Qualified DATA SYSTEMS

Regulatory Intelligence

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Regulatory Intelligence Overview

Regulatory Intelligence– *Acquiring knowledge through collection, aggregation, analysis, and interpretation of information sources which enable timely data-driven decision-making.*

The reality of today's Global Regulatory Landscape:

- Complex and continuously evolving. Not at same pace of Life Science Discovery and Innovation.
- Requires vigilance for a broad spectrum of issues at Local, State, Federal, and Country levels including Laws, Regulations, Directives, and Guidance.
- Industry is continuously challenged to do more with less and Regulatory Compliance is no exception. Cost pressures continue to influence data management strategies.
- Product Supply Chains are diverse and often require additional oversight. Intellectual Property is scattered across business unit portfolios.
- Requires the implementation of a robust Intelligence platform in order to maintain market advantage and derive meaningful insights.

Regulatory Information Sources

EU, APAC
USA, LATAM
ROW
(Regulations)

Pharma, Device, Biologics, Cosmetics, other Industry Groups
(Product Life Cycle Data)

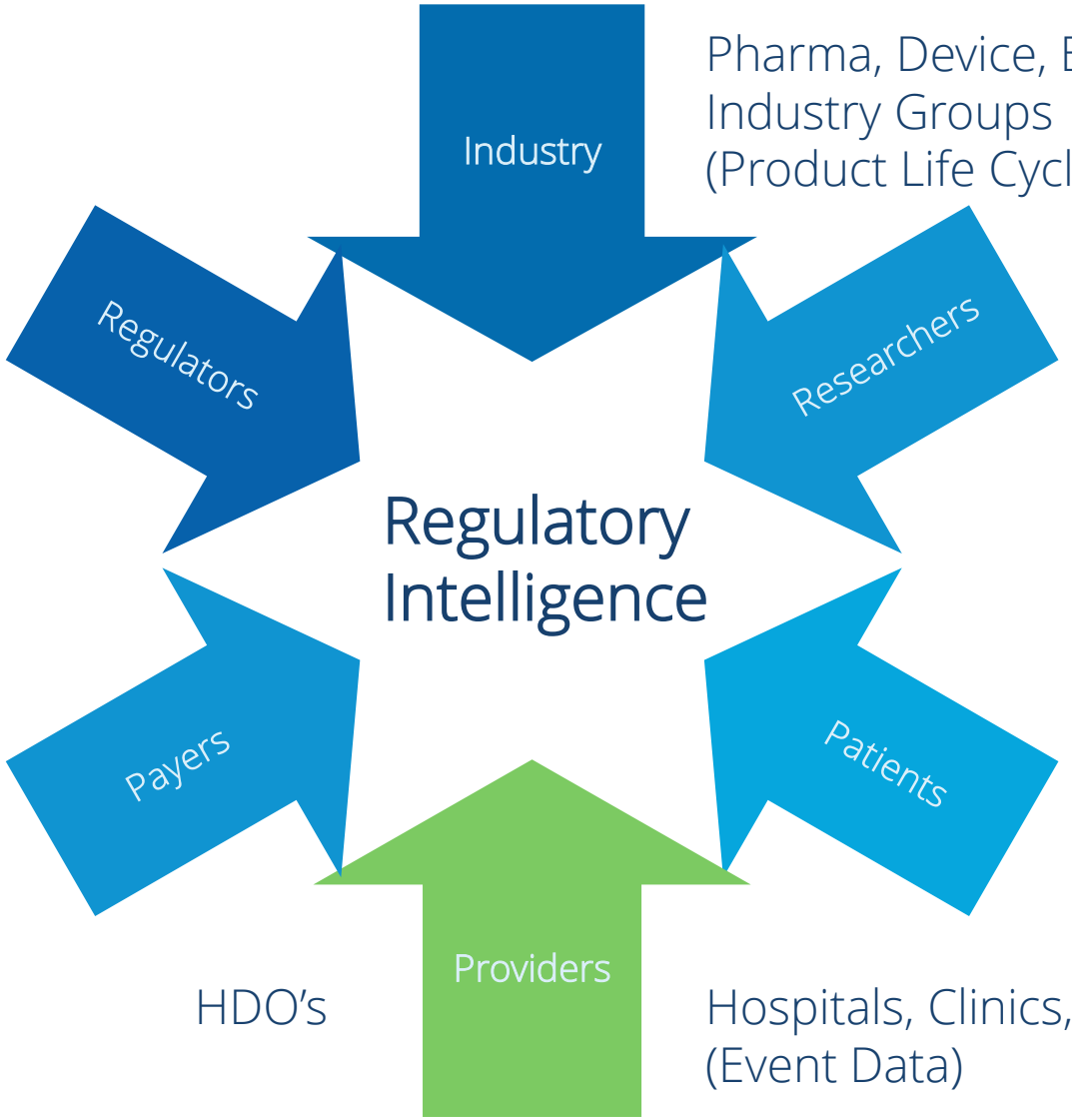
Academic, Independent, Consulting Studies, Medical Literature, Publications

User Experience Reporting
(Sentiment Data)

Insurance Companies
(Claims Data)

HDO's

Hospitals, Clinics, Diagnostic Centers
(Event Data)



Eco-System:

- Complex
- Diverse
- Rapidly Evolving
- Collaboration Required
- Shared Responsibility

Qualified DATA SYSTEMS

Regulatory Intelligence Platform

Post-Market Crowdsourced Data

MEDWATCHER
Make drugs, devices + vaccines safer

National Vulnerability Database
automating vulnerability management, security measurement, and compliance checking

openFDA

HealthData.gov

Project Open Data

All-Payer Claims Database

External Data Sources

Public Domain Data (API)

ETL PROCESS

EXTRACT

VALIDATE

CLEAN

LOAD

Data Remix & Mining

DATA WAREHOUSE

Products & Services

REPORTING

REGULATORY INTELLIGENCE

VISUALIZATION

ALERTS

STATISTICAL

Proprietary Data - Contextualization

Regulatory Science Innovation

Internal Data Sources

QMS

Supply Chain

Manufacturing

Customer Service

Adverse Event

CAPA

Deviations

Risk Mgt.

Development

Maintenance

Pre-Production, Production, & Distribution Data

Qualified DATA SYSTEMS

Benefits of a Regulatory Intelligence Platform

- Provides a holistic view of external environmental factors and internal performance data which can be measured, baselined, reported, and prioritized for improvement.
- Can help identify areas of regulatory overlap and gaps
- Assists in prioritizing Risk-based reviews based upon key performance indicators
- Facilitates Product & Service Quality improvements through the integration (i.e. "*RemiX*") of internal and external information sources
- Establishes ownership and accountability for meeting Quality Objectives and Compliance requirements.
- Establishes a solid foundation for Governance, Risk, and Compliance Management across the enterprise.

External Open Data?

Open Data Definition – "Open means **anyone** can **freely access, use, modify, and share** for **any purpose** (subject, at most, to requirements that preserve provenance and openness)."

In other words:

"Open data and content can be **freely used, modified, and shared** by **anyone** for **any purpose**"

Why is Open Data so important?

Because licenses and dedications are readily available such as Creative Commons, Open Data Common Public Domain Dedication, Open Data Commons Open Database License (ODbL), etc.

Source: http://opendatacommons.org/

External Data Brokers & Services

Look for trusted and validated data vendors who provide transparency and promote open standards for information sharing.

Use of External Data Brokers:

- Typically offer services for a fee (fixed or A-la-Cart)
- Services often include Searching, Filtering, aggregating, and limited downloading or reporting facilities
- Payment for these services does not necessarily translate into higher quality data. Choose wisely!
- Beware of Service Providers who repackage Open Data for a fee without proper disclosures or aggregate copyrighted information from the Web.
- Understand that there is an entire industry dedicated to filling Freedom of Information Requests for undisclosed recipients (FOIA.gov)
- Exclusions to the FOIA include some Law Enforcement and National Security Records.

Using External Open Data

Existing Challenges:

- Not all structured data sources use a common standards-based framework
- Often requires specialized IT skills and costly tools to prepare the data for use
- Use case for **Advanced Safety Signal Detection** still a long way off

Benefits:

- Large historical datasets readily available for data mining
- Self-Service Data discovery, Analysis, and Visualization tools for Lay-Users maturing rapidly. Vendor product eco-system is robust.
- ROI easier to demonstrate through efficient Proof-of-Concept use cases
- Can provide competitive advantage in some use cases where product performance can be benchmarked.

Advanced Signal Detection for Safety Surveillance

Technology Advancement:

- IOT use cases enabling greater speed of Voluntary data collection
  - Mobile devices
  - Advanced wireless sensor technology
  - Cloud computing environments
  - Electronic Regulatory Submission Portals/Gateways
  - Real-time Consumer feedback channels (Social Media)
  - Harvesting of Medical Device metadata by OEM's

Environmental Challenges:

- Government and Industry back-office Adverse Event systems not advanced enough today to process near real-time product safety feedback. Volume and Velocity of data key pain points.
- Regulatory and legal frameworks on data protection often apply the brakes on advanced feedback systems and processes.
- Cybersecurity, Privacy, and Intellectual Property rights important elements requiring continuous monitoring

The future of Advanced Signal Detection for Safety

Cyber-Physical Systems (CPS):

- Machine-2-Machine connectivity and advanced communications (Machine Learning)
- Interoperable Medical Devices
- Cloud Pharmacovigilance Data Repositories
- Automated Data Mining (internet robots)
- Natural Language Processing (NLP)
- Implementation of advanced Algorithms for Signal Processing (optimization of Signal to Noise ratio)
- Advanced Online Analytical Processing (OLAP)
- Artificial Intelligence applied to Health Data for assessment of better outcomes
- Industry 4.0: The rise of the Digital factories

Medical Devices and the IOT

Medical Devices are increasingly part of our connected world:

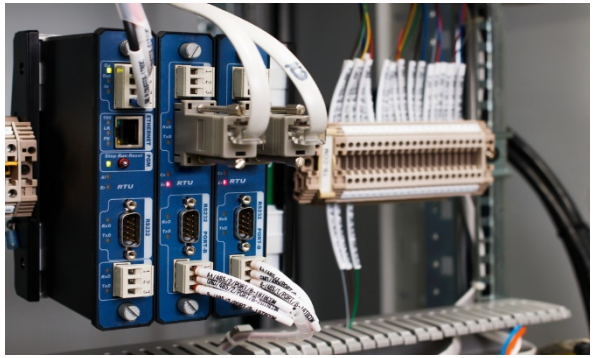
- Embedded systems
- Wireless Sensors
- Decision Support Software
- Therapy Delivery Systems
- Diagnostic Devices
- Cloud Computing Infrastructure
- Remote Patient Monitoring
- Cyber-Physical Systems
- Mobile Medical Apps
- Image Management Systems
- Connected autonomous systems
- Interoperable Devices

The Internet of things is changing the world quickly:

Changing Ecosystem:

- Lower costs and improve efficiency
- Aging Population
- Government stimulated digitization (HITECH)
- Oversight and legal (HIPAA)
- Back-end systems in cloud (EHR, PACS)
- Care models (home-based, mHealth)
- Design complexity vs. skillset

Digital Factories and their Data



Proactive assessment of Product Safety Signals

- Location where Product Quality is crafted
- Access to data is controlled by internal policies and procedures not external entities
- Timeliness and proximity to data means higher quality, integrity, and value
- Where the product knowledge lives
- Promotes safety innovation versus costly post-market design changes

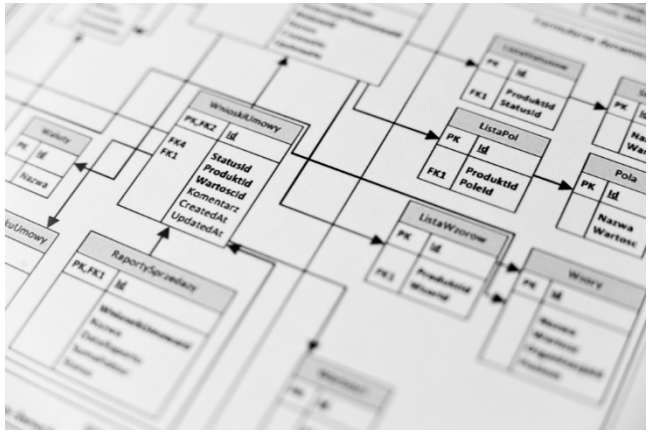
Internal Data Challenges

- Regulated Data scattered across the corporate environment and often insulated from rest of company
- Data is housed in vertical silos of vendor applications with little interoperability without additional pay walls being traversed.
- Organizations lacking clarity to enterprise Data Governance, Risk, and Compliance practices
- Data Management maturity highly dependent on company size and financial resources available
- Data Access many times is limited to a select few who posses licenses
- Heavy IT involvement still needed in some areas where skills or tools are not readily available for data analysis

Data Quality matters

- Recent focus on Quality Metric Programs in the Pharma and the Medical Device Industries in cooperation with FDA and ISPE highlights the need for a renewed emphasis on Data Integrity and Quality.
- While much of the Metric programs (PQLI-Quality Metrics and CfQ-Case for Quality) focus on metric definition and reporting schemes, many industry challenges remain to successful implementation. Examples include:
  - Making Raw Data available using the least burdensome approach
  - Cost of manual or automated data collection, review, and aggregation
  - Process development for Digital data extraction, cleansing, integration, and validation prior to reporting
  - Training and availability of resources for Data Analysis, Interpretation, and Visualization
  - Implementation of Tools for Analytical processing
  - Additional Software Validation requirements
  - Timely Management Reporting
  - Making data actionable in order to operationalize a data-driven culture

Quality Data Architecture



- Begins with robust Data Hygiene
  - Good documentation practice procedures
  - Data Entry field level verification for automated systems
  - Integrity and Business Logic verification for e-Records
  - Defined Data Management practices
  - 21 CFR Part 11 compliance (Security, Audit Trails, e-Signatures)
  - Comprehensive Software Validation Life Cycle for electronic Quality Systems

- Needs to Extend throughout the entire Quality Management System
  - To ensure Confidentiality, Integrity, and Availability of Regulated Information Systems
  - To promote cross-platform data integration, aggregation, and visualization
  - To enable efficient management reporting
  - To flatten silos of data for better collaboration, analysis, and problem resolution

The State of Data Driven Decision-Making

- Technology has made Data Analysis more accessible, but:
- Today's organizations still struggle with the basics of getting their hands around the data needed to make better decisions.
- Excel Spreadsheets and PowerPoint are still the main entry points for data collection, analysis, and presentation of descriptive historical information.
- It still takes way too long to aggregate data and contextualize for Sr. Management review (some take weeks to compile PowerPoints with hundreds of metrics which are tracked across the business). As a result, many reviews only performed quarterly.
- Near Real-time data review is still a utopian concept.
- Focus from the enterprise continues to be on structured Data Analytics. Show me the numbers!
- Organizations still have little demonstrated capabilities when it comes to managing and making use of unstructured data (e.g. Text Analytics). 80% of the world's data is of this kind.
- Data Analytics and self-service enable better data discovery but not necessarily delivers on better business outcomes.

Top Challenges in Incorporating Data Analytics

01 **Access to Data**
Difficulty in obtaining, accessing, and/or compiling the data.

02 **Time Commitment**
Time required to develop and execute analytical procedures

03 **Insufficient Resources**
Insufficient Resources or the need to train personnel.

04 **Lack of Knowledge**
Lack of understanding about data analytics.

05 **Lack of Management Buy-in**
Management not clear on scope, value, or outcomes.

06 **Results Interpretation**
Inability to interpret results and communicate effectively.

Source: The 2015 Data Analytics and Leadership Survey (The IIARF and Grant Thornton)

QMS Analytics Examples

Corrective and Preventive Actions (CAPA):

- Product/Process Non-conformance Analysis
- Complaint Trending
- CAPA Effectiveness Monitoring
- Internal Audit Trending
- MDR Compliance

Production & Process Controls (P&PC):

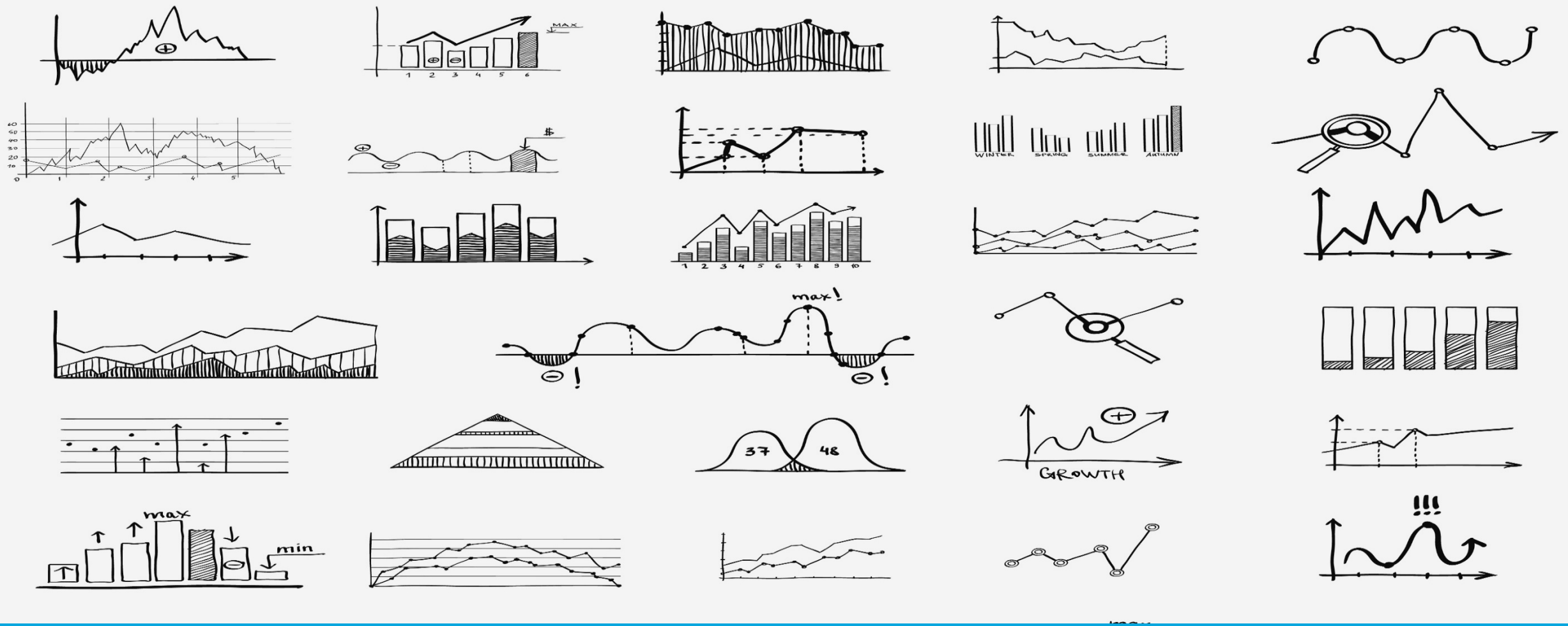
- Supplier Compliance Analysis
- UDI Compliance Trending
- Process Capability Analysis
- Continuous Process Verification (CPV)
- Statistical Process Controls
- OOT Trending
- Statistical Predictive Maintenance

Management Responsibility:

- Quality Metrics Program Monitoring
- Enterprise Risk Management Scorecards
- Training Effectiveness Monitoring
- Cost of Quality Evaluation
- Quality Actions Monitoring

Design Controls:

- Design Change Analysis
- Product Risk Likelihood Trending
- Software Defect Trending
- Product Reliability Analysis
- Verification & Validation Metrics
- Cybersecurity Vulnerability and Threat Monitoring
- Warranty Trending



Analytics in Action - FDA Safety Analytics

FDA Safety Analytics

Active Medical Product Surveillance

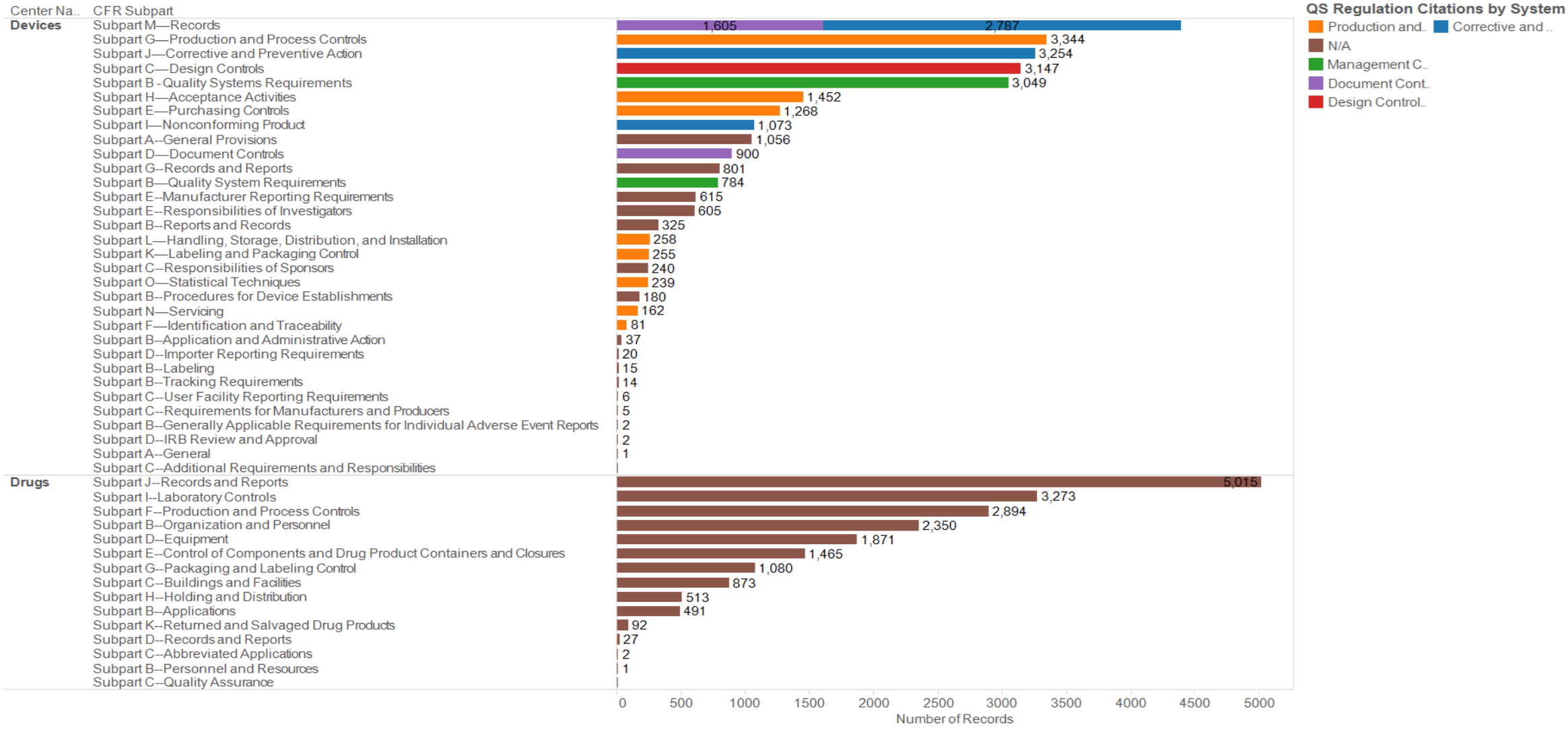
MD Data Sources:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/default.htm

Pharma Data Sources:
http://www.fda.gov/Drugs/InformationOnDrugs/default.htm

Biologics Data Sources:
http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/default.htm

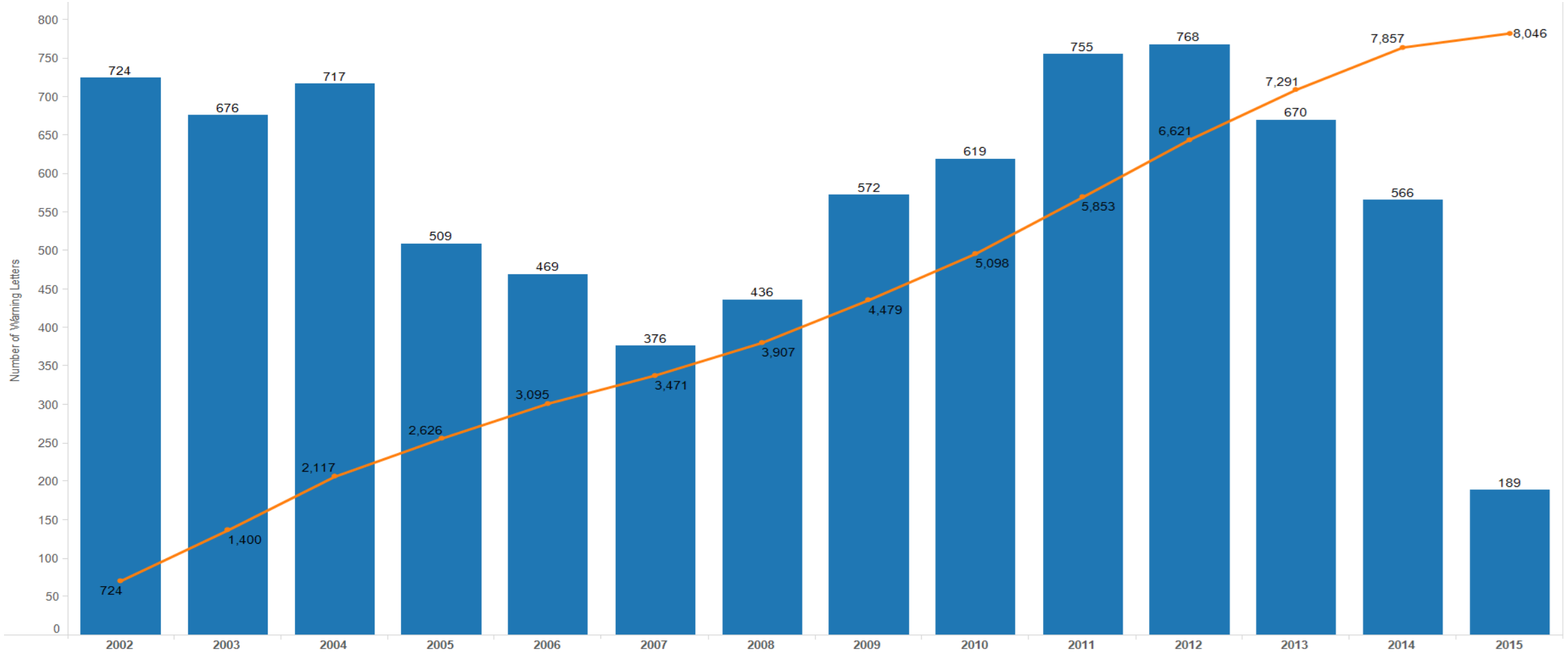
Compliance & Enforcement Data:
FDA 483's, Warning Letters, MDR's, and Recalls

Medical Device and Drug Manufacturers 483s by CFR Subpart 2005 to 2012



Data Source: FDA.gov

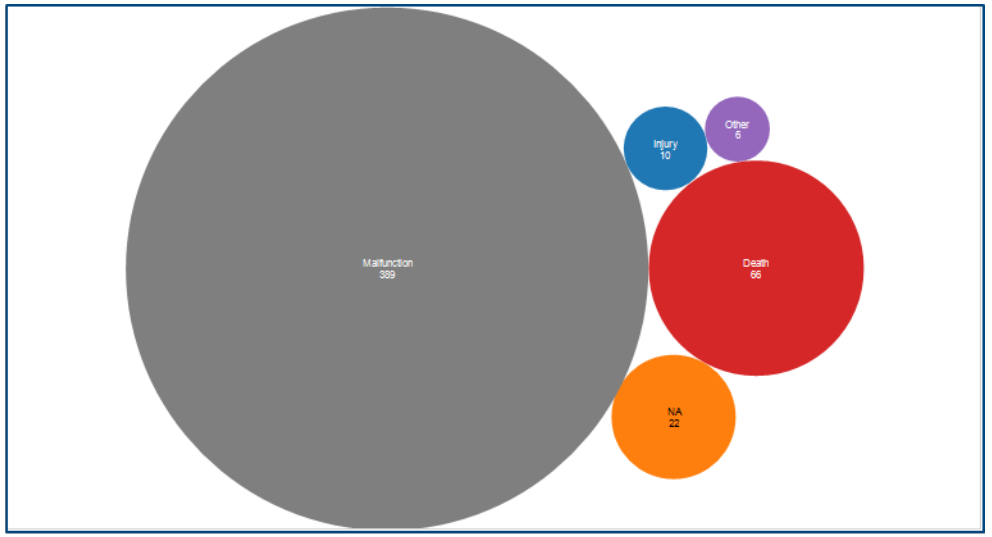
Warning Letter Yearly Trend 2002 to 12/7/2015

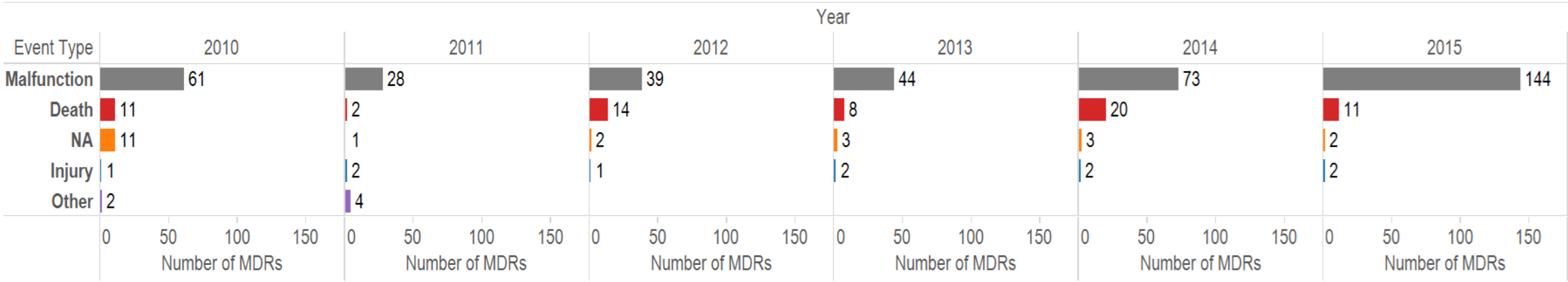


Data Source: FDA.gov

Manufacturer's MDR's 2011 to 2015

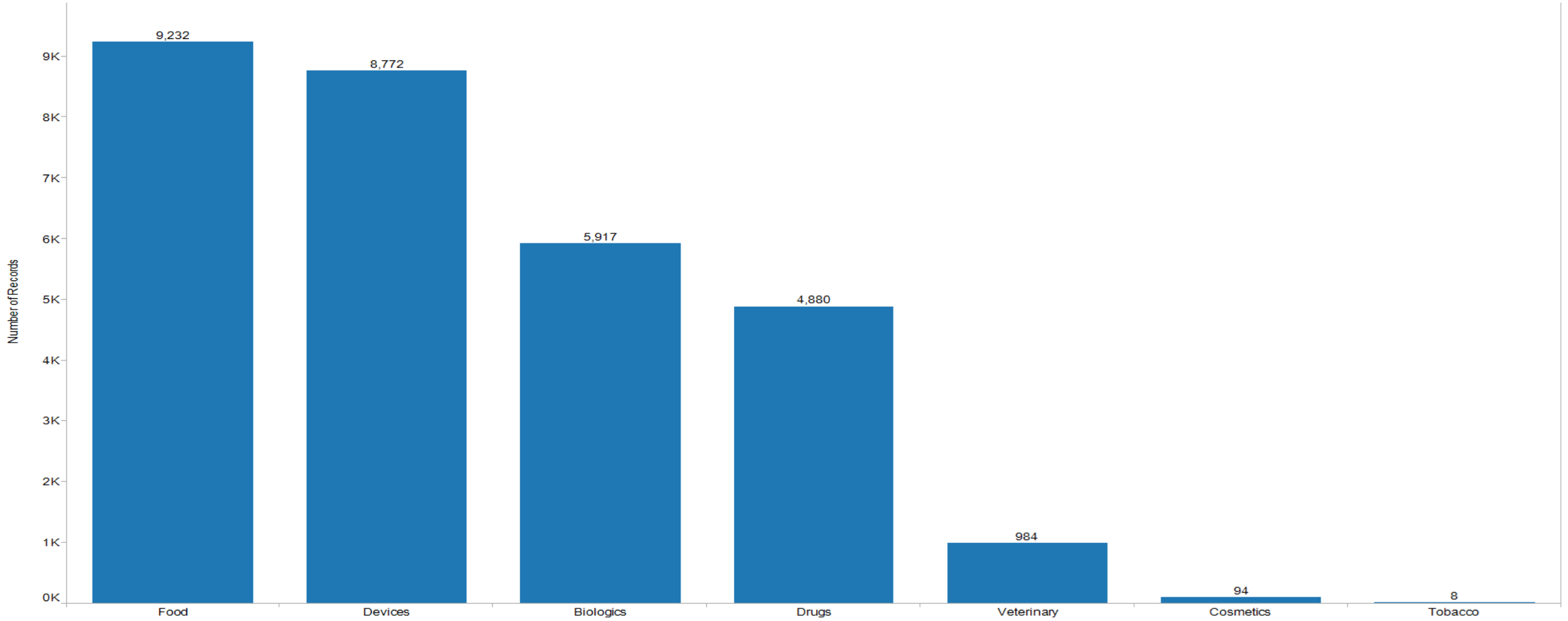
Event Type	Year 2010	2011	2012	2013	2014	2015	Grand Total
Malfunction	61	28	39	44	73	144	389
Death	11	2	14	8	20	11	66
NA	11	1	2	3	3	2	22
Injury	1	2	1	2	2	2	10
Other	2	4					6
Grand Total	86	37	56	57	98	159	493





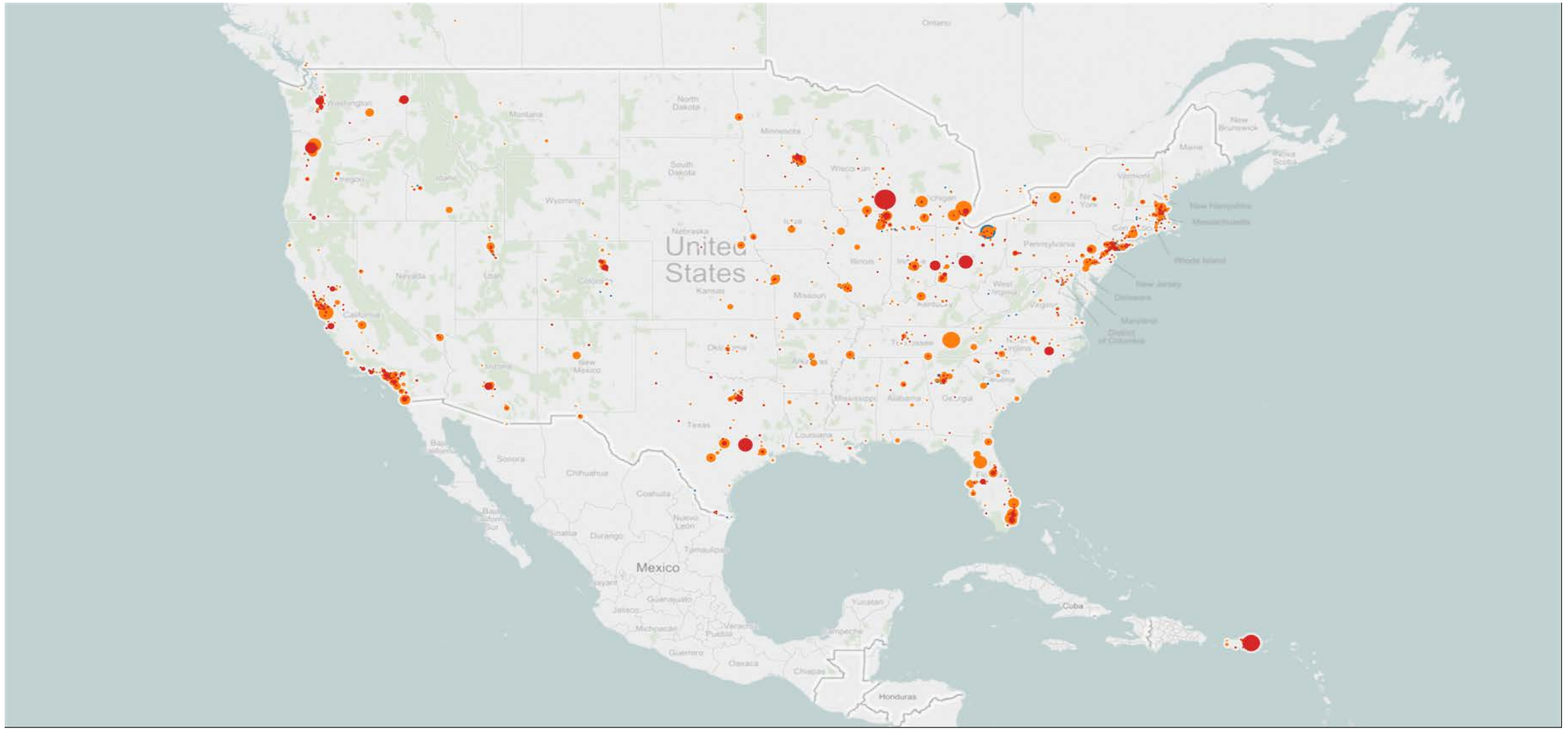
Data Source: FDA.gov

Enforcement Report
Recalls by Product Type 2002 to 12/7/2015



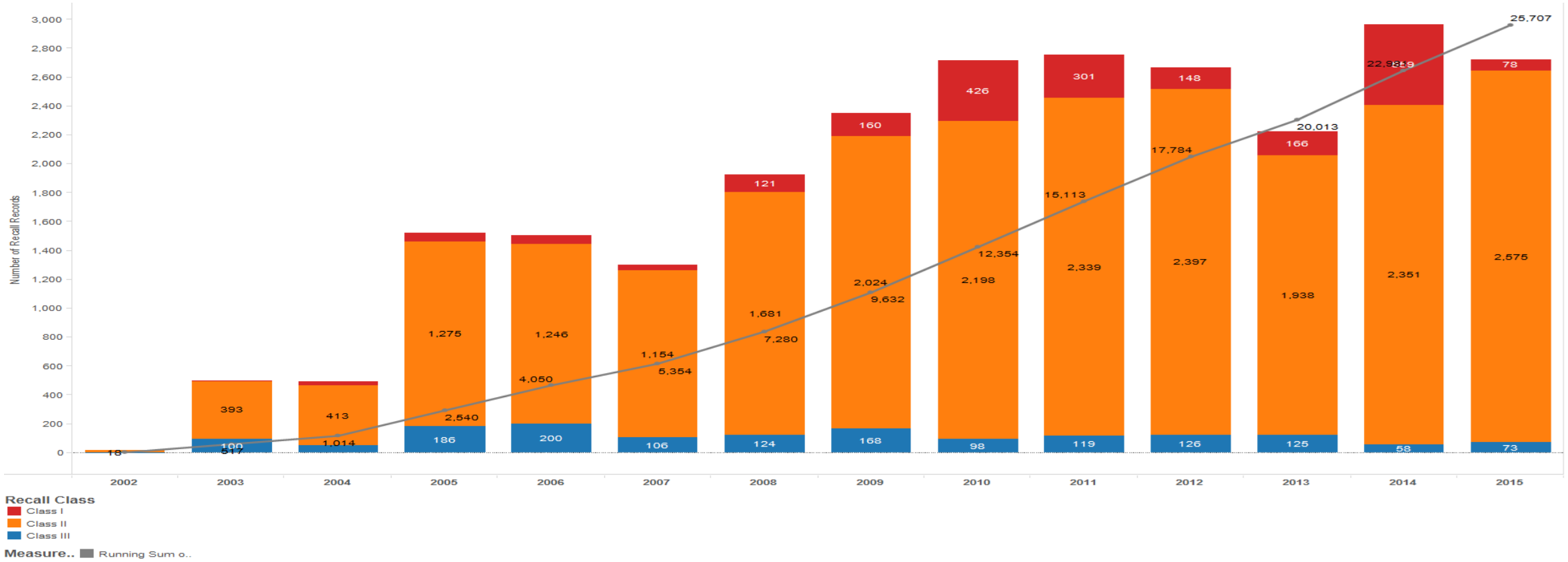
Data Source: FDA.gov

Geo-Spatial Recall Analysis



Data Source: FDA.gov

Medical Device Recalls Yearly Trend 2002 to 12/7/2015



Class I - Recall is a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.

Class II - Recall is a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability.

Class III - Recall is a situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences.

Data Source: FDA.gov

"Let's shrink Big Data into Small Data ...
and hope it magically becomes Great Data."

Questions?

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