



## WELCOME TO MARSQA 2018!

### Our Board of Directors:

**President:** Megan Lawhead  
**Vice President:** Nancy Gravino  
**Past President:** Stacy Wilson  
**Treasurer:** Tina Myers  
**Secretary:** Denise Wilson  
**Director:** Lyn Dugger  
**Director:** Christi Velez  
**Director:** Erin Range  
**Director:** Narith Flach

### Our Committee Members:

**Computer Validation:** Denise Botto, Chris Wubbolt, Calvin Kim  
**Education & Program Planning:** Roxanne McDonald, Tara Keener  
**Historical:** Nancy Gravino  
**Nominating:** Lyn Dugger  
**Membership:** Lyn Dugger  
**Newsletter:** Tina Myers, Amanda Hobson  
**Technology:** Kiet Luong

\*Please consider volunteering for the open committees or on any of the other committees. We would love to have you on board.

Contact the Board of directors for more information on volunteer opportunities: [board@marsqa.org](mailto:board@marsqa.org)

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### SPECIAL POINTS OF INTEREST

- Full Day MARSQA Member Meetings
- Free Webinars Through SQA
- CSV Training

# Call for Nominations!!

## MARSQA Board of Directors



MARSQA is seeking candidates for the 2019 Board of Directors (BoD) . The MARSQA BoD's encourage MARSQA members at all levels of experience to consider running for election. All you need is a commitment and a modest amount of time to participate. Positions to be filled will start working in their role **January 2019.**

An email appeal from the MARSQA Nominating Committee Chair to all MARSQA members will be sent 4Q2018 in search of candidates. If you are a current MARSQA member and would like to be considered, or you would like to nominate another MARSQA member who has consented, please respond to the Nominating Committee email to receive instructions and a biography template.

### **Vice President**

- ◆ One year term
- ◆ Plus one year succession to Presidency
- ◆ Plus one year succession as Past President
- ◆ Program Committee Advisor
- ◆ Member of Finance Committee

### **Treasurer**

- ◆ Two-year term
- ◆ Leads of the Finance Committee/liaison with SQA Accounting office
- ◆ Financial summaries at monthly MARSQA BoD meeting

### **Director** (two positions)

- ◆ Two-year term
- ◆ Voting member of the BoD
- ◆ Attends monthly meetings
- ◆ Optional duties include: Chairperson of MARSQA committees; MARSQA projects

Descriptions of Officer and Committee responsibilities can be found here:

[MARSQA.org/bylaws.com](http://MARSQA.org/bylaws.com).



What Floats Your Boat?  
We'd be sunk without  
volunteers!

**Get Involved With The MARSQA  
Organization!**

**All Committees are looking for new  
members for 2019 –2020**

If you are interested in participating Contact:

**board@marsqa.org**

Read MARSQA Bylaws: [http://  
www.marsqa.org/bylaws.shtml](http://www.marsqa.org/bylaws.shtml)

<u>COMMITTEE NAME</u>	<u>RESPONSIBILITIES</u>
Computer Validation	Provides current industry perspectives to the MARSQA membership on computer validation issues.
Education & Program Planning	Organizes training for Chapter members. Plans meeting programs. Coordinates with the hosts on the site to conduct Chapter meetings.
Historical	Collects and maintains information and artifacts related to the establishment and progression of the Chapter. Presents historical perspectives of the Chapter at Regional and National SQA meetings
Nominating	The Nominating Committee is responsible for recruiting the slate of candidates for Officer and Director Positions open for election. The Nominating Committee prepares the slate of candidates and sends it to the Board for approval. Once approved, the Committee emails the ballots to SQA for formal voting.  Prepares the slate of candidates for Chapter Officer positions for approval by the Chapter Board. Prepares the ballot and candidate biographies for mailing to the membership. Conducts the counting of ballots.
Membership	The Committee serves as the coordinator and liaison between the MARSQA Board of Directors and the general membership of MARSQA. The Committee works to attract new members, retain current members, and complete member surveys. In addition, take suggestions and make changes for improvements.  Maintains the roster of Chapter members. Prepares annual dues statements. Develops and conducts membership drives.
Newsletter	Edits the Chapter newsletter, MARSQA Monitor. Disseminates relevant information to the Chapter membership.
Technology	Oversees the MARSQA website and other uses of technology to advance the Chapter's mission.

# NEW FDA GUIDANCE!!!

## USE OF ELECTRONIC HEALTH RECORD DATA IN CLINICAL INVESTIGATIONS

Tina Myers, GCP

In July 2018 a new FDA Guidance was issued to outline recommendations primarily focused on the following (goals are italicized):

- ◆ Deciding to use EHR
- ◆ *Interoperability of with Electronic Data Capture systems*
- ◆ *Quality and integrity of data captured by EHR*
- ◆ Meeting the inspection/record keeping/record retention requirements of FDA.

The purpose of the guidance is for the use of EHR data in clinical investigations (drugs/biologics/medical device/combo products/in-practice investigations).

The Guidance is **not applicable** to the following **technologies**: Mobile, telehealth, medical devices, remote monitoring devices.

### Section IV: Interoperability and Integration of Systems

- ◆ Integrate the systems to avoid manual transcription errors
- ◆ Adopt open data standards as seen in the ONC Health IT Certification Program
- ◆ Create corresponding and structured data elements
- ◆ Validation interoperability

### Section V: Best Practices For Using EHR in Clinical Investigations

- ◆ Policies and processes in place
- ◆ Sponsors communicate EHR challenges with FDA
- ◆ EHR certification through ONC Health IT to comply with 45 CFR 170
- ◆ Sponsor Data Management Plan should include list of EHR systems used by each clinical investigator site
- ◆ The Informed Consent should include identification of entities that will have access to the patients records.

Find the Guidance here: <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM501068.pdf>

## Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)  
Center for Biologics Evaluation and Research (CBER)  
Center for Devices and Radiological Health (CDRH)

July 2018  
Procedural

### Understand the Difference

#### EHR vs EMR

**Electronic health records (EHRs)** EHRs focus on the total health of the patient—going beyond standard clinical data collected in the provider's office and inclusive of a broader view on a patient's care. EHRs are designed to reach out *beyond* the health organization that originally collects and compiles the information. They are built to share information with other health care providers, such as laboratories and specialists, so they contain information from *all the clinicians involved in the patient's care*. Although similar,

**Electronic medical records (EMRs)** are a digital version of the paper charts in the clinician's office. An EMR contains the medical and treatment history of the patients in one practice. (1)

(1) Health IT Buzz; Peter Garrett and Joshua Seidman PhD | January 4, 2011; <https://www.healthit.gov/buzz-blog/electronic-health-and-medical-records/>

# Data Integrity and Computer System Validation Perfect Together!

By: Cathlin Shapiro, Lead, GXP Data Integrity Governance, Bristol-Myers Squibb

August 27, 2018

## Data Integrity

...has been a hot topic for the past several years, with the focus on GMP QC laboratory data and laboratory software systems, along the increase in observations and warning letters with egregious examples of data falsification of QC testing data. But data integrity is a very broad area, and one overlooked segments of data integrity is the connection to computer system validation. Because many of the data integrity observations deal with control deficiencies in software, there is a natural connection between the two practices.

As a part of a robust data governance program, computer system validation processes should be evaluated for enhancements to include the data integrity elements suggested in this article. In fact, the MHRA “GxP Data Integrity Definitions and Guidance for Industry” has an entire section on “designing systems” for control of data integrity, which connects directly with system development and computer system validation.

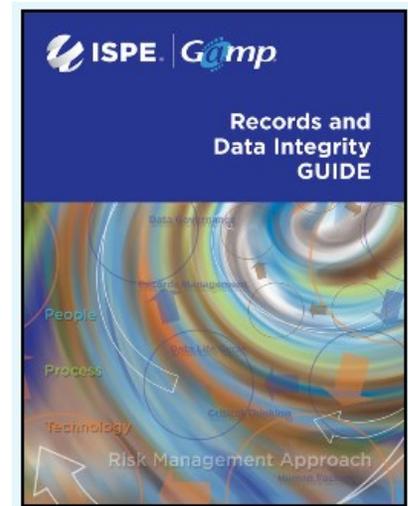
### The first step

...in ensuring that data integrity is included in your computer system validation processes is to ensure the organizational connection between the groups, depending on how your company is structured. Representatives from the validation group should be stakeholders in the overall data governance program. The validation group representative should provide the expertise on the existing validation process, while the data governance program should provide the current requirements and interpretation of data integrity associated with computerized systems. Data governance programs are sometimes sponsored by the Quality organization or Data Management groups.

### The second step

...is to examine the current requirements that may be in a template in your organization for functional or regulatory requirement specification documents. This is where the enhancements for building data integrity into system implementations begin.

You may find that there are similarities between 21 CFR Part 11 or Annex 11 requirements with those of data integrity requirements, especially in the area of security and audit trail. But at this intersection is where you should expand the focus of these requirements with the aspect of how the system is controlling the data.



**The ISPE GAMP Guide for “Records and Data Integrity” or “RDI Guide”** has a section with suggested data integrity requirements. You can use this resource to map to your organization’s standard requirements to include newer data integrity requirements that will then be tested later in the validation activities, which will in turn improve your data integrity compliance position.

**Some examples of data integrity requirements are:**

*The system should ensure that the accuracy, completeness, content, and meaning of data is retained throughout the data life cycle.*

*Original records and true copies should preserve the integrity (accuracy, completeness, content, and meaning) of the record.*

*Where appropriate, operational system checks should enforce permitted sequencing of GxP steps and events, and should disallow non-permitted sequencing of GxP steps and events.*

*Computerized systems exchanging data electronically with other systems should include appropriate built-in checks for the correct and secure entry and processing of data, in order to minimize the risks.*

**During the design phase**, make sure to include the documentation of the data flows in the system, or a “data map”. This should include validated interfaces, reports, manual entries and provide a holistic view of the types and methods of data usage and flows. Once the data map has been created, the data governance program should provide training and tools to assist teams in analyzing the data integrity risks associated with the data flows. The combination of understanding the data process flow risks, along with identification of “critical data” will assist the teams in assessing where to apply technical and procedural controls.

Once the implementation team reaches the **testing phase**, this is where it is recommended to expand testing to ensure data retains its integrity in the areas of negative testing and boundary testing. Many times computer system validation follows a “positive path” of testing because it is mirroring the business requirement of how the business process should work. In the case of negative testing, this questions of what happens to data if an interface failed or a user forgot to click a Save button? Is the data duplicated or lost? These are the scenarios

that robust data integrity testing should cover. It has been recently noticed in health authority observations about the lack of “challenge testing” during validation, so this is clear indicator that validation processes should expand beyond positive testing solely.

Another common area of health authority observations has been around the reliance on vendor provided **validation packages**. This is when no evidence is found of the testing for intended use or for a specific company’s configuration or data flows. This should also include the testing of specific security models and segregation of duties, which is a data integrity connection to ensure that those users who have interest in the data cannot modify the data without review and approval procedures.

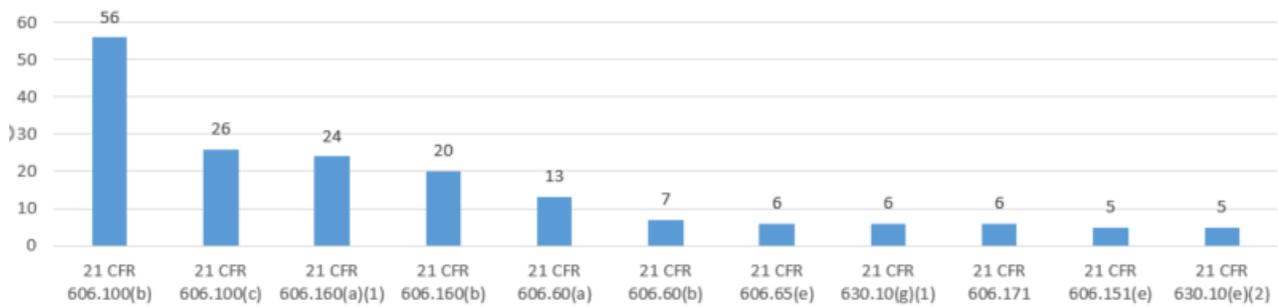
One of the most complex areas of any system is the **audit trail** and the associated review procedures, coupled with the fact that the lack of audit trail review is another highly cited observation in the scope of data integrity. During validation processes, ensure that the audit trail functionality is activated, is functioning as intended, and provided the required data elements are present in the audit trail logs themselves. Prior to the system’s implementation, procedures must be created for the review of the data or business audit trail, along with review of the system audit trail, which is more for ensuring the actions of the system administrator were under control and the system’s validated configuration is still in a validated state. It is recommended that validation teams thoroughly understand the functionality of the audit trails in order to guide teams in the creation of review procedures and robust testing scripts.

**Conclusion**

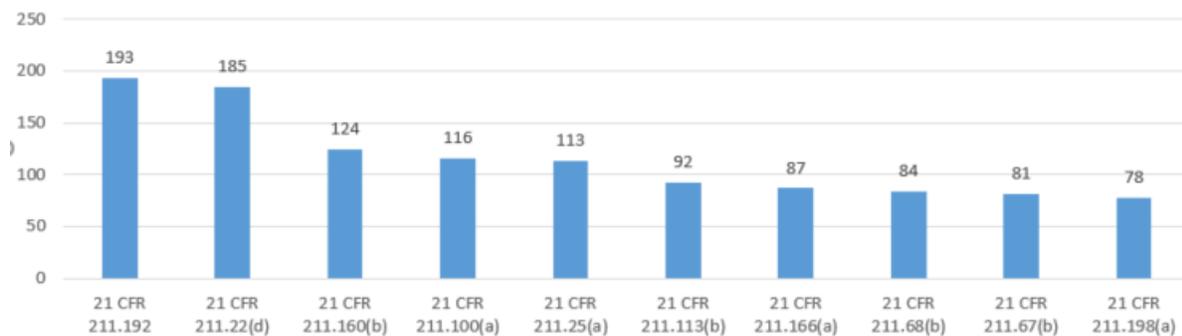
The current industry focus on data integrity should lead to enhancements on computer system validation process within your organization, including requirements, design, security, data maps and interfaces, testing and audit trail functionality. As data integrity requirements expand and refine for your company, so should your existing computer system validation processes.

# 2017 FDA Inspection Citations Summary

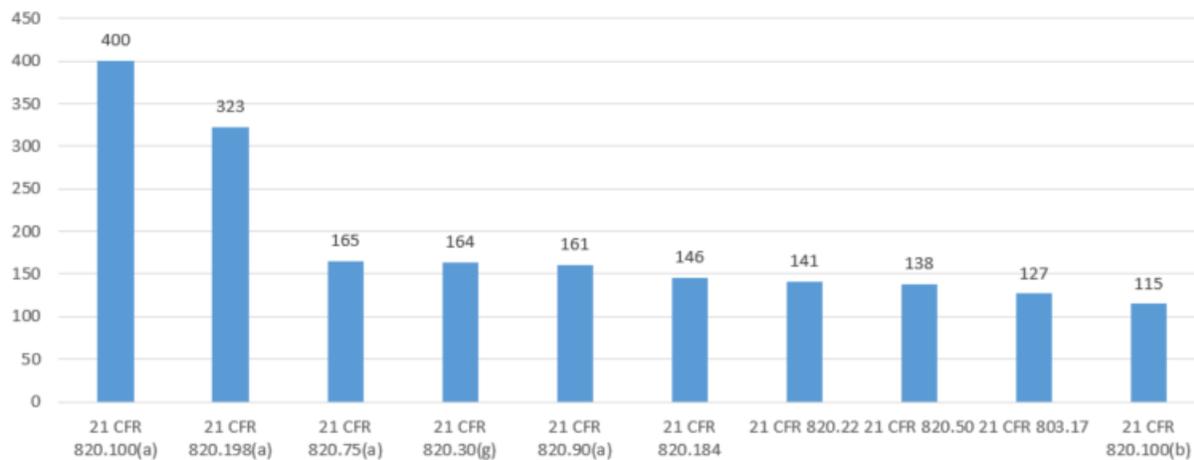
## Biologics Top 10 Citations



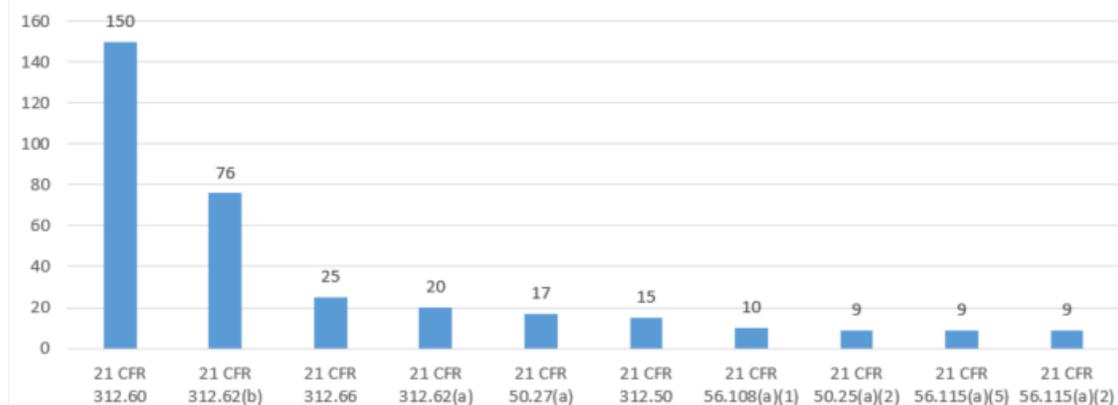
## Drugs Top 10 Citations



## Devices Top 10 Citations

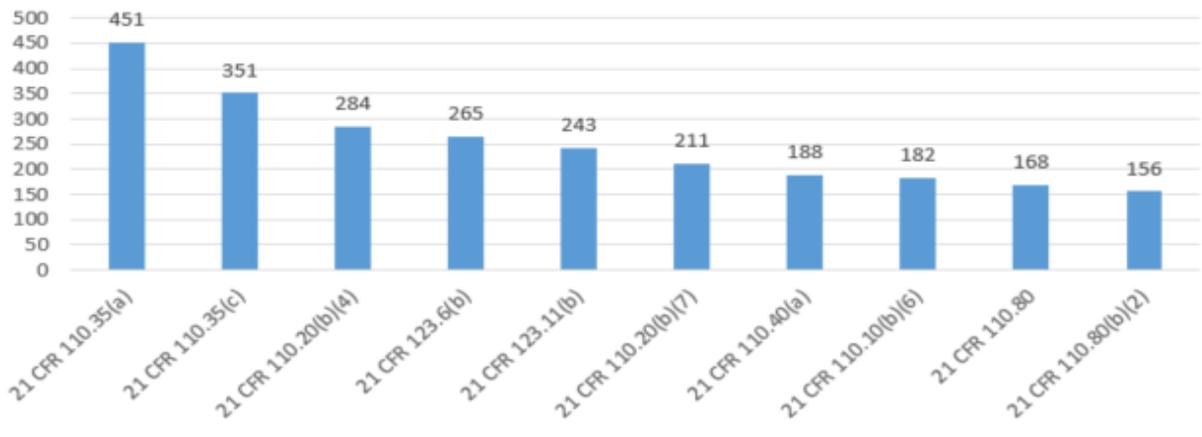


## Bioresearch Monitoring Top 10 Citations

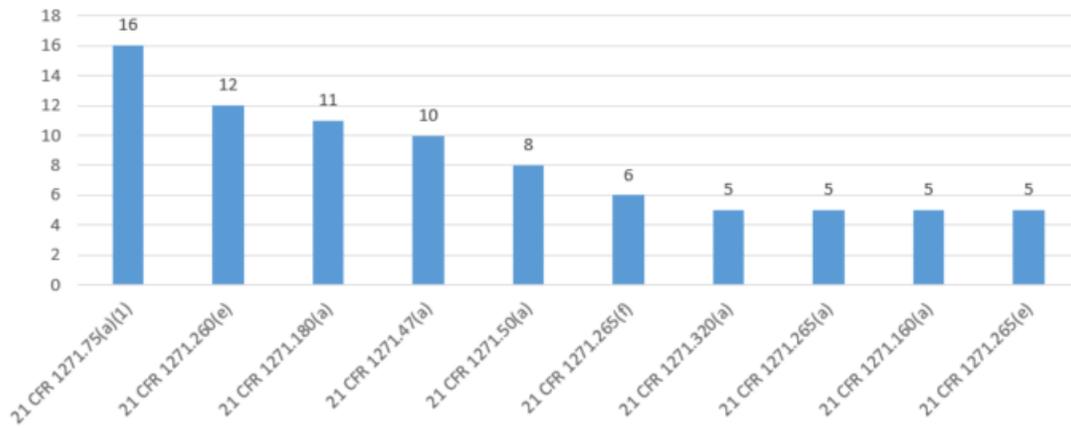


# 2017 FDA Inspection Citations Summary continued...

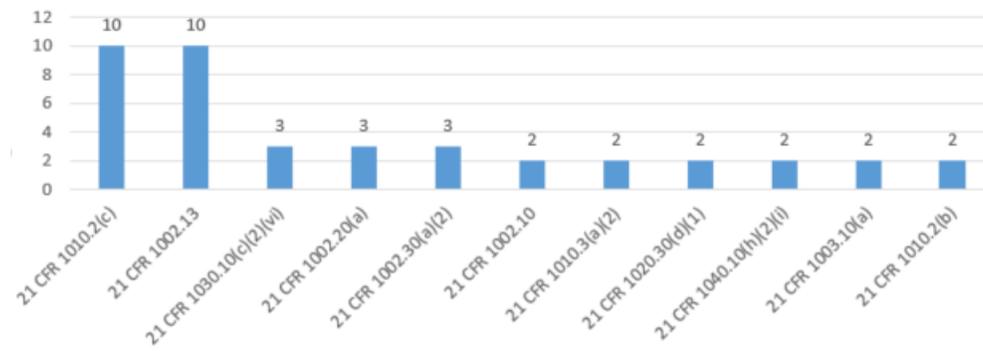
## Foods Top 10 Citations



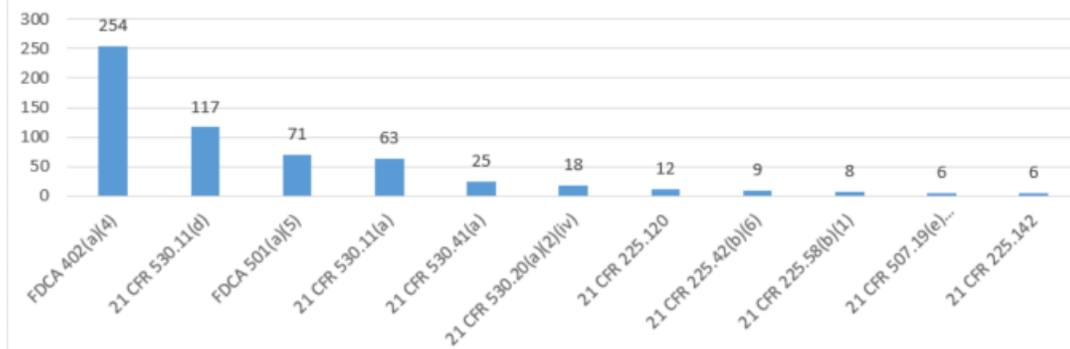
## Human Tissue Top 10 Citations



## Rad Health Top 10 Citations



## Vet Med Top 10 Citations



# “You can inspect but there’s no documentation to look at.”

## Analysis of FDA Inspection at a Clinical Investigator Site

Tina Myers, GCP

### The Observation on the FDA Form 483

#### “You failed

...to retain records required to be maintained under 21 CFR Part 312 for a period of two years following the date a marketing application is approved for the drug for the indication for which the drug is being investigated; or, if no application is filed or if the application is not approved for such indication, until two years after the investigation is discontinued [21 CFR 312.62(c)].”

*Failed to retain records of the disposition of the drug, including dates, quantity, and use by subjects. failed to retain adequate and accurate case histories including signed and dated in-*

### The Principal Investigator’s Defense

- ⇒ During the inspection: the Principal Investigator stated that all study records related to Protocols XYZ and ABC had been shredded or destroyed by my staff.
- ⇒ In the written response: I understand that records were to be retained for 2 years following study termination at a site and kept the records 2 years from the date of site closeout, after which the records were destroyed, and that the sponsor did not inform me of “any extension to the two-year record keeping period.” I will follow the document retention guidelines in the future.

### FDA’s response to the PI’s Rebuttal:

The **response is inadequate** because we/FDA remain concerned that you do not understand your record retention requirements, and because you did not provide any documentation that you retained the required records.

- ◆ Specifically, it is unclear whether you understand that you are required to retain records for studies conducted at your site for 2 years from the date of application approval or study discontinuation.
- ◆ The PI’s plan to follow document retention guidelines is **insufficiently detailed** to prevent similar violations in future studies.

### Result and Conclusion by the FDA

Failure to retain study records as required by FDA regulations compromises the validity and integrity of data significantly. Because you failed to retain drug accountability records and case histories for both studies, **we consider the data generated at your site for Protocols XYZ and ABC unreliable in support of a research or marketing application.**

#### GCP Angle:

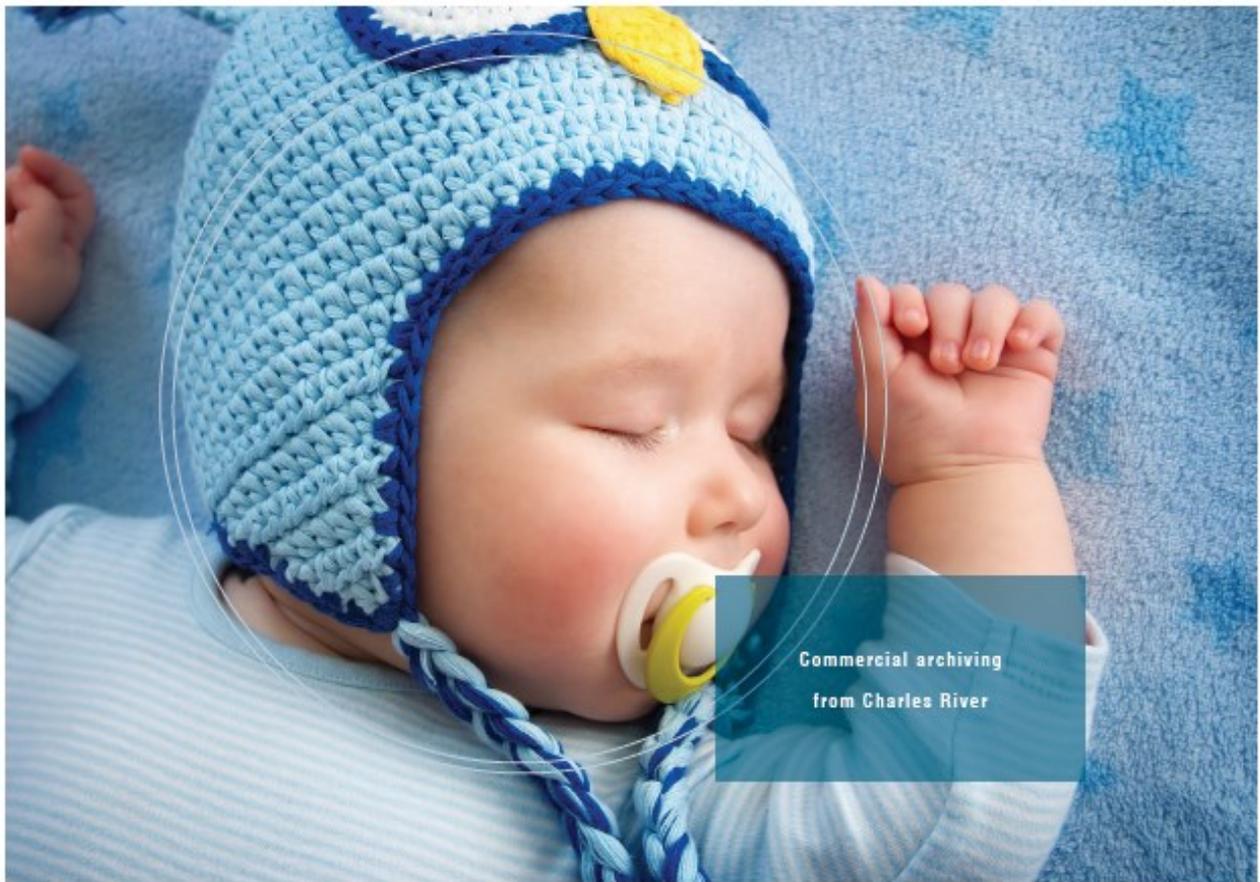
How could this have been prevented/ what could the sponsor have done to ensure the site would be in compliance with this regulation? Did the sponsor review this at the Investigator Meeting prior to study kick off? Did the sponsor check to see if the Principal Investigator and his staff had adequate GCP training? If they had training, did they miss this very important piece? Did the sponsor check to see if the site had an SOP on Document Retention/Data Integrity? Did the study monitor evaluate the sites understanding of document retention throughout the study? During the sponsor close out visit did the study monitor review the regulatory expectations of study document retention with the site? Was the site audited, and did the auditor review the site’s retention policy or understanding of document retention?

All the research resources allocated, and time spent performing the studies at this site were wasted.

All the subjects went through the trial, without having made a viable contribution to the study because the site did not maintain ORIGINAL SOURCE study documentation for the FDA to perform an evaluation, against the data recorded in the Case Report Forms. This resulted in unverifiable data that had to be excluded from the analysis.

Lastly, the principal investigator made another critical error. In his written response to the FDA, he underlined the root cause. He was oblivious in understanding basic regulatory requirements around retention of clinical trial documentation. Additionally, he/she did not know provide a detailed corrective and preventive action in the response further aggravating the outcome of the investigation.

When was the last time  
you slept like this?



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## Quality Assurance & Scientific Support



Quality Associates, Inc. (QAI) was established in 1986 to provide regulatory consulting services to the pharmaceutical and agrochemical industries. From inception, QA programs have been the cornerstone for providing services for both GLP and GCP studies.

- Establish GLP/GCP Programs
- Independent QAU, Full Time, Part Time, as Needed
- Conduct All Types of Study Audits, Both GLP & GCP
- CRO, Test Site, and Vendor Audits
- SOP Development
- Training Programs
- Validation Audits
- 21 CFR Part 11 Support
- CRO and Vendor Qualification Audits
- GLP Archiving

# SUMMARY OF UPCOMING EVENTS

Organization	Dates	General information
CQA	19 September 2018	<p style="text-align: center;">CQA Discussion Group</p> <p style="text-align: center;">GCP-focused discussion Group meets twice a year at Peddlers Village, Cock ‘n Bull Restaurant</p> <p style="text-align: center;">11:30-4:00pm</p> <p>For more details: <a href="https://www.linkedin.com/groups/5180873">https://www.linkedin.com/groups/5180873</a></p>
MARSQA	20 September 2018	<p style="text-align: center;">Full Day Membership Meeting.</p> <p style="text-align: center;">See page 13 for details &amp; Agenda</p>
CSV	3-4 October 2018	<p style="text-align: center;"><b><u>Selected Topics Training</u></b></p> <p style="text-align: center;">Full Day (8:30-4:30) Training with one or two day attendee option</p> <p style="text-align: center;">See page 14 for details</p>
CSV	7 November 2018	<p style="text-align: center;">On-site meeting at Bayer (100 Bayer Blvd, Whippany, NJ)</p> <p style="text-align: center;">4th floor Conference room:</p> <p style="text-align: center;">HNV_B100_04_1B416C-AV (32)</p> <p style="text-align: center;">Time: TBD/to be posted on MARSQA website in future</p>
SQA	28 April—03 May 2019	<p style="text-align: center;">Annual Meeting and Quality College</p> <p style="text-align: center;">Atlanta Marriott Marquis, Atlanta, Georgia</p>
CSV	<p>last Monday of each month 12:00-1:00</p> <p style="color: red;">Note: Next meeting is 9/24/2018</p>	<p style="text-align: center;">Teleconference number/code</p> <p style="text-align: center;">888-684-2443/4532615272</p> <p style="text-align: center;"><a href="mailto:denise.botto@syneoshealth.com">denise.botto@syneoshealth.com</a> OR <a href="mailto:calvin.kim@bayer.com">calvin.kim@bayer.com</a></p> <p style="text-align: center;">** please come prepared with discussion items**</p>
Webinars	Ad hoc	<p style="text-align: center;"><i>free</i> to SQA/MARSQA members</p> <p style="text-align: center;">Webinars are announced throughout the year. Keep an eye out for email announcements from SQA.</p>

## Full-Day... **MARSQA Member Meeting**

Thursday, 20 September 2018

Time: 9:00 am—4:00 pm includes Hot Buffet Lunch

Cock N Bull, Peddlers Village, Lahaska, PA

Cost \$50 Members/ \$70 Non-Members / discount: \$80 MARSQA membership + meeting

Register through SQA/SQA Store: "MARSQA" in search box OR

<http://marsqa.org/events.shtml>

\*\*\*\*\*

### **Agenda**

9:00 MARSQA President, Megan Lawhead

9:30 **Speaker:** Michael Rutherford, Syneos Health

Presentation Title: Computer System Validation and Data Integrity

A Marriage Made In...Regulations

10:15 GLP/Bioanalytical Forum

11:00 **Speaker:** Krista Valenuela, Sr. Cyber Threat Intelligence Analyst

12:00 Lunch Buffet

1:00 Computer System Validation Open Forum

2:00 **Speaker:** Will Bowen, Founder of Complaint Free Movement

3:00 Will Bowen Q&A session

4:00 Closing

Full Agenda is also available here: <http://marsqa.org/events.shtml>

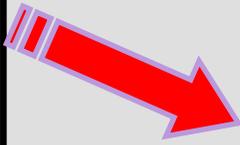
# CSV Training

## Selected Topics Training

3-4 October 2018; 8:30am-4:30pm

Registration will be open September 10-28, 2018

**Early registration pricing until September 24th**



<u>Attend One Day Training</u>	<u>by 9/24</u>	<u>after 9/24</u>
MARSQA Member	<b>\$150</b>	<b>\$175</b>
Nonmember	<b>\$200</b>	<b>\$225</b>
<u>Attend Both Days</u>		
MARSQA Member	<b>\$275</b>	<b>\$300</b>
Nonmember	<b>\$375</b>	<b>\$400</b>

### Location:

Earl's Restaurant, Peddlers Village, Lahaska, PA

### **Yep! Another volunteer opportunity!!!**

*Help is needed with:* course planning, presentation review, registration, etc.

Volunteers inquire with **Denise Botto: [denise.botto@syneoshealth.com](mailto:denise.botto@syneoshealth.com)**

For questions regarding the CSV training

Contact:

Chris Wubbolt: [chris.wubbolt@qacvconsulting.com](mailto:chris.wubbolt@qacvconsulting.com)

Denise Botto: [denise.botto@syneoshealth.com](mailto:denise.botto@syneoshealth.com)

Calvin Kim: [Calvin.Kim@bayer.com](mailto:Calvin.Kim@bayer.com)