MARSQA MONITOR

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MARSQA
Mid-Atlantic Region Society of Quality Assurance

Call for Nominations!

We are now seeking candidates for the 2017 MARSQA Board of Directors. The MARSQA Board of Directors encourages members at all levels of experience to consider running for election. All that is needed is a commitment to participate. Candidates for Vice President and Treasurer must also be members of SQA to quality for the ballot.

Positions to be filled include the following:

- **Vice President** – One-year current term (will become President and Past President for a term of three years total)
- **Treasurer** – Two-year term
- **Directors (two positions)** – Two-year term

Visit the MARSQA website for the responsibilities and estimated time required for each position. You may also contact Kiet Luong, MARSQA President, to discuss these important roles. MARSQA has an experienced group of officers already in place to guide those of you who may be concerned about being new to the Board.

Managers – MARSQA provides cost-effective training, networking and other professional development opportunities locally to help you develop your staff into seasoned quality assurance professionals. In the past several years, the preponderance of the efforts that keep MARSQA viable and valuable to you and your organization has been contributed by individuals representing only the companies that MARSQA serves. We are most grateful for those who have volunteered their time and efforts. We urge you to participate directly and/or encourage your staff to run for one of the available elected positions.

If you are a current MARSQA member and would like to put your name on the ballot, or you would like to nominate an individual you feel has the leadership skills, ability, and interest, please contact Penny Jegede or Kiet Luong by Friday, 14 October 2016. Be assured that no name will be placed on the ballot without the individual's consent.

Sincerely,
MARSQA

Inside this issue:

Contradictions to Ensuring Safety in Clinical Studies

An example of a clinical study where the outcome of their use caused serious harm

March 2006, Parexel Clinical Pharmacology Unit, London, UK: Phase 1 Study on healthy volunteers, to study a new class of monoclonal antibody (mAb) called IgG4k mAb, with a stimulatory action on regulatory T-cells. This was the first study/ first dose of this drug in humans. Most phase 1 studies are not anticipated to have pharmacologic effects based on the projections provided through pharmacokinetics analysis on data gathered from pre-clinical toxicity studies. The purpose of Phase 1 studies is to Test a small group of people (20–80) to evaluate safety, determine safe dosage ranges, and begin to identify side effects. A drug's side effects could be subtle or long term, or may only happen with a few people, so phase 1 trials are not expected to identify all side effects.[1] The purpose of research and development of IgG4k mAb is for potential therapeutic treatment of B-cell chronic lymphocytic leukemia, and rheumatoid arthritis however, the efficacy would have been studied in later phase studies after completion and analysis of safety data from the phase 1 study (is).

This study became coined as the TeGenero Incident, when the first intravenous infusions, a single dose, were given to six healthy volunteers that immediately required intensive organ support for eight to sixteen days due to "cytokine storm". A cytokine storm is a potentially fatal immune reaction consisting of a positive feedback loop between cytokines and white blood cells. As a result reported by the Sunday Times, 30 July 2006 reports that "the victims of the deadly TGN 1412 experiment have been told that the toxic effect of a single dose of this monoclonal antibody face contracting cancer and other fatal diseases as a result." There is inflammatory damage, and fibrotic healing when a cytokine storm is experienced causing permanent organ dysfunction.

What went wrong scientifically:

Pre-clinical study reports were not available/not required by the MHRA (Medicines and Healthcare Products Regulatory Agency), yet the pre-clinical studies did not predict a safe dose for humans even though the currently required regulations had been met. Monoclonal antibodies frequently have infusion reactions related to immunogenicity after the second dose however, it has been known that mAb's can have their most severe immunological effects upon receiving the first dose. It can be surmised that TeGenero, may not have designed their pre-clinical studies to detect this type of T cell activation.

Continued: Contradictions to Ensuring Safety in Clinical Studies

What went wrong clinically:

No sign of contaminants in or errors in manufacturing, formulation, dilution, or administration that would affect end result. As reported by The International Herald Tribune, one of the subjects stated that He believed "he was participating in a fairly standard trial of a painkiller like ibuprofen, for arthritis." He said that "the novelty of TGN 1412 never came up in upbeat pre-trial briefing, adding: "I had no idea it altered the immune system.'" "At Parexel's orientation meeting there was little time to read the study's 11-page consent form before signing, Rob O. said. Headaches and bruising were listed as potential side effects, as well as the possibility of a severe allergy. But that risk was downplayed." This is an indicator that the informed consent process contained significant weaknesses. An evaluation done by Norman M. Goldfarb, Managing Member of First Clinical Research LLC determined the following gaps per ICH E6, in the informed consent[2] document that could have impacted the study participant's willingness to participate:

- ◊ Missing statement of randomization possibilities
- ◊ Discussion of risks was not apparent based on the novelty and potential strength of TGN1212
- ◊ Missing statement on potential benefits
- ◊ The consent stated that concerns about the study should be communicated to the principal investigator sand the ethics committee secondarily however, the ethics committee is not listed in the Informed consent document
- ◊ Potential coercion with this statement: "If you leave the study and exercise your right to not give a reason…no payment need be made to you"
- ◊ Although this statement is written about a stipend paid to subject for participating in the trial/any additional costs "compensate for any inconvenience", the injured subject Rob O, still pays his own cab fare for follow up medical care from the incident

Preventive Action: The Creation of the EMEA Guideline: "Requirements for First-in-Man Clinical Trials for Potential High-Risk Medicinal Products" (EMEA 2007c, 2007d).

This guideline is intended to assist sponsors in the transition from non-clinical to early clinical development. It provides criteria to classify new investigational medicinal products as potential high-risk medicinal products. It also gives guidance on quality aspects, non-clinical testing strategies and designs for first-in-man clinical trials for high-risk medicinal products, including the calculation of the initial dose to be used in humans, the subsequent dose escalation and the management of risk.

1. Clinical Trials Wikipedia: https://en.wikipedia.org/wiki/Clinical_trial
2. First Clinical Research: http://www.firstclinical.com/journal/2006/0605_TeGenero.pdf
3. The TeGenero Incident and the Duff Report Conclusions: A Series of Unfortunate Events or an Avoidable Event? Christopher J. Horvath & Mark N. Milton

MARSQA Member Spotlight: Dana Wood

Where do you work and what is your specialty?
"I work at Janssen R&D in Spring House, PA. My official title is Compliance Analyst and my colleagues and I support clinical and non-clinical PK and ADA data generated from the Biologics Development Sciences group. We do 100% QC review of data and documentation and make sure work is done in a compliant manner based on our SOPs and federal regulations. I also support our department's outsourcing efforts to make sure our externally generated data meets our compliance expectations as well."

Describe your pathway to the regulatory world.
"I started out as a research scientist at Merck, then moved to the more regulated world of running clinical assays at PPD. With that experience I moved to Janssen to join their compliance group."

What is your favorite movie and why?
"Probably "Aliens". I like movies with strong female roles and Ripley takes the cake! Plus I like any alien/creature/dinosaur/zombie movie in general where the creature(s) obliterates almost everyone in an apocalyptic manner. It's my escape from reality."

What is one thing about the regulatory world that you enjoy?
"I really like the discussions surrounding regulatory rules and regulations. At first glance they may seem cut and dry, however, there can be many interpretations of the rules and it's always interesting to get other people's perspective. I like having these types conversations with people -it's my favorite part of the job!"

What is your favorite local restaurant?
"Kamita in Oaks, PA! It's a Japanese/Chinese/Thai restaurant that does all 3 incredibly well!! Pad Thai is my favorite comfort food."

What is the legacy you would like to leave behind?
"To know that I've contributed, even if it's in a small way, to medicines that make a difference in people's lives and nice, well-behaved children."

Call for MARSQA Presenter Volunteers !!!

Help MARSQA have another successful year and volunteer to be a meeting presenter!

- Are you a GLP Expert? GMP Expert? GCP Expert?
- Do you have an interesting Quality topic you would like to present?
- Are you a Quality Archives Expert?
- Do you know about Quality Risk Management?

If you answered yes to any of the above questions you are ready to be a MARSQA presenter.

Contact MARSQA Vice President, Stacy Wilson if you are interested in being a MARSQA presenter! Visit www.marsqa.org for contact information.

Outsourcing : Keys to Successful Sponsor and CRO Partnership

by Dana Wood

It is not surprising that Pharma companies are outsourcing more and more these days. With stagnant resources and increasing workload, it makes sense to contract with a CRO to meet deadlines. Whether the decision to outsource is purely resource related or additional expertise is needed, sponsors not only want good, sound science, they also want the quality of that work to be of high standard, especially if that work falls under GLP or another GxP regulation.

So how does a company ensure compliance and overall quality when outsourcing? Here are a few things to consider…

- **Vetting** – Do your homework!! it's critical to properly assess your vendor before placing work. An on-site audit is best in that it allows you to personally meet those who will be handling your projects. I recommend having both scientific/technical and quality representatives perform the audit to get the full picture of the CRO's capabilities.

- **Communication – this cannot be emphasized enough**! Proper communication is the key to any successful project. Ask your team: how will you communicate? Is email best? Teleconference? How often? Should the CRO expect on-site visits to monitor progress? Talk about these details at your introductory meeting and for every meeting thereafter, it is important to record minutes to be distributed so all parties are on the same page. Also, if GLP, ensure there is a clear communication procedure to the Study Director for deviations and other important study-related correspondence.

Continued: Outsourcing : Keys to Successful Sponsor and CRO Partnership

by Dana Wood

- **Expectations should be spelled out prior to the start of work –** Detailed contracts are critical to success. Nothing should be assumed. Not only should the technical end-goals of the project be described, but quality and data integrity expectations should be clearly stated in the contract as well. In addition, it's important to have a mutual understanding on both sides of what is written in the contract and protocols. **READ AND UNDERSTAND!**

- **Documentation –** Standards for documentation should be defined early in the process. Whose templates will be used for reports? How will approvals be handled? Are formal memos needed or is email okay?

- **Processes and SOPs –** again this comes down to good communication. Define whose SOP's are being used for the project. Is it the sponsor's or vendor's? In most cases it's best practice to use vendor's SOPs since it decreases the chance for deviations and study delays. In cases where sponsor's SOPs must be used, it should be communicated to the CRO in a timely manner and a full acknowledgment of the process should be demonstrated. Understanding what the differences between the processes are and getting agreement early on how to move forward will save time and keep the project moving smoothly.

These are just a few of the points to consider when initiating a project with a new vendor or CRO. In a sense, the Sponsor/CRO relationship is a partnership - the end goal is the same: bringing life-changing drugs or devices to the people who need them. Open communication, defined expectations, clear contracts and documentation are essential to successful projects and most importantly cultivates trust between the two parties. There will always be challenges (hey, this is science - nothing ever goes right 100% of the time) however, working through obstacles is a lot easier when there is a solid foundation of communication and trust in place.

Advertisements and MARSQA Contact Information

To contact the entire MARSQA board please e-mail:

board@marsqa.org

For individual Board Member e-mail addresses, please see:

http://www.marsqa.org/board.shtml

MARSQA Disclaimer:

Please note, during membership meetings, photography during the meeting may occur. If you do not wish you photograph to be included in upcoming MARSQA newsletters, please e-mail *newsletter@marsqa.org*

Upcoming Events

MARSQA Membership Meeting

06 Oct 2016

C*ck and Bull Restaurant
Peddler's Village,
Lahaska, PA

See www.marsqa.org

10:00—11:00:	GLP Discussion Group and Computer System Validation Quarterly Meeting
12:00—1:00PM:	**Lunch Buffet**
1:00PM -1:15PM:	MARSQA President—Introductions, Agenda, and MARSQA Business
1:15PM -2:00PM:	y
2:00PM - 2:45 PM:	**Bioanalytical Study Report - Reporting of Qualitative Bioanalysis,** *Mehmooda Shaikh, Research Scientist II, Bristol-Myers Squibb*
2:45 - 3:15 PM:	Afternoon Break/Networking and Beverages and Cookies
3:15 - 4:00 PM:	**Business Continuity: Best Laid Plans vs. Real Life Experience** (Previously presented at the 2016 SQA Annual Meeting), *Melissa Elliott, Director, Quality Assurance, Envigo*
4:00 - 4:15 PM	Business Card Prize Drawing
4:15 - 4:30 PM	Closing

Winter MARSQA Membership Meeting

December 6, 2016

Come celebrate MARSQA's 25th anniversary. Pre-registration is required.

A Murder Mystery luncheon with the theme "Murder at the Malt Shop" will be held.

More info coming soon!!