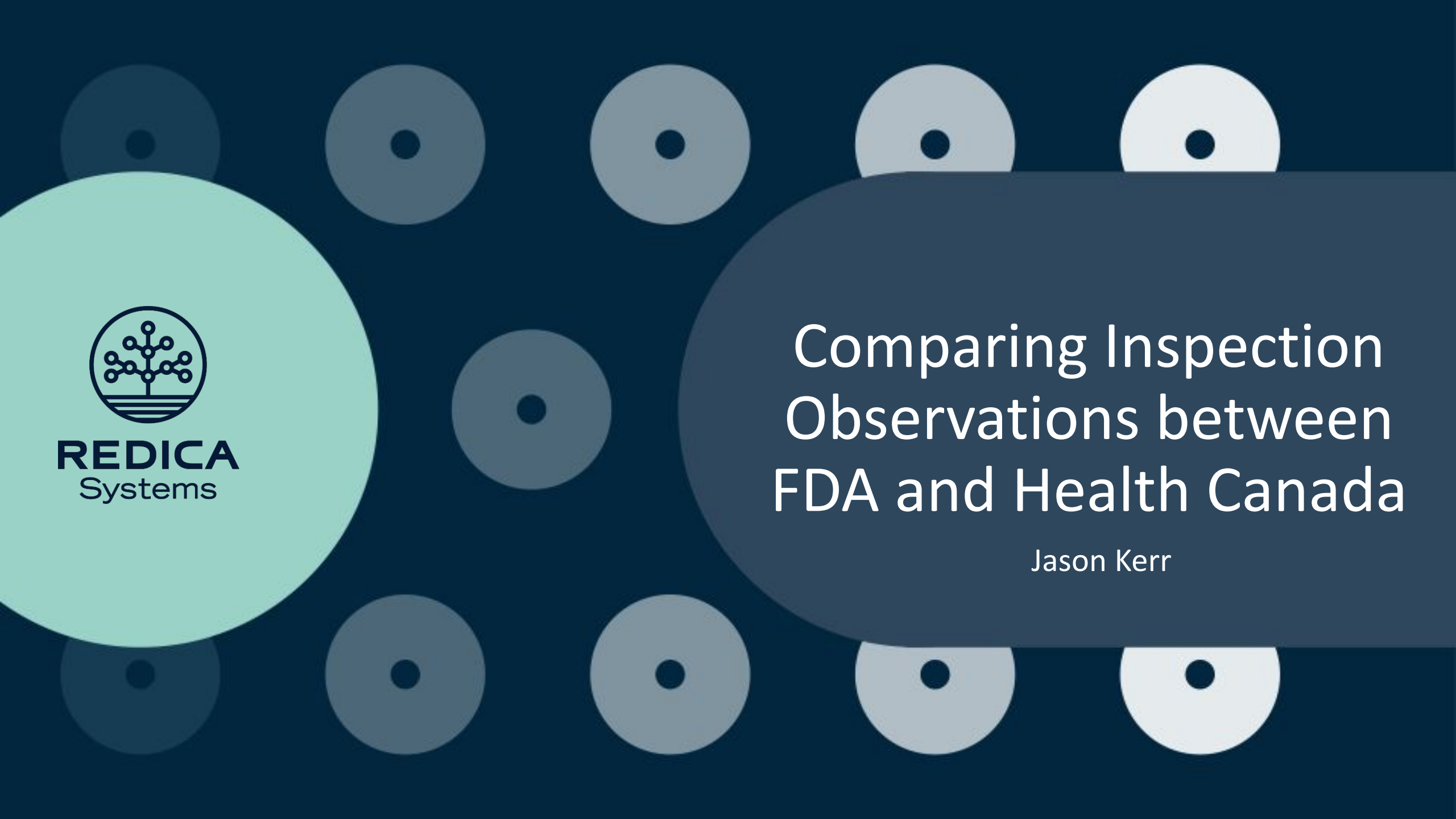


Comparing Inspection Observations between FDA and Health Canada

Jason Kerr

Agenda

- Quick Background on Redica Systems
- Question of the Day
- Data Foundation
- Data Comparison
- Deeper Analysis
- Quality System Labels
- Redica System Commercial

Who is Redica Systems?

Redica Systems - Quality and Regulatory Intelligence data analytics platform serves over 200 life sciences companies - from clinical-stage biotech to the largest global sponsors. Our customers rely on our comprehensive data sets to enable a fact-based approach to inspection preparation, vendor quality, and regulatory surveillance.

Representative customers

moderna, AstraZeneca, AMGEN, novo nordisk®, abbvie, J&J, Seagen, Lonza, patheon by Thermo Fisher Scientific, AGC Biologics, bluebirdbio, Kite A GILEAD Company, GBT, HERON THERAPEUTICS, KRONOS·BIO

Unmatched data sets

FDA, European Medicines Agency, MHRA Regulating Medicines and Medical Devices, Health Canada, ICH harmonisation for better health, ISO

- >15,000 regulatory and standards monitored daily from 200 agencies
- >1m regulatory inspections
- >25,000 Form 483s
- >17,000 Warning letters
- >16,000 EIRs and 483 Responses
- >35,000 EMA inspections and docs
- >1,500 MHRA GMP post-inspection reports
- >20,000 Health Canada inspections and docs

Question on the Day

- US – FDA Inspection Data
  - ~10,800 Human Drug Inspections from 2017-2022*
  - 3 Major Inspection Reason
  - Many Form 483's observations
- Canada – Health Canada Inspection Data
  - ~5,600 Human Drug Inspections from 2017-2022*
  - 4 Major Inspection Reasons
  - All Report Card's observations

Will the FDA's inspection reasons and observations be similar to that of the Health Canada's inspections reasons and observations?

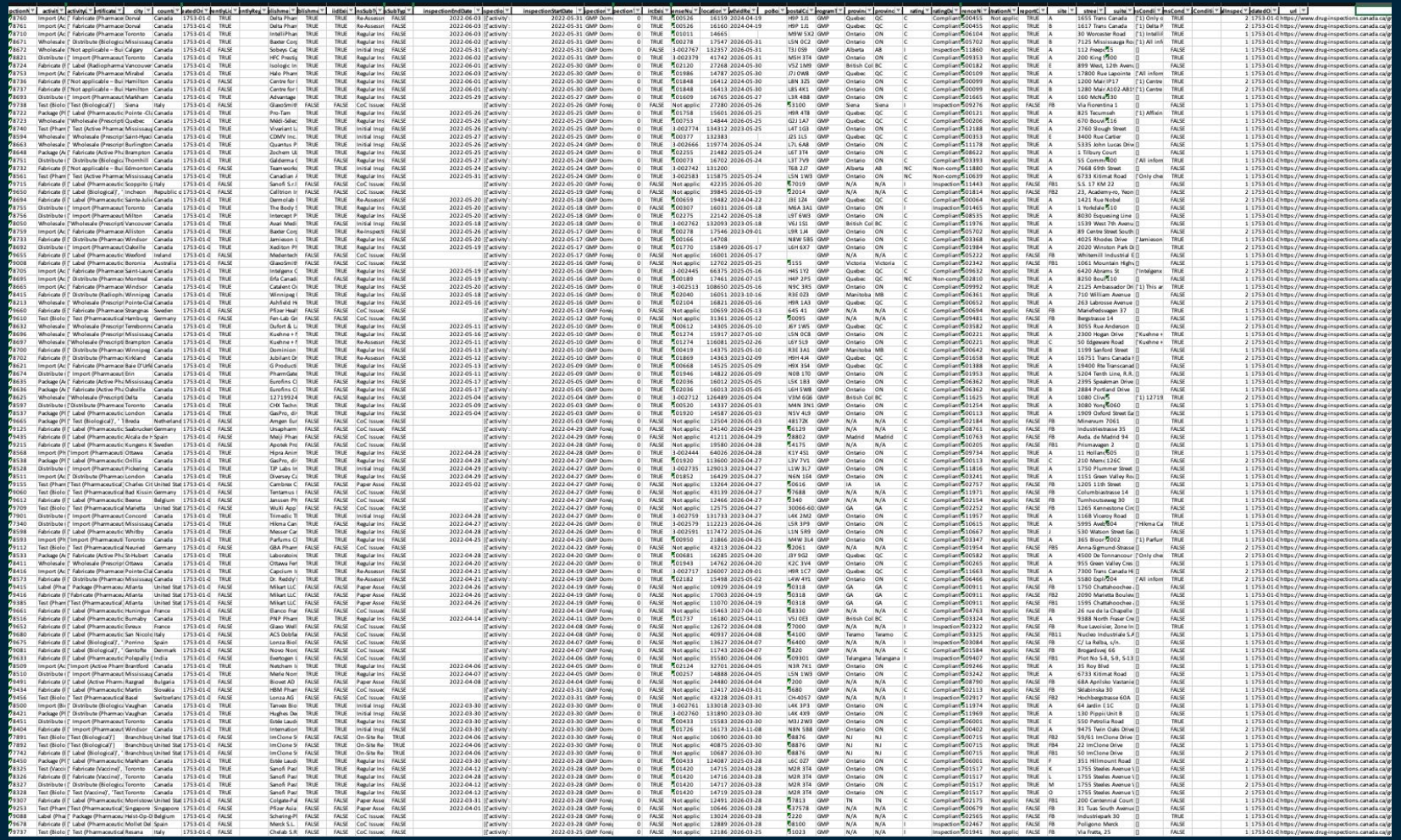
Set up the Scene – America

~10,800 Inspections

inspection	fei_number	inspection_s	inspection_	legal_name	address	city_name	st	zip_code	country_name	iss	full_name	district	center	Inspection Reason
1048175	1000021877	2018-02-21	2018-02-26	Gaylord Chemical	1880 Fairlaw	Tuscaloosa	AL	35401-2500	United States	N	Bradley, Sama	New Orleans	Human Drug:	Surveillance
1058496	1000036852	2018-06-18	2018-06-22	Astellas Pharma I	1 Astellas Wa	Northbrook	IL	60062-6111	United States	N	Yuscius, Susan	Chicago Distr	Human Drug:	Surveillance
	1000036852	2019-09-30	2019-10-04	Astellas Pharma I	1 Astellas Wa	Northbrook	IL	60062-6111	United States	N	Thai, Jeanne J	Chicago Distr	Human Drug:	Surveillance
1091840	1000043107	2019-03-18	2019-03-21	Elkhart General H	600 East Blvc	Elkhart	IN	46514-2483	United States	N	Jackson, Sherr	Detroit Distri	Human Drug:	Surveillance
1009921	1000056584	2017-04-24	2017-04-26	Whisk Products I	130 Enterpri	Wentzville	MO	63385-5544	United States	Y	Fuentes, Vero	Kansas City D	Human Drug:	Surveillance
1155133	1000056584	2021-10-18	2021-10-22	Whisk Products I	130 Enterpri	Wentzville	MO	63385-5544	United States	Y	Williams, Loga	Kansas City D	Human Drug:	Surveillance
NULL	1000065447	2017-04-27	2017-04-28	Airgas USA, LLC	323 Russell S	Craig	CO	81625-1936	United States	Y	Patel, Nayan J	Denver Distri	Human Drug:	Surveillance
1101842	1000066007	2019-09-09	2019-09-13	Lovelace Biomedi	Bldg 9217, A	Albuquerque	NM	87185	United States	Y	Chen, Zhou	Denver Distri	Human Drug:	Surveillance
1118971	1000066007	2020-01-27	2020-01-31	Lovelace Biomedi	Bldg 9217, A	Albuquerque	NM	87185	United States	Y	Campos, Jona	Denver Distri	Human Drug:	Surveillance
1160367	1000068559	2021-12-06	2021-12-13	Aldrich Chemical	3858 Benner	Miamisburg	OH	45342-4304	United States	Y	SenthamaraiK	Cincinnati Dis	Human Drug:	Surveillance
1017373	1000069268	2017-06-26	2017-08-09	Diamond Wipes I	1375 Isaac B	Bucyrus	OH	44820-9604	United States	Y	Barrowcliff, Ar	Cincinnati Dis	Human Drug:	Surveillance
1164257	1000069268	2022-02-16	2022-03-03	Diamond Wipes I	1375 Isaac B	Bucyrus	OH	44820-9604	United States	Y	Chudi-Nwanki	Cincinnati Dis	Human Drug:	Surveillance
1155946	1000071237	2021-10-20	2021-11-04	National Chemica	401 N 10th S	Philadelphia	PA	19123-3803	United States	Y	Casner, Micha	Philadelphia I	Human Drug:	Surveillance
NULL	1000071265	2017-10-23	2017-10-25	Diversified Chemi	60 Germay D	Wilmington	DE	19804-1105	United States	Y	Donald, Steve	Philadelphia I	Human Drug:	Surveillance
NULL	1000076625	2017-06-05	2017-06-16	Boothwyn Pharm	221 Gale Ln	Kennett Squar	PA	19348	United States	Y	Chou, Mindy M	Philadelphia I	Human Drug:	Surveillance
1153299	1000076625	2021-08-17	2021-09-08	Boothwyn Pharm	221 Gale Ln	Kennett Squar	PA	19348	United States	Y	Dissmeyer, Se	Philadelphia I	Human Drug:	For-Cause
1015411	1000086712	2017-06-12	2017-06-21	Charles River Lab	251 Ballardv	Wilmington	MA	01887-1096	United States	Y	Marcsisin, Sea	New England	Human Drug:	Surveillance
1118068	1000086712	2020-02-03	2020-02-11	Charles River Lab	251 Ballardv	Wilmington	MA	01887-1096	United States	Y	Koester, Erik W	New England	Human Drug:	Surveillance
NULL	1000100689	2017-07-17	2017-07-21	The Queen's Med	1301 Puncht	Honolulu	HI	96813-2402	United States	Y	Jackson, Sherr	San Francisco	Human Drug:	Surveillance
1149956	1000107122	2021-08-23	2021-08-27	Chastains Inc. db	1275 Highlar	Clarkston	WA	99403-2846	United States	Y	Zabinski, Roge	Seattle Distri	Human Drug:	Surveillance
NULL	1000110034	2017-09-11	2017-09-18	Similasan AG	Chriesiweg 6	Jonen			Switzerland	N	Fuentes, Vero	Office of Reg	Human Drug:	Surveillance
NULL	1000110299	2017-07-17	2017-07-20	Ortho Biologics, L	Road # 2, Km	Manati	PR	674	United States	N	Negron Rodrig	San Juan Dist	Human Drug:	Surveillance
1118152	1000110299	2020-01-21	2020-01-24	Ortho Biologics, L	Rd 2 Km 45.6	Manati	PR	674	United States	N	Negron Rodrig	San Juan Dist	Human Drug:	Surveillance
1016325	1000110364	2017-04-26	2017-05-10	Amgen Manufact	Rd 31 Km 24	Juncos	PR	777	United States	Y	Negron Rodrig	San Juan Dist	Human Drug:	Surveillance
1061201	1000110364	2018-07-23	2018-08-06	Amgen Manufact	Rd 31 Km 24	Juncos	PR	777	United States	Y	Negron Rodrig	San Juan Dist	Human Drug:	Surveillance
1093715	1000110364	2019-04-30	2019-05-08	Amgen Manufact	Rd 31 Km 24	Juncos	PR	777	United States	Y	Van Tassell, M	San Juan Dist	Human Drug:	Pre-Approval
1105967	1000110364	2019-09-23	2019-09-27	Amgen Manufact	Carr 31 KM 2	Juncos	PR	00777-3871	United States	Y	Muniz, Noreer	San Juan Dist	Human Drug:	Pre-Approval
1119286	1000110364	2020-02-24	2020-02-27	Amgen Manufact	24.6 Carr 31	Juncos	PR	777	United States	Y	Li, Zhong	San Juan Dist	Human Drug:	Pre-Approval
1074929	1000110770	2018-12-10	2018-12-13	Wellman Advanc	520 Kingsbu	Johnsonville	SC	29555-8011	United States	Y	Stevens, Jared	Atlanta Distri	Human Drug:	Surveillance
1089055	1000110808	2019-04-15	2019-04-18	Spangenthal Selv	1918 Randol	Charlotte	NC	28207-1114	United States	N	Greco, Debora	Atlanta Distri	Human Drug:	Surveillance
1156995	1000110808	2021-11-03	2021-11-08	Selwyn Spangent	8045 Provid	Charlotte	NC	28277-9724	United States	N	Ball, Tracy R	Atlanta Distri	Human Drug:	Surveillance
NULL	1000110912	2017-05-15	2017-05-19	Catalent Pharma	160 N Pharm	Morrisville	NC	27560-9570	United States	Y	Blackburn, Taj	Atlanta Distri	Human Drug:	Surveillance
1086471	1000110912	2019-01-28	2019-02-01	Catalent Pharma	160 N Pharm	Morrisville	NC	27560-9570	United States	N	Chennamanen	Atlanta Distri	Human Drug:	Surveillance
1081169	1000110912	2019-02-25	2019-03-04	Catalent Pharma	160 N Pharm	Morrisville	NC	27560-9570	United States	N	Edmonds, Son	Atlanta Distri	Human Drug:	Surveillance
1102199	1000110912	2019-07-30	2019-08-02	Catalent Pharma	160 N Pharm	Morrisville	NC	27560-9570	United States	N	Lugo, Libia M	Atlanta Distri	Human Drug:	For-Cause
1116748	1000110912	2019-12-16	2019-12-20	Catalent Pharma	160 N Pharm	Morrisville	NC	27560-9570	United States	N	Stevens, Jared	Atlanta Distri	Human Drug:	Pre-Approval
1131607	1000110912	2020-09-21	2020-09-28	Catalent Pharma	160 N Pharm	Morrisville	NC	27560-9570	United States	Y	Toms, Seneca	Atlanta Distri	Human Drug:	For-Cause
1004202	1000110937	2017-02-13	2017-02-22	Alchemix Corpora	2300 W Poin	College Park	GA	30337-5129	United States	Y	Oladeji, Susan	Atlanta Distri	Human Drug:	Surveillance
1081856	1000110937	2019-02-08	2019-02-14	Alchemix Corpora	2300 W Poin	College Park	GA	30337-5129	United States	Y	Fuentes, Vero	Atlanta Distri	Human Drug:	Surveillance
	1000110944	2018-12-17	2018-12-18	WestRock Conve	5950 Grassy	Winston Salem	NC	27105-1205	United States	N	Toms, Seneca	Atlanta Distri	Human Drug:	Surveillance
NULL	1000110956	2017-06-12	2017-06-19	Kiel Laboratories	5659 Southf	Flowery Branch	GA	30542-2838	United States	N	Oladeji, Susan	Atlanta Distri	Human Drug:	For-Cause
1035015	1000110990	2017-12-11	2017-12-15	Alcami Carolinas	4221 Faber F	Charleston	SC	29405-8510	United States	Y	Wang, Zhao	Atlanta Distri	Human Drug:	Pre-Approval
1080392	1000110990	2018-10-08	2018-10-10	Alcami Carolinas	4221 Faber F	Charleston	SC	29405-8510	United States	Y	Fong, Steven	Atlanta Distri	Human Drug:	Pre-Approval
1083831	1000110990	2019-02-18	2019-02-21	Alcami Carolinas	4221 Faber F	Charleston	SC	29405-8510	United States	N	Cooke, Adam	Atlanta Distri	Human Drug:	Surveillance
1156156	1000110990	2021-10-18	2021-10-29	Alcami Carolinas	4221 Faber F	Charleston	SC	29405-8510	United States	Y	Camara, Santo	Atlanta Distri	Human Drug:	Pre-Approval

REDICA Systems

Set up the Scene – Canada



~5,600 Inspections

FDA Inspection Metadata (shortened)

- Inspection ID
- FEI Number
- Inspection Start Date
- Inspection End Date
- Legal Name
- Address
- City Name
- State Code
- Country Name
- Classification
- Center
- Inspection Reason
- 483 Issued

Center
Human Drugs
Biologics
Medical Devices & Rad Health
Animal Drugs & Feeds
Foods & Cosmetics
Tobacco Products
OTHER

Inspection Reason
Surveillance
For-Cause
Pre-Approval

Form 483 Outcome
Form 483 Not Issued
Form 483 Issued

Health Canada
Drug Inspection Metadata (shortened)

- Inspection Number
- Reference Number
- Inspection Start Date
- Inspection End Date
- Establishment Name
- Address
- City
- Province
- Country
- Inspection Type
- Rating

Inspection Type
Regular Inspection
Partial Inspection
Regular On-Site Inspection
Re-Assessment
Re-Inspection
On-Site Re-assessment
On-Site Re-inspection
Initial Inspection
Initial On-Site Inspection
MRA/Audit Inspections

Rating
Compliant
Non-Compliant

Comparing the Data

FDA Inspection Reason	HC Inspection Type
Surveillance	Regular Inspection
Surveillance	Partial Inspection
Surveillance	Regular On-Site Inspection
For-Cause	Re-Assessment
For-Cause	Re-Inspection
For-Cause	On-Site Re-assessment
For-Cause	On-Site Re-inspection
Pre-Approval	Initial Inspection
Pre-Approval	Initial On-Site Inspection
N/A	MRA/Audit Inspections

Form 483 Outcome	HC Rating
Form 483 Not Issued	Compliant
Form 483 Issued	Non-Compliant

Question on the Day

- US – FDA Inspection Data
  - ~10,800 Human Drug Inspections from 2017-2022*
  - 3 Major Inspection Reason
  - Many Form 483's observations
- Canada – Health Canada Inspection Data
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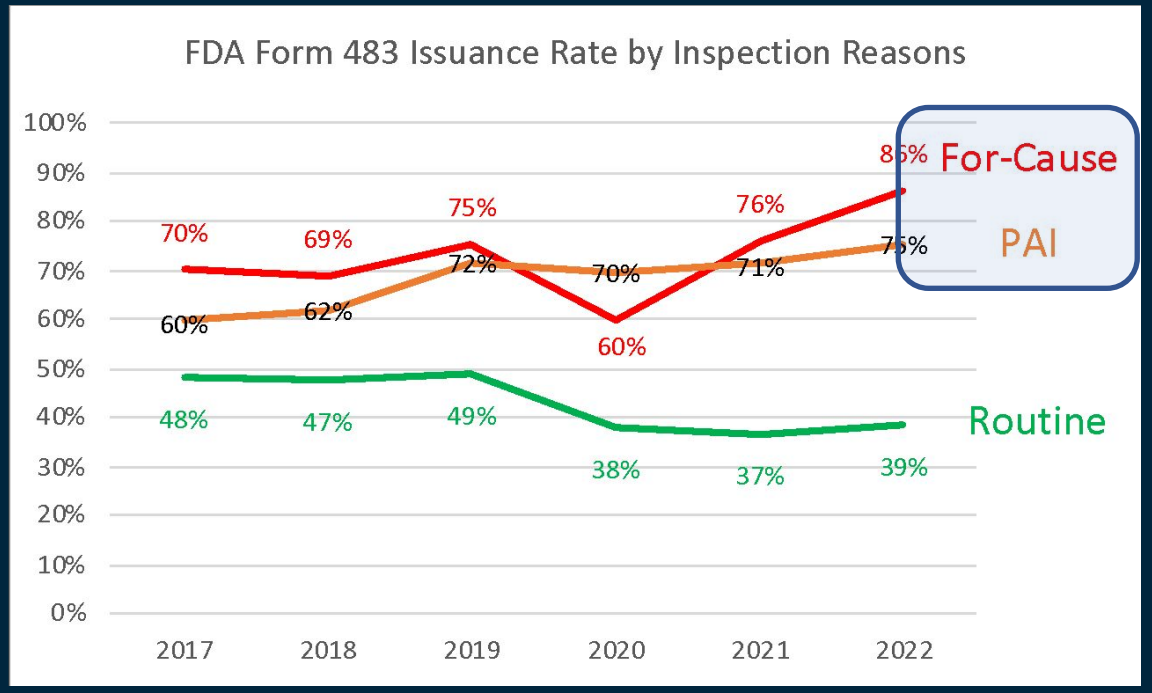
  - All Report Card's observations

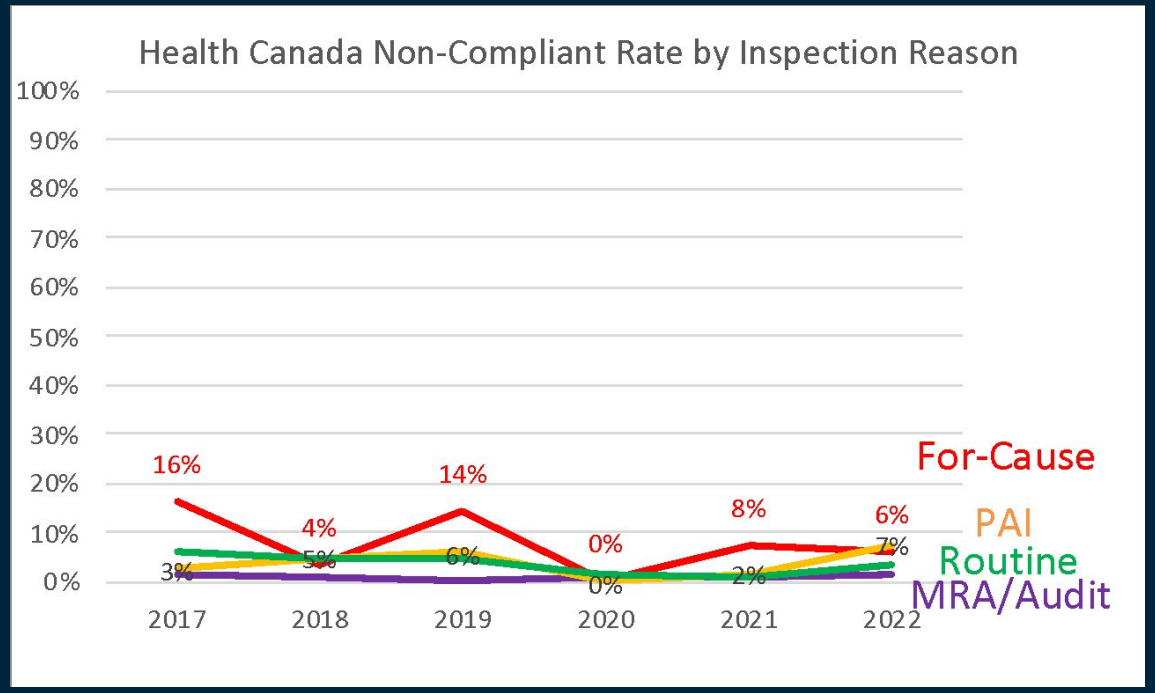
Will the FDA's inspection reasons and observations be similar to that of the Health Canada's inspections reasons and observations?

View by Inspection Reasons

~10,800^ total inspections

~5,600 total inspections

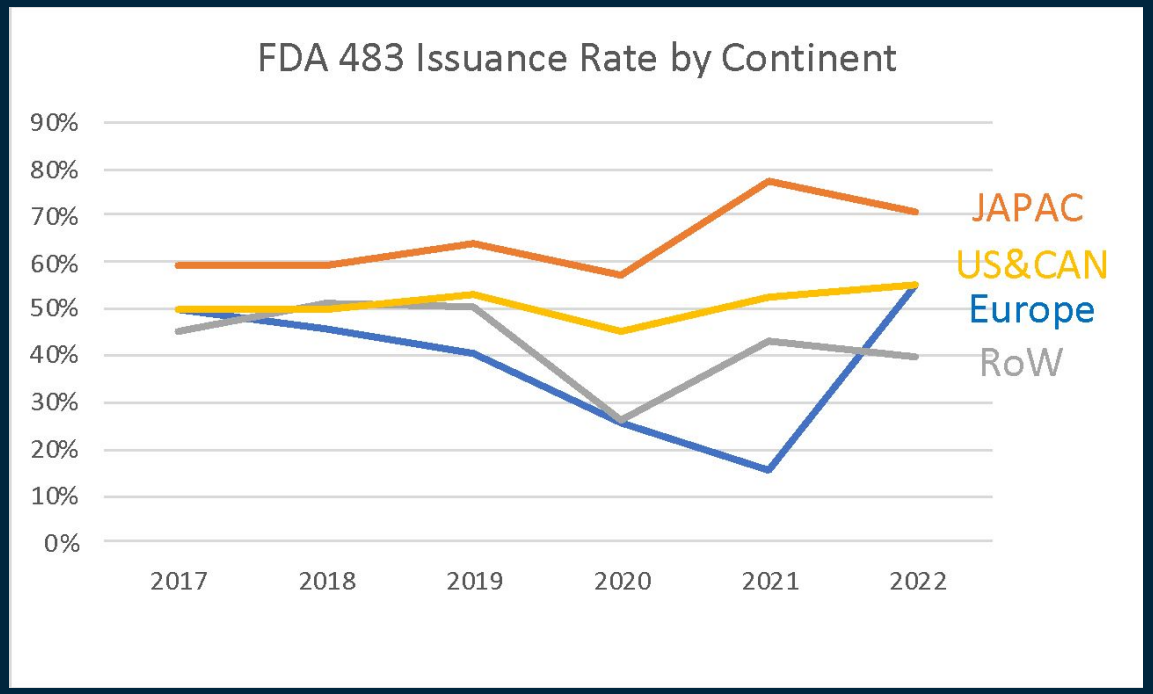


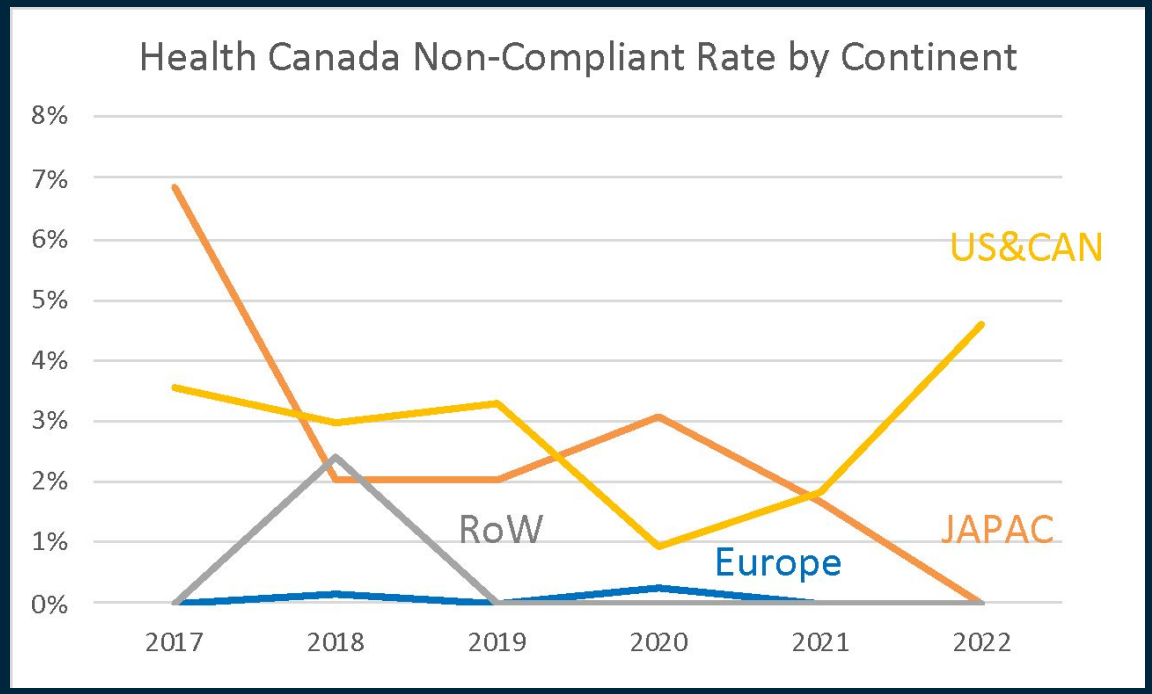


View by Continent

Continent	Inspections
Europe	1,552
JAPAC	2,229
RoW	327
US&CAN	6,732
Total	**10,840^**

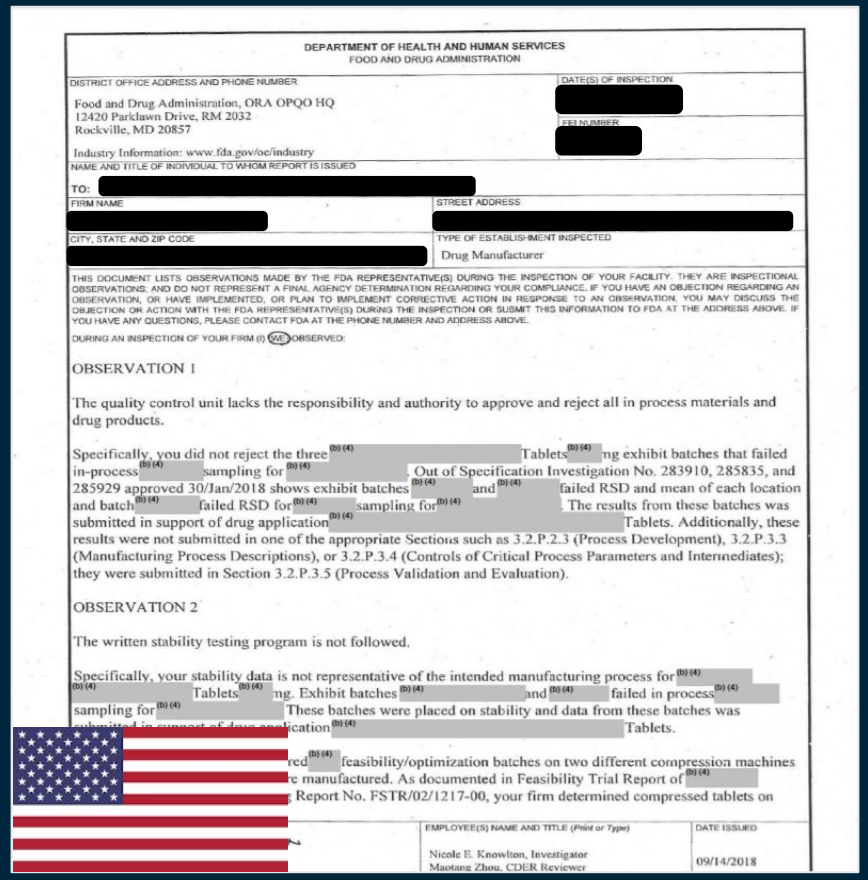
Continent	Inspections
Europe	2,177
JAPAC	795
RoW	114
US&CAN	2,497
Total	**5,583**





How can we go deeper?

- Typically, these inspections have the observations



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

Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION [redacted]

FEI NUMBER [redacted]

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: [redacted]

FIRM NAME [redacted]

STREET ADDRESS [redacted]

CITY, STATE AND ZIP CODE [redacted]

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 (I) (WE) 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) mg 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) (b) (4) Tablets (b) (4) mg. 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.

(b) (4) feasibility/optimization batches on two different compression machines e manufactured. As documented in Feasibility Trial Report of (b) (4) g Report No. FSTR/02/1217-00, your firm determined compressed tablets on

EMPLOYEE(S) NAME AND TITLE (Print or Type) | DATE ISSUED
Nicole E. Knowlton, Investigator
Maotang Zhou, CDER Reviewer | 09/14/2018

Observation number	Regulation	Summary of observation
1	C.02.013 - Quality control department	• The person responsible for making decisions about quality control requirements did not have adequate knowledge of on-site operations to fulfill the responsibilities of this position.
2	C.02.006 - Personnel	• The education, experience, and/or oversight of the individual in charge of the quality control department was inadequate. • The job descriptions for personnel, the authority given to personnel, and/or the delegation of duties was inadequate and/or undocumented. • The ongoing training of personnel was inadequate. • The training of personnel in good manufacturing practices and/or the maintenance of records was inadequate.
3	C.02.004 - Premises	• The qualification and/or verification of utilities and/or support systems was inadequate.
4	C.02.005 - Equipment	• The calibration, inspection, and/or qualification of the equipment, including computerized systems, was inadequate.
5	C.02.009 - Raw material testing	• The specifications for raw materials used to produce drugs did not meet pharmacopoeial standards. • The traceability, legibility, documentation, formatting, and/or the accuracy of records was inadequate. • The sampling plan for raw materials was inadequate. • The recorded information or details were inadequate.

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

Compliance Analysis Algorithm

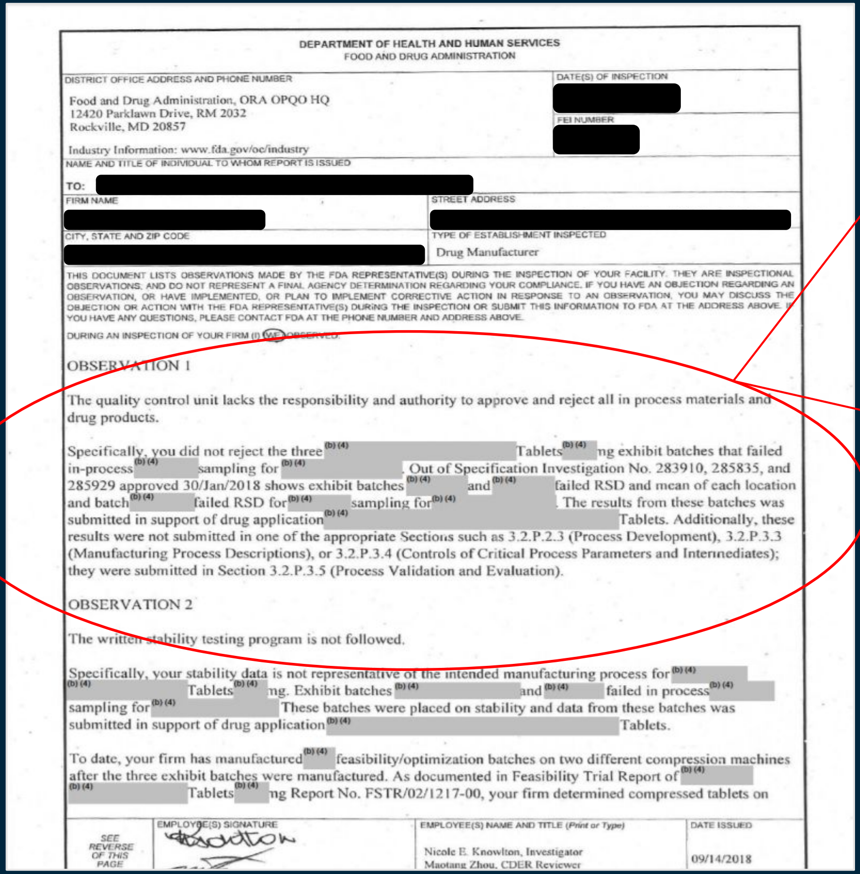
Redica Systems has created an AI tool – "expert model" – that allows deep and rapid analysis of compliance data sets.

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



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FIRM NAME
[redacted]

STREET ADDRESS
[redacted]

CITY, STATE AND ZIP CODE
[redacted]

TYPE OF ESTABLISHMENT INSPECTED
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Specifically, you did not reject the three (b) (4) Tablets (b) (4) mg 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).

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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) (b) (4) Tablets (b) (4) mg 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

Clean Observation Text: OCR, Retyping

Observation 1 of 2

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)~~mg 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 subitted 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 Intennediates); they were submitted in Section 3.2.P.3.5 (Process Validation and Evaluation).

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: Tokenization

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

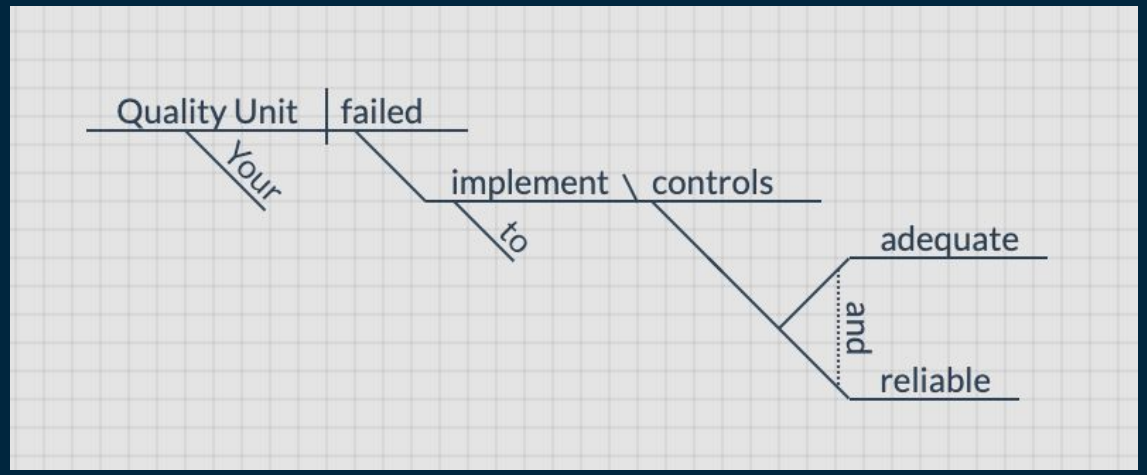
“Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed drug products always comply with the efficacy and quality they represent to possess.”

['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

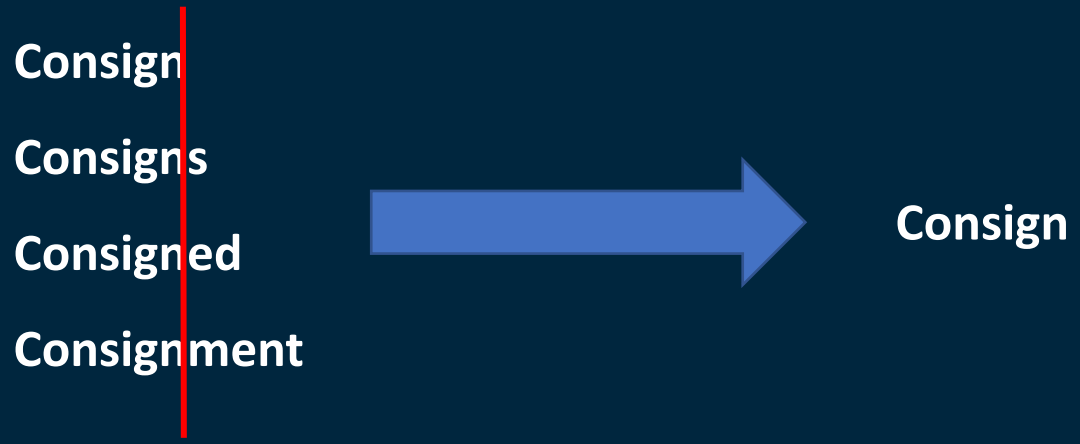
"Your Quality Unit failed to implement adequate and reliable controls for ensuring that distributed drug products always comply with the efficacy and quality they represent to possess."



[('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 efficaci 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')

Tri-gram
(**'Your', 'Quality', 'Unit'**)
(**'Quality', 'Unit', 'failed'**)
('Unit', 'failed', 'to')
('failed', 'to', 'implement')
('to', 'implement', 'adequate’)…….and longer ones

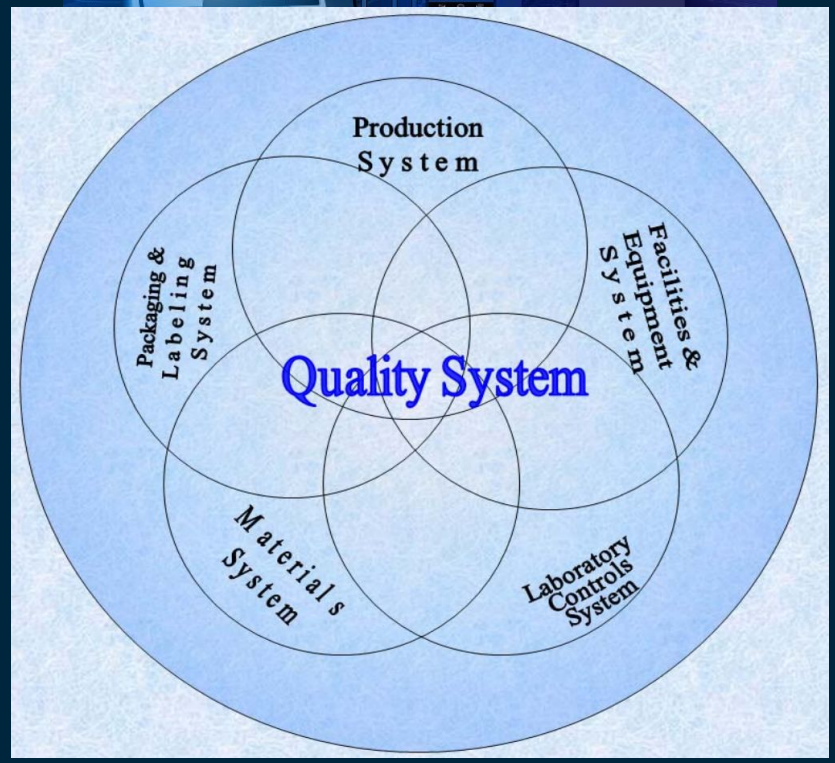
Subject Matter Experts create n-grams from experience and compliance document language; tested over time in model iterations.

Building and Applying the Models

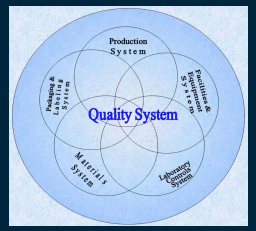
Experts create n-grams for each category and subcategory; also, TurboEIR 483 text

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

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



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



Quality System

- 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.

Packaging & Labeling

- Drug product containers and closures (3 subs)
- Label and Packaging Controls
- Line Clearance
- Serialization

Facilities & Equipment

- Cleaning (3 subs)
- Design (9 subs)
- Maintenance (3 subs)
- Alarm Management
- HVAC
- Pest Control
- Records and Reports

Materials

- Distribution
- Material Receipt and Handling (3 subs)
- Material Sampling and Testing (3 subs)
- Material Storage and Control
- Retain Samples

Laboratory

- Method Validation
- OOS/ OOT
- Stability (2 subs)
- Systems Controls
- Testing (4 subs)
- Reagents and Standards
- Records and Reports
- Sample Management

Production

- 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)

Data Integrity

- 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

Quick Summary for Quality System Labels (QSL)

Gathering the Data

- Redica System has a process to collect 25k+ Form 483s and retype observations into a machine readable format

Setting & Cleaning up the Data

- The FDA not only reviews Drugs and Devices, but also Food, Cosmetics, and Tobacco
- Redica System established a system to programmatically separate Form 483s to apply the right QSL model

QSL Model

- Observation are read and assigned the 6 Quality System + Data Integrity
- Experts review the output and ensures high quality

Example of Observations

2019 “For-Cause” Inspection Resulting in 483 & Non-Compliant

OBSERVATION 1

Investigations are inadequate in that they do not evaluate all potential root causes and because they do not extend to all potentially impacted products.

OBSERVATION 2

The validation of the firm's cleaning process for non-dedicated equipment is deficient in that the cleaning process was not evaluated to demonstrate removal of residual contaminant(s) that could alter the safety, identity, quality or purity of the drug substance. Specifically,

OBSERVATION 3

The Quality Unit failed to ensure that Corrective and Preventive Actions were adequate.

OBSERVATION 4

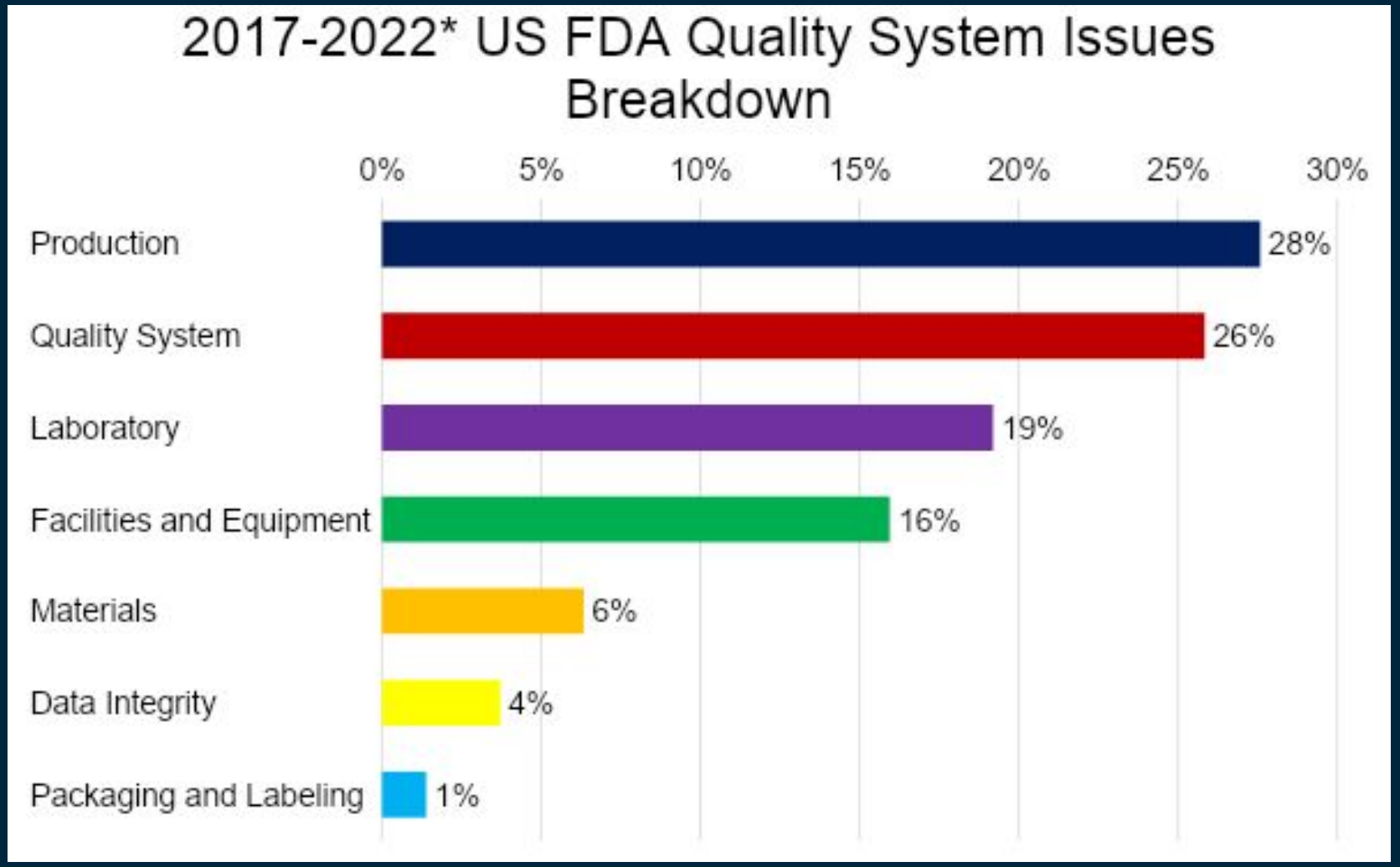
Analytical methods are not appropriately validated to include consideration of necessary characteristics.

OBSERVATION 5

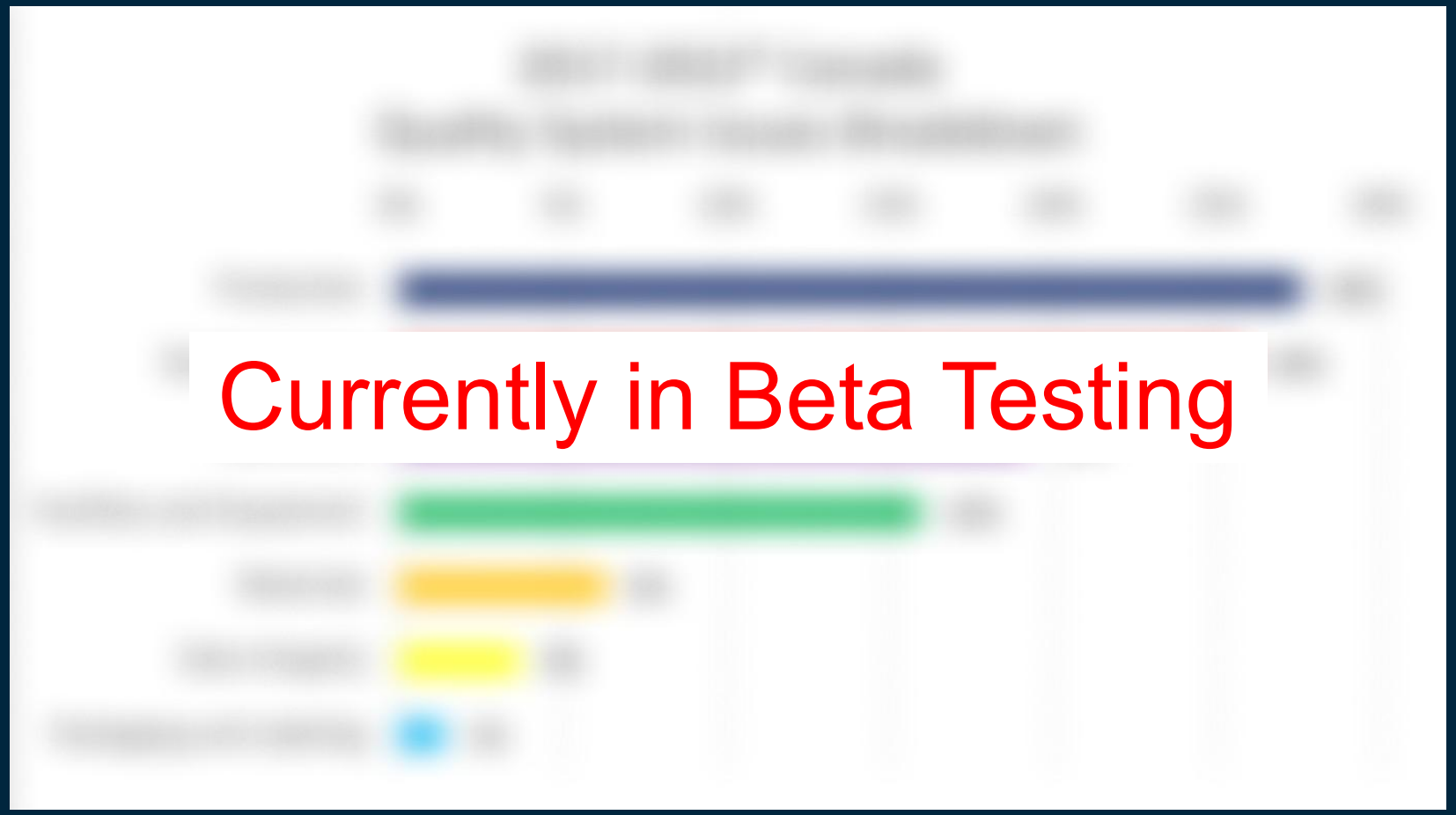
The laboratory failed to ensure that the calibration of the equipment, including computerized systems were adequate.

Summary of observation
The assessment, recording, follow-up, and/or investigation of complaints and/or other information about potentially defective products was inadequate.
The implementation, effectiveness, and/or validation of the cleaning procedures was inadequate for preventing unsanitary conditions.
Changes to production processes, systems, equipment, materials, and/or suppliers were not validated before they were implemented.
The validation of test methods was inadequate.
The calibration, inspection, and/or qualification of the equipment, including computerized systems, was inadequate.

Form 483 Observations QSL Model

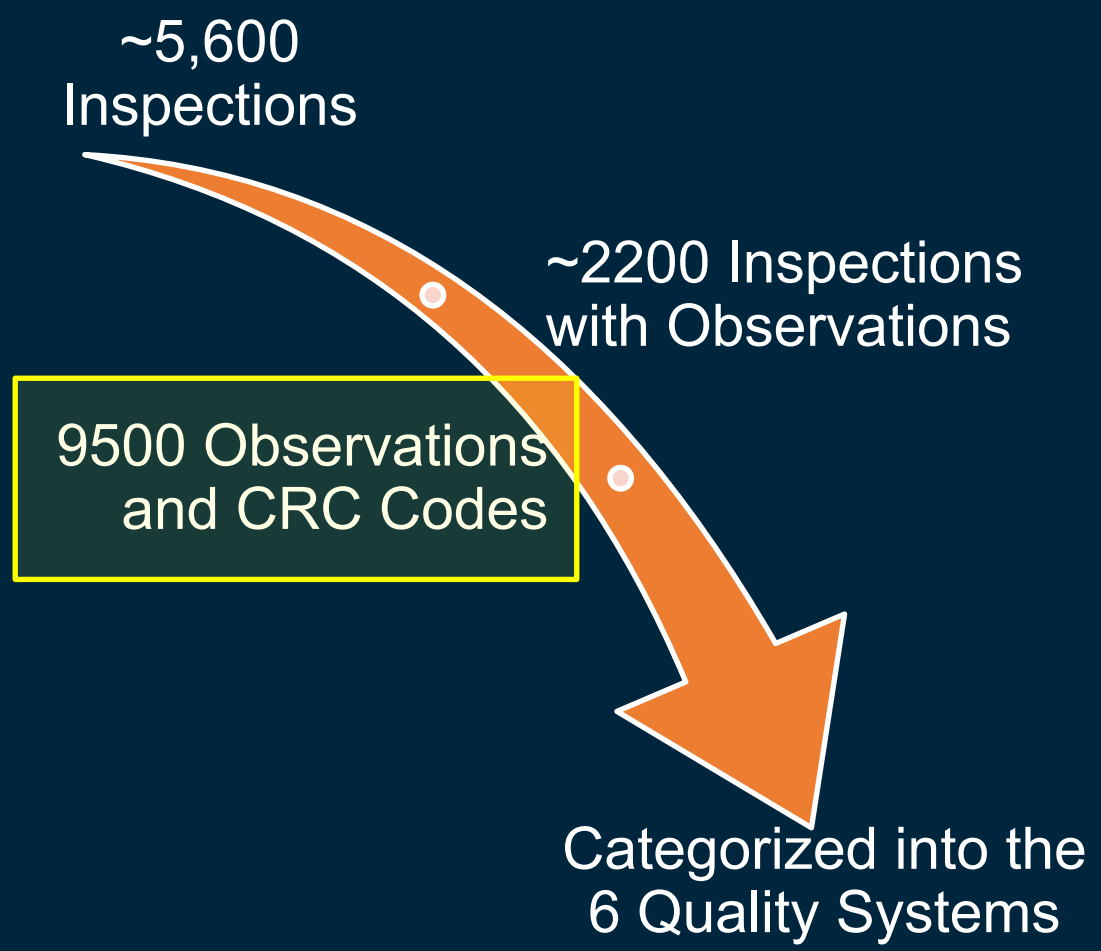


Health Canada Observations QSL Model

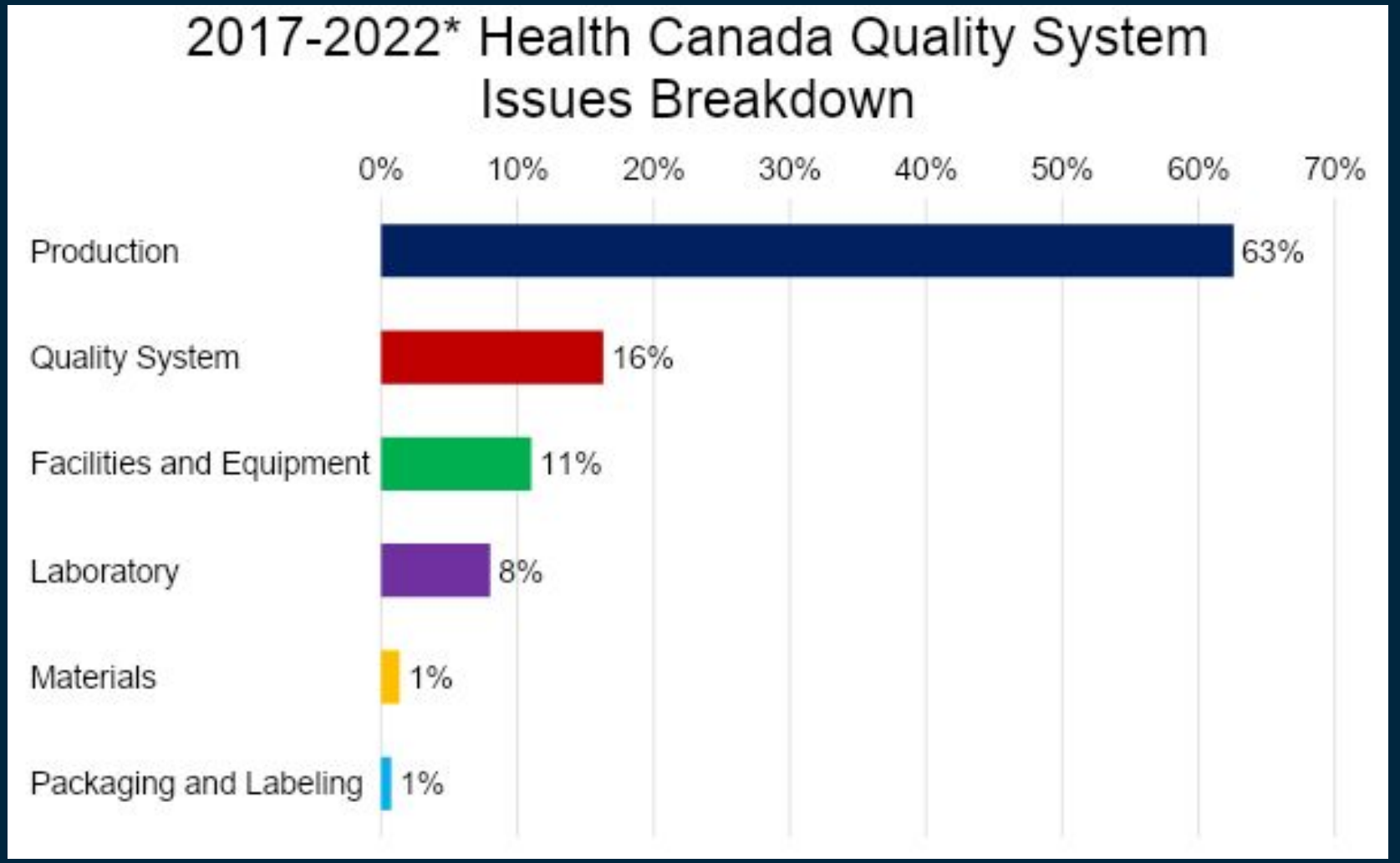


Health Canada Observations

- C.02.003: Sale
- C.02.004: Premises
- C.02.005: Equipment
- C.02.006: Personnel
- C.02.007 - C.02.008: Sanitation
- C.02.009 - C.02.010: Raw material testing
- C.02.011 - C.02.012: Manufacturing Control
- C.02.013 - C.02.015: Quality control department
- C.02.016 - C.02.017: Packaging Material Testing
- C.02.018 - C.02.019: Finished product testing
- C.02.020 - C.02.024: Records
- C.02.025 - C.02.026: Samples
- C.02.027 - C.02.028: Stability
- C.02.029: Sterile products

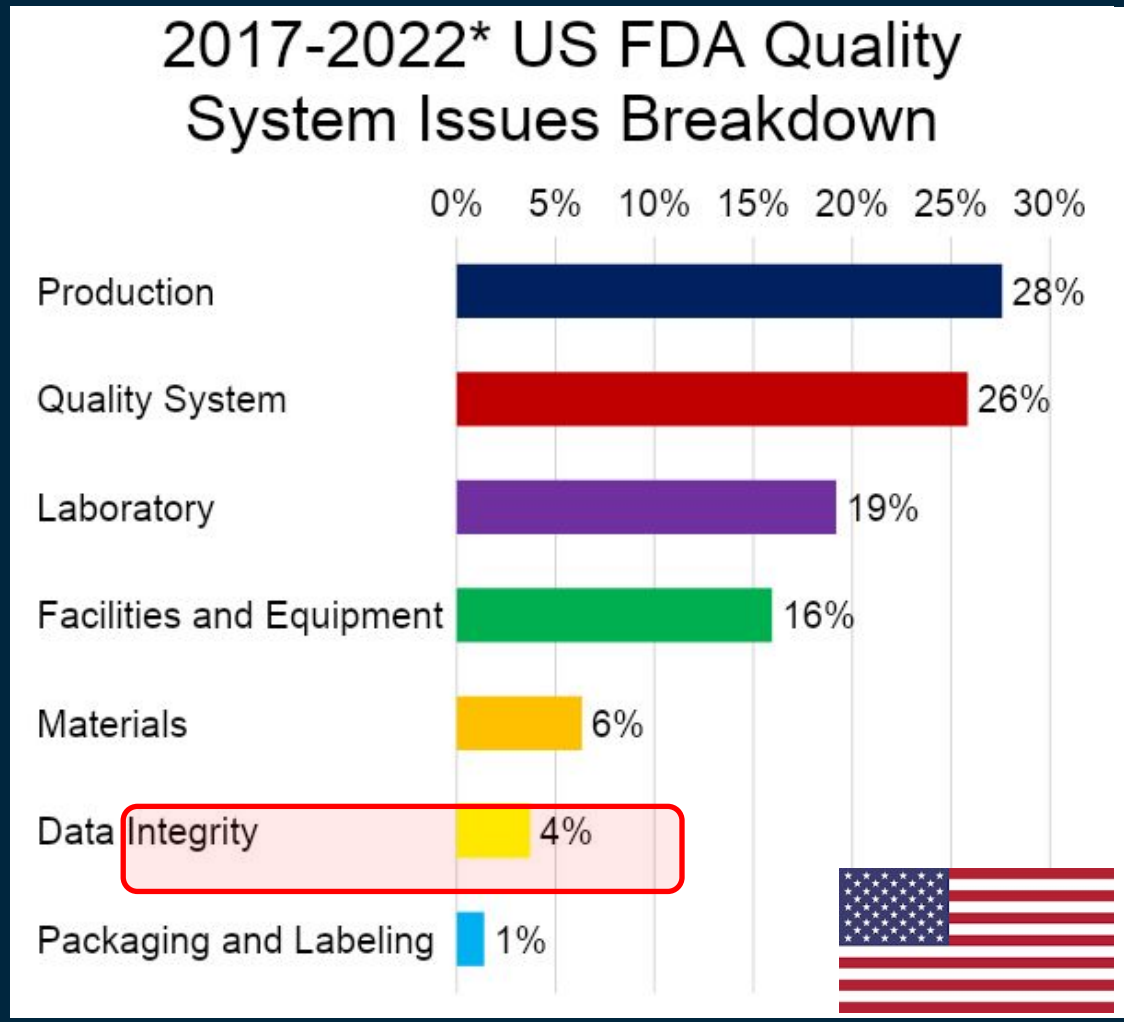


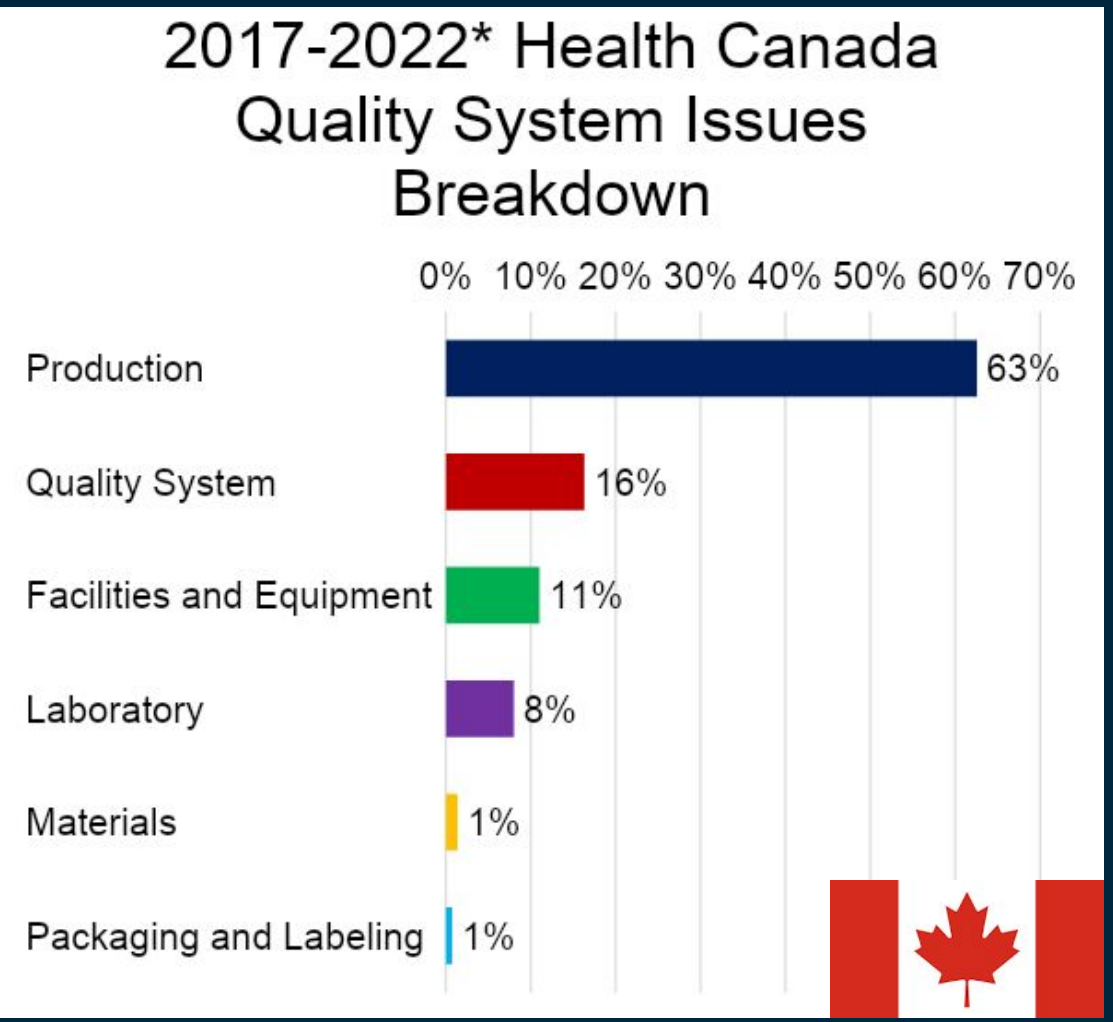
Health Canada Observations Sneak Peak



* Data up to June 2022

Comparing US FDA and Health Canada



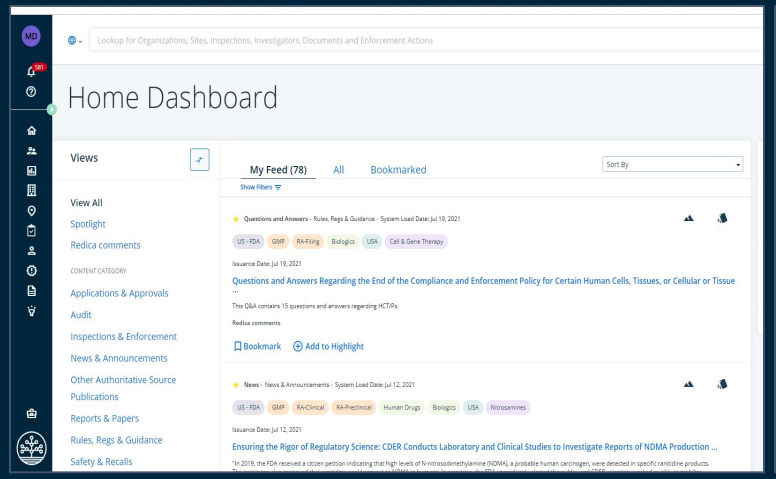


* Data up to June 2022

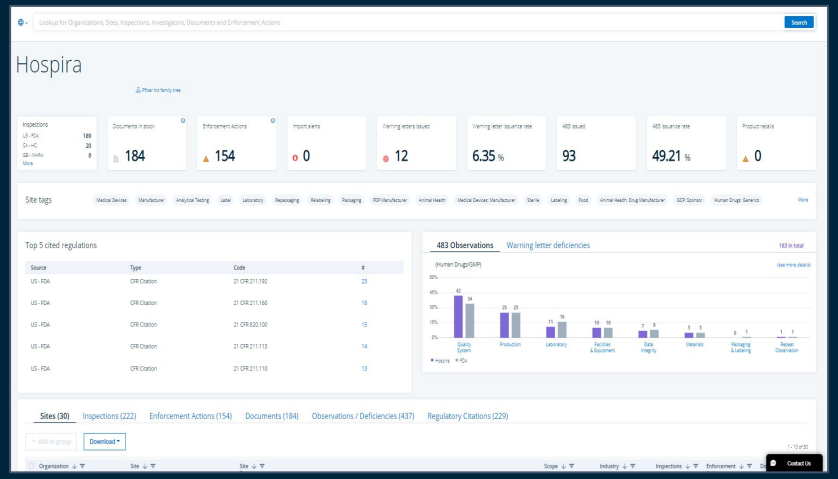
… and now a quick Redica Commercial …

Redica Systems: Our platform

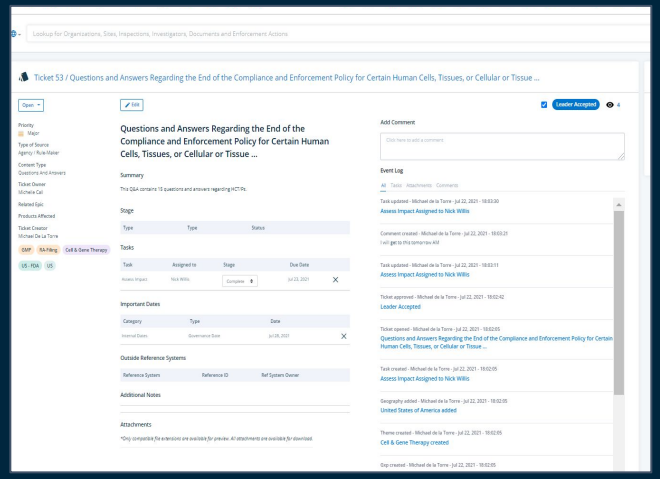
Daily Feed



Profiles and Reports



Workflows



Intelligence Layer

Thousands of sources

FDA, NSF, World Health Organization, edqm, USDA, European Medicines Agency, Department of Justice, ISO, MEE 生态环境部, swissmedic, Pmda, ICH harmonisation for better health, ANVISA, MHRA Regulating Medicines and Medical Devices, PIC/S, USP, OSHA, CDSCO, KFDA 식품의약품안전처, Cofepris

REDICA Systems

Redica Systems : How we work with Life Sciences

Inspection Preparation

- Investigator profiles
- Inspection outcomes mapped to quality system
- Inspection types
- Industry Trends mapped to GxP quality system
- Peer benchmarks

Vendor Quality

- Site and Organization profiles with full inspection history
- Monitoring and alerts for inspections and enforcement
- Vendor benchmarking

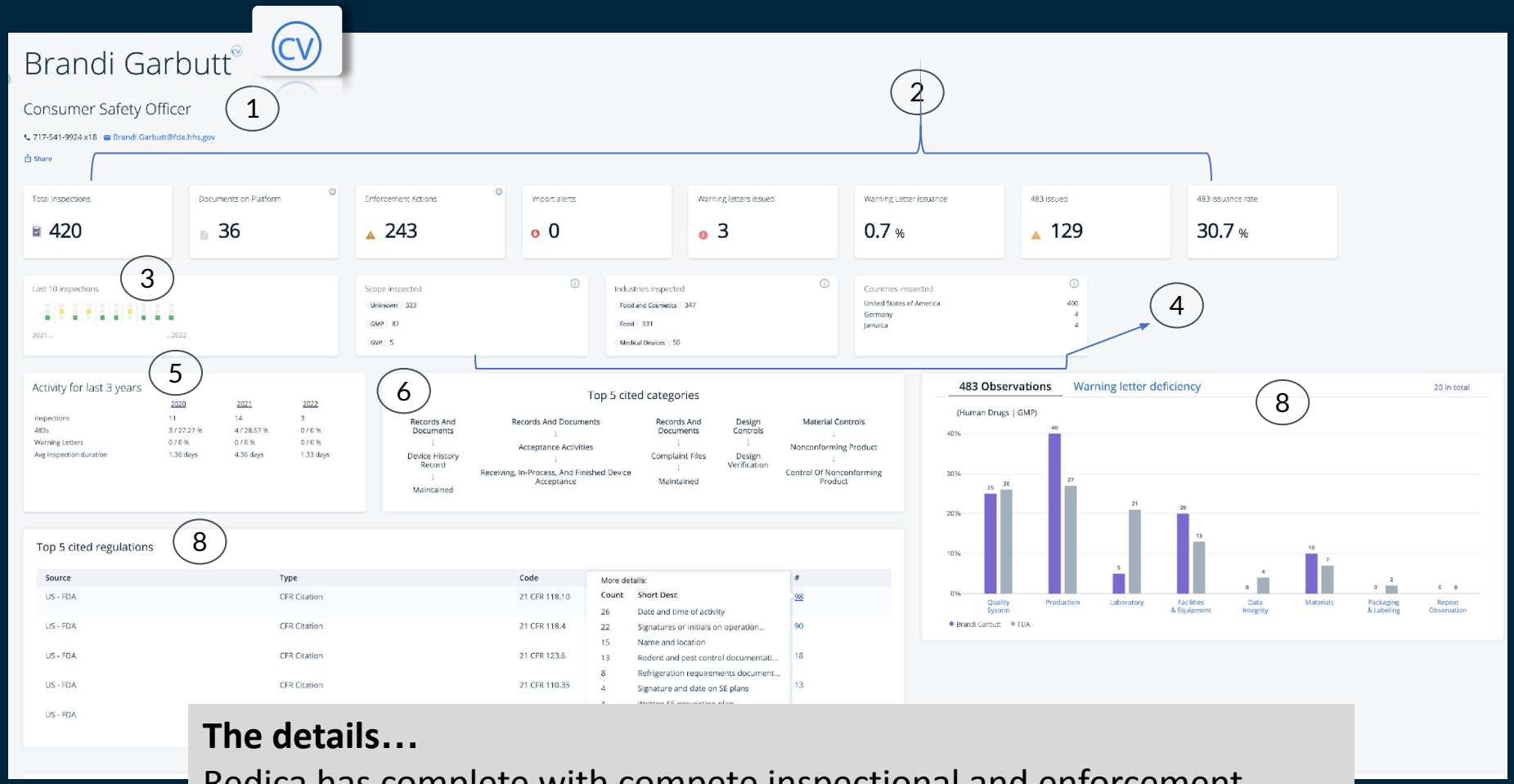
Regulatory Surveillance

- Global GxP coverage
- Unique labeling
- Simple dashboard
- Integrated workflows for triage and impact assessments

Redica **Reports, Visualizations and Automation**

FDA Inspector Profiles

1. Investigator information, including CV's in some profiles
2. View at a glance key details to quickly understand the Investigator's inspection history and outcomes.
3. Scan the inspection outcome through Inspection Patterns to easily understand outcomes
4. Quick view of the types of Scope, Industry, and Countries inspected by the Investigator
5. Spot year over year Investigator trends based on the past three years
6. A breakdown of the top five cited categories of observations based on the six quality systems
7. Compare the Investigator vs others in the FDA in Human Drugs/GMP built from the 483 observations in the six quality systems to spot trends
8. View Top 5 cited regulations given, including the count and short descriptions



The details…
Redica has complete with compete inspectional and enforcement history and benchmarks to industry averages for all FDA inspectors going back to the year 2000

Redica **Reports, Visualizations and Automation**

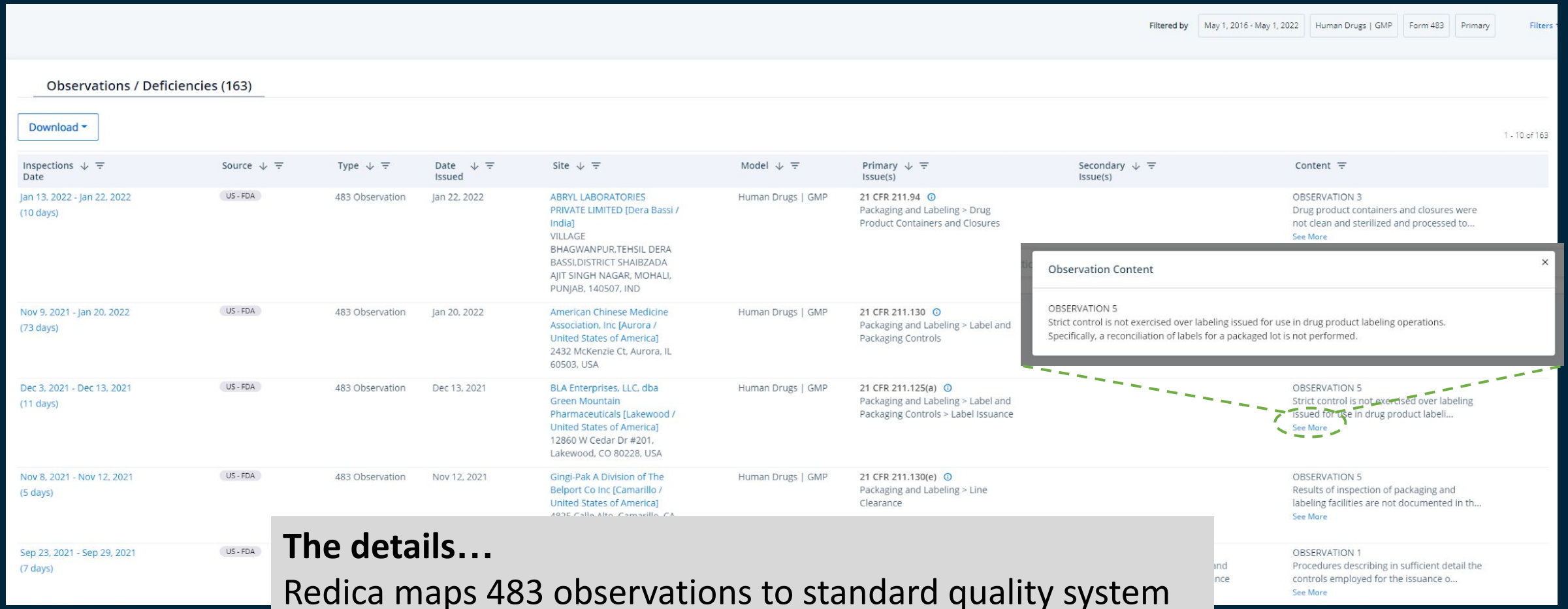
Site & Org Profiles

1. Site information, including address and Site Registry ID's
2. Family Trees provides visibility on parent and sister companies, great to keep up with mergers and acquisitions
3. At a glance key details of each Site for a quick risk assessment
4. Quickly add Sites to your Groups to run reports and be notified of activity
5. Be in the know of how the Site is registered with the FDA through Site Tags
6. View the inspection interval days to be prepared to expect a visit from the FDA
7. Top 5 cited regulations given, including count and a short descriptions
8. Compare the Site vs others in the FDA in Human Drugs/GMP built from the 483 observations in the six quality systems
9. See the count of the available data in each tab and click to drill

The details…
Redica has >250,000 Site profiles with compete inspectional and enforcement history and benchmarks to industry averages. Redica can send email alerts when the Site is inspected or receives an Enforcement Action

Redica **Reports and Automation**

Example 483 Observation Report –> Primary Issue = Packaging and Labeling

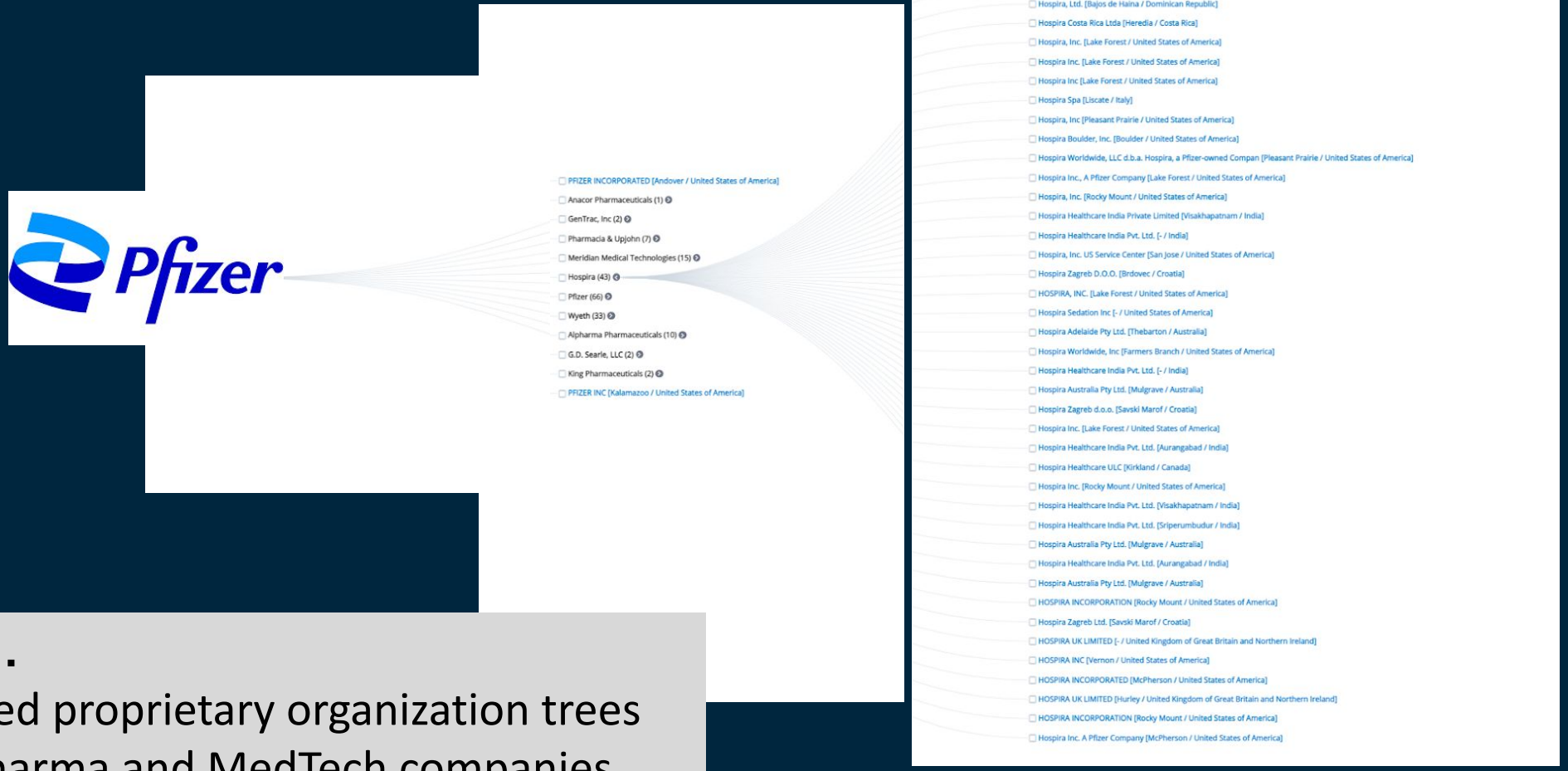


The details…

Redica maps 483 observations to standard quality system categories – taking the guess work out of 483 trends!

Redica **Reports, Visualizations and Automation**

Organization “family trees”



The details…

Redica created proprietary organization trees of the top Pharma and MedTech companies

Redica **Blogs**

- Health Canada GMP Inspectors Turning to Video, Teleconferencing; Three Case Studies Presented
- Who Decides if my FDA Inspection is Classified OAI?
- Where is My EIR?
- Redica Responds: How Many GMP Inspections Have Resulted in a 483?
- Japan's PMDA Formalizing Post-Approval Change System Based on Recent Pilot
- Senior Management Failures Lead to Patient Deaths, Prison Sentence

Q&A and Thank You

Presenter

- Jason.Kerr@Redica.com
- Senior GXP Specialist

Special Thanks

- Jerry.Chapman@Redica.com
- GMP Expert

- Go to www.Redica.com to learn more about how we can help you