US FDA and CDRH in 2020

Peering out the window

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Agenda

quick review of 2019
wider trends in 2020
2020 forecasts
wildcards

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Presentation Objectives

1. Understand how FDA's 2019 activities are continuing into 2020 including data integrity enforcement
2. Recognize business implications of FDA's anticipated 2020 enforcement priorities
3. Identify the real-world implications of FDA's 2020 guidance focus points to your quality system and business objectives
4. Improve your business and regulatory plans to align (or better prepare for) FDA initiatives in 2020 and beyond

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About Your Presenter

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John Avellanet gives practical, real-world compliance solutions and streamlines quality systems for clients around the world. Winner of the 2009 & 2011 Best of Business Services award by the Small Business Commerce Association, Mr. Avellanet has earned international acclaim for his business-savvy, pragmatic advice

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overall enforcement
CDRH specifics
devices and data integrity
other points of note

QUICK REVIEW OF 2019

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FDA's Enforcement Evolution

<u>High benefits</u> to patients with **<u>little risk</u>** to public safety → FDA exercises **<u>enforcement discretion</u>**

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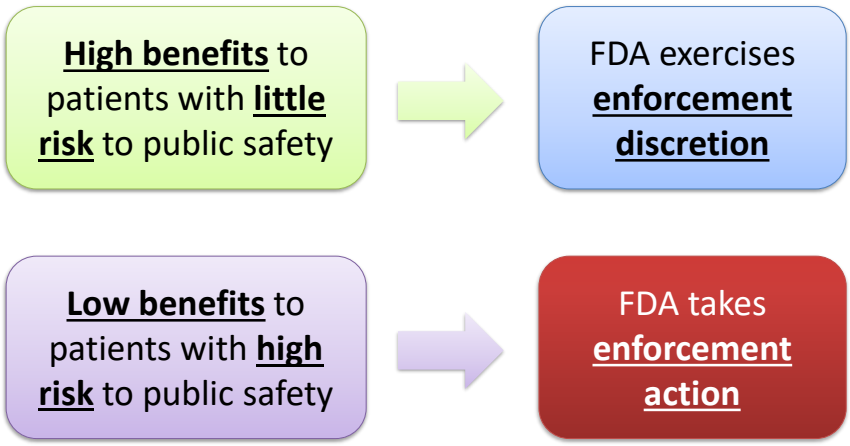
FDA's Enforcement Evolution



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FDA's Integrated Enforcement

- Beginning in 2012, FDA now evaluates and reacts to a firm's FDA-483 response letter, attachment and detailed plans
- This has directly led to a **significant reduction in Warning Letters since 2013** … e.g., "enforcement discretion"
- This trend is likely to continue through 2025

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Enforcement Sparks Litigation

- FDA enforcement actions are public
- FDA-483 forms, warning letters, and untitled letters admissible as "official sanctions" of non-compliance
- Impact under §10(b) and §20(a) of the SEC Act of 1934 targeting senior executives
- Increasingly see this in litigation:
  1) Disgruntled large shareholders and investment groups
  2) Product liability
  3) Consumer protection (and privacy)

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Device Summary Statistics for 2019

Enforcement Action	Total Count
Inspections Conducted	1,874
FDA-483 Observations	905
Recall Events	49

Source:
US FDA, 483 Citation Dataset (see online at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-citation)

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Example CDRH Numbers

Regulation	Issue	No. of FDA-483s
21 CFR 820.198	Complaint handling SOPs, controls and records	224
21 CFR 820.100(a)	CAPA SOPs and controls	192
21 CFR 803.17	MDR procedures and controls	93
21 CFR 820.50(a)	Purchasing controls and SOPs	91
21 CFR 820.90(a)	Non-conforming product procedures and control	81
21 CFR 820.22	Quality audit procedures, plans, et al	74
21 CFR 820.75(a)	Process validation SOPs, execution, etc.	67
21 CFR 820.40	Procedures over record control and integrity	53
21 CFR 820.72(a)	Calibration, maintenance and generate data	50
21 CFR 820.100(b)	Documentation, records management controls	39

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Device Data Integrity

In 2004, FDA conducted an inspection of GE Medical focused on **device complaint data handling and control**

During the inspection, FDA found:

- complaint **data was missing** from SalesForce.com (used by GE to intake complaints)
- GE **knowingly allowed software and system updates without conducting data impact risk assessments**
- GE conducted **no independent verification and comparison of data in SalesForce versus what was reported** to management (and then to FDA)
- as a result, GE **did not take actions to protect the public** health – and this earned FDA's ire

Root Cause:
GE did no pre-change and post-change data verifications – this allowed data to be inadvertently lost and altered

GE, FDA and the DOJ signed a public 5-year consent decree in January 2007

GE lost $100M in first quarter of 2007 – and revenue drops continued for next 3 years

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CDRH and Data Integrity

- September 4-8, 2017 – First set of CDRH investigators receive detailed "inspecting for data integrity" training in St. Louis
- FDA trains device investigators to **cite device firm records** for Part 11 data integrity requirements under the specific FD&C citations of 21 USC §§ 331(e)(w), and 360i(a), and under the specific predicate citations of 21 CFR §§ 803.18(c)(d), 807.26(c), and 820 (var.)
- FDA views cybersecurity of devices, collected and transmitted information, etc. as part of data integrity controls

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Example Data Integrity QSR Citations

Specific Citation	Key Requirements
21 CFR § 820.30 (b) (d)(f)(g)(h)(i)(j)	Requires trustworthy data for design verification, validation, and transfer; controls over design history file
21 CFR § 820.40	Establish and maintain procedures that ensure **all records** – digital, paper, or hybrid – are **controlled with integrity** (including data changes – requires audit trails; see 820.40(b) – this is "hook" for data integrity into QSR)
21 CFR § 820.70(i)	Requires **computerized system validation and change control for systems associated with data and/or regulated activities**
21 CFR § 820.72(a)	Requires equipment to be able to **generate valid and trustworthy data** (complete, accurate, available, etc.)
21 CFR § 820.75(b)(2)	Requires **process validation to include data integrity controls**
21 CFR § 820.80(d)	Requires all **final production and release testing data to be trustworthy and maintained with integrity**
21 CFR § 820.180	Requires **all data and records – including relevant raw data – to be retained with data integrity controls** such as disaster recovery backups
21 CFR § 820.198(a-e)	**Complaint data and correspondence shall be trustworthy and maintained with integrity** from initial input and through reporting, long-term archival, etc.

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Example Data Integrity QSR Citations

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Example FDA-483 C

Examples:
- shared usernames
- editable testing results
- print-outs not containing all the data claimed as "raw data"

"Electronic records are used, but they do not meet requirements to ensure that they are trustworthy, reliable and generally equivalent to paper records. Specifically, **while computers connected to your firm's equipment generate electronic records during the manufacture and testing** of licensed in-vitro diagnostic devices, **you have not considered maintaining these records in a way that guarantees their authenticity, legibility, contemporaneity and accuracy**. For example:…."

- FDA-483 to Bio-Rad, August 2018

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Example Data Integrity Citations

August 2019

- WatchChild
- Beds by George
- Mark Two Engineering
- Abbott Sylmar

Most device data integrity FDA-483 observations cite missing (paper and/or digital) documents, files, and data – so unless you know what you are looking for, it is difficult to learn from the mistakes of others

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Other Points of Note in 2019

- NO premarket approval application (PMA) advisory panel meetings were held
- Theranos litigation discovery efforts are a resource drain vortex (through April 2020)
- ORA continues to merge CDER, CVM and CDRH inspection techniques (e.g., more use of digital record reviews and "live" system review)
- CDRH has started adding in ISO 13485:2016 specifics into its internal inspection documents, manuals, etc. (ala GHTF and PIC/S guidance for inspectors)

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Key Points So Far…

- Initial analysis of available enforcement statistics shows continuing trends from the past 10+ years – but more emphasis on records
- FDA is increasingly scrutinizing device firms and devices for data integrity controls (including cybersecurity controls) – 3 of top 10 483s
- FDA is leveraging the specifics ISO 13485:2016 for its investigators

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Business Implications So Far…

- Enforcement is increasingly driving litigation – especially from investors and shareholders – which directly name senior executives as part of the litigation

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current administration impact
US 2020 election and trade
increasing elderly population

WIDER TRENDS

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Current Administration Impact

- FDA is struggling to balance new guidance docs with regulation revisions (no new regs pronouncement)
- FDA is unable to replace retiring employees easily (federal hiring freeze with exemptions)
- Multiple acting directors and assistant directors, commissioner focused on keeping job (3 commissioners in 2019)
- Encourage faster device, less expensive device approvals (healthcare costs)
- Key focus – tobacco (and vaping/ENDS in particular)

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US 2020 Election and Trade

- FDA will "keep its head down" in 2020 (priorities will be highly public profile items, high-risk enforcement)
- FDA commissioner(s) and directors will have to constantly "testify" in front of Congress
- Trade negotiations may spur enforcement – especially for firms that have outsourced manufacturing overseas

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Increasing Elderly Population

As the boomer population "ages out" while device technological innovations and scientific knowledge increase, firms run two key risks:

1) **Designing out their customer** - elderly patients struggle with technology complexity; consider usability design factors for elderly caretakers – typically Gen-X age group (note: this is also the age of FDA management…)
2) **Cost factors** – "Obamacare" simply slowed down (temporarily) health care costs; costs are rising rapidly again and fixed income elderly are very vulnerable – this is likely to be a major public health issue through 2025 (and multiple elections)

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- FDA is very sensitive to political pressure…up to a point; expect rapid reversal and strict enforcement if widespread public danger
- FDA no longer has the manpower to keep up with publishing summaries of activities (enforcement, new devices approved, etc.)

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Business Implications So Far…

- Enforcement is increasingly driving litigation – especially from investors and shareholders – which directly name senior executives as part of the litigation
- Very business-friendly regulatory environment to push for low-risk exemption status (especially if your device is low-cost)
- Do not be surprised if your oversight of international (non-US) critical suppliers is scrutinized during inspections and premarket approvals
- Products need to be designed for both “boomers” and Gen-X in mind (Gen-X are often the caretakers of the elderly boomers)

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finalized guidances expected

draft guidances expected

ISO 13485:2016 alignment

2020 GUIDANCE FORECAST

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Finalized Guidance Expected

- New device approval point that FDA expects to help firms speed applications (examples: 510(k) Third Party Review Program, Safety and Performance Pathways, etc.)
- Continuing review and revisions to consensus standards
- Guidance related to public-facing risks and usage (examples: Labeling Recommendations, Multi-Function Device Policy, and so on)

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Draft Guidance Expected

- More guidance on cybersecurity and software that generates patient, diagnostic and/or treatment data
- More guidance on UDI – specifically enforcement discretion for Class I devices
- Multiple updates and revisions to currently existing guidance documents (either in draft form or finalized years ago)

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ISO 13485:2016 Alignment

- FDA plans a series of town hall meetings (no published schedule yet)
- Goal is for industry to use 13485:2016 and MDSAP inspection preparation to self-regulate (inspections will still cite QSR, MDR, etc.)
- Downside – allows **easier citation for failure to follow specific regulation** by interpreting the old regs through the lens of 13485:2016
- FDA remains concerned that ISO can make changes to 13485 without FDA approval

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high public-risk priority
design control data integrity
continuing shift to postmarket surveillance

2020 ENFORCEMENT FORECAST

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Overall

Unfortunately, because of current directives, much of this will be reactive

FDA will prioritize high-risk and trust issues

- Review of claims – especially around new devices (including SaMD) – on websites, social media, et al **and the data that support such claims** (or lack thereof)
- Scrutiny on **tracing safety and efficacy features and testing from design through post-market surveillance reporting and investigation** (public safety risk aligned with MDSAP and ISO)
- More review of supply chain and supplier oversight controls
- Increased **look for data integrity issues** during an inspection (e.g., is the device firm's design specification data and final release testing TRUSTWORTHY?)

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Data Integrity

- Continued expansion of the 2010 "special focus" **data integrity portions of inspections to device firms**
- Assessment of data trustworthiness controls around trustworthiness of data informing **final device design control specifications**, **final device and component testing**, in **post-market reporting**, and in **supplier oversight**
- Includes scrutiny of cybersecurity controls on any computerized medical device, app and 3D printing schematics
  - documentation and validation as part of design control
  - change management as part of postmarket changes and reporting
  - management of changes for devices that rely upon COTS
  - prevention of hacking/alterations to 3D device schematics

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Postmarket Surveillance Shift

- FDA continues its shift to emphasize faster device approvals combined with more stringent postmarket surveillance (philosophically aligned with EU's new device directives)
- This allows firms easier integration between EU and US device regulations (and allows FDA easier alignment with IMDRF for 2025 harmonized enforcement target)
- Expect multiple guidances and CPMs to be published in 2020 detailing FDA's postmarket expectations, policies and rules:
  - servicing versus remanufacture
  - postmarket inspection feedback (90-day letters from pharma…?)
  - post-approval studies revisions

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- FDA will prioritize devices with high-risk and/or high public profile (e.g., low risk devices used by everyone will see inspections)
- Data integrity continues its slow burning growth in device enforcement
- FDA continues to try to harmonize its device enforcement with global device regulators and expectations

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- FDA's increasing emphasis on global harmonization should allow for some economies of scale in compliance organizations and budgets
- Monies are going to have to be spent on modernizing record and data integrity controls (both in the firm and in any devices); includes strengthening cybersecurity (especially for litigation protection)

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Wildcards for 2020

- **Global economy** (especially Europe post-Brexit)
- **Trade struggles** (China and the US are drifting apart)
- **US election crisis** (widescale tampering and electronic vote-rigging)
- Widespread natural disaster impacting supply chains

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Longer Term (2021 and beyond)

- **Telemedicine** – this is a major area of growth and FDA is only at exploration stage for rules and boundaries (first public workshop on VR in telemedicine in March 2020)
- **3D printing** – AAMI joint guidance will likely need to be supplemented by regulatory guidance to avoid state-by-state litigation precedents
- **IMDRF harmonization** – goal is to enforce IMDRF guidances (as with ICH guidances) by 2025

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Agenda Recap

quick review of 2019 ✓
wider trends in 2020 ✓
2020 forecasts ✓
wildcards ✓

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