U.S. FOOD & DRUG ADMINISTRATION

Quality Surveillance Dashboard Enabling Comprehensive Surveillance

Alex Viehmann

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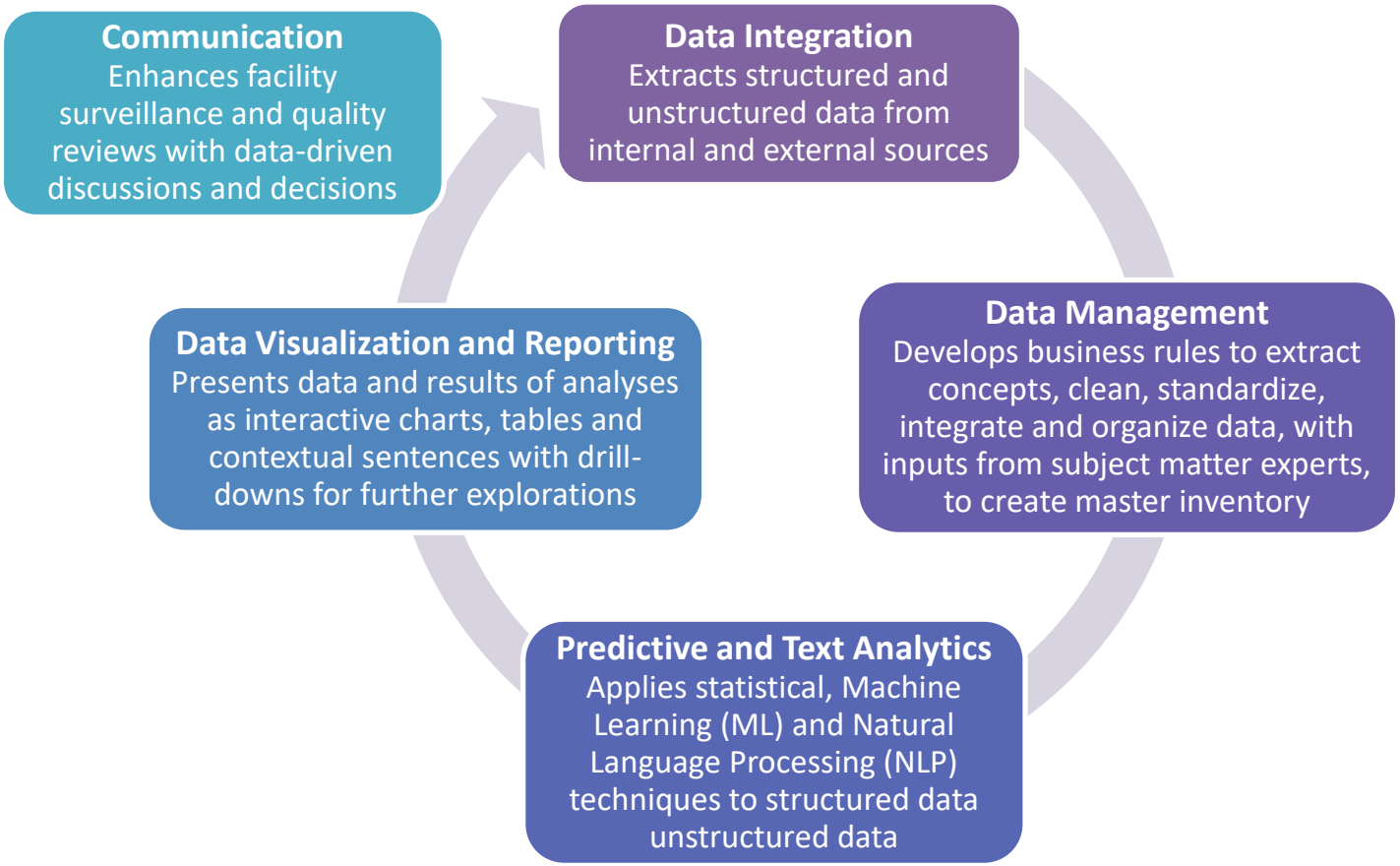
Quality Surveillance Dashboard Overview

- Provides a framework for consistent and up-to-date evaluation of facilities
- Integrates and governs facility and post-market product quality data from across multiple systems
- Search information about firms and compare firms
- Navigate details about a firm's products such as application status, supply chain, route of administration, drug shortages, pediatric flags, indications, and storage conditions
- Track and trend quality signals within a product lifecycle such as those related to MedWatch, Field Alert Reports, and Recalls
  - Potential link to distribution data for normalization
- Incorporates results of predictive analytics (e.g., ML models) on Pharmaceutical Quality Systems (PQS) effectiveness, manufacturing capabilities, and potential product quality issues
- Utilizes natural language processing (NLP) to enable efficient data mining (examples include Establishment Inspection Reports and 483s) to enable efficient and risk-based assessments
- Better harness database resources by applying programming codes to systematically correct typographical errors and incomplete data fields, conduct data validation, and provide data enhancement

How is the dashboard created?

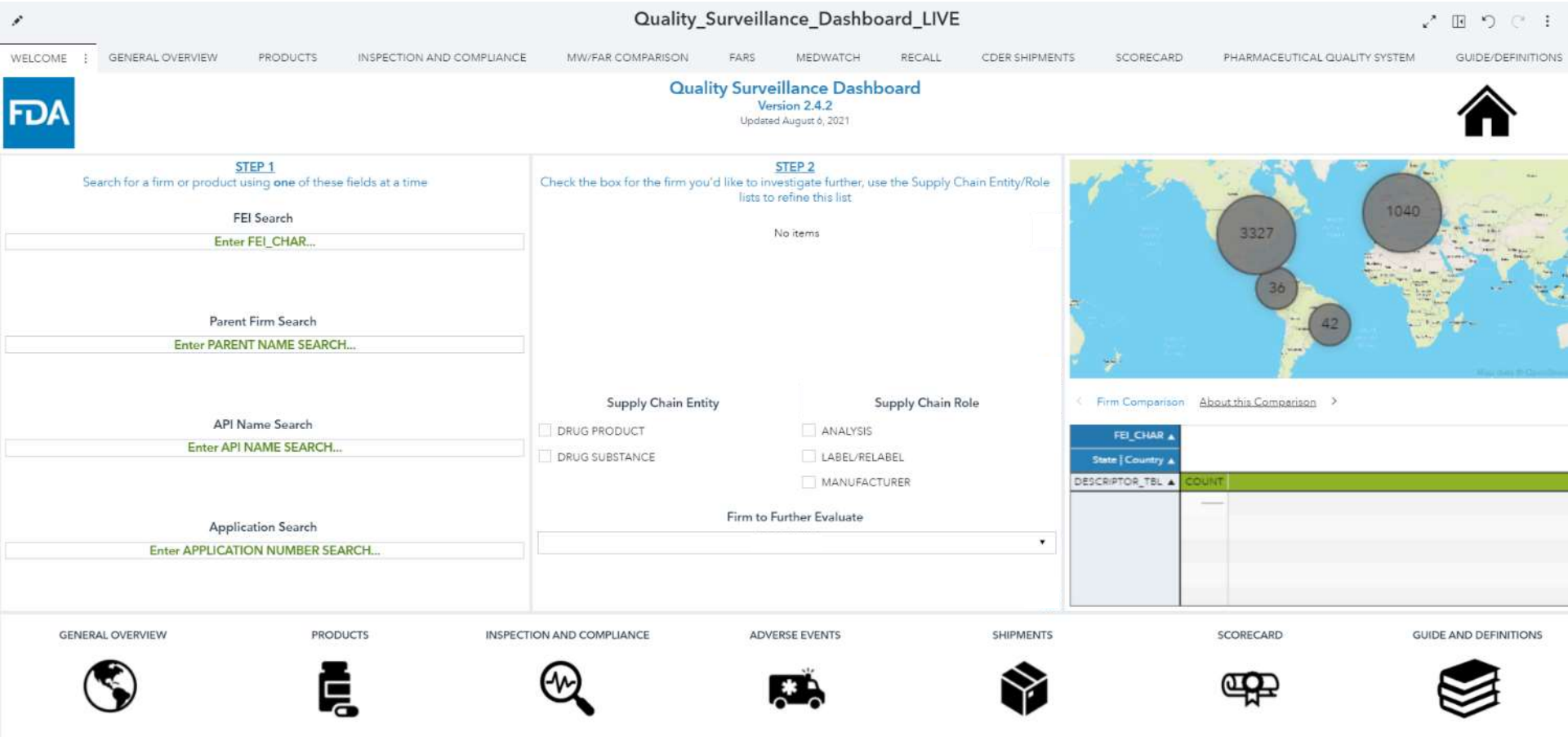


Why was this important?

Current processes showed:

- Ineffective use of time searching in multi-sources
- Inconsistent methods for organizing data
- Use of static data that needs constant refresh/updating
- Assumption about data
- Fishing for insights in unstructured (text) data

QSD Use Case Example - Welcome Page



Firm Comparison table

- The firm comparison table on the *Welcome* tab provides counts of the different descriptors and enables efficient comparison of multiple firms

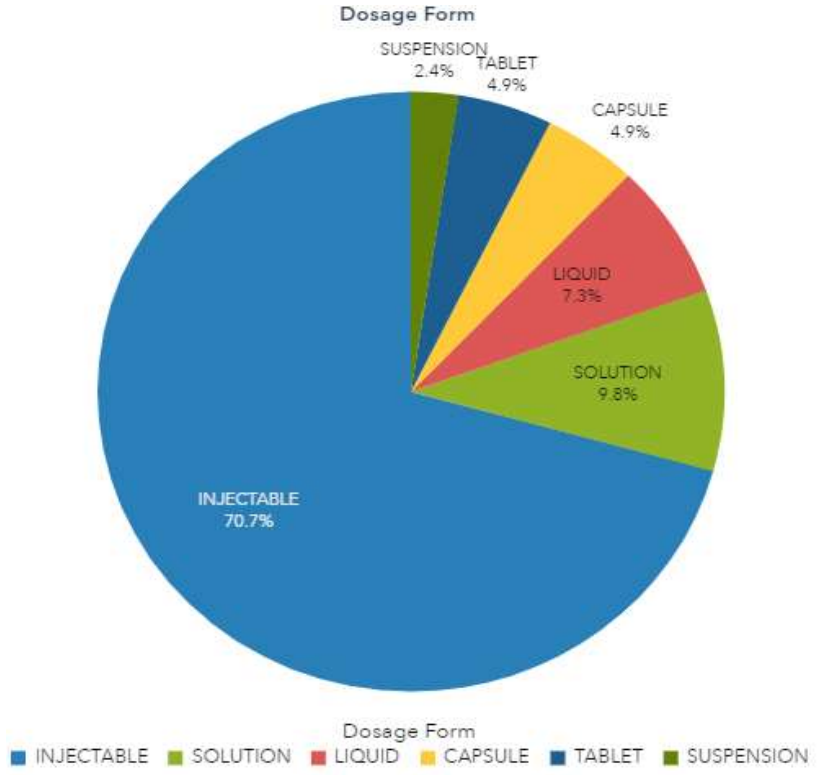
State | Country ▲	CA | UNITED STATES	WESTFALEN | GERMANY	BAYERN | GERMANY	INCEON-SI | KOREA, SOUTH	| SINGAPORE
DESCRIPTOR_TBL ▲	COUNT	COUNT	COUNT	COUNT	COUNT
A) Application Products	32	42	22	5	22
B) Non-Application Products	4	13	1	1	3
C) Shortage Products	1	0	1	0	1
D) LDL Products	0	0	0	0	0
E) Narrow Ther. Ind. Products	0	2	0	0	0
F) Inspections	11	7	8	5	7
G) OAI Inspections	0	0	0	1	0
H) Cases	2	0	0	1	0
I) FARs (Last 5 Yrs.)	1	0	0	0	0
J) MedWatch (Last 5 Yrs.)	37	34	0	3	0
K) Class I Recalls (Last 5 Yrs.)	1	0	0	0	0
L) Recalls (Last 5 Yrs.)	1	1	0	0	0

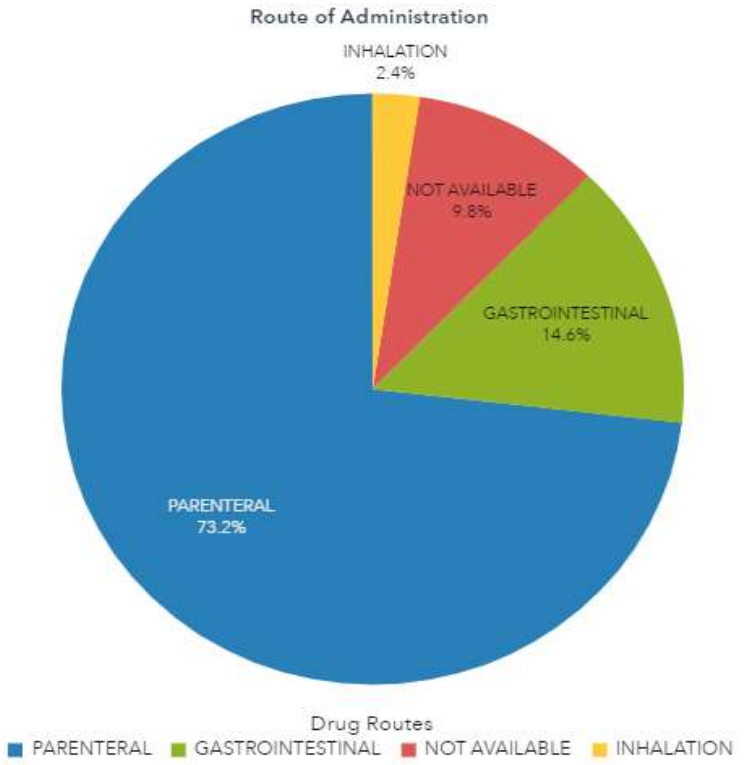
Products

- 40 unique Applications
  - 26 approved| 2 pending BLAs
  - 6 approved| 2 withdrawn NDAs
  - 4 non-applications

PRODUCT_TYPE ▲	APPLICATION_STATUS ▼	API(s) Count	Product Count
Total		28	40
BLA	PENDING	2	2
	APPROVED	21	26
NDA	WITHDRAWN	2	2
	APPROVED	4	6
NON-APP	REGISTERED	4	4

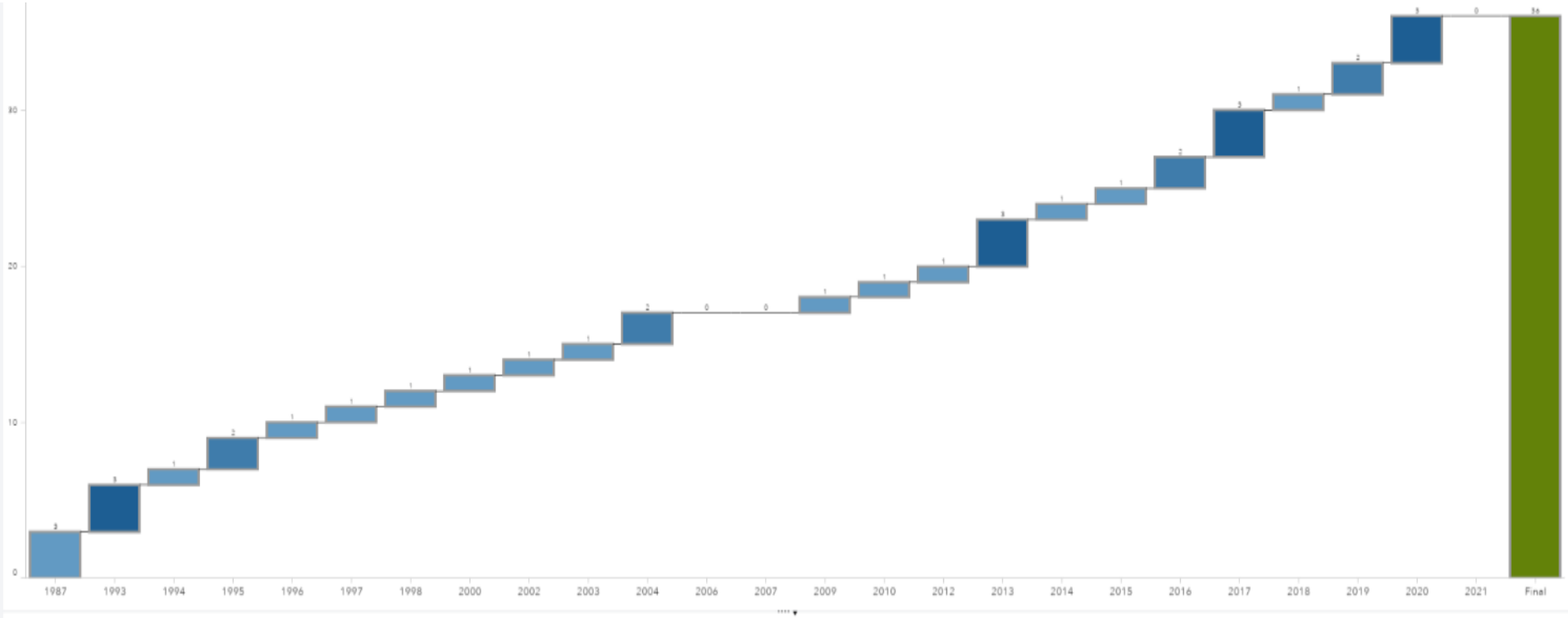
- Applications are mostly injectables (~71%) with a ROA of Parenteral (~73%)





Products

- The waterfall chart shows how the number of approved applications have changed over time
- This firm started with 3 approved applications in 1987, and throughout the years, some applications were withdrawn, and more were approved, and it currently has 36 approved applications in the market

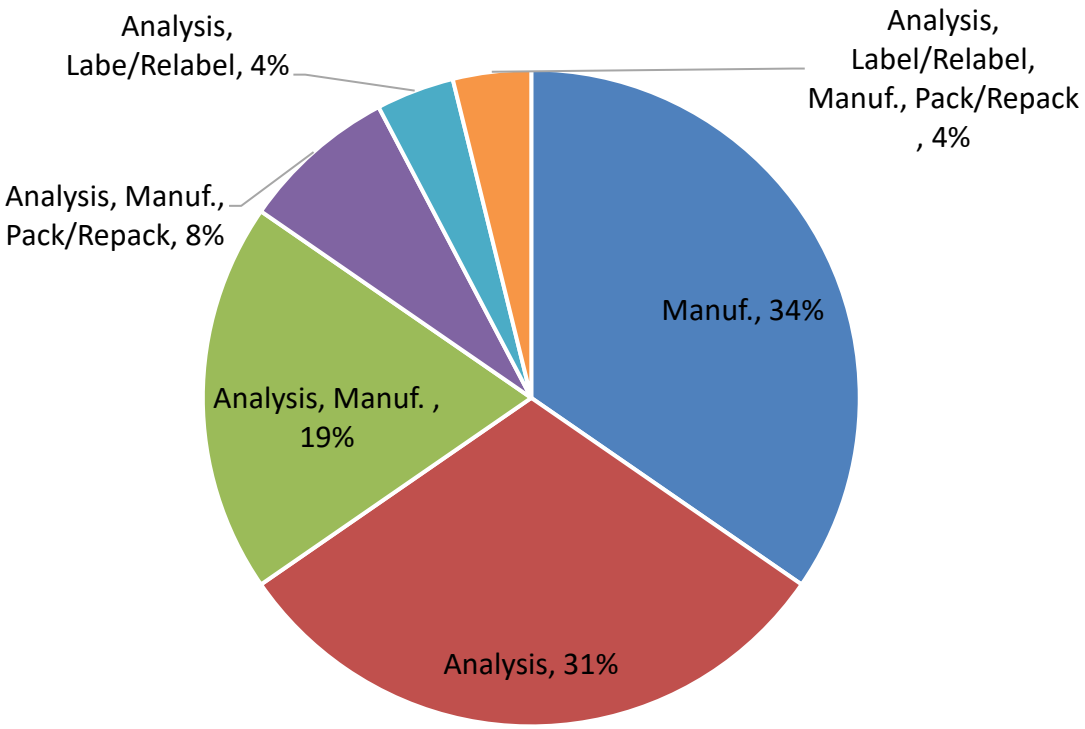


APPL_STATUS_EFF_DATE	waterfall measure	Product Count (Net)	APPROVED APPLICATIONS	PENDING APPLICATIONS	WITHDRAWN APPLICATIONS	API(s) Count
2021	0	0	0	2	0	3
2020	3	3	3	0	0	3
2019	2	2	2	0	0	2
2018	1	1	1	0	0	1
2017	3	3	3	0	0	3
2016	2	2	2	0	0	1
2015	1	1	1	0	0	1
2014	1	1	1	0	0	1
2013	3	3	3	0	0	3

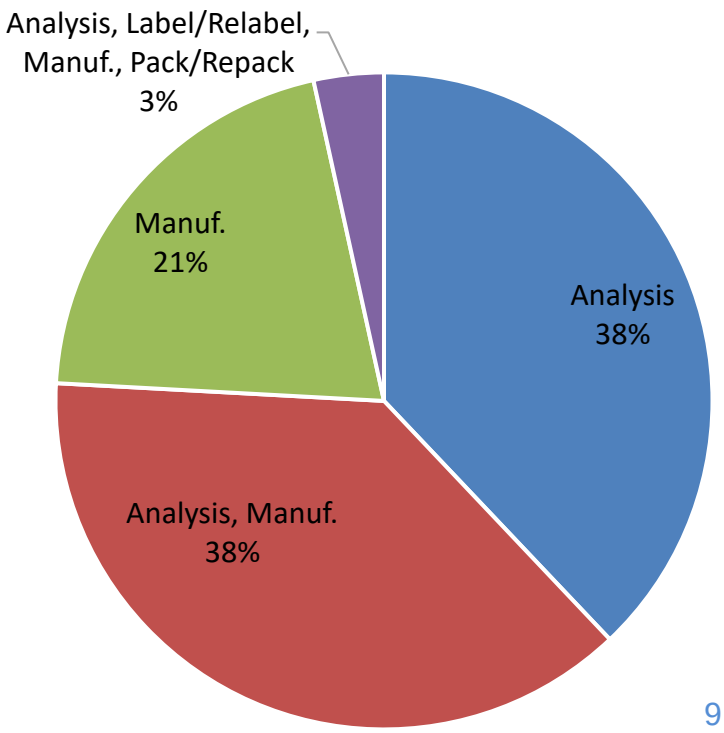
Products

- The following pie charts display the supply chain roles of this facility as a Drug Product and Drug Substance
  - There are 29 products where this facility is the drug product firm, and 26 products where this facility is the drug substance firm
  - For example, as a Drug Product, this facility takes on the role of the manufacturer for 34% of the products

Drug Product

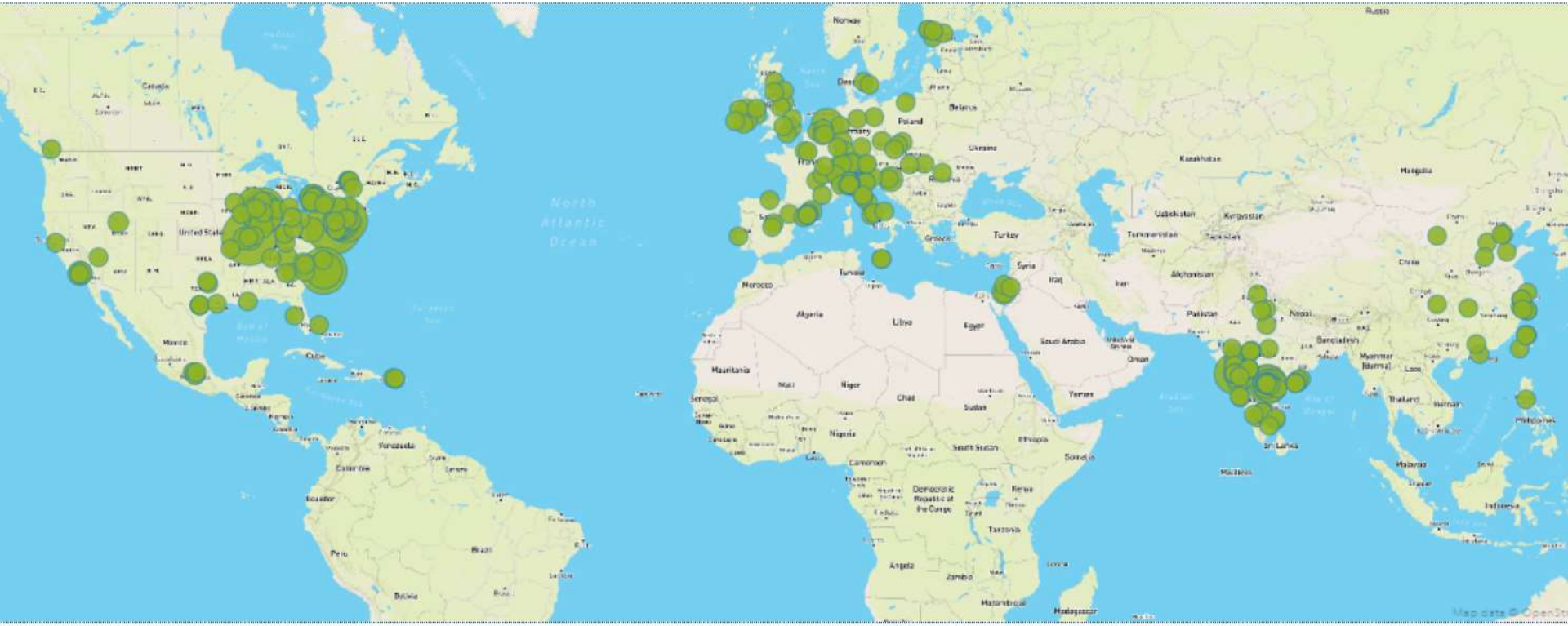


Drug Substance



Facility Supply Chain Map

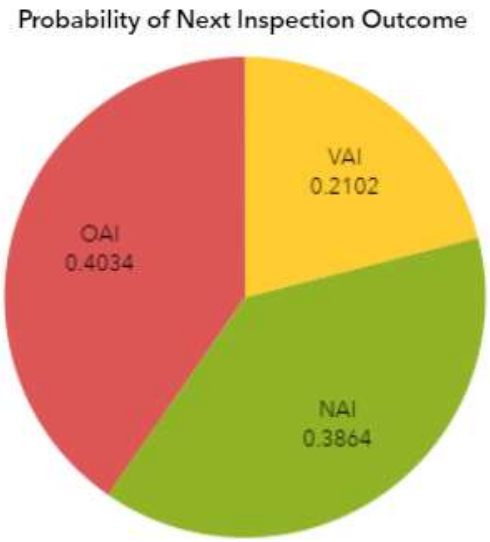
- A particular FDA Establishment Indicator (FEI) can be mapped to other associated FEIs based on application number. The associated sites map shows these related FEIs.



Inspections and Compliance

- Inspection timeline shows inspections from FY 2010-current

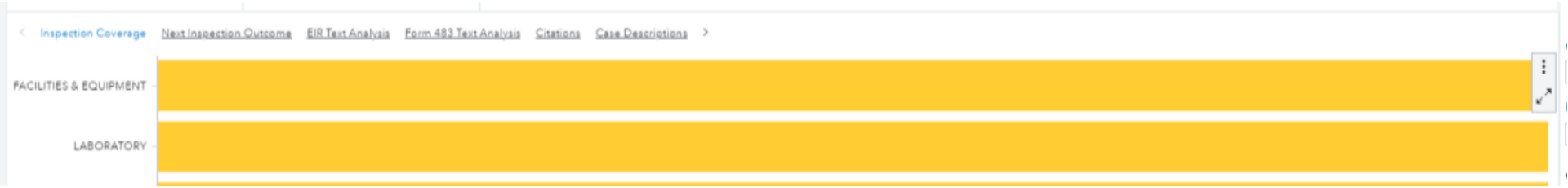
- 11 inspections with 5 VAI outcomes, and 0 OAI outcomes
  - Most recent surveillance inspection was on July 12, 2017, and it was an NAI



- Next inspection outcome model uses historical data that considers key trends and patterns in data for prediction
  - Facility operations (manufacturer type, packer, labeler, control lab)
  - Product types processed (dosage forms, non- and/or application products)
  - Quality defect reports; etc.

Inspections and Compliance

- Summary text of EIR can be found on the dashboard:



- The previous inspection covered the Quality System; Facilities and Equipment System; Materials System; Production System; and Laboratory Control system. There were no refusals encountered and no samples were collected. **The previous inspection was classified NAI**. The current inspection covered the Quality System; Facilities and Equipment System; Materials System; Production System; and Laboratory Control system**. The current inspection resulted in a 2-item Form FDA 483, Inspectional Observations, which was issued to the Interim Site Head at the firm for: 1.) The quality control unit lacks authority to fully investigate errors that have occurred. 2.) Records are not maintained so that data therein can be reviewed at least annually to evaluate the quality standards of each drug product to determine the need for changes in specifications or manufacturing or control procedures**. Two (2) verbal discussion items were also brought to the attention of firm management: 1.) The inspection revealed an Analyst in the Quality Control Laboratory had access privileges to delete data files X software. 2.) The review of X and Trend Reports revealed “alert limits” and “action limits” of X that were greater than 1, because the firm uses formulas to calculate averages for these limits. The firm acknowledged the Observations and Discussion Items and promised corrections. Firm management stated that a written response would be submitted to FDA.

Inspections and Compliance

- NLP enables an efficient data mining process that can extract information pertaining to custom concepts – see examples from EIR documents below:

Text Topics	Summary of Text/Text from EIR
Laboratory system -> stability program	"The firm's **stability program** is governed by ……..
Laboratory system -> data integrity	"We observed **data integrity issues** within …….. We observed that Ms. X, as an analyst, had extra administrative privileges in the software where she had the ability to delete data files."
Laboratory system -> methods	"To cover the firm's Laboratory Control System, we reviewed **Quality Control Methods** and Procedures; Associated **SOPs** included but were not limited to: **SOP** A, B and C. No apparent deficiencies related to analytical instruments or equipment were observed."
Production -> production documentation	"The executed **batch record documented** critical process parameters……
Production-> Media fill	"Non-routine interventions are challenged once per year during a **media fill** to assess……"

MedWatch

- This firm has 27 MWs and 5 applications
- Dashboard enables visualizations of trends over time; forecasting potential
- Ability to visualize by Dosage Form, product, defect, etc., which supports data-driven and risk-based decision making

Pharmaceutical Quality System

- ML models were trained to make predictions on four metrics that were chosen to align with industry and academic research
- These metrics include median investigation time, % repeat deviations, % root cause related to human error, % CAPA retraining only
- Model outputs are tracked for trending and visualizations enable benchmarking against ‘similar’ facilities

Conclusion

- The Quality Surveillance Dashboard (QSD): Bringing it together
  - Data integration and management: Automation – boosting productivity
  - Application of natural language processing (NLP), machine learning, and predictive analytics
    - Data extraction
    - Proactive signal detection
    - Enhancing future inspections
    - Supporting pre/post approval decisions (e.g., ICH Q12 implementation)
    - Facilitating data-driven/objective/efficient decision making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