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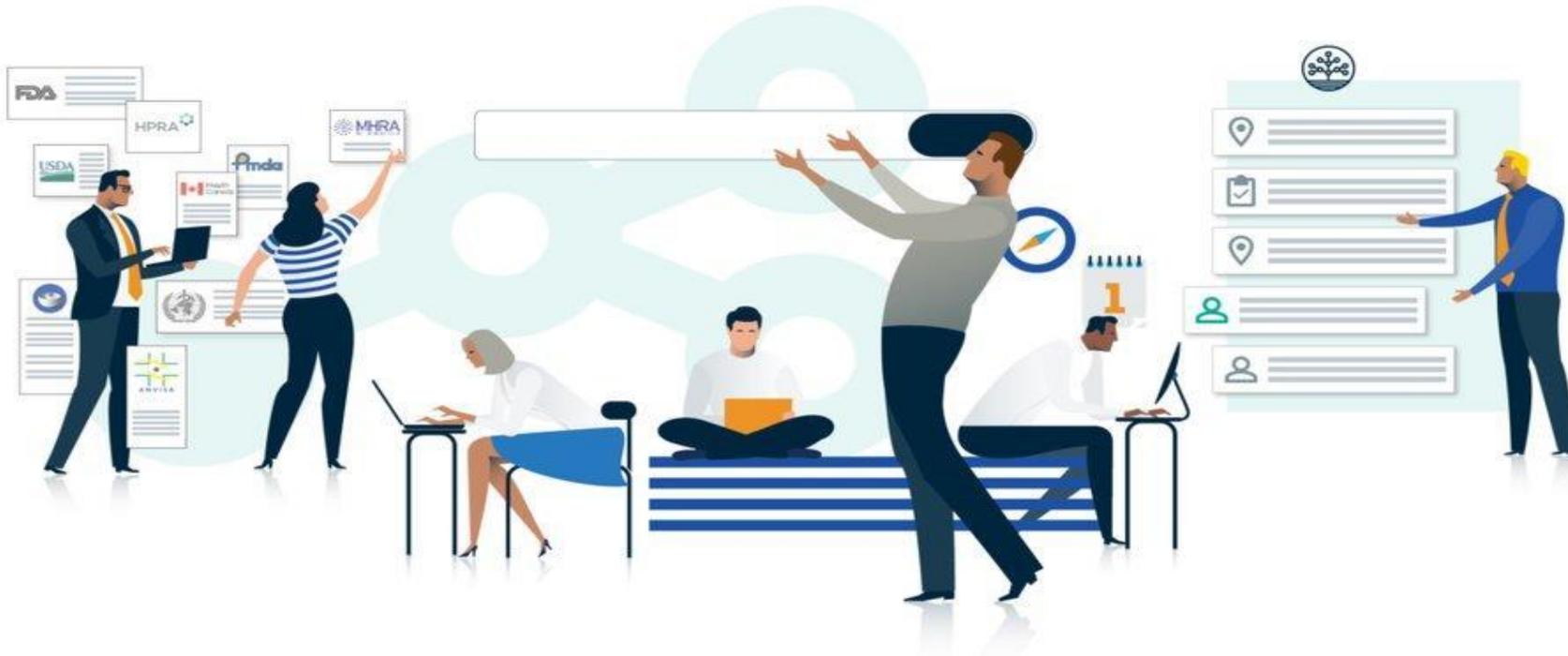
The Insider's Guide to Audit Readiness

Presented by:

Sam Klooster
VP of Software, SIMCO

Jerry Chapman
Senior GMP Quality Expert, Redica Systems

In theory, the mission is simple: make safe, high quality great products while meeting regulatory requirements and business demands. But...



Growth in number of regulatory agencies and requirements.

Health agencies rules and regulations vs. *how they are enforced on inspection.*

What are their expectations for your plant?

Where are those changing expectations found?



Introduction

Mining enforcement data: 483 observations, warning letter citations.

Time consuming and difficult, requires expertise.

Where is enforcement data found?

Redica Systems has built the largest dataset of inspection and enforcement documents in the world – *the data sets used for the following analysis.*



Introduction

Includes all FDA inspected and registered sites since 2000. 20 times more data than has been released on FDA.gov (targeted FOIA). More than 350,000 sites and 800,000 inspections.

Once you get the inspection data, do you have the experts to analyze it?

And if so, do they still print hard copies and use highlighting markers to analyze them?

Built proprietary AI “expert models” using machine learning and honed by industry experts



Machine Learning, Natural Language Processing (NLP), AI: Data Sources

Data Sources

- *All data are from PUBLIC sources*
- FDA Inspections databases (CLIL and FACTS)
- FDA CFR Citations database
- Warning Letters from FDA.gov
- 50,000+ 483s, responses and EIRs obtained via FOIA and FDA.gov
- FDA registration databases (e.g., GDUFA)
- FDA 21 CFR 211 catalogue (Cornell University)
- Experts - Jerry Chapman (GMP), Barbara Unger (GMP), Jane Wastl (GMP), Mark Agostino (Devices), Alison Sathe (Devices), Fran Lambetecchio (GVP/GCP), others

Site Tags

CDER

- Rx manufacturing (API and FDF)
- Over-the-Counter (OTC)
- Other CDER (e.g., unapproved drugs)
- GCP (Clinical Investigators, IRBs, Sponsors)
- Compounding Pharmacies

CBER

CDRH

MHRA

Health Canada

etc.

How do we use the data?

- Investigator profiles
- CMO/CRO due diligence
- Vendor selection
- **Inspection preparation**
- Keeping PQS up to date
- Tracking changes to authoritative sources
- Tracking and trending inspection observations
- Finding observations and citations “hiding in plain sight” (case studies)
- Tip of the iceberg...

Machine Learning, Natural Language Processing (NLP), AI: Expert Model Algorithm

Compliance Analysis Algorithm

Redica Systems has created an AI tool – “expert model” – that allows deep and rapid analysis of compliance data sets.

Created an algorithm using machine learning, NLP and other AI tools and associated data sets to analyze FDA warning letters, 483s, and other documents.

To begin to train the AI algorithm and prepare the documents for examination, there are initial, important steps that must be taken first.

Natural Language Processing: Making Scanned Documents Human and Machine Readable

Processed >50,000 483s, 483R, and EIRs

Clean Observation Text: OCR, Retyping

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION			
DISTRICT OFFICE ADDRESS AND PHONE NUMBER Food and Drug Administration, ORA OPQO HQ 12420 Parklawn Drive, RM 2032 Rockville, MD 20857	DATE(S) OF INSPECTION 9/10/2018-9/14/2018		
Industry Information: www.fda.gov/oc/industry NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED TO: Mr. Prashant G. Pathak, Assistant Vice President Plant Head-Mohali	FBI NUMBER 3002807979		
FIRM NAME Sun Pharmaceutical Industries, Inc.	STREET ADDRESS SEZ Unit 1, Plot No. A-41, Ind. Area Phase VIII-A, S.A.S. Nagar		
CITY, STATE AND ZIP CODE Mohali, Punjab, 160071 India	TYPE OF ESTABLISHMENT INSPECTED Drug Manufacturer		
THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.			
DURING AN INSPECTION OF YOUR FIRM (100) OBSERVED			
OBSERVATION 1			
The quality control unit lacks the responsibility and authority to approve and reject all in process materials and drug products.			
Specifically, you did not reject the three (b) (4) Tablets (b) (4) ng exhibit batches that failed in-process (b) (4) sampling for (b) (4) . Out of Specification Investigation No. 283910, 285835, and 285929 approved 30/Jan/2018 shows exhibit batches (b) (4) and (b) (4) failed RSD and mean of each location and batch (b) (4) failed RSD for (b) (4) sampling for (b) (4) . The results from these batches was submitted in support of drug application (b) (4) Tablets. Additionally, these results were not submitted in one of the appropriate Sections such as 3.2.P.2.3 (Process Development), 3.2.P.3.3 (Manufacturing Process Descriptions), or 3.2.P.3.4 (Controls of Critical Process Parameters and Intermediates); they were submitted in Section 3.2.P.3.5 (Process Validation and Evaluation).			
OBSERVATION 2			
The written stability testing program is not followed.			
Specifically, your stability data is not representative of the intended manufacturing process for (b) (4) Tablets (b) (4) ng. Exhibit batches (b) (4) and (b) (4) failed in process (b) (4) sampling for (b) (4) . These batches were placed on stability and data from these batches was submitted in support of drug application (b) (4) Tablets.			
To date, your firm has manufactured (b) (4) feasibility/optimization batches on two different compression machines after the three exhibit batches were manufactured. As documented in Feasibility Trial Report of (b) (4) Tablets (b) (4) ng Report No. FSTR/02/1217-00, your firm determined compressed tablets on			
SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE 	EMPLOYEE(S) NAME AND TITLE (Print or Type) Nicole E. Knowlton, Investigator Maotang Zhou, CDER Reviewer	DATE ISSUED 09/14/2018

Observation 1 of 2

OBSERVATION 1

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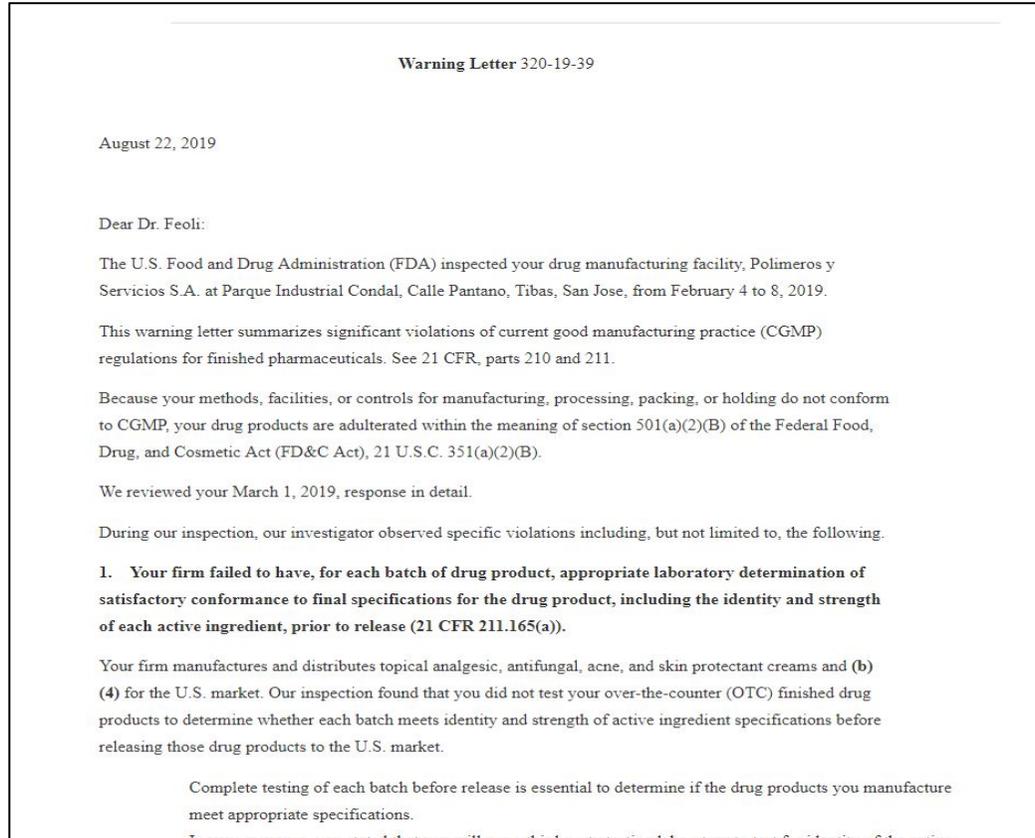


Parse “main topic” of Observation

The quality control unit lacks the responsibility and authority to approve and reject all in process materials and drug products.



Natural Language Processing: Text Parsing



Drug GMP Warning Letter “parts”

- name
- recipient
- introduction
- **deficiency title 1**
- deficiency description 1
- deficiency action 1
- deficiency feedback 1
- **deficiency title 2**
- deficiency description 2
- deficiency action 2
- deficiency feedback 2
- **deficiency title n**
- deficiency description n
- deficiency action n
- deficiency feedback n
- **cgmp consultant recommended**
- format_type
- conclusion
- reply_to
- identification number
- footer

Natural Language Processing: Text Parsing

Not all sections are searched. **Parsing is key**; without it the results are **worse than meaningless with an abundance of incorrect search results that will mislead and drive incorrect actions and behaviors – for example:**

*CFR citation: “Your firm failed to clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals **to prevent malfunctions or contamination** that would **alter** the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements. **(21 CFR 211.67(a))**”*

Specifically...

It is the “specifically” or “for example” text that contains rich content



Natural Language Processing: Text Cleaning

Text Cleaning is the process of clearing out the “junk” from a sentence.

Examples:

- Remove extra spaces
- Make all words lowercase
- Remove typos & misspelling

Natural Language Processing: Tokenization

Splitting up a sentence into tokens. The most basic of which is just to split a sentence into individual words.

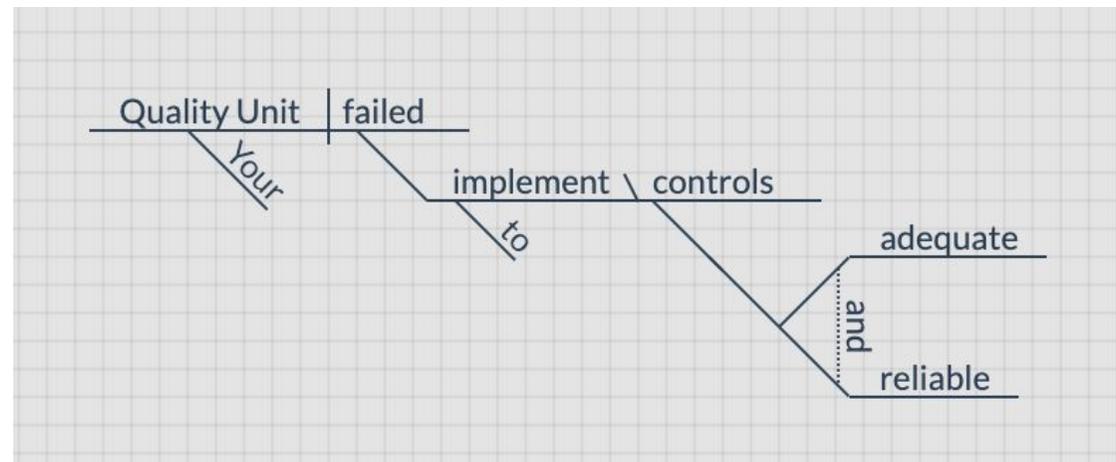
“Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed drug products always comply with the efficacy and quality they represent to possess.”

['Your', 'Quality', 'Unit', 'failed', 'to', 'implement', 'adequate', 'and', 'reliable', 'controls', 'for', 'ensuring', 'that', 'distributed', 'drug', 'products', 'always', 'comply', 'with', 'the', 'efficacy', 'and', 'quality', 'they', 'represent', 'to', 'possess', '.']

Natural Language Processing: Tokens and Parts of Speech (POS) Tagging

Tokens can be much more complex, in the example below the sentence was broken up into “Part of speech” tokens

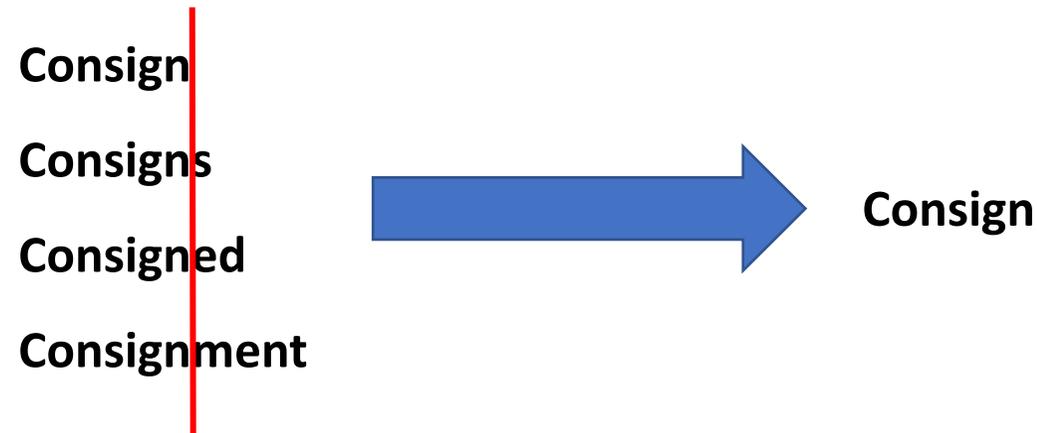
“Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed drug products always comply with the efficacy and quality they represent to possess.”



[('Your', 'PRP\$'), ('Quality', 'NNP'), ('Unit', 'NNP'), ('failed', 'VBD'), ('to', 'TO'), ('implement', 'VB'), ('adequate', 'JJ'), ('and', 'CC'), ('reliable', 'JJ'), ('controls', 'NNS'), ('for', 'IN'), ('ensuring', 'VBG'), ('that', 'IN'), ('distributed', 'VBN'), ('drug', 'NN'), ('products', 'NNS'), ('always', 'RB'), ('comply', 'VBP'), ('with', 'IN'), ('the', 'DT'), ('efficacy', 'NN'), ('and', 'CC'), ('quality', 'NN'), ('they', 'PRP'), ('represent', 'VBP'), ('to', 'TO'), ('possess', 'VB'), (',', ',')]

Natural Language Processing: Stemming/Lemmatization

Stemming is the process of reducing each word in a written document into its word stem, base or root form. This will not necessarily become a proper word, but all permutations of a word will stem to the same root. Lemmatization is a similar process that considers the parts of speech and context in which the word is used, reducing each to a *lemma*.



“Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed drug products always comply with the efficacy and quality they represent to possess.”

your qualiti unit fail to implement adequ and reliabl control for ensur that distribut drug product alway compli with the efficaciaci and qualiti they repres to possess

Natural Language Processing: N-grams

An n-gram is a contiguous sequence of n items from a given sample of text or speech

“Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed drug products always comply with the efficacy and quality they represent to possess.”

Bi-gram

- ('Your', 'Quality')
- ('Quality', 'Unit')
- ('Unit', 'failed')
- ('failed', 'to')

Subject Matter Experts create n-grams from experience and compliance document language; tested over time in model iterations.

Tri-gram

- ('Your', 'Quality', 'Unit')
- ('Quality', 'Unit', 'failed')
- ('Unit', 'failed', 'to')
- ('failed', 'to', 'implement')
- ('to', 'implement', 'adequate').....and longer ones

Building and Applying the Models

Experts create n-grams for each category and subcategory; also, TurboEIR 483 text

For drugs, organized by FDA's 6 quality systems + 1 (DI)

Models for human drugs, medical devices, and clinical trial investigators are completed and deployed

Other FDA models for • clinical trials (GCP) (institutional review boards) • APIs • human cell and tissue/GTP • human drug recalls, and • models for Health Canada inspections and other geographies – e.g., MHRA, EMA – in various testing phases

Different parsing models, n-grams, TurboEIR text, and SMEs: **contextual (contemporaneous)**



Building and Applying the Models: GMP Classification Categories (Human Drugs)

Quality System	Packaging & Labeling	Facilities & Equipment	Materials	Laboratory	Production	Data Integrity
<ul style="list-style-type: none"> •Agency Notification (4 subs) •Audit (2 subs) •CAPA •Change Control •Complaint Management •Records and Reports (13 subs) •Deviations / Investigations (8 subs) •Qualified Personnel (3 subs) •Quality Unit Inadequate (1 sub) •Risk Mgmt. 	<ul style="list-style-type: none"> •Drug product containers and closures (3 subs) •Label and Packaging Controls •Line Clearance •Serialization 	<ul style="list-style-type: none"> •Cleaning (3 subs) •Design (9 subs) •Maintenance (3 subs) •Alarm Management •HVAC •Pest Control •Records and Reports 	<ul style="list-style-type: none"> •Distribution •Material Receipt and Handling (3 subs) •Material Sampling and Testing (3 subs) •Material Storage and Control •Retain Samples 	<ul style="list-style-type: none"> •Method Validation •OOS/ OOT •Stability (2 subs) •Systems Controls •Testing (4 subs) •Reagents and Standards •Records and Reports •Sample Management 	<ul style="list-style-type: none"> •API •Batch Records •Clean Utilities •Cleaning validation or verification •Contamination Control •High Potency/ Allergenic •Nonsterile products (2 subs) •Penicillin and Cephalosporin •Personnel Responsibilities •Process control (5 subs) •Process Monitoring / Continued Process Verification •Process Validation (2 subs) •Product Contamination •Records and Reports •Retain Samples •Sterile Products (8 subs) 	<ul style="list-style-type: none"> •Accurate •Attributable (3 subs) •Backup and Archival •Contemporaneous •Data Destruction •Data Manipulation •Legible •Original Data •Paper Record Controls •System Controls •Testing into Compliance

NOTE: Different models will have different categories: drugs use FDA quality systems



Building and Applying the Models

Build the parser and the model

- Process FDA warning letters, 483s – NLP tools
- Run the algorithm against them
- Experts grade parsing and tagging, iterative, “machine learning” – why is it not right?
- Changes to n-grams, algorithm, fuzzy matching
- Find secondary potential areas of concern in addition to those listed by CFR

“Hiding in plain sight”



Model Insights

Redica Systems data can be used for a variety of purposes to support our mission:

*“Empowering the champions of quality and safety
with actionable data intelligence”*

Sam Klooster from SIMCO will present insights his company has been working on using our systems and data platform

Specifically, he used the Human Drug GMP model to look at data integrity issues related to Part 11 compliance



Maintaining FDA Compliance is a Top Industry Challenge

90% of Quality Leaders say maintaining compliance is their top challenge

Recent Inspection Citations Manufacturers Received from the FDA:

- "Written procedures are not established and followed for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product."
- "The calibration of instruments and apparatus is not done at suitable intervals."
- "Electronic records are used, but they do not meet systems validation, system access limitation, audit trail, operational system check, authority check, device check, personnel qualifications, employee accountability/responsibility policy, systems documentation control, open systems control, signature manifestation and signature to record linking requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records."



About 21 CFR Part 11 Compliance

What is FDA 21 CFR Part 11?

- FDA Regulation governing the use of electronic records and digital signatures to store, track and transfer records pertaining to the manufacture of products
- Defines the criteria under which electronic records and e-signatures are considered trustworthy, reliable, and equivalent to paper records
- Electronic systems are not required, but increasingly used by manufacturers to improve compliance faster and at lower cost

Benefits of using electronic systems for 21 CFR Part 11 compliance:

- Reduced errors
- Increased data confidentiality, integrity, and accessibility
- Faster information exchange
- Increased cost savings

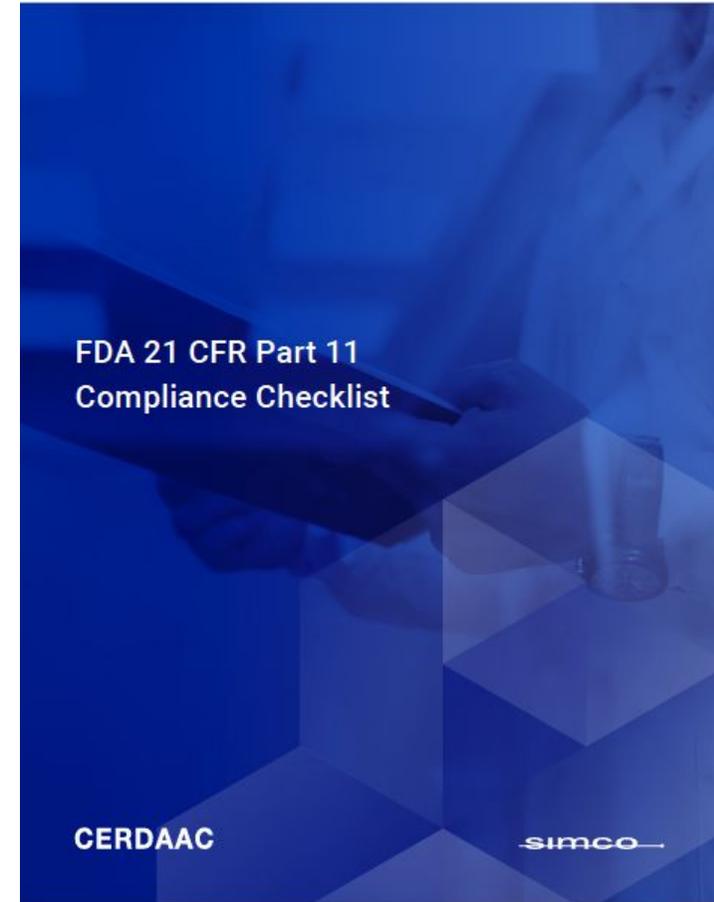
Penalties for non-compliance can include:

- FDA Form 483, a warning letter, an injunction (which can include a market recall or ban on importation), or a consent decree.
- Criminal penalties, fines, etc.



Five Key Areas of the Regulation

- **Systems Compliance:** are the electronic systems being used to store records in compliance
- **Audit Trails:** are records kept of alterations and changes, with previous versions stored and available?
- **Electronic Signatures:** who can sign, are signatures validated?
- **Access and Control:** are roles and permissions properly defined and controlled?
- **System Validation:** the difference between “validatable” and prevalidated, and key requirements



Systems Compliance

- Does the system include workflows that enforce compliance?
- Control and limit delete capabilities included?
- Are proper sequence of steps and processes enforced?
- Are roles and permissions properly controlled?
- Can results be altered, and if so, are changes easily tracked and identified?
- Is training provided and documented?

Home Assets x Asset: 12383 x

Edit Print Show Enrollment Form Quality Engineer

Asset: 12383 Tags: none

Asset Information

Asset ID	12383	Active	Yes
Manufacturer	Mitutoyo	Condition	Operational
Model	500-196-30	Department	R&D
Serial Number	3213256	Location	Research Cell A
Description	0-6" Digital Caliper	Owner	Laurissa Primavera [Change]
Model Type	Caliper	No Calibration Required	No
Acquisition Cost	\$ 127.00	Standard	No
Parent		Calibration Interval	12 Months

Procedural Methods

Manufacturer Procedure	Yes	Manufacturer Procedure Name	Caliper Procedure ABC
Industry Accepted Method	Yes	Industry Accepted Method Name	Caliper Procedure
Custom Procedure	No	Custom Procedure Details	

Calibration Specification

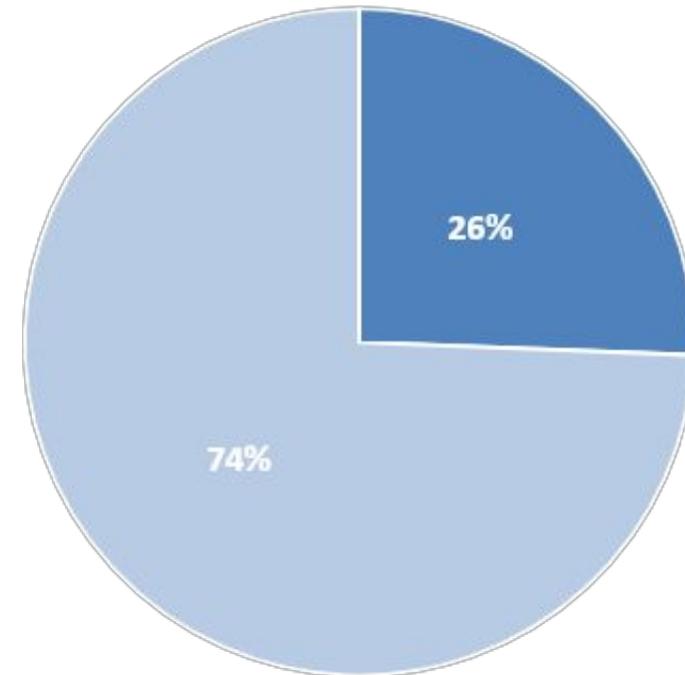
Process / Operating Range	0-6"	Calibration Range	0-6"
Process / Operating Set Point Tolerance	0.001	Calibration Tolerance	0.001

Classification

Rigorous Keyword Search vs Expert Model

- Redica Systems' Human Drug model was used as the expert model to review data over the last 5 years
- A rigorous key word search was also used to identify relevant 483 observations as it relates to FDA 21 CFR Part 11 compliance
- The key word search only identified $\frac{1}{4}$ of the observations across the data

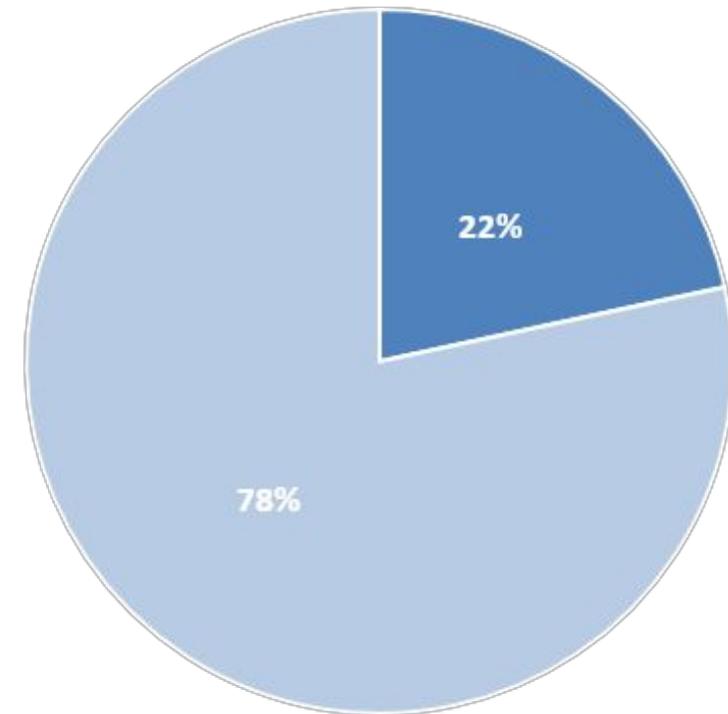
FDA 21CFR Part 11 Relevant Findings
(Jan 2018 to Oct 2022)



■ Rigorous Key Word Search ■ Additional Results from Expert Model

5 Years of “Systems Compliance” Observations

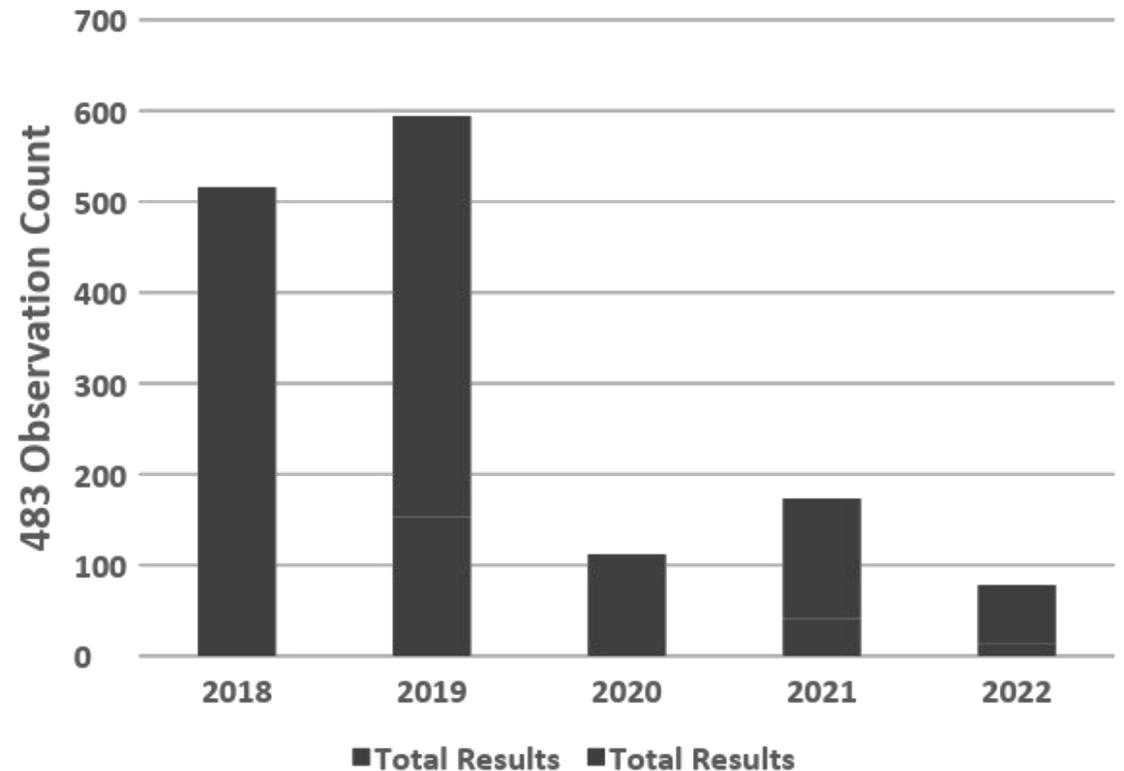
- Redica Systems’ Human Drug model shows nearly 1500, 483 observations focused on “Systems Compliance” in the last 5 years
- 22% of “Systems Compliance” 483 observations were identified by a rigorous key word search, while 78% more were only identified by the expert model



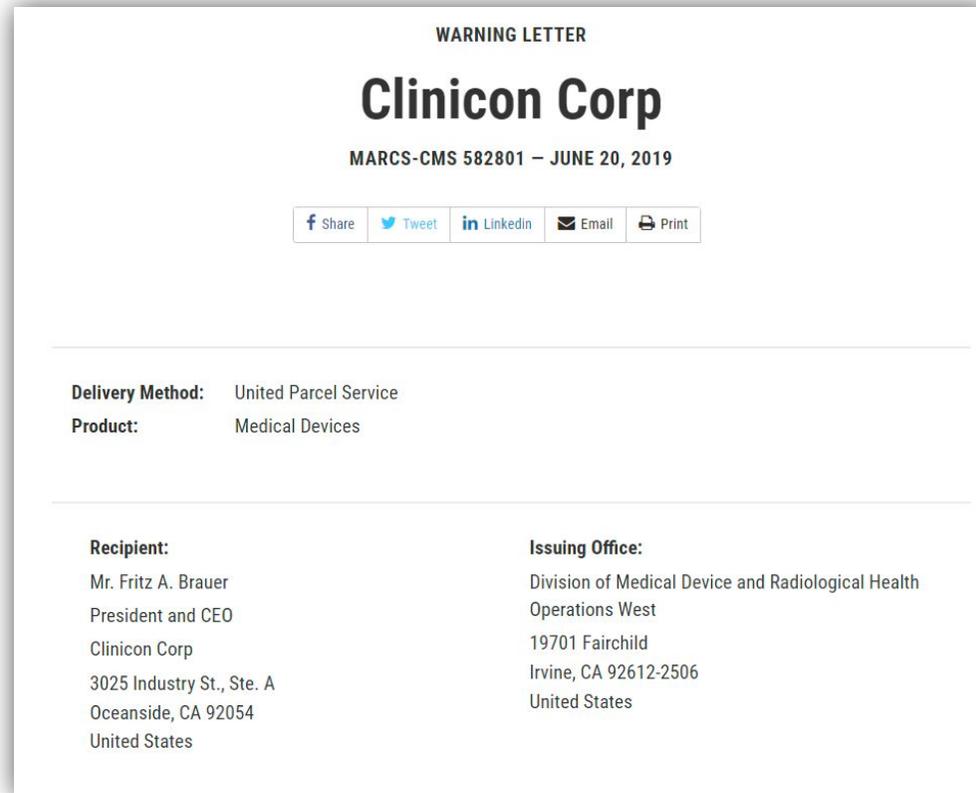
■ Rigorous Key Word Search ■ Additional Results from Expert Model

5 Years of “Systems Compliance” Observations

- “Systems Compliance” referenced 483 observations decreased 74% due to COVID
- USA vs International observations were fairly even with 55% cited US companies while 45% cited International companies



FDA “Systems Compliance” Citation Example



The documentation maintained by your firm does not demonstrate a validation has been maintained for the (b) (4) process, or performed for your packaging process. Please review the requirements of 21 CFR Part 820.75 and provide information as to how you are ensuring sterilization and maintaining the sterile barrier for your products currently being distributed and in future. We also request that you **review your procedures to ensure they meet the requirements, and implement those procedures to include retention of applicable records.** Please provide our office a timeframe for when this can be completed, a copy of the procedure if it is updated, and records such as the final report showing results of each validation.

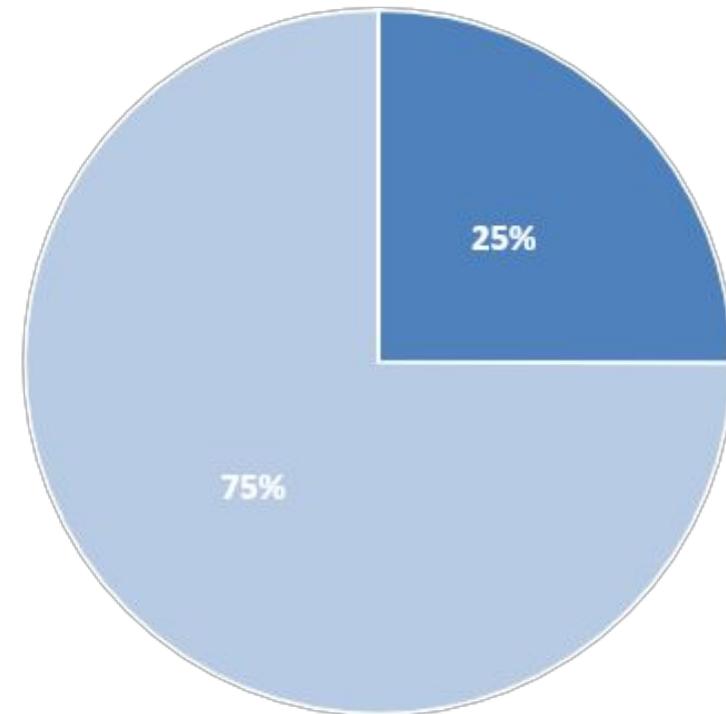
Audit Trails

- Time stamped audit trails with complete histories?
- Are change histories available, and previous versions stored?
- Audit trails retrievable and available for review?
- Device checks to confirm source data validity?
- Evidence of system checks?
- Written policies that deter record and/or e-signature falsification?

Date Created	Created By	Description
05/17/2022 11:48:17 AM	Judy Young	Modified Owner from John Ashworth to Laurissa Primavera of record - 00040
03/04/2021 08:39:30 AM	John Ashworth	Record Name: 00040 Modified Service Completed to 03/04/2021 Modified Initial Asset Condition to Out of Tolerance Modified On Time Status from In Process to Serviced On Time Modified Final Asset Condition to Operational Modified Work Finished to 03/04/2021 Modified Next Service to 00199 Modified Actual Turnaround Days to 78 Modified Next Due Date to 03/04/2022 Modified Processing Status from In Process to Completed Modified Open from Yes to No
11/16/2020 09:35:00 AM	John Ashworth	Completed By Signature Invalidated - 00040
11/16/2020 09:35:00 AM	John Ashworth	Reviewed By Signature Invalidated - 00040
11/16/2020 09:35:00 AM	John Ashworth	Record Name: 00040 Modified Procedure to MITU-001
11/16/2020 09:12:19 AM	John Ashworth	Reviewed By Signed
11/16/2020 09:12:06 AM	John Ashworth	Completed By Signed
		Record Name: 00040 Modified Start Date to 11/16/2020

5 Years of “Audit Trails” Observations

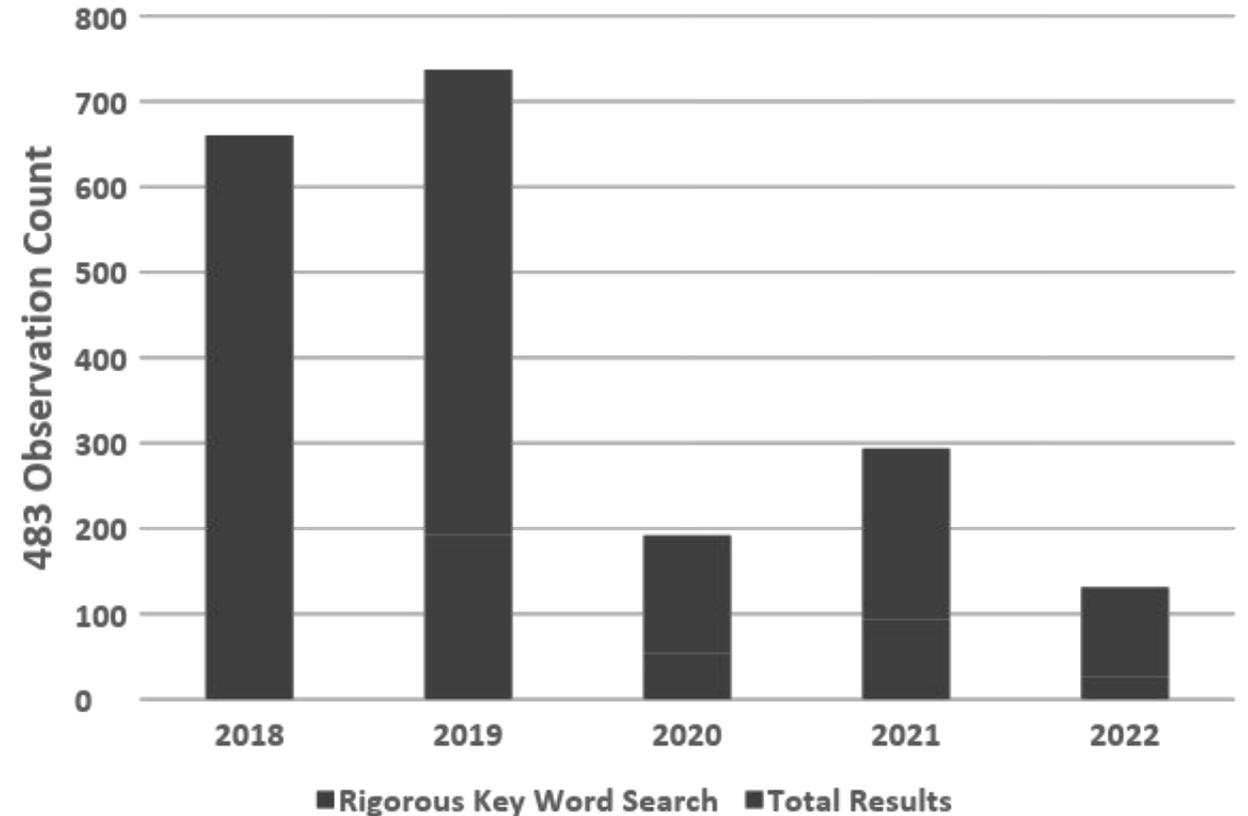
- Redica Systems’ Human Drug model shows nearly 2150, 483 observations focused on “Audit Trails” in the last 5 years
- 25% of “Audit Trails” 483 observations were identified by a rigorous key word search, while 75% more were only identified by the expert model



■ Rigorous Key Word Search ■ Additional Results from Expert Model

5 Years of “Audit Trails” Observations

- “Audit Trails” referenced 483 observations decreased 65% due to COVID
- USA vs International observations were slightly skewed towards the US with 62% cited US companies while 38% cited International companies



FDA “Audit Trails” Citation Example

WARNING LETTER

International Trading Pharm Lab Inc

MARCS-CMS 598537 – APRIL 24, 2020

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Delivery Method: Via Email
Product: Drugs

Recipient: Mr. Ismail Elchagea President and Owner International Trading Pharm Lab Inc 470 Chamberlain Ave., Suite 12 Paterson, NJ 07522-1000 United States	Issuing Office: Division of Pharmaceutical Quality Operations I United States
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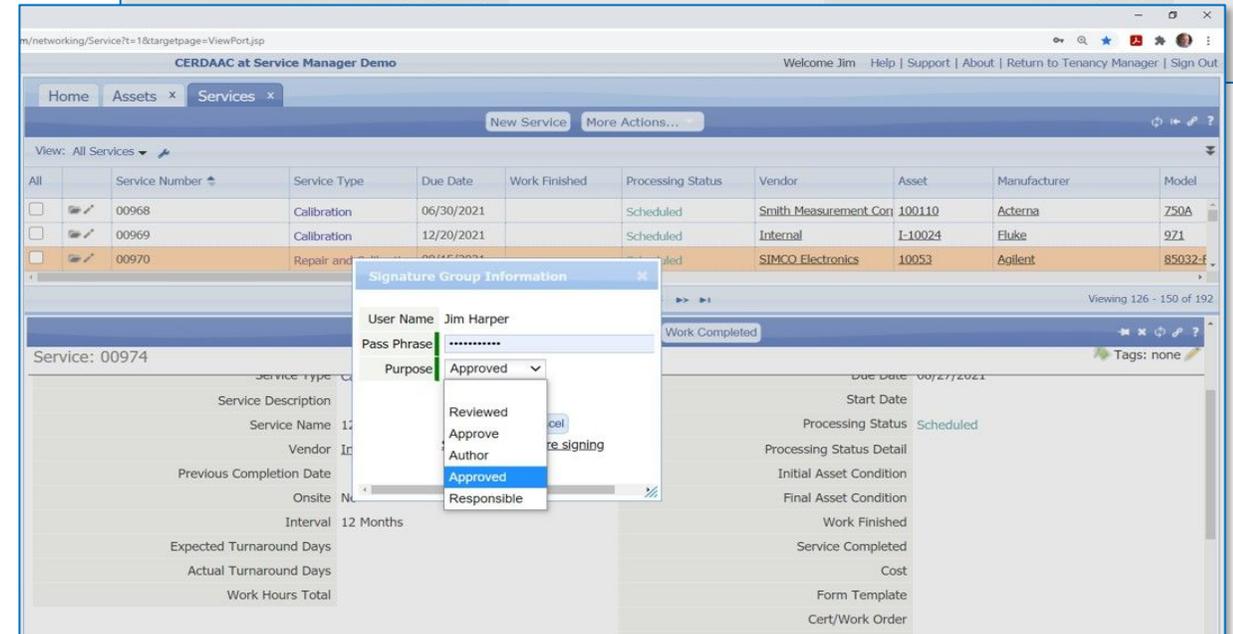
4. Failure to exercise sufficient controls over computerized systems to prevent unauthorized access or changes to data, and failure to have adequate controls to prevent omission of data.

Your firm lacks controls to assure the integrity of electronic test data generated by high performance liquid chromatography (HPLC) and gas chromatography (GC) systems. For example, during the inspection our investigator observed that stand-alone computers used to run an HPLC and a GC allowed analysts who test drug samples the ability to delete raw data files and alter date and time stamps. In addition, **audit trails were not enabled, so there would be no way to determine whether analysts manipulated data.**

Electronic Signatures

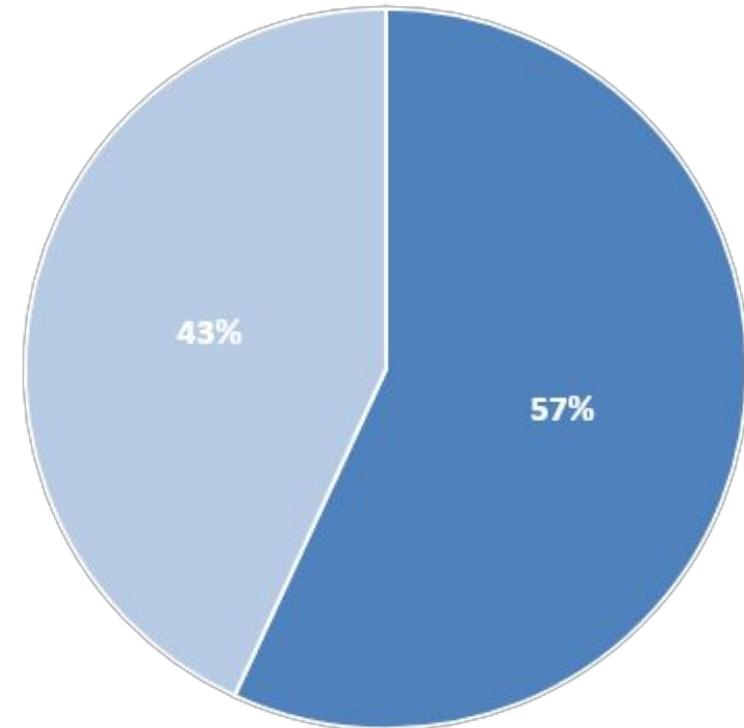
E-signatures can accelerate review and approval processes, BUT there are key requirements for FDA regulated manufacturers to make sure e-signatures are compliant:

- Include printed name and date, as well as signature?
- Meaning of signature included? (review, approval, etc.)
- Are e-signatures linked to their respective electronic records?
- Cannot be cut, copied, falsified?
- Verification of signer's identity?
- Cannot be reused or reassigned?



5 Years of “Electronic Signatures” Observations

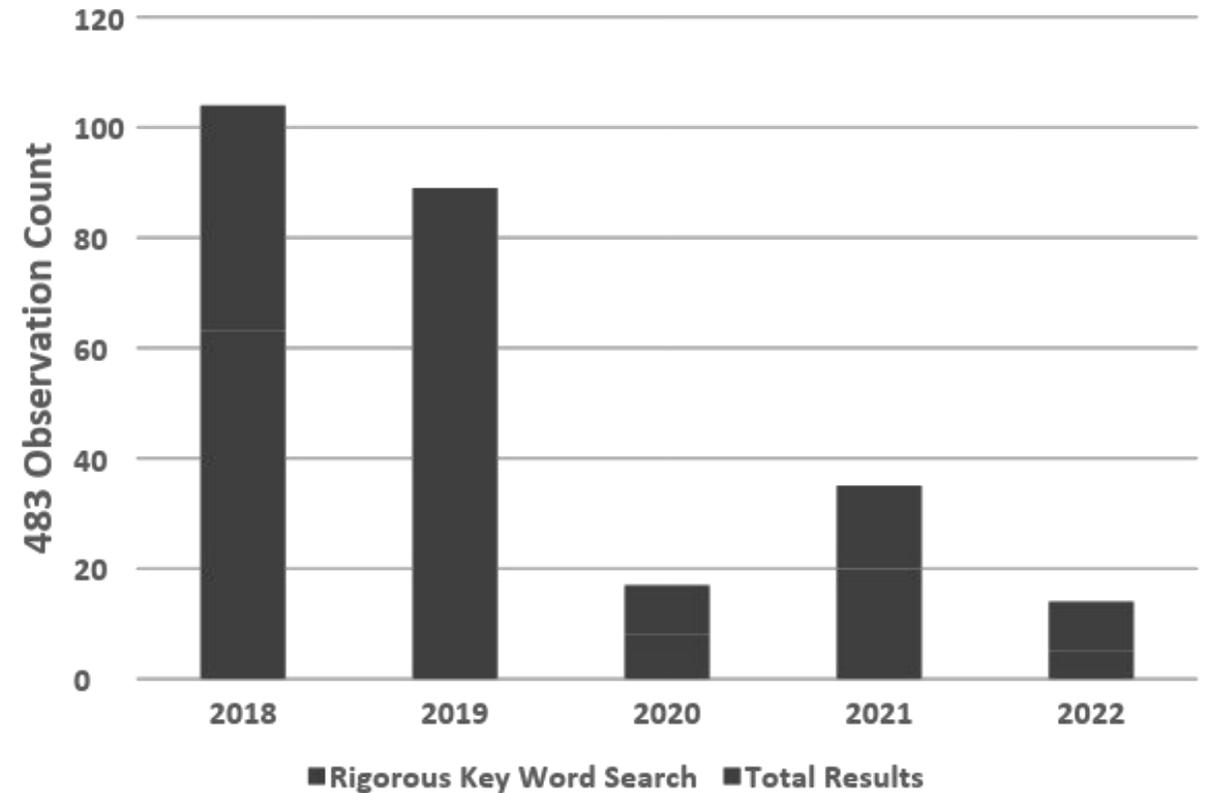
- Redica Systems’ Human Drug model shows nearly 300, 483 observations focused on “Electronic Signatures” in the last 5 years
- 57% of “Electronic Signatures” 483 observations were identified with a rigorous keyword search, while 43% more were only identified by an expert model. This split is significantly higher than the other observations.



■ Rigorous Key Word Search ■ Additional Results from Expert Model

5 Years of “Electronic Signatures” Observations

- “Electronic Signatures” referenced 483 observations decreased 73% due to COVID
- USA vs International observations were even with 49% cited US companies while 51% cited International companies



FDA “Electronic Signature” Citation Example

WARNING LETTER

Green Wave Analytical, LLC

MARCS-CMS 630965 – AUGUST 19, 2022

[f Share](#) [t Tweet](#) [in LinkedIn](#) [✉ Email](#) [🖨 Print](#)

Delivery Method: Electronic Mail
Product: Drugs

Recipient: Mr. James P. Polansky Co-owner/Scientist Green Wave Analytical, LLC 10366 Roselle St., Suite C San Diego, CA 92121-1543 United States ✉ jpolansky@ecalab.com	Issuing Office: Division of Pharmaceutical Quality Operations IV United States
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In addition, the HPLC instrument was found to be operating in the absence of an activated audit trail to record information about each analytical test, such as:

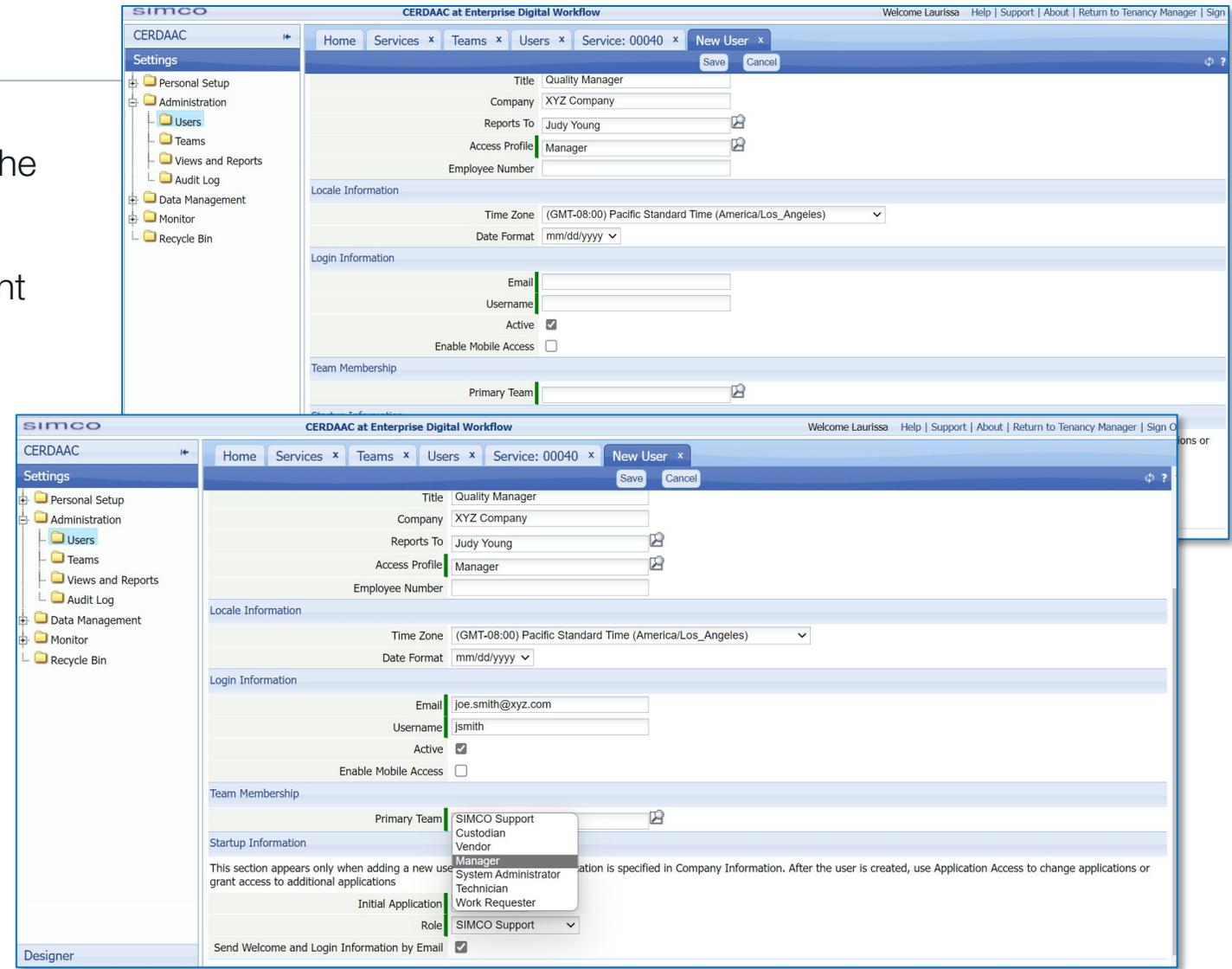
- Type of injection
- Date and time
- Identity of analyst
- Nature of action taken and reason

You also stated that data from the HPLC was not securely backed up and you did not review the HPLC audit trail data. In addition, you failed to **validate electronic signatures used to approve analytical testing records for release testing** of drugs performed from at least January 2020, to September 2021.



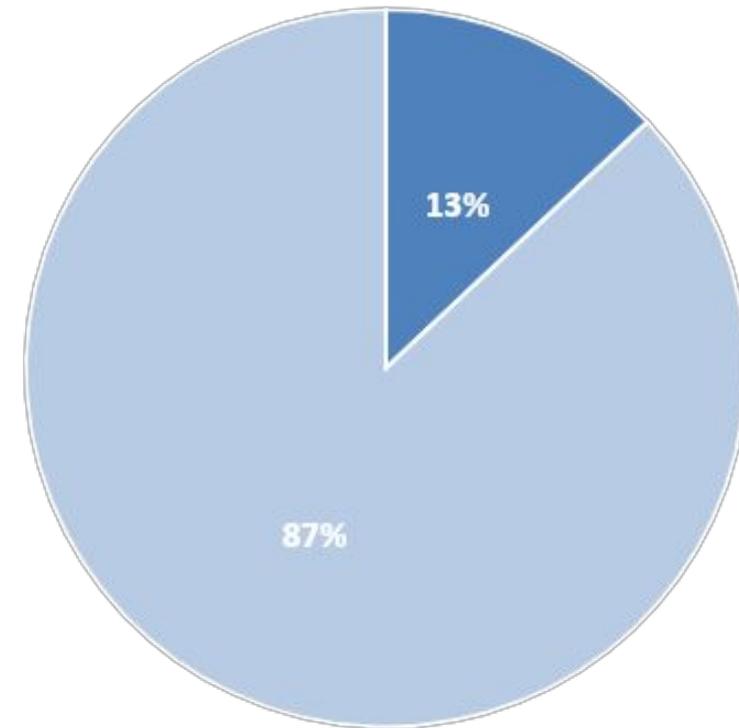
Access and Control

- Individual access control to confirm the identity of the person accessing the system?
- Sophisticated password security measures, frequent password updates, password expirations
- Procedures for recalling passwords
- Unauthorized access attempt notifications
- Loss management procedures for devices
- Controls for testing of devices



5 Years of “Access & Control” Observations

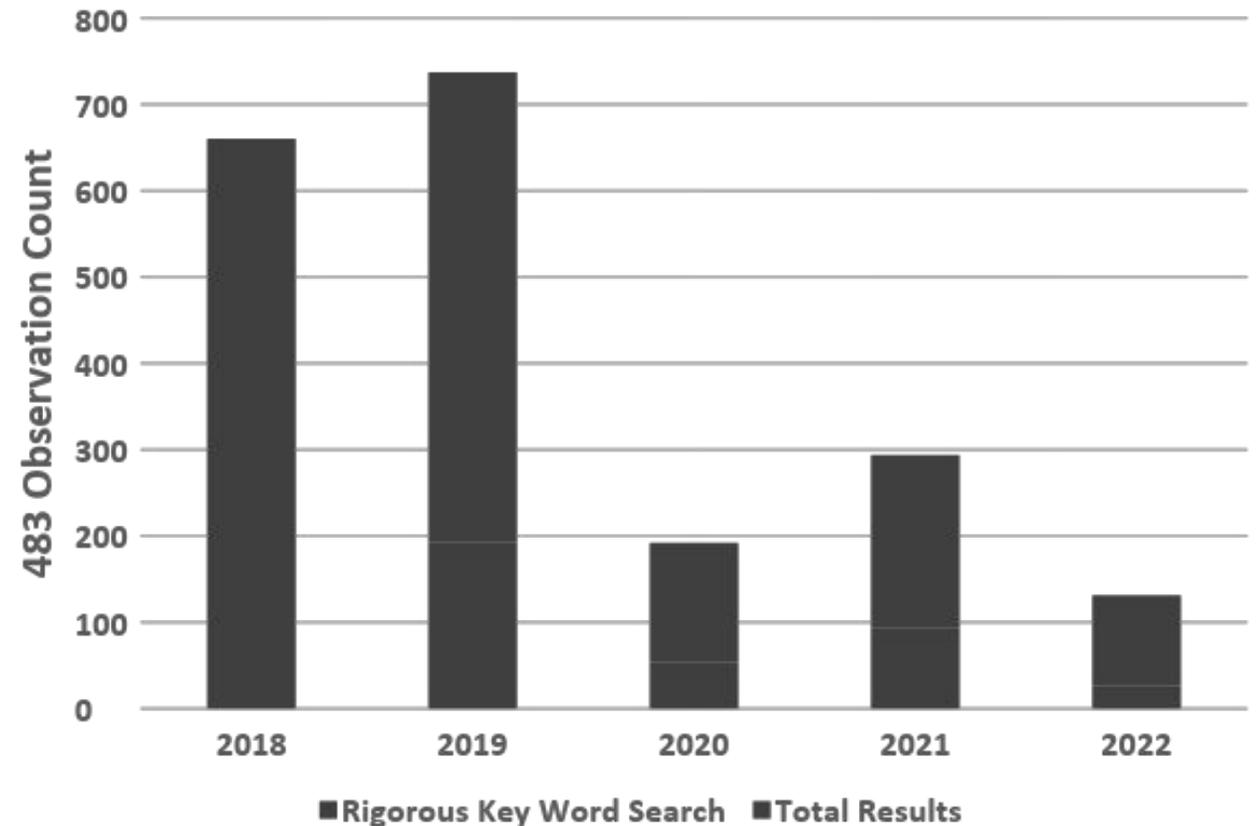
- Redica Systems’ Human Drug model shows 500+, 483 observations focused on “Access & Control” in the last 5 years
- 13% of “Access & Control” 483 observations were identified by a rigorous key word search, while 87% more were only identified by the expert model. This is the lowest number of keyword results across all 5 sections



■ Rigorous Key Word Search ■ Additional Results from Expert Model

5 Years of “Access & Control” Observations

- “Access & Control” referenced 483 observations decreased 71% due to COVID
- USA vs International observations were skewed with 71% cited US companies while 29% cited International companies



FDA “Access and Control” Citation Example



4. Your firm failed to exercise **appropriate controls over computer or related systems to assure that only authorized personnel institute changes in the master production and control records, or other records (21 CFR 211.68(b)).**

Your firm failed to implement adequate controls to support the integrity of your electronic data and to ensure that only appropriate individuals had administrative rights. For example, your (b)(4) microbiological testing instrument used for drug product release testing is controlled by a stand-alone computer which does not have appropriate controls in place to prevent deletion of raw laboratory data. All QU users utilized a shared generic account to access the computer which had administrative privileges capable of changing and deleting files. During the inspection, one of your employees opened the computer’s recycle bin and noted that approximately (b)(4) files and folders were deleted. Further, these deleted items included at least (b)(4) files of the “(b)(4)” format which your personnel stated were most likely (b)(4) data files. The names of (b)(4) of those deleted files were similar to drug product formulas produced since 2017.

System Validation

- Has the system been validated?
- The difference between “*validatable*” or *pre-validated*? The answer can save you considerable time and money!
- Does the system validate for:
 - IQ (Installation Qualification)
 - OQ (Operational Qualification)
 - PQ (Performance Qualification)—”Does This Process Produce the Right Result”? “Is This Process Safe and Consistent?”

The screenshot displays the SIMCO CERDAAC Service Manager interface. A central pop-up window titled "SIMCO CERDAAC Service Manager + Compliance" is overlaid on the dashboard. The pop-up features a green checkmark icon and the word "VALIDATED" in green. Below this, it states "Version 4.0, July 2019" and includes a "Browse details" button. At the bottom of the pop-up, it reads "Copyright © 2009-2020 SIMCO Electronics" and "CERDAAC is a registered trademark of SIMCO Electronics", with a link to "CERDAAC availability report".

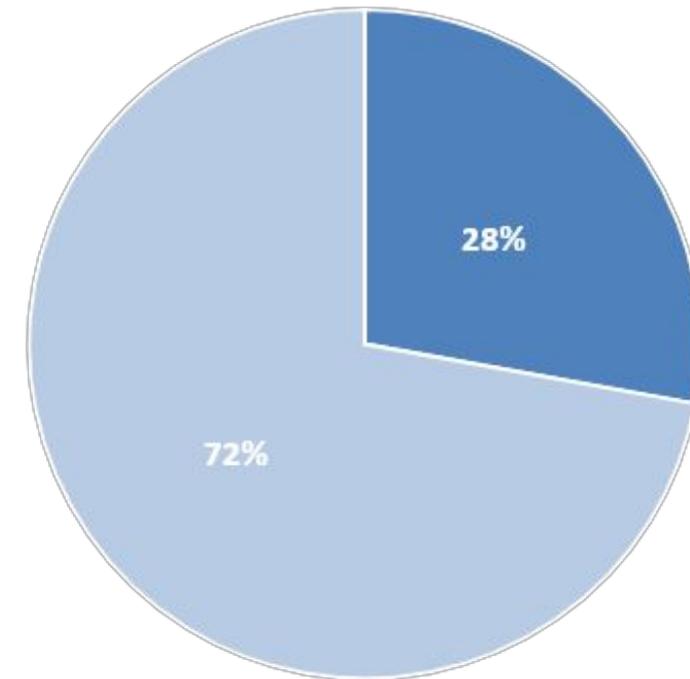
The background dashboard shows several widgets. On the left, a navigation menu lists various system components. The main area contains a "Manager Dashboard" with a "Page: Manager Dashboard" dropdown. Key widgets include:

- On Time Status - AI**: A pie chart showing the following data:

Category	Percentage
Current	66%
In Process	7%
Due Within 30 Days	5%
- Out Of Tolerance Summary**: A gauge chart showing a needle pointing to 21.4% on a scale from 0% to 30%.
- Number of Calibrations that Met or Missed Turnaround Target by Vendor - Past 365 Days**: A bar chart with a value of 15.
- Number of On Time vs. Late Service Starts**: A bar chart with a value of 24.

5 Years of “System Validation” Observations

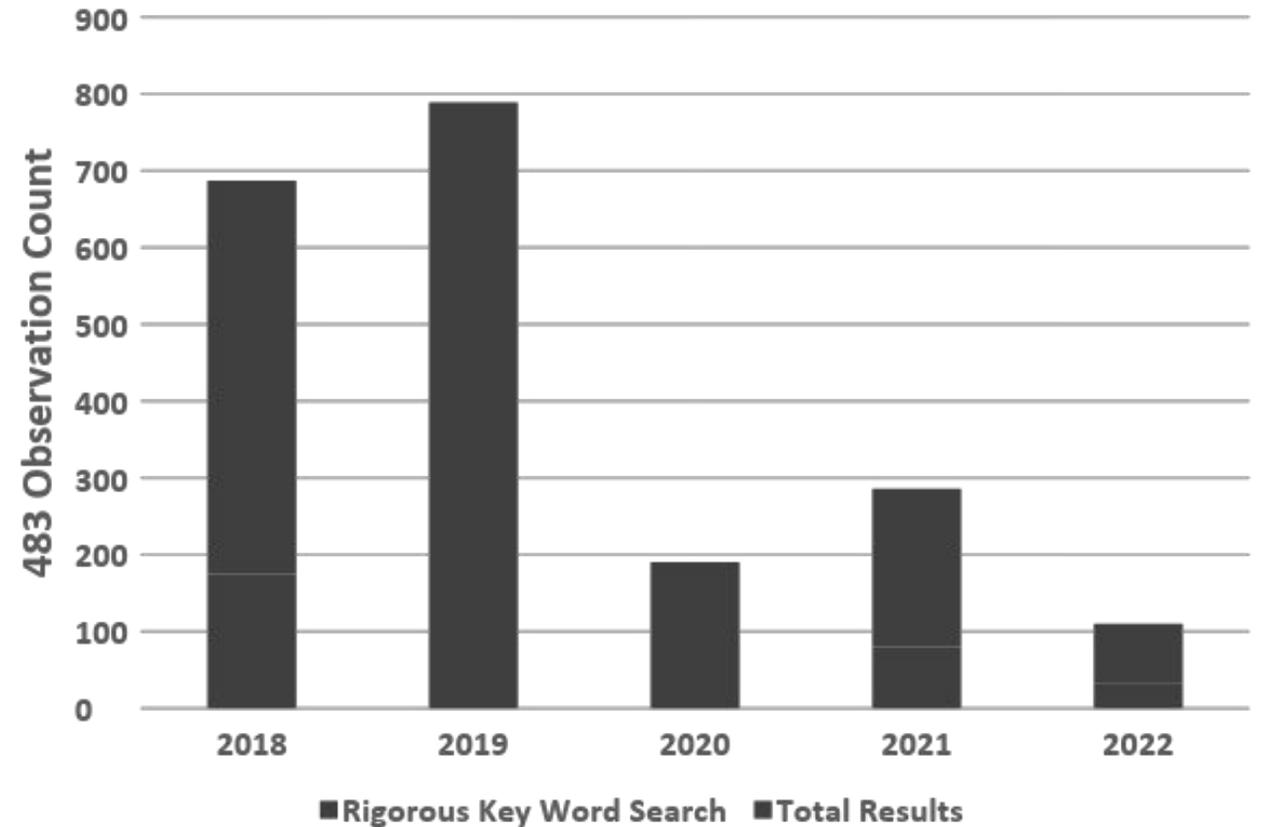
- Redica Systems’ Human Drug model shows nearly 2000, 483 observations focused on “System Validation” in the last 5 years
- 28% of “System Validation” 483 observations were identified by a rigorous key word search, while 72% more were only identified by the expert model



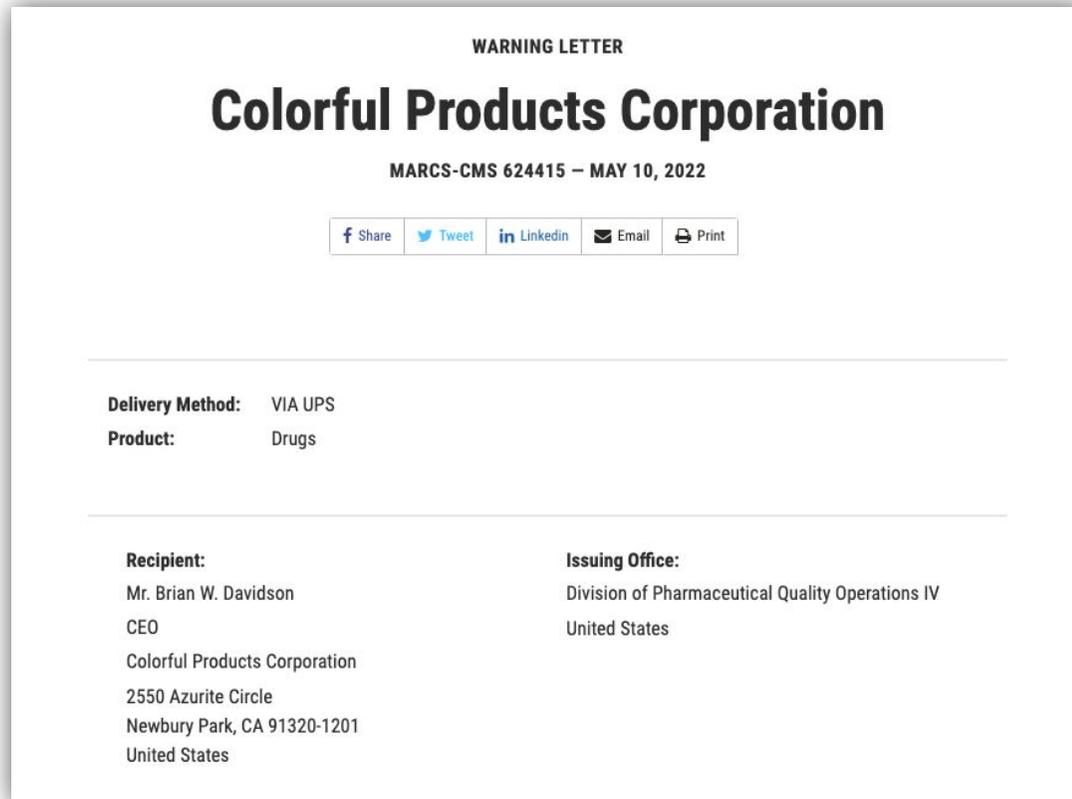
■ Rigorous Key Word Search ■ Additional Results from Expert Model

5 Years of “System Validation” Observations

- “System Validation” referenced 483 observations decreased 68% due to COVID
- USA vs International observations were slightly skewed with 60% cited US companies while 40% cited International companies



FDA “Software Validation” Citation Example

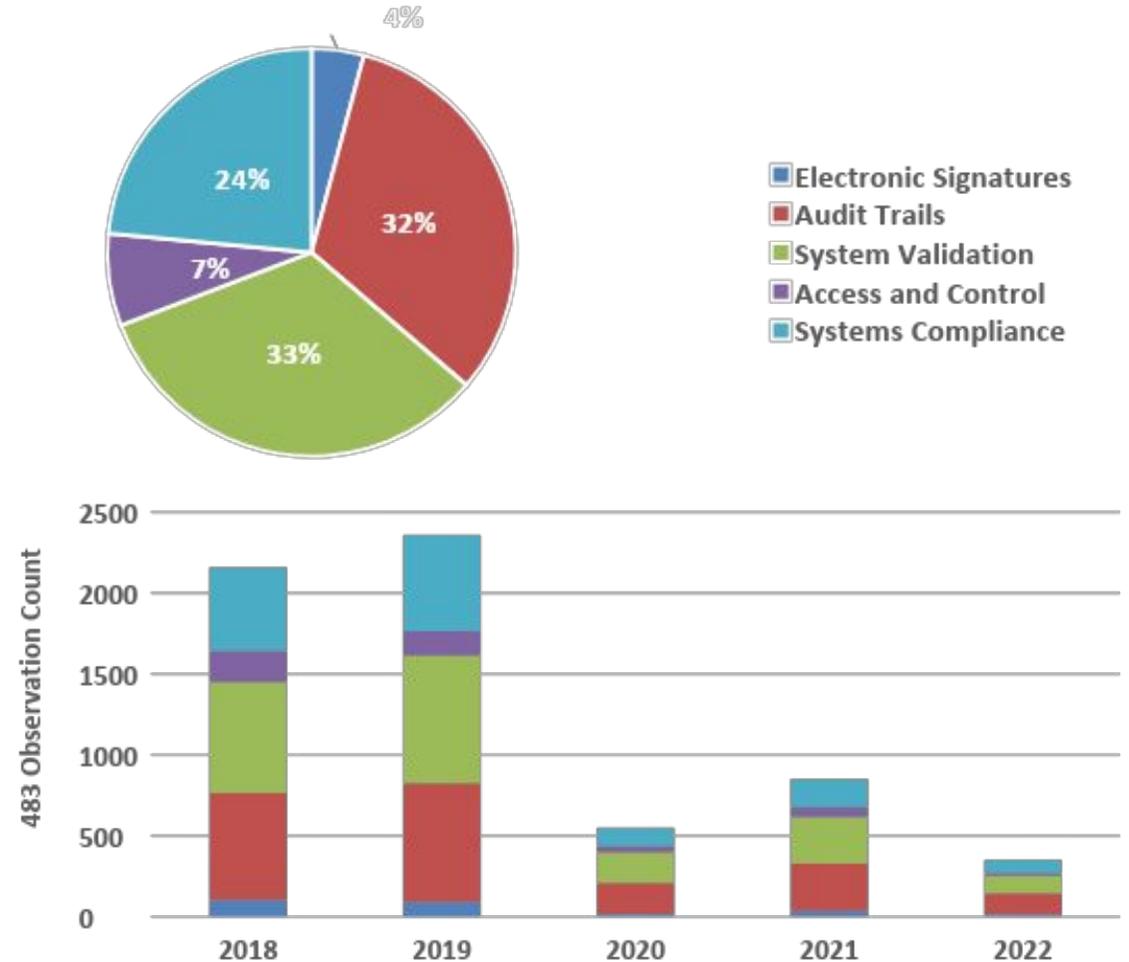


4. Your firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records, or other records. (21 CFR 211.68(b)).

Your firm lacked controls to assure the integrity of (b)(4) used in the manufacturing of your drug products. For example, your firm utilized software (i.e., (b)(4)) for the retention of data, including your drug product formulations and the quarantine and release status of drug products. This software is also used to document the completion of manufacturing steps on batch records, including (b)(4) amounts, manufacturing activities, and calculations. You stated to our investigator that this (b)(4) software was not validated and lacked audit trails.

Summary of 5 Years of 483 Observations

- FDA 21 CFR Part 11 Compliance was cited more than 6,250 times in the last 5 years
- “System Validation” and “Audit Trails” were observed the most frequent
- “Electronic Signatures” was cited the least
- COVID caused a 69% decrease in Human Drug 483 observations



CERDAAC: Ensures FDA 21 CFR Part 11 Compliance without Increasing Costs:

Purpose-built for highly regulated industries:

- 16 of the top 20 global life sciences companies
- 14 of the top 20 global aerospace & defense companies
- 60 years in business
- 15M+ services performed
- FDA 21 CFR Part 11 Compliant: e-signatures, workflows, records, data, etc.
- **Prevalidated** system saves you time and money
- Manage quality and compliance of assets, people and processes
- Cloud solution makes it easy to access, deploy, and maintain
- Highly configurable to your business needs
- Easy to use
- Secure, controlled access



Thank you for attending!

“The Insider’s Guide to Audit Readiness”



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Does anyone have any questions?

