



DATA INTEGRITY A CLOSER LOOK

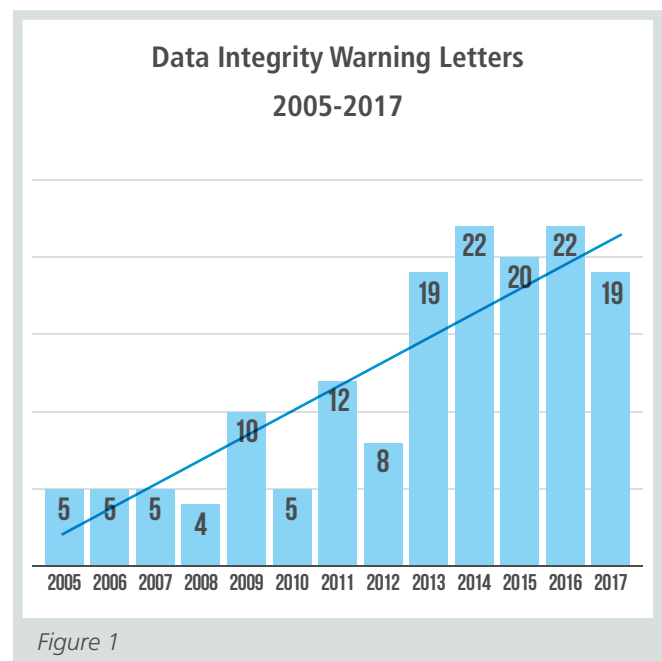
by George Toscano

Data integrity remains a perennial hot topic impacting the pharma biotech industry and the trend has been picking up steam; the number of data integrity-related warning letters has increased consistently since 2010. A number of new guidance documents came out in 2016 by FDA, MHRA, EMA PIC/S and the WHO and yet companies continue to grapple with data integrity issues.

FDA enforcement has been ramping up as evidenced by the number of warning letters citing data integrity deficiencies between 2005 and 2017 (see **Figure 1**). A clear uptick starts after 2010, which is no coincidence. FDA began incorporating data integrity into its Pre-Approval Inspection (PAI) process as one of the primary inspection objectives in 2010 as defined in its Compliance Program Guidance Manual 7346.832. Better training for inspectors, incorporating data integrity as an inspection objective and companies not having robust systems to ensure data integrity have contributed to this trend.

WHAT ARE THE MAIN ISSUES YOU SEE RELATED TO DATA INTEGRITY?

At NSF we have conducted extensive research into data integrity looking at our own clients, new guidance documents and regulatory enforcement actions. We decided to take a closer look to see where companies were struggling most. We reviewed warning letters issued from 2005 to 2017 for data integrity deficiencies. We then grouped these deficiencies into common themes and what we found was revealing (see **Figure 2**).



FINDINGS HIGHLIGHTS

Topping the list is **incomplete or missing records** which was cited 107 times in the 154 warning letters (67 percent). Examples include data being processed multiple times, but only one set being presented. Other examples include injections in a sequence which are not included in the data package; missing flasks, solutions or microbial test plates for tests that are supposed to be in process; or missing data to support analytical results.

Access control deficiencies were cited 50 times (32 percent). These include shared login accounts, users having inappropriate privilege levels such as administrator rights, and systems having inadequate controls that allow users to modify or delete files.



Reintegration, reprocessing and inappropriate manual integration was cited 39 times (25 percent). These include instances when samples are reprocessed multiple times with no justification and only one set of data is reported. This category also includes excessive manual integration with no justification or procedure to define the practice.

Deleting or destroying original GMP records was cited 36 times (23 percent). Items cited include analysts deleting data on electronic data systems as well as official records including sample notebooks and test records found in the trash.

Rounding out the top five, **audit trail deficiencies** had 32 citations (21 percent). Audit trail issues run the gamut from systems without audit trail capabilities, to audit trails being disabled by users, to audit trails not being reviewed to detect deletion or manipulation of data.

FDA RECOMMENDS THIRD-PARTY CONSULTING SUPPORT

FDA has been increasingly recommending that companies reach out to a qualified third-party consultant to help with addressing certain data integrity issues (**Figure 3**). NSF has served as an independent third-party on many occasions and is a recognized expert in this capacity.

WHAT ARE SOME OF THE CONSEQUENCES OF DATA INTEGRITY-RELATED FINDINGS?

Data integrity findings are taken very seriously by the FDA as they erode trust between the FDA and the company, and can result in FDA 483s, warning letters, import alerts, injunctions and, in severe cases, FDA invoking application integrity policy.

WHAT CAN COMPANIES DO?

Companies should first evaluate data integrity holistically and consider the entire data lifecycle when they think about data integrity and data governance. Secondly, companies should take a risk-based approach to addressing data integrity concerns, factoring in data criticality and data risk. The level of effort to mitigate

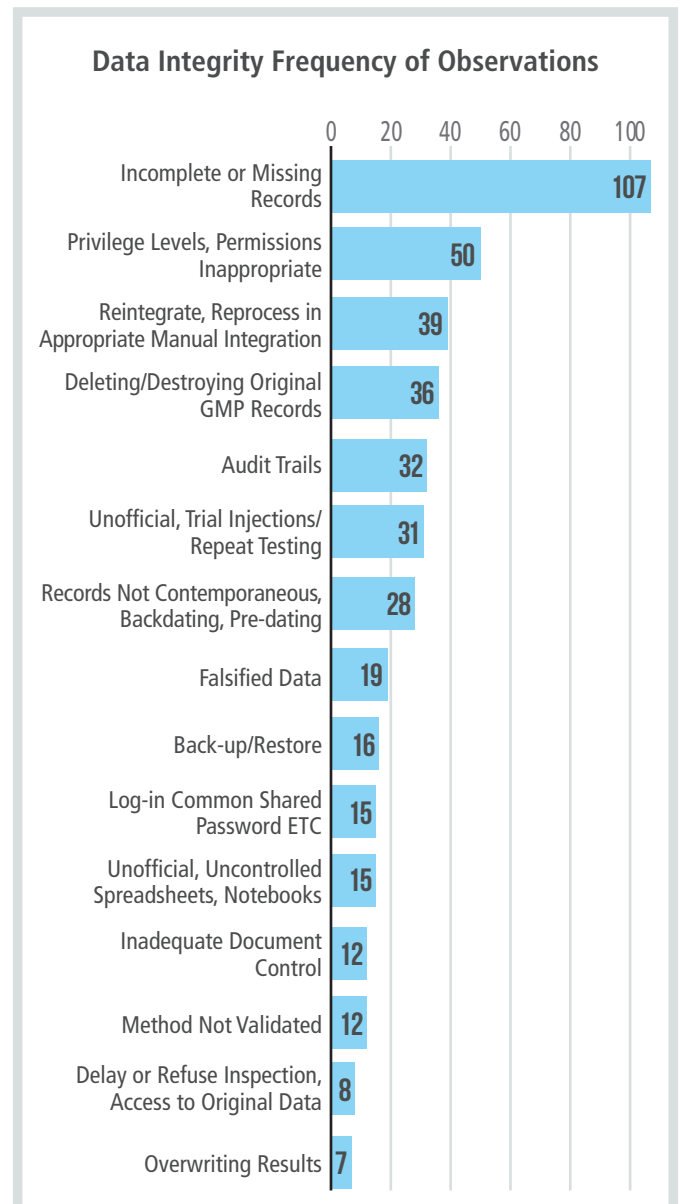


Figure 2

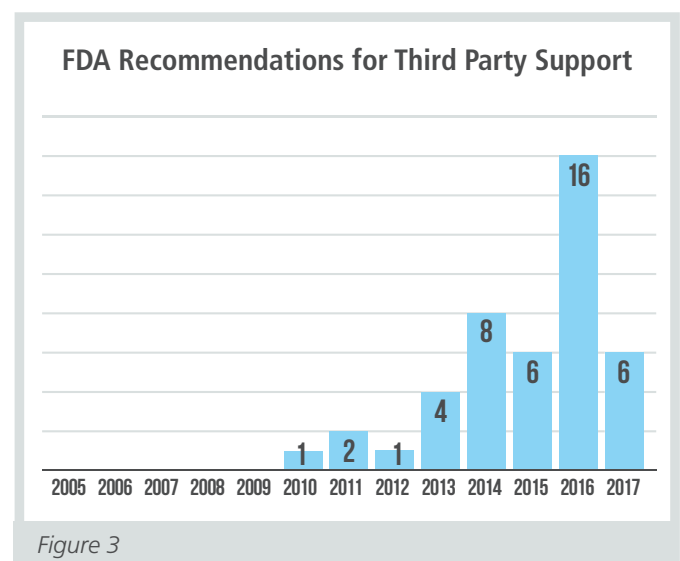


Figure 3



data integrity gaps should be commensurate with the risk present.

I have seen many companies move along the data integrity maturity curve from initial awareness to basic understanding and ultimately to implementation of robust data governance programs. Most clients are struggling with implementation of data integrity concepts, and I am often asked questions such as:

- > Do I need to review audit trails?
- > How often do I need to review them?
- > And what in particular should I be looking at?

We have helped many clients answer these questions and implement simple yet compliant solutions. If you feel that your company can use some help with implementation of data integrity controls, contact us at USpharma@nsf.org or pharmamail@nsf.org to discuss how we can meet your needs.

DATA INTEGRITY – IS EUROPE DIFFERENT?

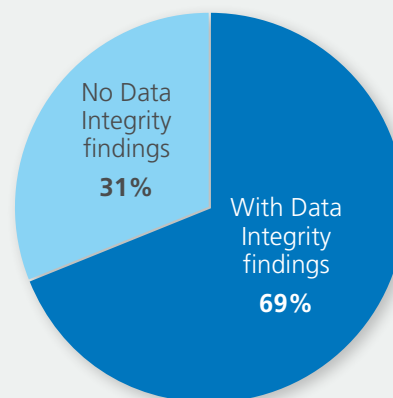
by Lynne Byers, Executive Director, Pharma Biotech, NSF International

The level of detail about European regulatory inspections is not as fully available to the public as it is in the U.S. where warning letters are published. However, an excellent source of information is the EudraGMDP database, <http://eudragmdp.ema.europa.eu/inspections>. Here you may glimpse the reasons for suspending a GMP authorization.

An assessment of the data available in Europe would indicate that European regulators are finding the same issues as the U.S. FDA. At NSF we offer in-house courses on data integrity, as well as public courses in specific topics. For up-to-date information on our public pharmaceutical courses, visit www.nsf.org/info/pharma-training.

European Data, Jan 2017-Feb 2018

16 Non Conformance Reports



Typical findings

- > Reporting testing not performed.
- > Issues with log in to computerized systems.
- > System security in computerized systems.
- > Falsification of records; e.g. test, calibration, sampling and manufacturing records.
- > Falsification of location of manufacture.



Watch NSF's latest video **Data Integrity – A Closer Look** available in our resource library (www.nsf.org/info/pblibrary) under Videos.

A special thank you to Andy Barnett, Director of Pharma Biotech Quality Systems at NSF, for conducting the research that made this article possible.



ABOUT THE AUTHOR



George Toscano has more than 20 years of experience helping companies in the global pharmaceutical, biologic and biotechnology markets develop and execute comprehensive quality systems solutions. He is a recognized data integrity expert and has conducted numerous audits and assessments to evaluate companies' systems. In addition, he has led remediation activities related to data integrity deficiencies to help clients address regulatory enforcement actions.

As Vice President of Quality Systems, Mr. Toscano assists companies in the pharmaceutical, biologic and biotechnology industries, both foreign and domestic, in developing compliant quality and regulatory strategies. He also specializes in conducting GMP assessments of facilities and support to help companies address quality system deficiencies.

For more information, contact pharmamail@nsf.org or visit www.nsfpharmabiotech.org

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