocol. It is the Study Director's responsibility to conduct the study according to the regulations (58.33 (e)) and SOPs, and record whatever data is necessary for supporting the conclusions of the study. The Study Director is responsible for the interpretation of the data. Every moment of a study does not need to be recorded--- only sufficient data so that a Study Director may reasonably interpret that the protocol was followed and that the conclusions are valid. In the real world, GLP data consists of a matrix of original observations

that should reflect study conduct and results, and support analysis. Therefore the number and detail of observations are made not by tradition, but at the Study Director's discretion. The demand for positive documentation denies the Study Director's role as interpreter, and creates a situation where data is always incomplete, because there is always something more that can be recorded. If valid conclusions are not to be devalued in a mass of meaningless data issues, it is critical that the Study Director consciously make the decision when 'enough is enough'.

Not all data has the same value. Again this is why the Study Director has the power to evaluate data, and determine its usefulness. For example, indicating that a Standard Operating Procedure is followed may have less value than a sequential recording of all actions, but either probably could equally well support a conclusion. Only when a process itself is being evaluated does the level of detail become critical to the study conclusions. Likewise, it should be expected that a Study Director would reject data that does not meet that Study Director's minimum expectations and that data would not be reported.

It is a common misconception that the Quality Assurance Unit (QAU) is responsible for both compliance and data. The QAU is only responsible for conducting periodic phase inspections, maintaining a Master Schedule of Studies, maintaining a set of protocols, assuring the final report reflects the raw data, periodically submitting a status report of all studies to management, and notifying management and Study Director of any deviations from the regulations. (58.35) It is interesting to note that since all interpretation resides with the Study Director, as does the responsibility for compliance, then any compliance issue is an issue only if the Study Director evaluates that it is. The only real power that the GLP QAU has is that which derives from persuasion.

Since the Study Director is legally the single-point of control in a non-clinical study, (58.33), the Study Director is in a unique position from all other study personnel. As long as a Study Director records data in a compliant format, that data must be accepted as long as it is not ridiculous. The difference between observation and interpretation may not always be black and white. Data may be reported by the Study Director in whatever form that Study Director chooses. Once a certain Study Director was questioned about how he could report that pigs were gelded, when this detail was not in the data. He made a comment to data, and properly said, that he was there, he knew the pigs were gelded, and he was Study Director, and the report stands. The principle here is that a Study Director can manage a study however that Study Director chooses within the confines of the regulations.

The report is the final objective of all data. The regulations indicate that the Quality Assurance Unit shall assure that the reported results accurately reflect the raw data. (58.35 (B) (6)). The word "reflect" is carefully used here. Even a broken mirror can reflect. There is no expectation to report all data, nor even all items in a protocol. There is a specific list of items that must be addressed, (58.185), and there must be sufficient raw data reported to support the conclusions of the study. Those data used to support an evaluation are at the Study Director's discretion and do not need to be all-inclusive.

If it is necessary to evaluate whether data is compliant, the principles above allow a simple series of questions to clarify the issue, and indicate any corrective actions.

Does the data exist?

Is the data written directly, promptly, legibly, in ink?

Is there attribution?

Does any change clearly show what was changed, what is new, why it was changed, and by whom and when it was done?

Is this described in Standard Operating Procedure? (Process or Product)

Would a "reasonable person" agree that there is sufficient information recorded to reconstruct study conduct indicated in a protocol?

If yes is answered to all these questions, then the data is compliant. This process can be used for any compliance issue. The value and of any QAU will be enhanced the more the regulations govern our thinking and interpretations.



Audit Committee Report – 2007

Janet Cunningham

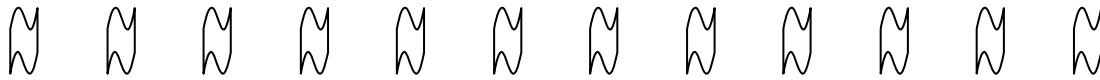
Eli Lilly

The 2007 MWSQA Audit Committee was comprised of Janet Cunningham – Committee Chair, Carol Thompson and Marcia Rexroat, all of Eli Lilly & Company, Indianapolis, IN. The audit committee conducted its review of the MWSQA Chapter's 2006 and 2007 to date financial records in March 2007.

The audit consisted of reviewing the 2006 bank statements, invoices/receipts, cancelled checks, Form 990 and the year-end treasurer's report for clarity, consistency, accuracy and completeness. Minor discrepancies were noted during the audit and were discussed with the Chapter Treasurer who provided the records. The following are the discrepancies and the anticipated corrective actions:

1. A deposit of \$260.00 is recorded on the Treasurer report and ledger as occurring on 3/28/05. This is actually the date the deposit was posted by the bank; the actual transaction date was 3/26/05. Corrective action – the ledger and Treasurer report will be corrected to reflect the transaction date.
2. There was a deposit of \$1410.00 on 9/9/05, with a returned check of \$200.00 on 9/16/05. The Treasurer report indicated the deposit was actually \$1210.00 (factoring in the returned check). Corrective action: The Treasurer report will be updated to indicate the actual deposit of \$1410.00 on 9/9/05 and the returned check of \$200.00 on 9/16/05. The overall balance will not be affected.
3. There was a check written for a charge of \$120.11 on 9/25/05 for Board of Director dinner. An invoice or receipt for this charge was not in the records. Corrective action: The receipt for this charge was located and copied for the records.
4. There was a check written to the Holiday Inn for room charges, which included charges for two individuals. There was not a written receipt/invoice for these charges, but hand written information. Corrective action: The records will be clarified to indicate that the hand written information was provided by the hotel clerk at the time of check-out from the hotel.
5. A check was written to MARSQA on 10/1/05 for a re-payment of advertisements. There were invoices, but a copy of the check written to MARSQA was not included, but a cancelled check was in the bank records. This was an inconsistency with the processes. Corrective action: Clarification will be added to the records by the Treasurer.
6. There was a deposit on 10/1/05 for \$120.00, from a check received by the Treasurer. A copy of the check was not included in the records. Corrective action: Clarification will be made to the records.
7. Deposit on 10/8/05 for \$1180.00, bank receipt and bank statement both agree with the amount listed in the Treasurer report, ledger and check register. However, upon review of the copied checks, only \$1080.00 was copied. Corrective action: Since the bank receipt and bank statement agree that they received \$1180.00 then clarification will be made to explain the missing check.
8. There was a service charge of \$10.00 that was documented as being assessed in November according to the Treasurer report. However, the bank made this charge in October. Corrective action: The Treasurer report will be updated to indicate when the charge was assessed.

The Financial Audit Form was provided to the Chapter Treasurer for retention. Once the Board approves this report, it will be provided to the Chapter Treasurer for retention. The audit of the Chapter's 2006 financial records will be completed within the first quarter of 2007.



JOB OPPORTUNITY CERTIFIED QUALITY ASSURANCE SPECIALIST

ChanTest (www.chantest.com) is a Cleveland, Ohio-based, internationally-recognized ion channel company providing drug safety and discovery services to the biopharmaceutical industry and has been recognized as the world's most trusted ion channel services company. Our company is undergoing a major expansion of staff and is seeking to add a certified QA specialist to its Quality Assurance Unit (QAU). The QAU consists of two full-time QA specialists, one QA/QC specialist and a team of GLP-trained and qualified Study Directors.

Job Responsibilities:

- Coordinating and performing study-specific inspections and inspections of the testing facility, including its processes, documentation, and personnel to ensure compliance to internal standard operating procedures
- (SOPs) and applicable international, federal, and state regulations
- Reporting inspection findings to Study Directors and Management
- Securing/maintaining QAU records separately from other facility records
- Helping to identify and develop systems/processes needed to support the quality function of the company, including identifying needed SOPs, writing and revising SOPs and serving as a resource to assist others in writing SOPs
- Ensuring compliance with internal SOPs
- Maintaining Master Schedule of all nonclinical laboratory studies
- Supervising sponsor and regulatory inspections of the testing facility and, with the support of management, addressing reported observations
- Planning growth of the QAU to support services

Minimum Qualifications:

- Bachelors degree in science, preferably biology or chemistry
- Three years GLP or related quality assurance experience in the pharmaceutical industry
- Experience with Part 11 validation preferred
- RQAP-GLP a plus

ChanTest provides a competitive benefits package. Salary is commensurate with experience. Please send your resume with salary requirements and three references to: humanresources@chantest.com, or fax to (216) 332-1706. Equal Employment Opportunity.

Contact: Dee Groynom
ChanTest Corp.
14656 Neo Parkway, Cleveland, OH 44128
dgroynom@chantest.com
Phone: 216-332-1665





Note from your Editor

Greetings All,

Hope your summer has been wonderful and that you're refreshed and ready to send an article to the newsletter. Special thanks to Mark Sullivan as the most prolific contributor who is not also a board member in the last seven years! Much as we appreciate hearing from him, is there anyone else out there who has knowledge or opinions to share? Please don't be shy.

Paula

Paula N. Wehmeyer
Bioanalytical Systems, Inc. (BASi)

Thank You to All Who Contribute to Our Newsletter!!!

*Opinions are those of the authors and not necessarily those of MWSQA.
The editor, MWSQA and national SQA are not responsible for any damage.*