NERC SQA
New England Regional Chapter
Society of Quality Assurance

# Northern Highlights

September 2005
Volume 8 –Issue Number 1

# President's Message

## Make NERCSQA Your Organization

By Beth Moulaison

Here we are, already more than six months into the year, with an outstanding new and returning group of NERCSQA directors and officers. We have already accomplished so much this year and are still working on creating a meaningful and informative fall program for you, our members.

One of the initiatives of the chapter has been to breed new life back into our newsletter. A Publication Committee was formed this year and is spear-headed by two of our board members, Denise Hayes and April Brunelle. I would like to take the opportunity to thank the entire committee for all the work they have done to make this, our first newsletter of 2005, a success.

*"Quality is the result of a carefully constructed cultural environment. It has to be the fabric of the organization, not part of the fabric."*
*- Philip Crosby*

Our Program Committee has also been working really hard to offer training programs to meet the needs of our area. Our first program in the spring featured discussions on Clinical compliance issues and our summer session dealt with the issues surrounding archiving and e-signatures. Soon you will receive notice of our fall training and member's meeting in October, which will focus on medical devices.

We are always looking for ways to reach out to our current members to become a voice. The Nominating Committee, which is led by Kathy Vanderhoof this year, is actively seeking candidates for open officer and director positions. Serving on the NERCSQA board is an excellent opportunity to expand your QA knowledge and leadership skills and to build a network of colleagues and friends. If serving as an elected official is not a possibility for you at this time, there are many other ways to participate. Our committees are always looking for member involvement, so don't hesitate to throw your hat into our Membership Committee, Program Committee, Sponsorship Committee or Publication Committee. Also, share your training flyers with colleagues and let them know what NERCSQA has to offer.

Finally, NERCSQA will be celebrating our 10th anniversary in 2006. We are beginning planning our celebrations already! Jump in and help us celebrate.

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# 2005 NERCSQA COMMITTEES

Program Committee Volunteers at Registration Desk

**Program Committee**

*The Program Committee develops educational programs, makes arrangements for speakers or other features, and arranges for meeting places.*

Chair: Lynn Burtner
Charles River Laboratories – Preclinical Services
Email: VP@NERCSQA.org

**Nominating Committee**

*The Nominating Committee is appointed by the Board at least 3 months prior to the annual election to identify candidates for election. The Nominating Committee Chair is appointed by the Board each year.*

2005 Chair: Kathleen Vanderhoof, CRL Discovery and Development Services
Email: Nominating@NERCSQA.org

**Historical Committee**

*The Historical Committee compiles and maintains files of documents and information that map the development and history of the Chapter such as photographs, newsletters, national meeting presentations and other documents.*

Chair: Sharon Mercando, Pfizer, Inc.
Email: PastPresident@NERCSQA.org

**Membership Committee**

*The Membership Committee identifies opportunities for NERCSQA to serve its members and performs outreach to identify new members.*

Chair: Melanie Noland, Separcor, Inc,
Email: DirectorM@NERCSQA.org

**Publication Committee**

*The Publication Committee compiles and publishes the Chapter Newsletter "Northern Highlights, manages the content of the NERCSQA website (www.NERCSQA.org), and prepares the Chapter poster for the annual SQA meeting.*

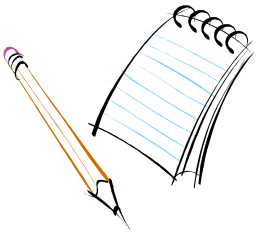
Chair: Denise Hayes, Vertex Pharmaceuticals Incorporated
Email: DirectorP@NERCSQA.org

**Sponsorship Committee**

*The Sponsorship Committee solicits corporate sponsor to support the NERCSQA mission and activities and facilitate the Sponsor's use of the benefits associated with their participation.*

Chair: Randy Covill, Wyeth Bio-Pharma
Email: DirectorS@NERCSQA.org

## Newsletter Information



*Your comments on and contributions to Northern Highlights are welcomed.*

Submit articles and information to DirectorP@NERCSQA.org

**Schedule for Next Issue**
Submission Deadline: October 15, 2005
Publication Date: November 2005

**Contributors to this Issue**

Lynn Burtner
Denise Hayes
Beth Moulaison
Melanie Noland
Sharon Shiner
Mark Sullivan
Kathleen Vanderhoof

# The Characteristics of Robust Data

**Contributed by Mark Sullivan**

**Reprinted from "News from the Heartland" Midwest Society of Quality Assurance Newsletter August 2004**

Saying that you 'know it when you see it' is insufficient when advising a Study Director on how to improve data. Data should record the conduct of a study sufficiently so that each aspect that might effect the interpretation of the data can be reconstructed and repeated. "Robust Data" here indicates data that is thorough enough to reconstruct a GLP study with a maximum of reliability.

Often the best way to guide a Study Director is to present a simple, easy to remember principle that illustrates the issue, and then explain it. The Study Director may not agree with your explanation or suggestions, but they will rarely argue with the principle. Therefore even if our suggestions are ignored, compliance is improved.

This article is an explanation of the elements of data and some simple talking points that any QA auditor can carry into the laboratory.

**Robust data reflects that which directs it.** A GLP study can be divided into a series of activities, and each activity will have direction, a record of conduct, and record of all variables. Clear guidance must be provided either by protocol or Standard Operating Procedures.

**Robust data consists of positive documentation.** Each individual study activity should be represented by a recorded data point. An animal 'observation by exception' recorded by no data point is inherently less robust than a recorded observation of "normal". But care must be taken not to over record. It is possible to bury critical data in mountains of data of little value, and create a situation in which the data is not clear. For example, putting animals into a stainless steel cage for a study is a single activity, and daily record of the animal in a stainless steel cage is needless and redundant.

**Robust data has data attribution in all aspects of the study.** All samples, data, or reports must be able to survive a "dump test." Could you take any part of a study and dump it on the floor and put it back together without any questions? Every piece of a study must be uniquely identified and have a logical chain of custody throughout the whole study. Likewise, all aspects of a study must be attributed to a time and a person. It must be possible to reconstruct a chronology of a study, and know exactly who did what.

**Robust data records and accounts for all variables.** Generally, these variables consist of all the measured values and unplanned events that at the report stage support or detract from the scientific evaluation of the study. One of the basic tenets of Good Laboratory Practices is that there must be data to support the accuracy of measured values. Without this supporting the data, any data indicating a measured value is no longer robust and its value becomes questionable to the study director.

Continued on the next page

**The Characteristics of Robust Data (continued)**

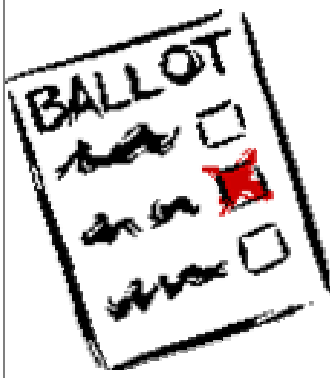
**Robust data is understandable and has utility.** Data must be understandable to the average man, and be in a form that can be used and archived. In the real world, reports are written from the data, and the writer is often a person of less education than the Study Director. Obscure data, even if correct, only promotes error and inefficiency in the report writing process.

**Robust data contains a record of systematic review.** Verification of data is a Study Director responsibility, and a part of the GLPs. Oddly, review of data, which is a study function, is often done by Quality Assurance Units, which could be argued to be a non-compliant event. Nevertheless, it is critically important that robust data be "verified" in a consistent and systematic way.

These principles should provide clarity and direction when next confronted with a data issue. Just remember to focus on the data, apply the principle to the situation, and your argument will be hard to refute.

## Nominating Committee News

**Contributed by Kathleen Vanderhoof**




Nominations are now being accepted for the following Officer and Board positions:

Vice President – one opening with a 3-year commitment

The VP also serves as the Chair of the Program Committee. Following the 1-year term as VP, this person will automatically become the NERCSQA President for 1-year and then will serve as the Past President for 1-year. The VP must be a NERCSQA and SQA member.

Secretary—one opening for a 2-year term

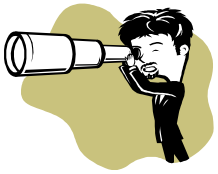
The Secretary works closely with all Board members and committees to capture information and communicate it to the membership. Serving in this leadership role provides an excellent opportunity to learn new skills and interact with some great people. The Secretary must be a NERCSQA and SQA member.

Director – two openings for 2-year terms

Directors serve on the Board and lead a NERCSQA Committee. Directors must be NERCSQA members.

## Fall 2005 Training is Coming.

**Watch our your email, mail or our website for more information!**



# Able Laboratories - Tipping the Compliance Balance

**Contributed by Denise Hayes**

Earlier this year, the FDA advised consumers that Able Laboratories (Able) was conducting a nation-wide recall of all of its manufactured drugs, which are primarily generic pharmaceuticals, and had ceased production of any new inventory. In its press release, FDA listed more than100 products branded by Able as well as private label products for 5 other firms that were part of the recall. The FDA press release also cited that there were "serious concerns that [drugs manufactured by Able] were not produced according to quality assurance standards."

Based on the observations listed on the Amended FDA 483 that Able posted on its website, fundamental cGMP principles were found to be deficient by the FDA Investigators including:

- Quality Unit releasing drug batches that failed to meet specifications
- No documentation of out-of-specification results to explain retesting and re-injection of test results that did not meet specifications. The FDA 483 included more than 20 specific examples of failed in-process, stability, and finished product test results that had been accepted.
- ANDA Annual Reports included only passing data; OOS results were not reported. The FDA 483 identified 4 ANDAs that were withdrawn due to "submission of erroneous data."
- Field Alert Reports were not routinely filed when products did not meet specifications.
- In the laboratory records, OOS results were replaced with passing results by modifying processing methods, cutting and pasting chromatograms and changing samples weights.
- Employees were not trained in cGMP and procedures required by cGMP.

With the news of the recall Able stock price fell from $24.63 to $6.26 in one day. (May 18-19 2005). In the subsequent 9 weeks, there were several management resignations, a workforce reduction, a voluntary Chapter 11 (bankruptcy) filing and an eventual delisting of the company's stock from the NASDAQ exchange. This is a sad chapter in the story of a company that increased sales from $19.6 million to $103.2 million between 2001 and for 2003 and in 2003 and 2004, the company was granted 28 ANDAs in 2003, of which t6 were 'first to file' products.

Beyond the business impact of a major recall due to quality and compliance issues, consumers and their health care providers are forced to find substitute products that will ensure that treatment continues and the reputation of the pharmaceutical industry as a whole is once again called into question.

As a QA Professional I am left to wonder - How did this happen?, Where was they quality function (QA, QC)? Did this result from ignorance of the basic QA and compliance standards, an over-stretched work force, greed, and/or other business pressures? I am glad that I have always worked in organizations strive to find the right balance between compliance and business. It is not always easy but the cost when the balance tips too far in one direction or the other can be very high.

# NEW FDA GUIDANCE DOCUMENTS

## ICH Draft Consensus Guideline, Quality Risk Management, Q9

Released for Consultation at Step 2 of the ICH Process on 22 March 2005

This document provides guidance on the principles and tools to support a scientific and practical approach to quality risk management. ICH points out that "The risk of its quality is just one component of the overall risk. " The guidance is not intended to create any new expectations beyond the current regulatory requirements. Risk management methods and tools described include

- Failure Mode Effects Analysis
- Fault Tree Analysis,
- Hazard Analysis
- Control Points and Preliminary Hazard Analysis

## Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers

Final July 2005

Pharmacology and Toxicology

This guidance outlines a process (algorithm) and vocabulary for deriving the maximum recommended starting dose (MRSD) for first-in-human clinical trials of new molecular entities in adult healthy volunteers, and recommends a standardized process by which the MRSD can be selected. The purpose of this process is to ensure the safety of the human volunteers.

## FDA Pilot Program on Submission of CMC Information in a NDA Under the New Pharmaceutical Quality Assessment System

In a July 14 Federal Register posting, the FDA announced that it is seeking pharmaceutical companies to volunteer to participate in a pilot program involving the submission of chemistry, manufacturing, and controls (CMC) information consistent with the new risk-based pharmaceutical quality assessment system. This pilot program will be limited to 12 original NDAs to be submitted by December 31, 2006, in the CTD format, paper or electronic.

Under this quality assessment approach, the agency intends to facilitate innovation and improvement throughout the product lifecycle and provide some regulatory flexibility by applying quality-by-design principles. While it is expected that a CMC submission under the new system will contain more comprehensive and expansive information than in current submissions, the FDA also believes that this may lead to less need for information that could be handled through inspectional oversight of current good manufacturing practices (cGMP) requirements.

Through this pilot program, the agency hopes to enable the public and regulated industry to provide feedback that will assist FDA to develop a Guidance for Industry on the new quality assessment system.

Written and electronic requests to participate in the pilot program must be submitted to the agency by October 31, 2005.

# The Birth of NERCSQA

## An Interview with Jane Snell, First NERCSQA President

**Contributed by Sharon Shiner**

**What were your reasons for forming NERCSQA?**

At the time there was no training available for the bench QA person and money being spent on revenue generating groups often ran out by the time it got to QA training. I thought if there was something local the expenses would be less and the likelihood of QA people getting to go would increase. There was also the issue of networking with other QA professionals.

**How did you go about getting the organization started? Did you look to SQA to help you get started?**

I did. I received the procedure from SQA for starting a chapter and followed the instructions. There were a couple people at other chapters that helped me by reviewing the documents.

**What did you find critical to getting the chapter going?**

Getting other individuals involved was critical because there is no way I could have done this alone. Denise Hayes, Linda Chin and Anne Kowalewski (Trainor) were extremely supportive and instrumental in launching this chapter.

**Were there any specific requirements necessary for starting the chapter?**

Yes. SQA had detailed the process in a policy document.

**What was the hardest thing about starting the chapter?**

Writing the By-laws.

**Was there anything you would have done differently?**

I don't think so. At one time I did think that it would have been better to get the clinical and manufacturing QA people involved at the beginning of the process but they already have well established groups and have not been all that excited about ours.

**What were the first meetings like?**

They were small (15-25 people) and were held in the evenings with a single speaker. They were held at one of the member sites because our treasury was non-existent and free was all we could afford. The meetings lasted for a couple of hours with networking at the local bar before the meeting got started.

**Can you share a particular memory about the early NERCSQA years?**

We had a meeting scheduled at our site and I had a client audit going on. The topic was QA and Study Director Conflict Management and as I was getting ready to leave they asked how much it would cost to attend the NERC-SQA meeting. As they were MARSQA members, I took this as a sign that our chapter had arrived!

**What is your favorite thing about NERCSQA as it stands today?**

I think it has matured and the chapter is a good source for networking as well as a way to get good, inexpensive training. I like seeing all the new faces and it is really nice when I hear someone say that they are glad they came because they learned something that will enable them to do their job better.

**What are some of the challenges and opportunities for NERCSQA today?**

Attracting new members is a big challenge (as is keeping the ones you have). Many regulatory groups are vying for that membership dollar so the Chapter will have to make sure it can offer a good return on that investment. Once convinced to join, the challenge will be getting new members to volunteer to be active committee members.

The link to SQA should be strengthened. There are some benefits to having a big sister and I think this avenues need to be explored.

I also think that every year NERCSQA should sponsor training events for both beginner and advanced QA profes-sionals. These events could even be co-sponsored with another chapter and focus on "reality training" with mock inspections as well as the basics.

# Program Committee Update

**Contributed by Lynn Burtner**

This year has been a very successful one for the Program Committee. Our first training of the year was held in March at the Sheraton hotel in Framingham, MA, focused on "Clinical Compliance: Audits, Inspections, and New Technologies". This was a full-day training that included five speakers on the topics of eSource, CDISC, clinical bio-analytical assays, and FDA GCP inspections.

Participants at a NERCSQA Training Session

The June training took us to the beautiful Publick House in Sturbridge, MA, where we learned about "Administering, Archiving, and Auditing Documentation Systems". We had three great speakers who presented on electronic regulatory submissions, e-signature systems, and archiving design.

We have had great feedback from those in attendance and welcome ideas from all of the NERCSQA membership. Currently the Program Committee is working on plans for our fall training and member's meeting in October, with a focus on medical devices. Keep an eye out for the flier in September and be sure to register early to take advantage of the pre-registration discount!

If you or someone you know is interested in being a presenter or becoming part of the Program Committee, please contact Lynn Burtner at VP@nercsqa.org.

# Membership Committee Update

**Contributed by Melanie Noland**

NERCSQA will be celebrating our 10th anniversary in 2006. We are very excited about our upcoming milestone! Our membership number is currently at approximately 117 members. We are counting down the top 5 member benefits. Also remember you do not have to work in Quality Assurance to join NERCSQA. Please tell a friend or colleague about NERCSQA!

### Membership Benefits

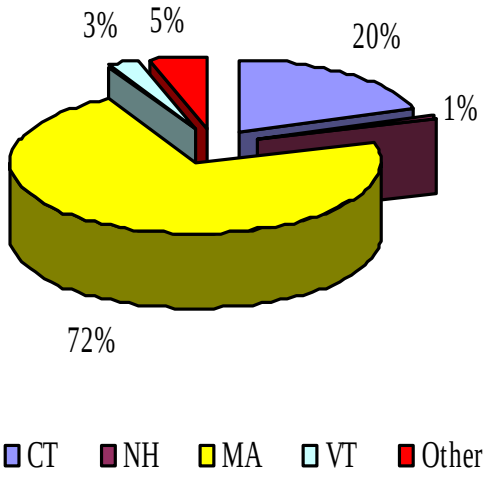
FREE Subscriptions to Northern Highlights, our quarterly newsletter.

Career Services: job listings.

Continuing education & professional development: regional meetings and events. Members get discounted prices!

Professional networking opportunities at our local meetings.

Personal benefits: end of the year social. Local meeting door prizes.




2004 member demographics by state

NERC SQA
New England Regional Chapter
Society of Quality Assurance

**We're on the Web!**
**www.NERCSQA.org**

## NERCSQA MISSION

To serve as a focal point for Quality Assurance "GXP" professionals in the New England Region by establishing a forum for education, training, communication and information exchange among QA professionals in the environmental, pharmaceutical and biotechnology fields of government, private in-

Serving the needs of Quality Professionals in Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont since 1996

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