Data Reliability - Internet

- Wikipedia
  - https://en.wikipedia.org/wiki/Reliability_of_Wikipedia
- Others
  - http://www.dailymail.co.uk/health/article-2639910/Do-NOT-try-diagnose-Wikipedia-90-medical-entries-inaccurate-say-expertsDo.html
  - http://www.dailymail.co.uk/sciencetech/article-2131458/Up-articles-Wikipedia-contain-factual-errors.html
  - http://www.foxbusiness.com/features/2015/09/02/just-how-accurate-is-wikipedia.html

DATA INTEGRITY AND DATA MANAGEMENT FOR GXP REGULATED FIRMS

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Training Disclaimer

This document is an overview training document and is provided "as is", to be used as a reference only. Use of this document for any purposes other than as reference material (i.e., for the purposes of training and testing users on data related items by other commercial entities or individuals) is not advised. In no event shall the authors and or presenter of this material, be liable for any claim, damages, or other liability whether in action or contract, arising from, out of, or in connection with the use of the information in this document for training, testing, or on-going safe and compliant use of data. Please consult your own lawyers and subject matter experts if you are looking to develop your own data integrity and data management curriculum. Data users are responsible for their knowledge, skills and ability, including reading and understanding applicable regulations, guidelines and standards.

Welcome

Today's Overview

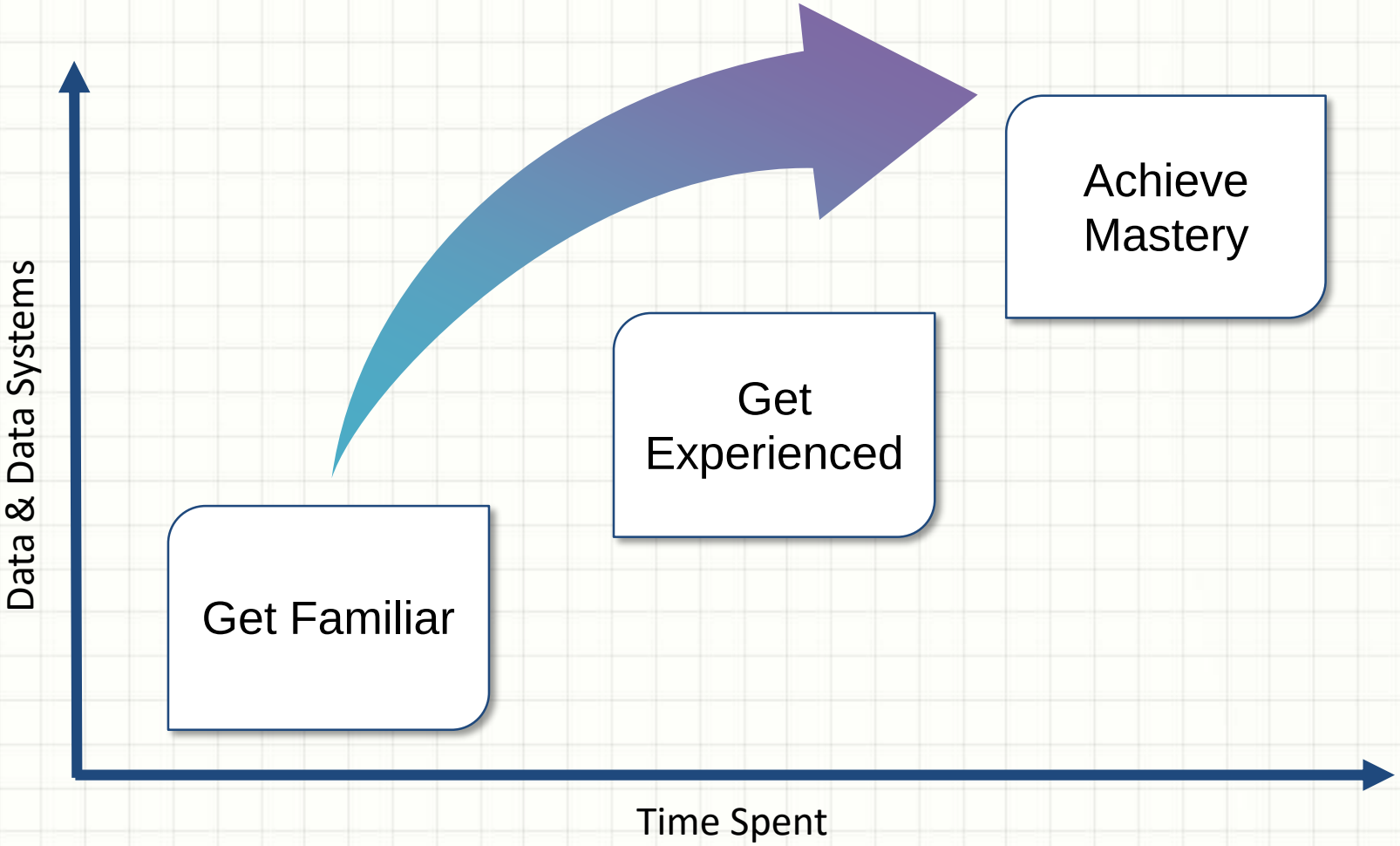
1

- Familiarize yourself with Data (Integrity & Management)

2

- Understand Your role

Working Toward Mastery



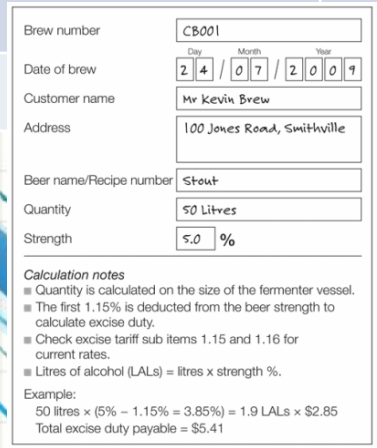
Data

facts and statistics collected together for reference or analysis.

Computing
the quantities, characters, or symbols on which operations are performed by a computer, being stored and transmitted in the form of electrical signals and recorded on magnetic, optical, or mechanical recording media.

Data Continuum

Personal	Finance	GCP	GLP	GMP
MEDICAL RECORDS	STOCK MARKET	CLINICAL TRIAL SPECIFICATIONS	EQUIPMENT VALIDATION	IQ/OQ/PQ
LEGAL RECORDS	BANKING	FORMS	TEST RESULTS	BATCH RECORD
	PAYROLL			PRODUCT RELEASE

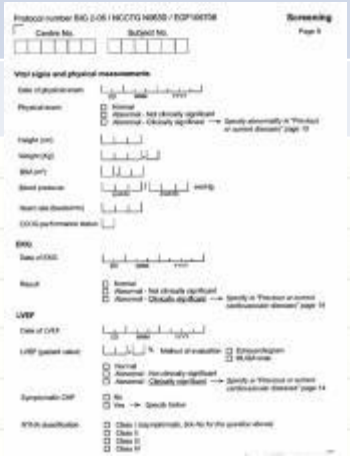


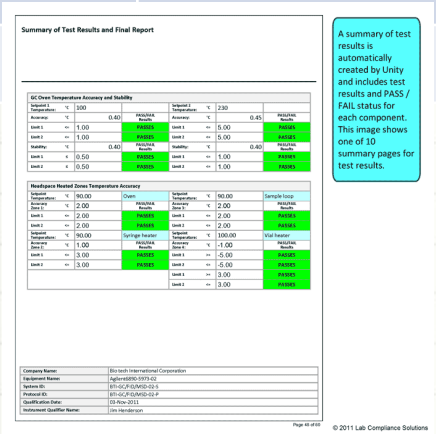
Brew number	CB001
Date of brew (Day / Month / Year)	24 / 07 / 2009
Customer name	Mr Kevin Brew
Address	100 Jones Road, Smithville
Beer name/Recipe number	Stout
Quantity	50 Litres
Strength	5.0 %

Calculation notes

- Quantity is calculated on the size of the fermenter vessel.
- The first 1.15% is deducted from the beer strength to calculate excise duty.
- Check excise tariff sub items 1.15 and 1.16 for current rates.
- Litres of alcohol (LALs) = litres x strength %.

Example:
50 litres × (5% – 1.15% = 3.85%) = 1.9 LALs × $2.85
Total excise duty payable = $5.41





Data Integrity

- Data integrity is the assurance that data records are accurate, complete, intact and maintained within their original context, including their relationship to other data records.
- Ensuring data integrity means protecting original data from accidental or intentional modification, falsification or even deletion, which is the key to reliable and trustworthy records that will withstand scrutiny during regulatory inspections.

PAPER

Hybrid

Electronic

DATA STANDARDS - ALCOA

Accurate	Data must be accurate. Where appropriate, correctness should be 2nd person verified. This extends, for example, to data / information that are presented in multiple locations such as an equipment log, laboratory notebook, and electronic chromatography data where data should be in agreement.
Legible	Data and results must be legible / readable. Electronic data much also have the capability to be made human readable.
Contemporaneous	Thus, data are recorded at the time of the event / action, not transcribed at a later date. Data are not transcribed from post-it notes or scrap paper to the official documents such as batch records or laboratory notebooks.
Original	Original data are similar to "raw data". The following is taken from the MHRA guidance and appears to also represent FDA's opinion: "**Original record:** Data as the file or format in which it was originally generated, preserving the integrity (accuracy, completeness, content and meaning) of the record, e.g. original paper record of manual observation, or electronic raw data file from a computerized system." The paper print out of a chromatogram is no longer considered the official raw GMP data because it does not include the complete information, including but not limited to meta-data, audit trails, and system configuration for the analysis in question. FDA addresses this in their GMP Q&A.
Attributable	This term requires the ability to determine who collected the data, when it was collected, from which instrument it was collected and who made any data modification or data manipulations. For example, for HPLC chromatography, this includes all integration events. Use of shared passwords renders makes it impossible for the reviewer to attribute the data to a specific person.

Data Management

Data management is the development and execution of architectures, policies, practices and procedures in order to manage the information lifecycle needs of an enterprise in an effective manner.

SDLC

Your Role in Ensuring Data Integrity

Mandates to Manage Data

The “generics scandal” of the 1980’s raised the issue of falsified data submitted to FDA in support of drug approvals. One outcome of this scandal was the shift in focus of the FDA pre-approval inspection (PAI) to evaluate raw laboratory data included in the marketing application and evaluate whether the site was capable of manufacture as described in the application.

This scandal also prompted implementation of the Application Integrity Policy in 1991 which “describes the Agency's approach regarding the review of applications that may be affected by wrongful acts that raise significant questions regarding data reliability”.

Five firms are on the current CDER Application Integrity Policy List effective October 1, 2015.

SDLC

SECURE

Data Management

RELIABLE

RETRIEVABLE

VALIDATED

DATA INTEGITY REGULATIONS

- **Broad Laws**
  - Sarbanes-Oxley Act (SOX); Payment Card Industry Data Security Standard (PCI DSS); Gramm-Leach-Bliley Act (GLB) Act; Electronic Fund Transfer Act, Regulation E (EFTA); Customs-Trade Partnership Against Terrorism (C-TPAT); Free and Secure Trade Program (FAST); Children's Online Privacy Protection Act (COPPA); Fair and Accurate Credit Transaction Act (FACTA), including Red Flags Rule; Federal Rules of Civil Procedure (FRCP)
- **Industry Specific Guidelines & Requirements**
  - Federal Information Security Management Act (FISMA); North American Electric Reliability Corp. (NERC) standards; Title 21 of the Code of Federal Regulations (21 CFR Part 11) Electronic Records; Health Insurance Portability and Accountability Act (HIPAA); The Health Information Technology for Economic and Clinical Health Act (HITECH); Patient Safety and Quality Improvement Act (PSQIA, Patient Safety Rule); H.R. 2868: The Chemical Facility Anti-Terrorism Standards Regulation

DATA INTEGITY REGULATIONS

- FDA inspects for electronic data integrity during the pre- and post market product approval process under 21 CFR Part 11, which is commonly referred to as the “data integrity regulation.”
  - When FDA published its intent to raise the enforcement profile of 21 CFR 11 (Part 11) in 2010, it listed four goals:
    - 1. Assess the industry’s comprehension or continuing misinterpretations of Part 11.
    - 2. Determine how firms are ensuring the integrity of electronic records.
    - 3. Extend scrutiny of data, quality-related and computerized system validation-related Form 483 inspectional observations since 2007.
    - 4. Determine next steps for Part 11, including whether to issue a revised regulation or simply draft more guidance.

DATA INTEGITY REGULATIONS

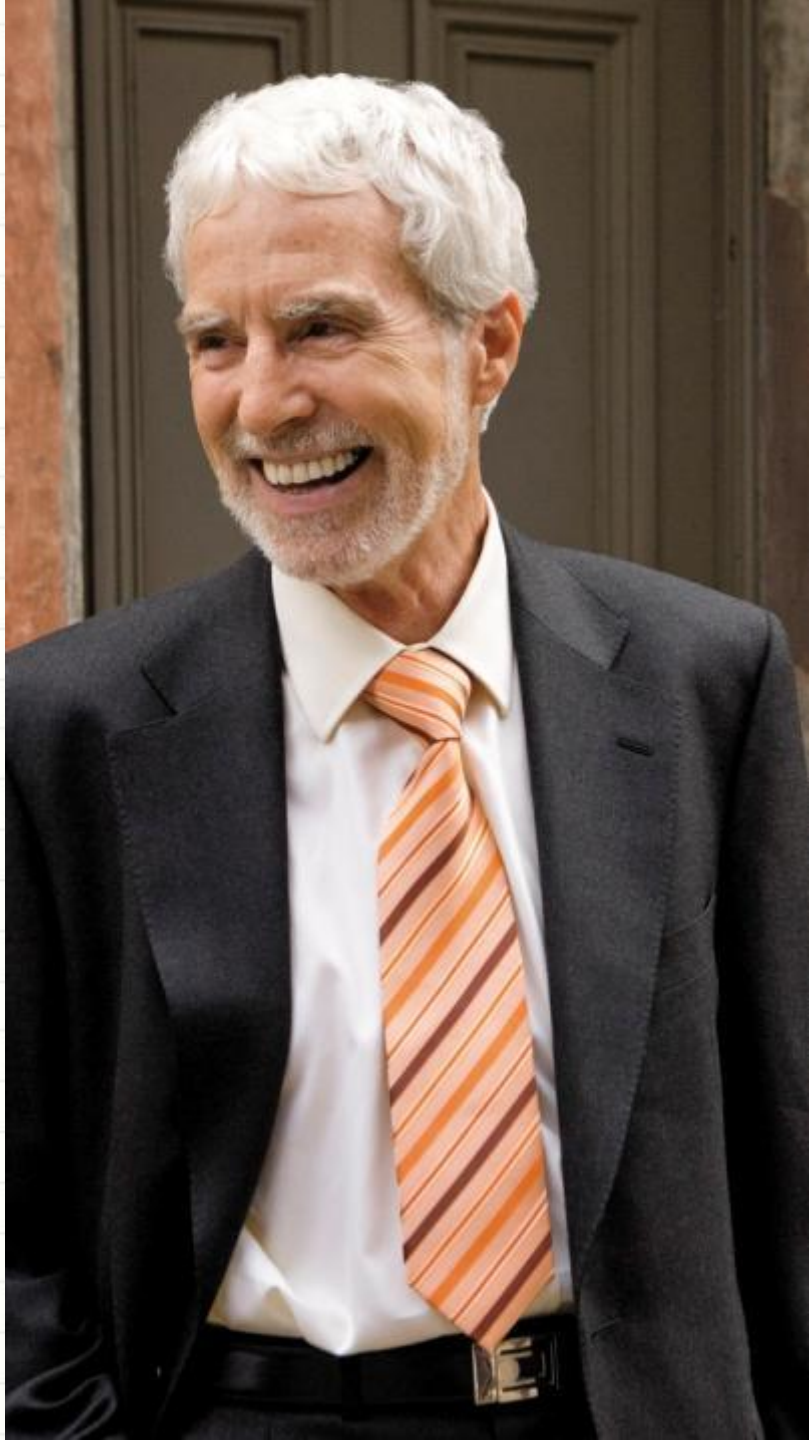
- The **General Data Protection Regulation (GDPR)** is a Regulation by which the European Commission intends to strengthen and unify data protection for individuals within the European Union (EU). It also addresses export of personal data outside the EU.
- The three main cybersecurity regulations are the 1996 Health Insurance Portability and Accountability Act (HIPAA), the 1999 Gramm-Leach-Bliley Act, and the 2002 Homeland Security Act, which included the Federal Information Security Management Act (FISMA).

GDPR: Businesses that fail to comply with the regulation....

- can be fined up to $20 million, or 4 percent of global revenues. That's huge. Here's what a hypothetical fine could look like for just a handful of well-known, global brands based on total revenues for 2014:
- Twitter: $56 million
- General Mills: $716 million
- Goodyear: $725 million
- Vodafone: $2.3 billion
- HP: $4.5 billion
- Apple $9.3 billion

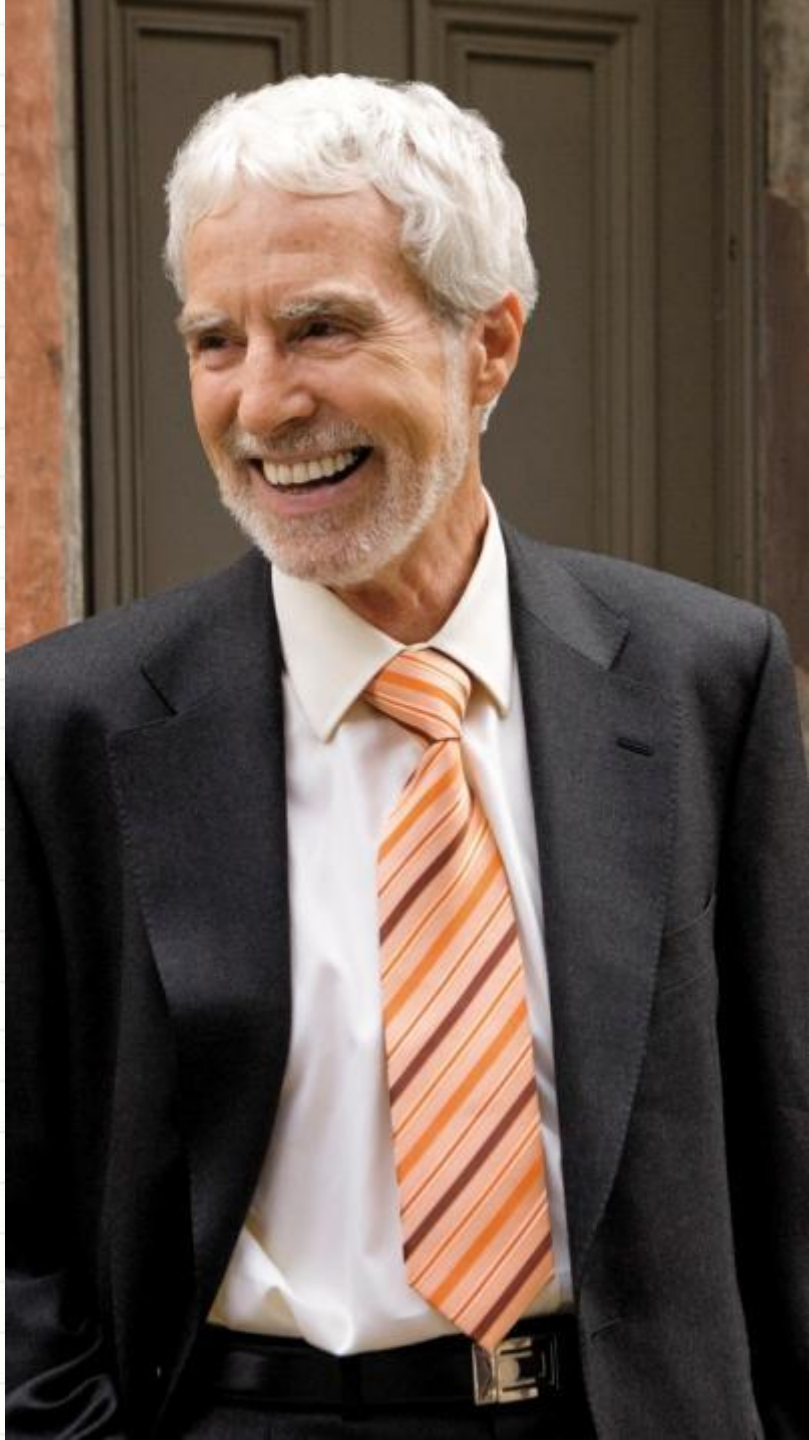
Case Study

- Jimmy works for a small BioBest Company
- His first day he learns:
  - SOP System is not version controlled
  - Clinical Protocols have multiple uncontrolled versions in use
  - Batch Records are missing data and have errors recorded
  - Lab testing results recorded have been found to be altered
  - Product release is missing signatures



Discussion

- What we can learn from Jimmy
- Best practices
- Take-aways



Characteristics of Trustworthy Records

National Archives & Records Administration

- Reliability: trusted to be complete & accurate
- Authenticity: proven to be what it purports to be
- Integrity: complete and unaltered
- Usability: can be located, retrieved, presented & interpreted.

Review

1

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2

- Understand Your role

References

- FDA *21 CFR Part 11*, *Electronic Records*; *Electronic Signatures*, 1997
- Preamble to the final rule, 21 CFR Part 11, March 20, 2997
- Guidance for Industry, General Principles of Software Validation, January, 2002
- FDA *21 CFR Part 211*. Current Good Manufacturing Practice for Finished Pharmaceuticals.
- FDA Compliance Program Guidance Manual, Chapter 46 – New Drug Evaluation, *Pre-Approval Inspections*, *Program 7346.832*
- FDA slide deck describing *GMP audits of Data Integrity and Automated Systems*. This presentation was given by Robert D. Tollefsen National Expert – Computers on April 27, 2010. He delivered the same slide deck at many industry conferences.
- FDA Guidance for Industry, Part 11*, Electronic Records; Electronic Signatures –Scope and Application*, 2003
- FDA *Guidance for Industry, Electronic Source Data in Clinical Investigations*, September 2013 formally addresses the ALCOA acronym.
- 15-page *form 483* issued to Able Laboratories in 2005.
- Rules Governing Medicinal Products in the European Union. Good Manufacturing Practice, *Annex 11*, Computerized Systems, effective 30 June 2011
- Rules Governing Medicinal Products in the European Union, Good Manufacturing Practice, *Part II*: *Basic Requirements for Active Substances Used as Starting Materials*
- MHRA *GMP Data Integrity Definitions and Guidance for Industry*, March 2015
- MHRA *expectations regarding self inspection and data integrity*, December 2013. See also the explanation from the European Compliance Academy *HERE*.
- MHRA Inspectorate Blog on Data Integrity, 3 parts starting June 25, 2015.
- MHRA Presentation on Data Integrity in Goa, India, September 2014. See the link to download the slides at the *bottom of the page*.
- ICH Q7, Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
- PIC/S Guidance, Good Practices for Computerized Systems in Regulated “GXP” Environments, 25 Sept 2007. *Guidance for Inspectors*, PI 011-3
- PIC/S Annexes to GMP Guide, Annex 11, Computerized Systems in the *GMP Guide (Annexes)*
- WHO published a 35-page draft document on their website for comment, *Guidance on Good Data and Record Management Practices* for GXP regulated activities.
- WHO Notice of Concern issued to Quest Life Sciences Pvt. Ltd on 30 June 2015. This site conducts clinical studies
- WHO Notice of Concern issued to Svizera Labs Private Limited on 2 September 2015.
- Addressing the historical issue of data integrity in FDA enforcement actions: *The Financial Value of a Comprehensive GMP Regulatory Intelligence Program*, March 25, 2015, Unger Consulting, Inc., includes links to associated warning letters, particularly those from 2000-2008.
- Notre Dame Law Review, Volume 75, Issue 1, October 1, 1999, page 312. Describes the nature and outcome the US generic drug scandal.
- *Unger Consulting Inc*. data, available upon request. Delineates the common regulations cited in FDA warning letters associated with data integrity.

QUESTIONS?