Postmarket Compliance and Enforcement Trends for Medical Devices

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November 2022

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Agenda

- Prohibited Acts and Penalties
- FDA's Enforcement Tools
- Quality System Enforcement Trends
- Promotion-Related Enforcement Trends
- DOJ Enforcement & Trends

Prohibited Acts and Penalties

Prohibited Acts: FDCA § 301 (21 U.S.C. § 331)

301(a): Introduction/delivery for introduction into interstate commerce of adulterated or misbranded device

301(b): Adulteration of misbranding of device that is in interstate commerce

301(c): Receipt in interstate commerce of adulterated or misbranded device and delivery/proffered delivery thereof

301(e): Refusal to permit entry/inspection of establishments

301(k): Doing of act that results in a device being adulterated or misbranded while the device is held for sale after being shipped in interstate commerce

301(p): Failure to register establishments and/or list devices

301(q): Failure to comply with MDR obligations

301(jj): Failure to submit required clinical trial information

Adulteration and Misbranding: FDCA §§ 501 & 502 (21 U.S.C. §§ 351 & 352)

Adulteration	Misbranding
• 501(c): Device does not comply with claimed performance standard • 501(f): Unapproved class III device (unless subject to IDE) • 501(g): Banned device • 501(h): Device not manufactured according to QSR • 501(i): Investigational device not compliant with IDE regulations • 501(j): Inspection refused at establishment where device manufactured	• 502(a): Labeling is false or misleading • 502(b) & (c): Label does not bear required information with required conspicuousness • 502(f): Labeling does not contain adequate directions for use • 502(o): 510(k) was not submitted, or manufactured in an establishment that was not registered • 502(q): Restricted device distributed in violation of restrictions • 502(r): Restricted device distributed without required advertising statements • 502(s): Device subject to performance standards does not include required labeling statements • 502(t): Failure to comply with mandatory notification or repair/replace/refund requirements, failure to submit MDRs, or failure to comply with postmarket study obligations • 502(u) & (v): Failure to include certain labeling on reprocessed single-use devices

Sources of Evidence

Inspections:

- Routine
- For-Cause

Complaints

- Public
- Whistleblowers

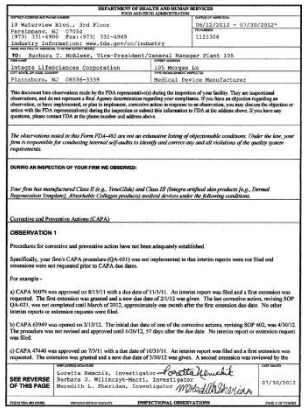
Voluntary Disclosures

Criminal Investigations

IG Investigations

FDA's Enforcement Tools

Overview of Traditional Enforcement Tools



Inspectional Observations (FDA 483)

Untitled Letter

Regulatory Meeting

Warning Letter

Mandatory Recall

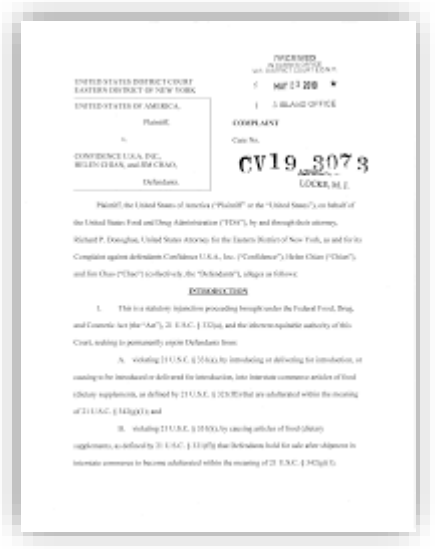
Civil Money Penalty

Consent Decree

Seizure

Injunction

Prosecution



Other Enforcement Tools:

- NIDPOE
- Application Integrity Policy
- Recidivist Warning Letter
- Import Alert
- Banned Devices

FDCA Penalties: FDCA § 303 (21 U.S.C. § 333)

Criminal:

- First conviction**:**
  - Up to $1,000 fine and/or
  - Up to 1 year imprisonment
- Not first conviction *or* intent to defraud or mislead**:**
  - Up to $10,000 fine, and/or
  - Up to 3 years imprisonment

Civil:

- Up to $15,000 per violation, up to $1,000,000 for all violations adjudicated in a single proceeding
  - *Except* for certain minor violations (e.g., insignificant MDR/QSR violations that do not pose risk to public health; minor violations of device tracking and correction/removal reporting requirements)

Individual Liability

Park Doctrine

- Criminal liability for corporate officers in positions of "responsibility and authority"
- Applies to unknowing and unintentional violations
- Generally applies to Presidents & CEOs

Consent Decrees

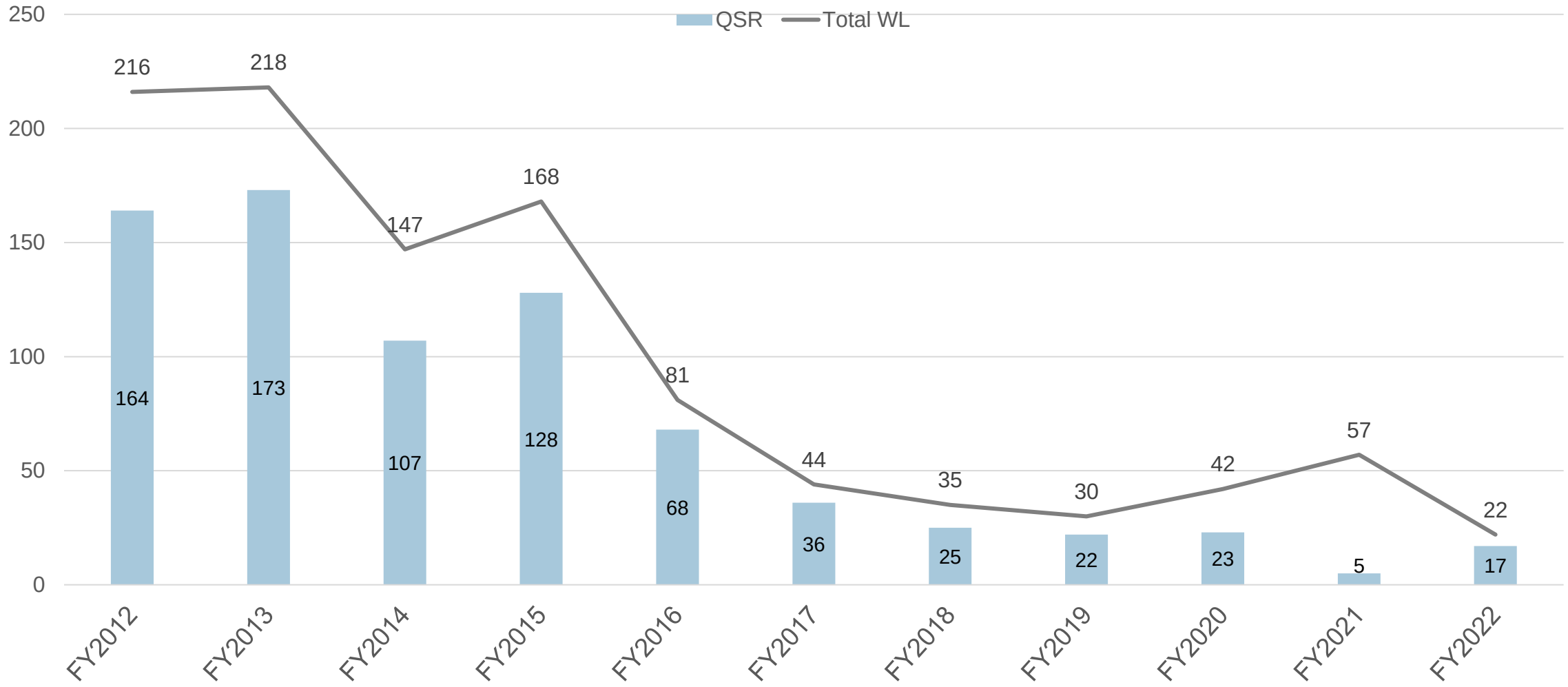
- Generally civil agreements between company & DOJ
- Often name top management as defendants & require management certifications

Corporate Integrity Agreements

- Generally civil agreements between company & HHS
- Often require management certifications

Quality System Enforcement Trends

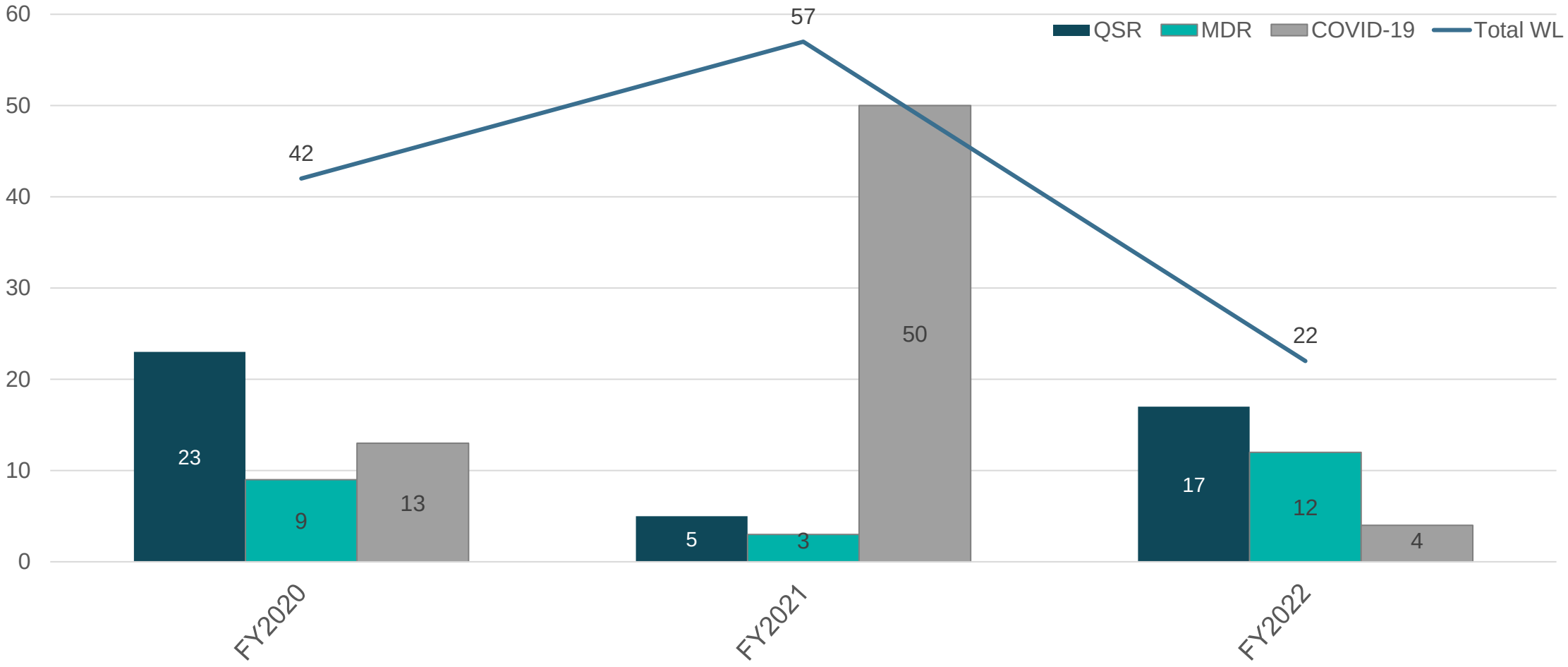
Steady, Multi-Year Decline in Warning Letters



As of 31 AUG 22

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters

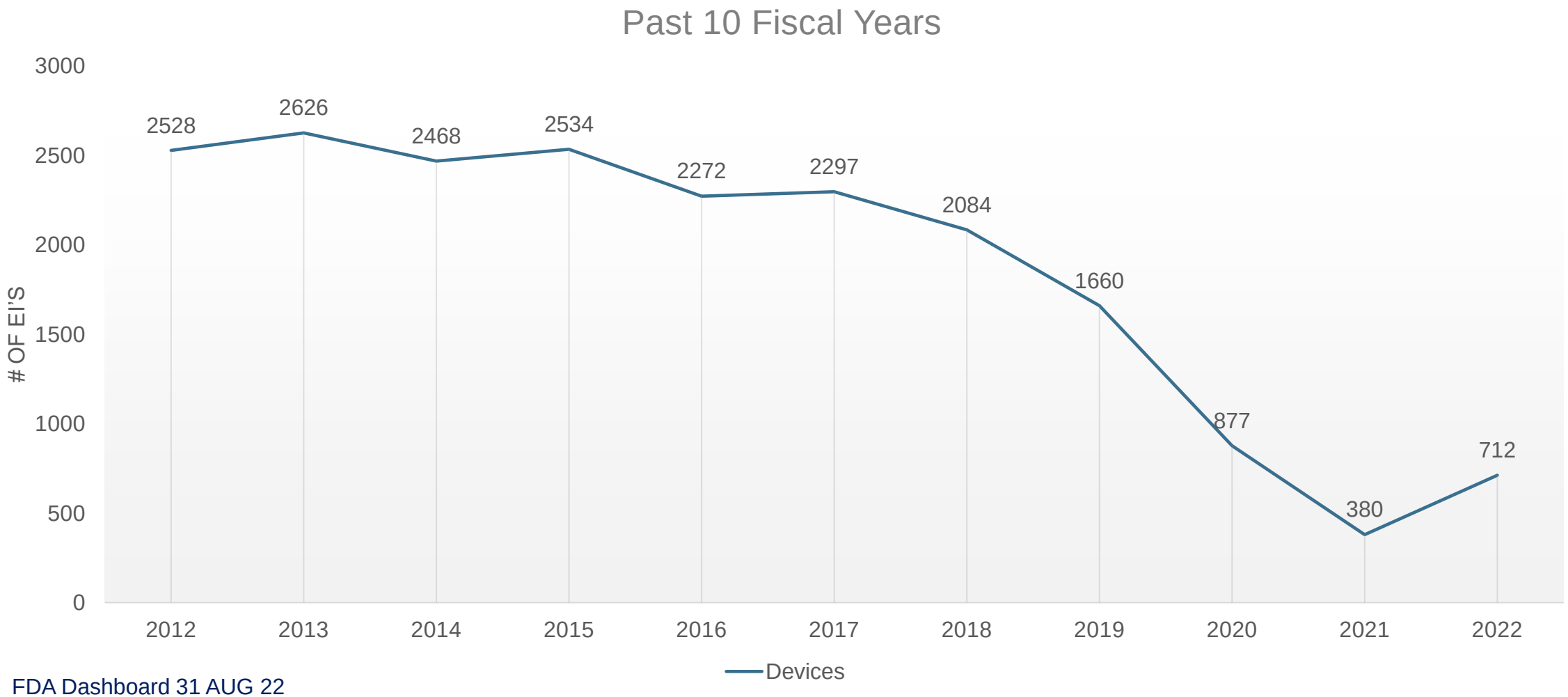
Device Warning Letters: Total and QS, MDR, COVID Citations FY20 – FY22



As of 31 AUG 22

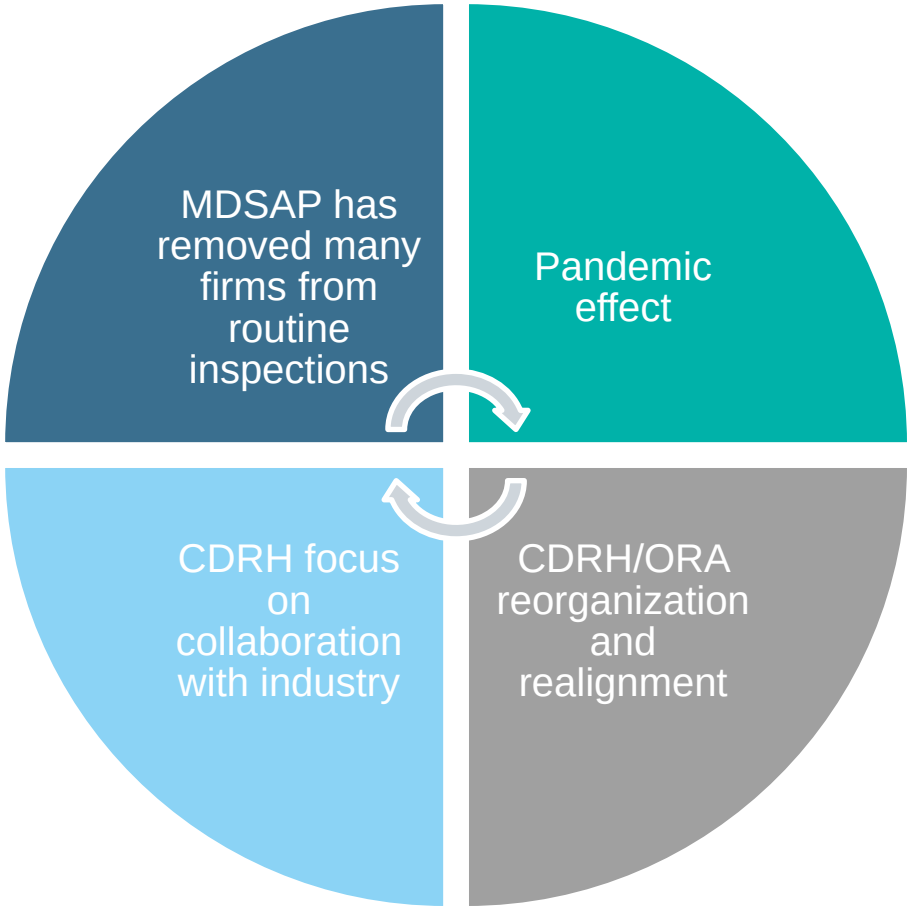
https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters

Decline in Device Inspections



FDA Dashboard 31 AUG 22

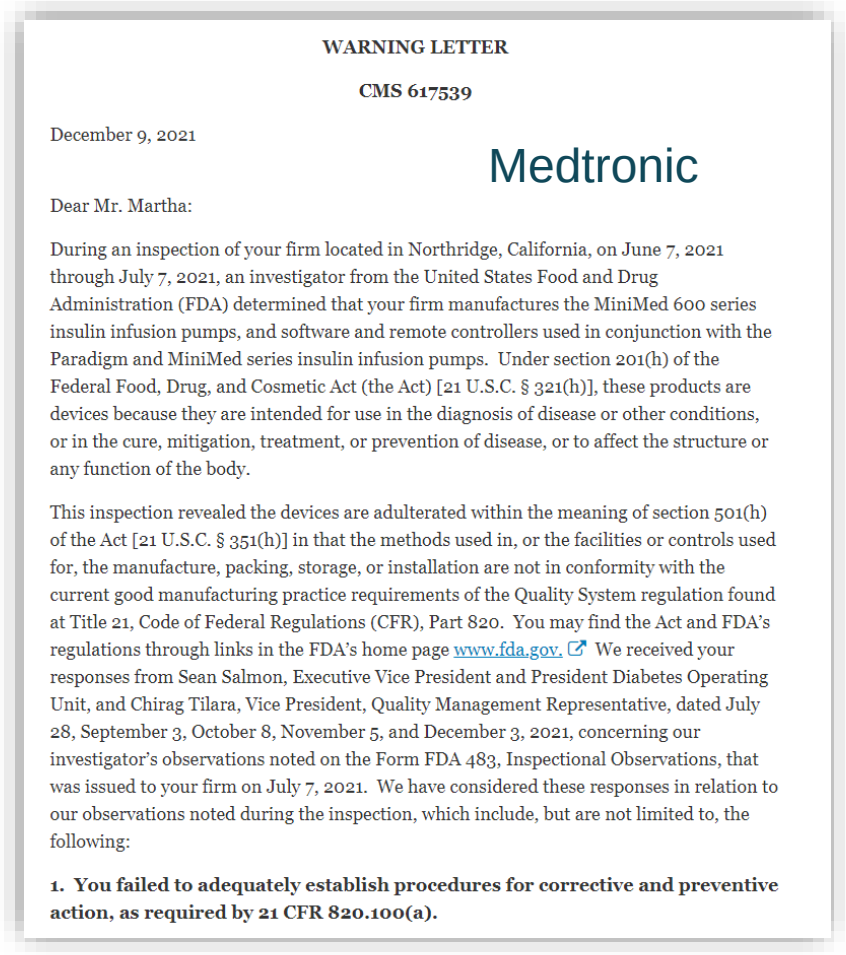
Drivers of the Decline In Inspections and Warning Letters



Recent Warnings Letters Focused on Core QS Issues

Multiple major QSR violations	CAPA
	Complaint handling
	Design control
	Process validation
Risk assessment deficiencies	Underestimating occurrence of harm
	Failure to address high risk situations
	Failure to assess risk of distributed devices
	Lack of addressing reasonably known hazards
MDR procedural and execution failures	Inadequate procedures
	Not reporting malfunctions
	Late reports

Warning Letter Example



WARNING LETTER

CMS 617539

December 9, 2021

Medtronic

Dear Mr. Martha:

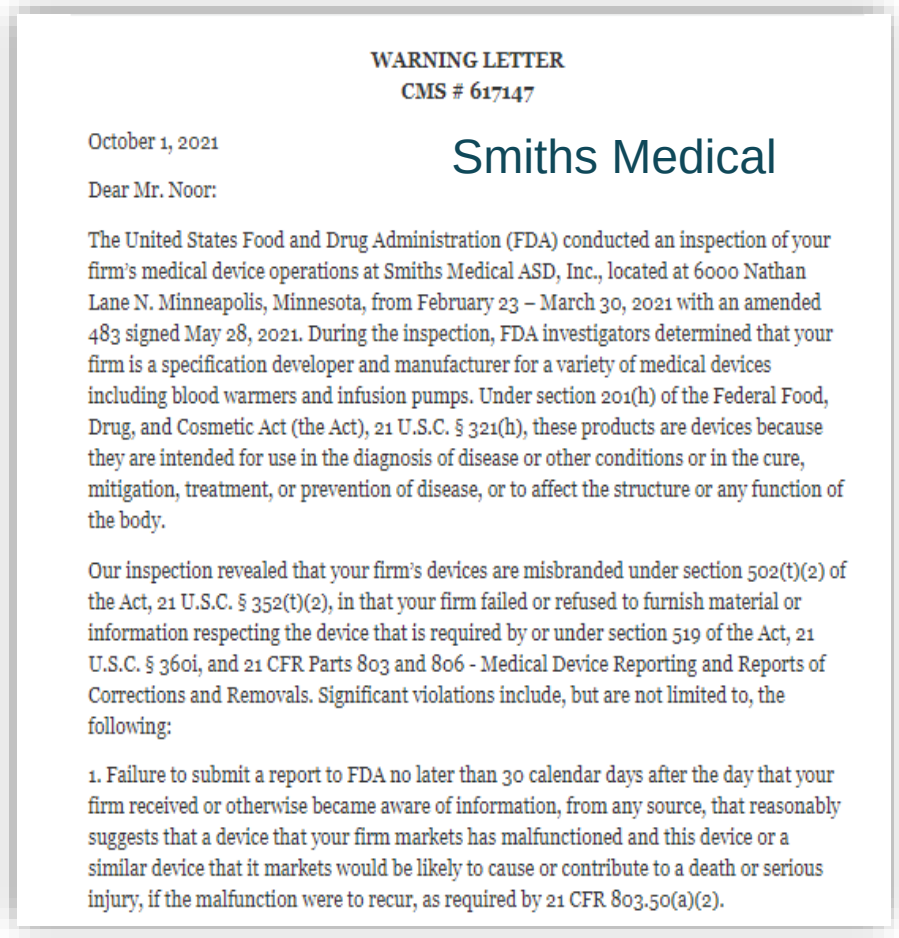
During an inspection of your firm located in Northridge, California, on June 7, 2021 through July 7, 2021, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures the MiniMed 600 series insulin infusion pumps, and software and remote controllers used in conjunction with the Paradigm and MiniMed series insulin infusion pumps. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 321(h)], these products are devices because they are intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.

This inspection revealed the devices are adulterated within the meaning of section 501(h) of the Act [21 U.S.C. § 351(h)] in that the methods used in, or the facilities or controls used for, the manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. You may find the Act and FDA's regulations through links in the FDA's home page www.fda.gov. We received your responses from Sean Salmon, Executive Vice President and President Diabetes Operating Unit, and Chirag Tilara, Vice President, Quality Management Representative, dated July 28, September 3, October 8, November 5, and December 3, 2021, concerning our investigator's observations noted on the Form FDA 483, Inspectional Observations, that was issued to your firm on July 7, 2021. We have considered these responses in relation to our observations noted during the inspection, which include, but are not limited to, the following:

1. You failed to adequately establish procedures for corrective and preventive action, as required by 21 CFR 820.100(a).

1. CAPA
    a) Risk assessment activities underestimated the probability of occurrence of harm, leading to a failure to identify the actions needed to control devices already in distribution
    b) Correction of cybersecurity vulnerabilities did not address distributed product
2. Complaints
    a) Failure to investigate 800 complaints by incorrectly relying on a previous investigation
    b) Failure to obtain device information required to conduct a thorough investigation
3. MDRs
    a) Failure to report an event where medical intervention was required to preclude permanent impairment of a body function or permanent damage to a body structure
    b) Failure to report malfunctions associated with recall

Warning Letter Example



WARNING LETTER
CMS # 617147

October 1, 2021

Smiths Medical

Dear Mr. Noor:

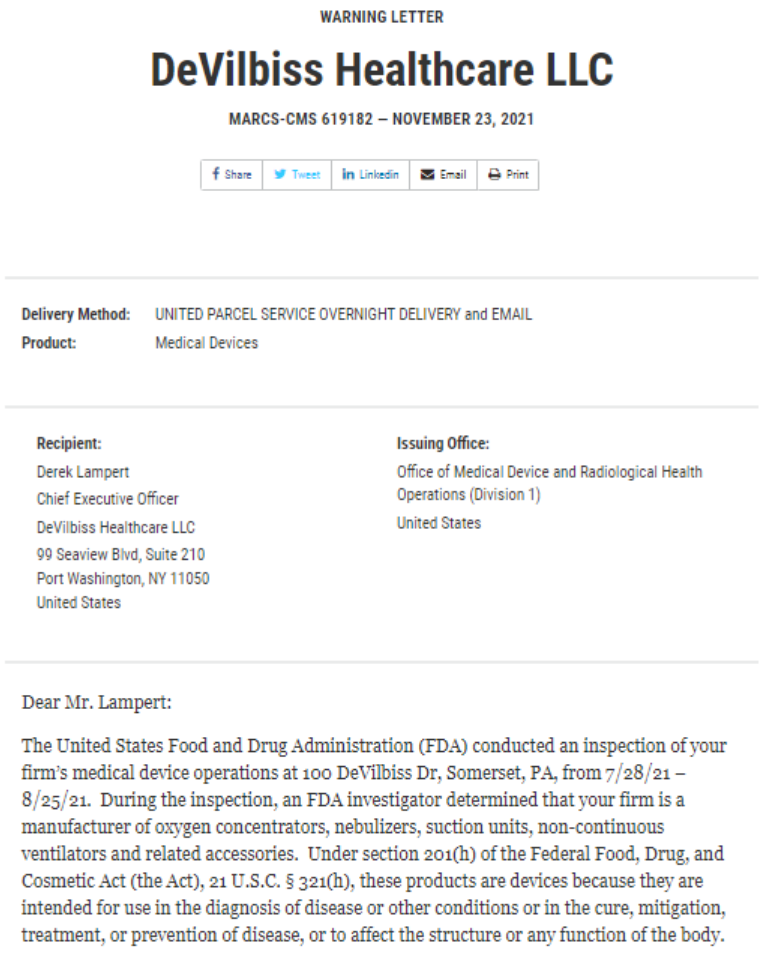
The United States Food and Drug Administration (FDA) conducted an inspection of your firm's medical device operations at Smiths Medical ASD, Inc., located at 6000 Nathan Lane N. Minneapolis, Minnesota, from February 23 – March 30, 2021 with an amended 483 signed May 28, 2021. During the inspection, FDA investigators determined that your firm is a specification developer and manufacturer for a variety of medical devices including blood warmers and infusion pumps. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.

Our inspection revealed that your firm's devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Parts 803 and 806 - Medical Device Reporting and Reports of Corrections and Removals. Significant violations include, but are not limited to, the following:

1. Failure to submit a report to FDA no later than 30 calendar days after the day that your firm received or otherwise became aware of information, from any source, that reasonably suggests that a device that your firm markets has malfunctioned and this device or a similar device that it markets would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur, as required by 21 CFR 803.50(a)(2).

1. MDRs
    a) Not reporting malfunctions associated with recall
    b) Failure of MDR SOP to address reporting criteria, timely transmission of MDRs, and documentation of investigation
2. Failure to submit 806 report for a component change needed to prevent pump failure
3. Lack of design validation for device software
4. Multiple CAPA deficiencies
5. Failure to document complaints received via phone
6. Failure to retain device modification Letters to File

Warning Letter Example



WARNING LETTER

DeVilbiss Healthcare LLC

MARCS-CMS 619182 – NOVEMBER 23, 2021

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Delivery Method: UNITED PARCEL SERVICE OVERNIGHT DELIVERY and EMAIL
Product: Medical Devices

Recipient:
Derek Lampert
Chief Executive Officer
DeVilbiss Healthcare LLC
99 Seaview Blvd, Suite 210
Port Washington, NY 11050
United States

Issuing Office:
Office of Medical Device and Radiological Health Operations (Division 1)
United States

Dear Mr. Lampert:

The United States Food and Drug Administration (FDA) conducted an inspection of your firm's medical device operations at 100 DeVilbiss Dr, Somerset, PA, from 7/28/21 – 8/25/21. During the inspection, an FDA investigator determined that your firm is a manufacturer of oxygen concentrators, nebulizers, suction units, non-continuous ventilators and related accessories. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.

1. Failure of design verification to address actual operating conditions
2. Complaints
    1. Failure to document complaints in a timely manner
    2. Failure to document the determination of whether or not the complaint is reportable under 21 CFR Part 803
    3. Failure to investigate service records
3. Failure of CAPA procedure to consider severity of harm of quality issues; instead, reliance solely on the frequency of occurrence of quality issues
4. Failure to review complaints that may be subject to medical device reporting requirements

Current Administration Seems More Focused on Enforcement

Anecdotally, more "directed inspections"

Instead of going straight to WL, FDA sometimes convenes a Regulatory Meetings and/or issues an Untitled Letter

Continuing to target pandemic related healthcare fraud

Shift in FDA-Industry Interactions

CDRH's total life cycle approach to devices

- Deeper inquiries into technical issues, risk assessments
- Traditional postmarket concerns being raised during premarket reviews

ORA's utilization of voluntary Remote Regulatory Assessments (RRA)

- Additional regulatory tool to remotely examine records to evaluate compliance and prioritize on site inspections
- Does not replace on site inspections
- Upon completion of an RRA, FDA may have a meeting with the establishment's management and may present a written list of RRA observations

Preventive Actions

QSR Focus

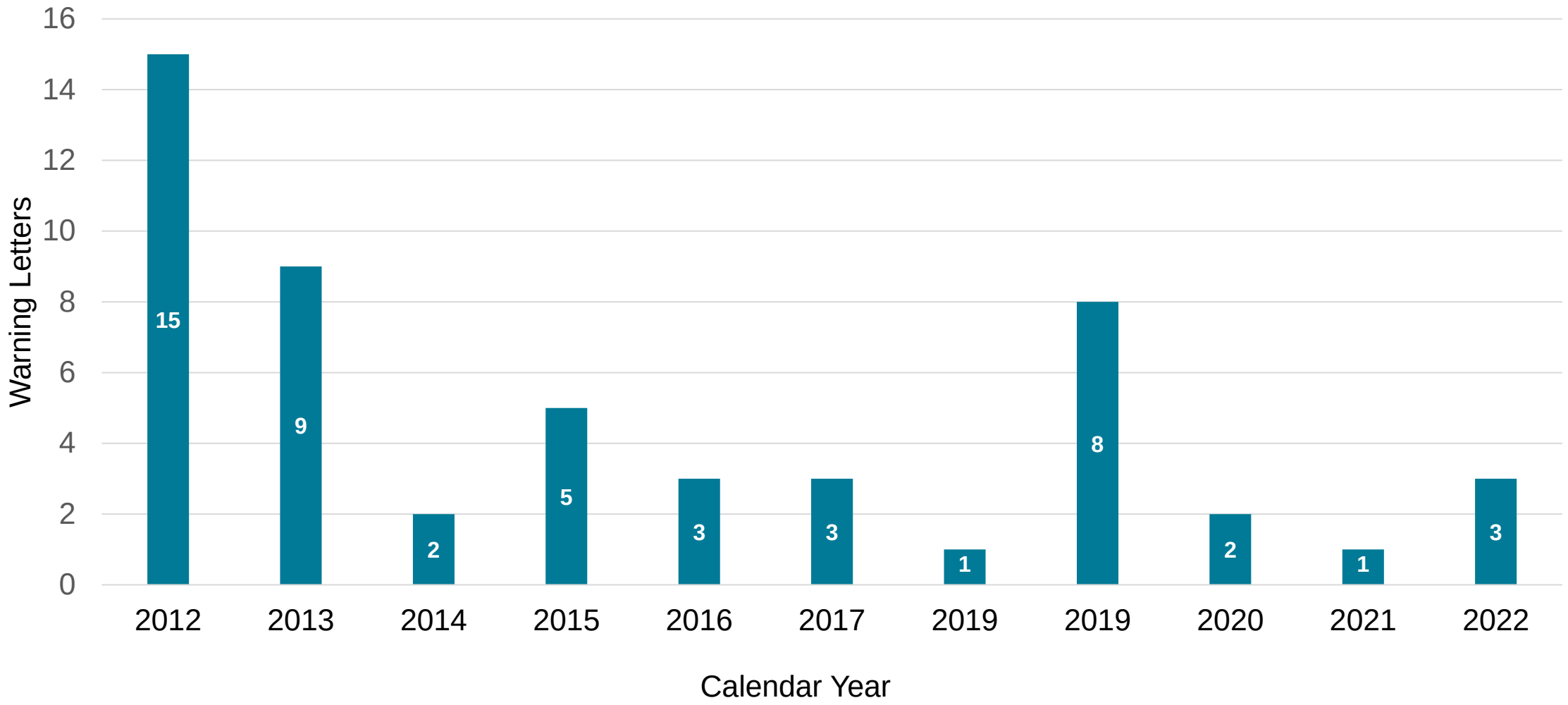
- Robust design control
  - Utilize cross functional design team
  - Apply risk management
  - Complete Design History File
  - Understand design verification vs. validation
    - Use appropriate recognized standards
    - Validate design changes, including IFU changes
- Comprehensive CAPA process
  - Risk based
  - Define triggers for quality data monitored
  - Utilize appropriate investigational tools
  - Consider impact on distributed product
  - Verify and/or validate any changes

Prepare for FDA Interaction

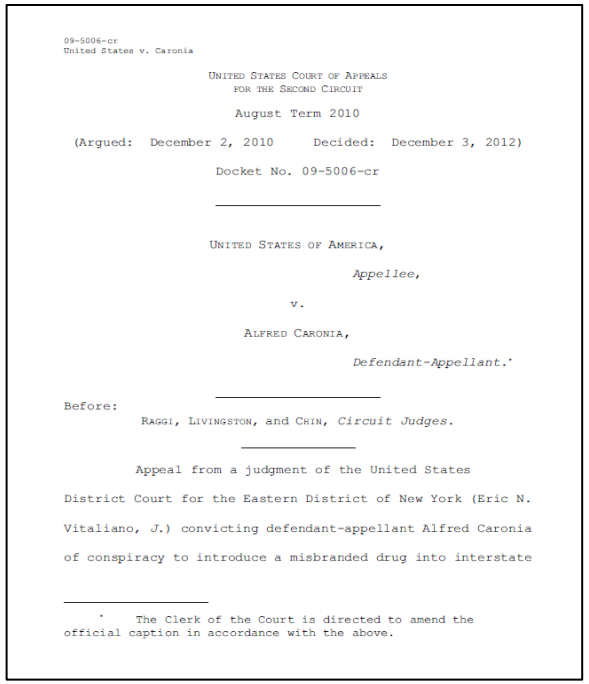
- Mock audits
- Inspection SOP
- SME training
- 483 response training

Promotion-Related Enforcement

Significant Decline in Promotion-Related Warning Letters



Off-Label Communications: What's Happened?



09-5006-cr
United States v. Caronia

UNITED STATES COURT OF APPEALS
FOR THE SECOND CIRCUIT

August Term 2010

(Argued: December 2, 2010 Decided: December 3, 2012)

Docket No. 09-5006-cr

UNITED STATES OF AMERICA,

Appellee,

v.

ALFRED CARONIA,

Defendant-Appellant.

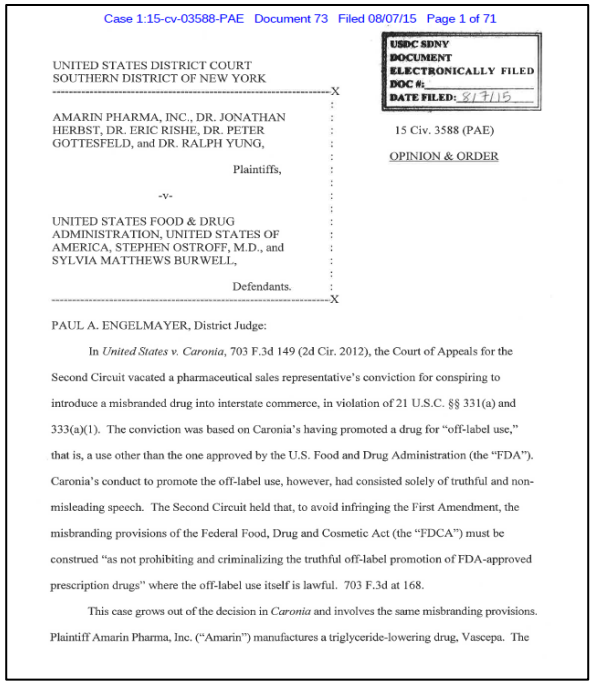
Before:

RAGGI, LIVINGSTON, and CHIN, *Circuit Judges*.

Appeal from a judgment of the United States District Court for the Eastern District of New York (Eric N. Vitaliano, *J.*) convicting defendant-appellant Alfred Caronia of conspiracy to introduce a misbranded drug into interstate

The Clerk of the Court is directed to amend the official caption in accordance with the above.

United States v. Caronia (2nd Cir. 2012)



Case 1:15-cv-03588-PAE Document 73 Filed 08/07/15 Page 1 of 71

USDC SDNY
DOCUMENT
ELECTRONICALLY FILED
DOC #:
DATE FILED: 8/7/15

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

AMARIN PHARMA, INC., DR. JONATHAN HERBST, DR. ERIC RISHE, DR. PETER GOTTESFELD, and DR. RALPH YUNG,

Plaintiffs,

-v-

UNITED STATES FOOD & DRUG ADMINISTRATION, UNITED STATES OF AMERICA, STEPHEN OSTROFF, M.D., and SYLVIA MATTHEWS BURWELL,

Defendants.

15 Civ. 3588 (PAE)

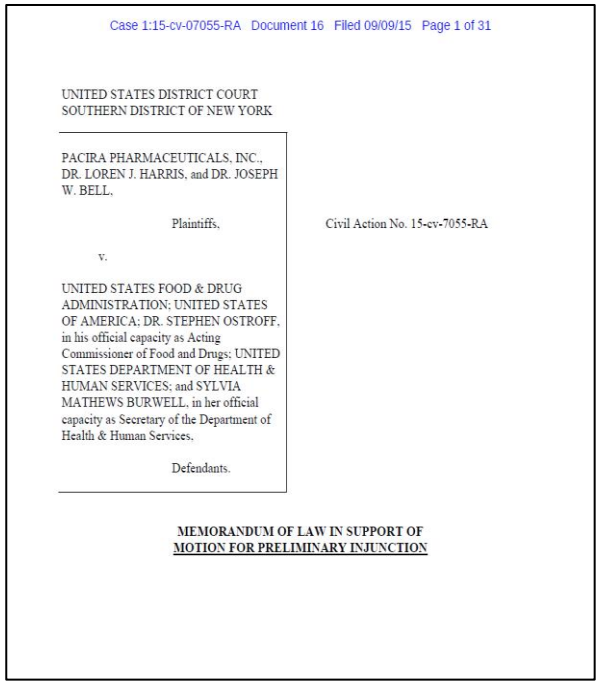
OPINION & ORDER

PAUL A. ENGELMAYER, District Judge:

In *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012), the Court of Appeals for the Second Circuit vacated a pharmaceutical sales representative's conviction for conspiring to introduce a misbranded drug into interstate commerce, in violation of 21 U.S.C. §§ 331(a) and 333(a)(1). The conviction was based on Caronia's having promoted a drug for "off-label use," that is, a use other than the one approved by the U.S. Food and Drug Administration (the "FDA"). Caronia's conduct to promote the off-label use, however, had consisted solely of truthful and non-misleading speech. The Second Circuit held that, to avoid infringing the First Amendment, the misbranding provisions of the Federal Food, Drug and Cosmetic Act (the "FDCA") must be construed "as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs" where the off-label use itself is lawful. 703 F.3d at 168.

This case grows out of the decision in *Caronia* and involves the same misbranding provisions. Plaintiff Amarin Pharma, Inc. ("Amarin") manufactures a triglyceride-lowering drug, Vascepa. The

Amarin Pharma. v. FDA (S.D.N.Y. 2015)



Case 1:15-cv-07055-RA Document 16 Filed 09/09/15 Page 1 of 31

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

PACIRA PHARMACEUTICALS, INC., DR. LOREN J. HARRIS, and DR. JOSEPH W. BELL,

Plaintiffs,

v.

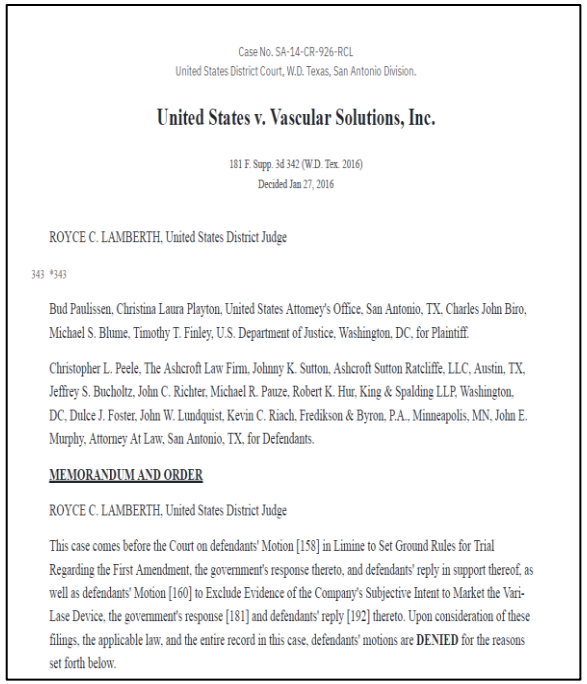
UNITED STATES FOOD & DRUG ADMINISTRATION; UNITED STATES OF AMERICA; DR. STEPHEN OSTROFF, in his official capacity as Acting Commissioner of Food and Drugs; UNITED STATES DEPARTMENT OF HEALTH & HUMAN SERVICES; and SYLVIA MATHEWS BURWELL, in her official capacity as Secretary of the Department of Health & Human Services,

Defendants.

Civil Action No. 15-cv-7055-RA

MEMORANDUM OF LAW IN SUPPORT OF MOTION FOR PRELIMINARY INJUNCTION

Pacira Pharma. v. FDA (Settled 2015)



Case No. SA-14-CR-926-RCL
United States District Court, W.D. Texas, San Antonio Division.

United States v. Vascular Solutions, Inc.

181 F. Supp. 3d 342 (W.D. Tex. 2016)
Decided Jan 27, 2016

ROYCE C. LAMBERTH, United States District Judge

343 *343

Bud Paulissen, Christina Laura Playton, United States Attorney's Office, San Antonio, TX, Charles John Biro, Michael S. Blume, Timothy T. Finley, U.S. Department of Justice, Washington, DC, for Plaintiff.

Christopher L. Peele, The Ashcroft Law Firm, Johnny K. Sutton, Ashcroft Sutton Ratcliffe, LLC, Austin, TX, Jeffrey S. Bucholtz, John C. Richter, Michael R. Pauze, Robert K. Hur, King & Spalding LLP, Washington, DC, Dulce J. Foster, John W. Lundquist, Kevin C. Riach, Fredikson & Byron, P.A., Minneapolis, MN, John E. Murphy, Attorney At Law, San Antonio, TX, for Defendants.

MEMORANDUM AND ORDER

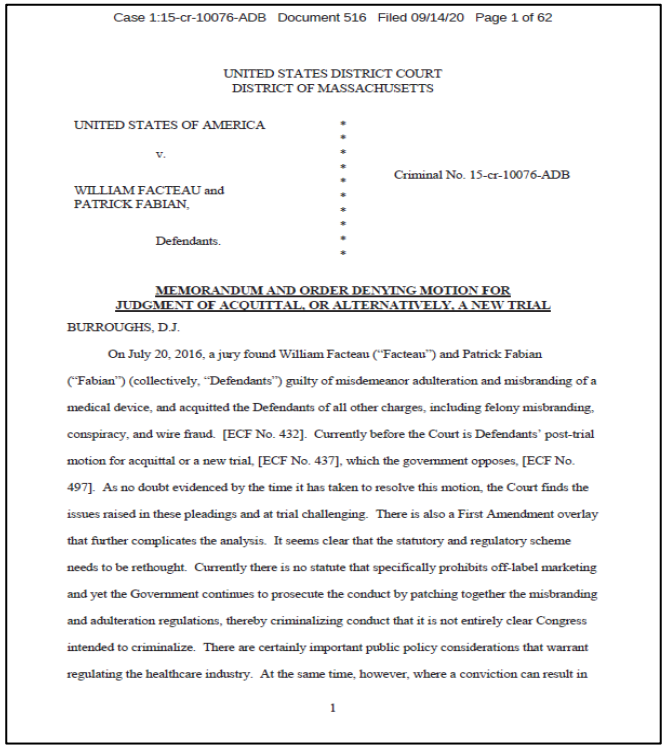
ROYCE C. LAMBERTH, United States District Judge

This case comes before the Court on defendants' Motion [158] in Limine to Set Ground Rules for Trial Regarding the First Amendment, the government's response thereto, and defendants' reply in support thereof, as well as defendants' Motion [160] to Exclude Evidence of the Company's Subjective Intent to Market the Vari-Lase Device, the government's response [181] and defendants' reply [192] thereto. Upon consideration of these filings, the applicable law, and the entire record in this case, defendants' motions are **DENIED** for the reasons set forth below.

United States v. Vascular Solutions (W.D. Tex 2016)

Increasing consensus that truthful, non-misleading off-label promotion is protected by First Amendment

But … not so fast?



Case 1:15-cr-10076-ADB Document 516 Filed 09/14/20 Page 1 of 62

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA
v.
WILLIAM FACTEAU and PATRICK FABIAN,
Defendants.

Criminal No. 15-cr-10076-ADB

MEMORANDUM AND ORDER DENYING MOTION FOR JUDGMENT OF ACQUITTAL, OR ALTERNATIVELY, A NEW TRIAL

BURROUGHS, D.J.

On July 20, 2016, a jury found William Facteau ("Facteau") and Patrick Fabian ("Fabian") (collectively, "Defendants") guilty of misdemeanor adulteration and misbranding of a medical device, and acquitted the Defendants of all other charges, including felony misbranding, conspiracy, and wire fraud. [ECF No. 432]. Currently before the Court is Defendants' post-trial motion for acquittal or a new trial, [ECF No. 437], which the government opposes, [ECF No. 497]. As no doubt evidenced by the time it has taken to resolve this motion, the Court finds the issues raised in these pleadings and at trial challenging. There is also a First Amendment overlay that further complicates the analysis. It seems clear that the statutory and regulatory scheme needs to be rethought. Currently there is no statute that specifically prohibits off-label marketing and yet the Government continues to prosecute the conduct by patching together the misbranding and adulteration regulations, thereby criminalizing conduct that it is not entirely clear Congress intended to criminalize. There are certainly important public policy considerations that warrant regulating the healthcare industry. At the same time, however, where a conviction can result in

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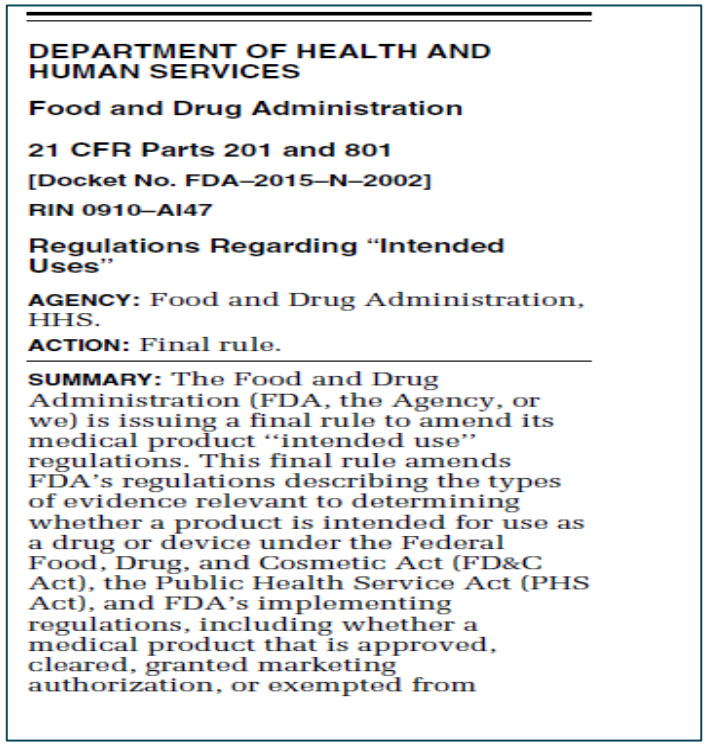
United States v. Facteau
(D. Mass 2020)



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 201 and 801

[Docket No. FDA–2015–N–2002]

RIN 0910–AI47

Regulations Regarding "Intended Uses"

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is issuing a final rule to amend its medical product "intended use" regulations. This final rule amends FDA's regulations describing the types of evidence relevant to determining whether a product is intended for use as a drug or device under the Federal Food, Drug, and Cosmetic Act (FD&C Act), the Public Health Service Act (PHS Act), and FDA's implementing regulations, including whether a medical product that is approved, cleared, granted marketing authorization, or exempted from

FDA Final Rule Amending Regulations
on Intended Use (August 2, 2021)

Recent developments reflecting traditional FDA views on off-label issues.

Off-Label Communications: Where are we today?

- The "law of the land" has not changed
- Premature for firms to revise their promotional policies
  - Court decisions and settlements are very case-specific and should not be applied more broadly
  - FDA and DOJ have continued to pursue cases and open new investigations
- But, certain core precepts are being successfully challenged, which could, in the future, lead to more leeway on what has historically been considered impermissible, off-label promotion
- FDA could issue guidance in future on key aspects of off-label promotion (*e.g.*, scientific exchange)

Promotional Enforcement Landscape

FDA losses in First Amendment cases are likely the main driver of the decline in promotion-related Warning Letters

However, FDA continues to engage on a more informal basis (e.g., via email inquiries) with industry on promotion-related concerns

WLs often issued after extended correspondence between FDA and manufacturer, and sometimes following the issuance of an It Has Come To Our Attention Letter

DOJ

False Claims Act

Four elements:

- Claim or statement for payment or approval of payment
- False or fraudulent
- "Knowledge" of the falsehood – actual knowledge, reckless disregard, or deliberate ignorance
- Materiality

Can be brought by U.S. Government or citizens (*qui tam*)

Penalties are significant: treble damages + statutory penalties

Brings in:

- Anti-kickback statute
- Off-label promotion
- Sunshine Act
- Product quality

and more...

Other Potential Theories

- General federal criminal statutes, e.g., False statements in violation of 18 U.S.C. § 1001
  - Applies to "any matter within the jurisdiction" of any branch of the federal government and criminalizes:
    - Falsifying, concealing, or covering up any material fact
    - Making any materially false, fictitious, or fraudulent statement or representation
    - Making or using any false writing or document with knowledge that it is false

- State consumer protection laws
  - Each of 50 states + DC has a broad "UCL" statute
  - Applies generally to any business practice that is "unfair, unlawful, or fraudulent"

Recent DOJ Device Settlements

Company	Date Settled	Total Recovery
DJO Global Inc.	January 2018	$7.62 M
Abiomed, Inc.	March 2018	$3.1 M
Alere Inc.	March 2018	$33 M
AngioDynamics, Inc.	July 2018	$12.5 M
Ev3, Inc.	December 2018	$17.9 M
Olympus Medical Systems Corporation	December 2018	$85 M
ACell, Inc.	June 2019	$3 M
Pentax Medical Company	April 2020	$43 M
Merit Medical Systems Inc.	October 2020	$18 M
Medicrea International	May 2021	$2 M
Alere Inc.	July 2021	$38.75 M
Avanos Medical Inc.	July 2021	$22 M
St. Jude Medical Inc.	July 2021	$27 M
Arthrex	November 2021	$16 M
Biotronik Inc.	July 2022	$13 M
BSN Medical Inc.	August 2022	$780,000
Philips North America LLC	August 2022	$ 4.2M
Philips RS North America LLC	September 2022	$24 M

Questions?