Introduction to Medical Device Law and Regulation: *Enforcement and Compliance*

November 18, 2021

Presenters:

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ROPES&GRAY

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Agenda

- FDA Jurisdiction: Prohibited Acts
- FDA Enforcement Tools
- FDA Inspections
- Relevant Actors at FDA/DOJ
- Other Enforcement/Remedial Possibilities

Agenda

- **FDA Jurisdiction: Prohibited Acts**
- FDA Enforcement Tools
- FDA Inspections
- Relevant Actors at FDA/DOJ
- Other Enforcement/Remedial Possibilities

Polling Question

Where do you work with medical devices?

a. Medical device manufacturer

b. FDA

c. Law firm

d. Trade association

e. Other

Prohibited Acts: Adulteration & Misbranding

The FDCA prohibits the following acts, among others, and the causing thereof:

- Introduction or delivery for introduction into interstate commerce of any device that is adulterated or misbranded. *FDCA Sec. 301(a)*
- Adulteration or misbranding of any device in interstate commerce. *Sec. 301(b)*
- Receipt in interstate commerce of any device that is adulterated or misbranded, and the delivery or proffered delivery thereof. *Sec. 301(c)*

Prohibited Acts: Other

The FDCA prohibits the following acts, among others, and the causing thereof:

- Failure to maintain or permit access to any required records; failure to make required reports, including medical device reports (MDRs). *Sec. 301(e)*
- Alteration, destruction, or removal of the labeling of a device or doing of any other act that causes a device that is held for sale after shipment in interstate commerce to be adulterated or misbranded. *Sec. 301(k)*
- Failure to comply with manufacturer registration and listing requirements. *Sec. 301(p)*
- Submission of a required report for a device that is false or misleading. *Sec. 301(q)*

Adulteration

A device is adulterated if the device, among other things:

- Includes any filthy, putrid, or decomposed substance or is prepared, packed, or held under unsanitary conditions. *FDCA Sec. 501(a)(1); (a)(2)(A)*
- Has a container composed, in whole or part, of any poisonous or deleterious substance. *Sec. 501(a)(3)*

Adulteration

A device is adulterated if the device, among other things:

- Fails to comply with a required a performance standard if it is subject to or represented to be in compliance with such standard. *FDCA Sec. 501(e)*
- Is a Class III device that requires, but has not received, FDA approval of a premarket approval application ("PMA") or notice of completion of a product development protocol. *Sec. 501(f)*
- Is in violation of quality system regulation ("QSR") requirements established under Sec. 520(f). *Sec. 501(h)*
- Fails to comply with an Investigational Device Exemption (IDE). *Sec. 501(i)*

Misbranding

A device is misbranded if, among other things:

- It is manufactured in an establishment that is not duly registered with FDA or device was not listed in accordance with listing requirements. *FDCA Sec. 502(o)*
- A required premarket notification (510(k) submission) has not been submitted with respect to the device. *Sec. 502(o)*
- Device manufacturer or importer fails to comply with MDR obligations, fails to provide notifications about recalls or corrections, or fails to comply with post-market surveillance requirements. *Sec. 502(t)*
- It is dangerous to health when used in the manner or with the frequency or duration prescribed or suggested in the label. *Sec. 502(j)*

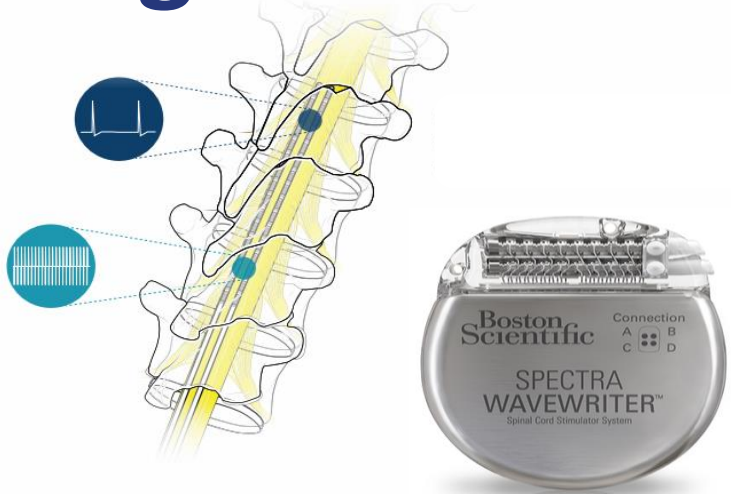
Misbranding

A device is misbranded if its labeling, among other things:

- Is false or misleading in any particular. *FDCA Sec. 502(a)(1)*
- Does not display required wording clearly or prominently as compared with other wording in the labeling. *Sec. 502(c)*
- Does not bear adequate directions for use by laypersons, including statements of all uses for which the device is intended, instructions for preparation and administration or application, warnings against use in certain conditions where use may be dangerous to health, and warnings against unsafe dosage or methods or duration of administration or application. *Sec. 502(f); 21 C.F.R. § 801.5*

Labeling and Advertising Concerns

- FDA regulates advertising of “restricted” devices; FTC regulates advertising of non-restricted devices
  - Restricted device advertisements may not be false or misleading and must include a “brief statement” of intended uses and relevant warnings, side effects, and contraindications. *FDCA Sec. 502(q)-(r)*
- For prescription devices, labeling must bear adequate information, including indications, methods of administration, and relevant hazards and contraindications, for the safe and effective use of the device by practitioners licensed by law to administer the device. *21 C.F.R. § 801.109(c)-(d)*



US Indications for Use: The Boston Scientific Spinal Cord Stimulator Systems are indicated as an aid in the management of chronic intractable pain of the trunk and/or limbs including unilateral or bilateral pain associated with the following: failed back surgery syndrome, Complex Regional Pain Syndrome (CRPS) Types I and II, intractable low back pain and leg pain. Associated conditions and etiologies may be: radicular pain syndrome, radiculopathies resulting in pain secondary to failed back syndrome or herniated disc, epidural fibrosis, degenerative disc disease (herniated disc pain refractory to conservative and surgical interventions), arachnoiditis, multiple back surgeries. Contraindications, warnings, precautions, side effects. The SCS Systems are contraindicated for patients who: are unable to operate the SCS System, have failed trial stimulation by failing to receive effective pain relief, are poor surgical risks, or are pregnant. Refer to the Instructions for Use provided with the SCS System or ControlYourPain.com for potential adverse effects, warnings, and precautions prior to using this product. Caution: U.S. Federal law restricts this device to sale by or on the order of a physician.

Labeling and Advertising Concerns

- Regardless of the kind of device, device labeling cannot be misleading. *Sec. 502(a)*
- In determining whether the labeling or advertising is misleading, FDA will consider:
  - Representations made or suggested by statement, word, design, device, or any combination thereof. *Sec. 201(n)*
  - Extent to which the labeling or advertising fails to reveal material facts or material consequences which may result from use. *Sec. 201(n)*
- Off-label promotion and comparative claims present heightened risks

Enforcement Discretion

FDA may exercise “enforcement discretion” by declining to enforce certain provisions of the FDCA. Heckler v. Chaney, 740 U.S. 821 (1985).

Also, FDCA Section 309 expressly does not require action for “minor violations” where FDA believes “the public interest will be adequately served by a suitable written notice or warning.” 21 U.S.C. § 336

Polling Question

Which of the following images reflect medical devices that have been subject to FDA or DOJ enforcement action?

a. 

b. 

c. 

d. all 3

Agenda

- FDA Jurisdiction: Prohibited Acts
- **FDA Enforcement Tools**
- FDA Inspections
- Relevant Actors at FDA/DOJ
- Other Enforcement/Remedial Possibilities

FDA Enforcement Tools

FDA tools for enforcing the FDCA include both administrative and judicial actions:

Administrative	Judicial
• Advisory Notices • Recalls • Administrative Detention • Import Alerts & Refusal • Banned Devices • Use of Publicity	• Seizure • Civil Money Penalties • Injunction • Criminal Prosecution/Fines

Administrative Enforcement Tools

- Advisory Notices
- Recalls
- Administrative Detention
- Import Alerts & Refusal
- Banned Devices
- Use of Publicity

Advisory Notices

Warning Letters

- Informal, advisory letter which provides notice of a significant regulatory violation, such as failure to comply with cGMPs or reporting requirements, or improper promotion
- Include a warning statement that failure to take prompt correction may result in enforcement action
- Provide individuals and firms an opportunity to take voluntary and prompt corrective action before FDA initiates enforcement action
- FDA's principal means of achieving prompt voluntary compliance

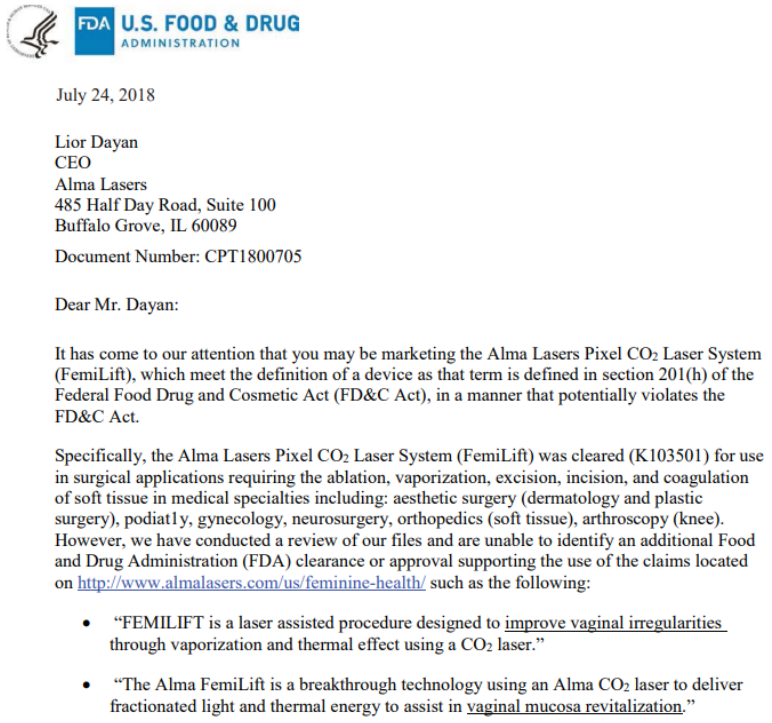
Untitled Letters

- Letter, which cites violations that do not meet the threshold of regulatory significance for a Warning Letter

Advisory Notices

"It Has Come to Our Attention" Letters

- Letter from CRDH or the Office of In Vitro Diagnostics and Radiological Health (OIR) expressing FDA's belief that a product is a regulated medical device requiring 510(k) clearance or approval



FDA U.S. FOOD & DRUG ADMINISTRATION

July 24, 2018

Lior Dayan
CEO
Alma Lasers
485 Half Day Road, Suite 100
Buffalo Grove, IL 60089

Document Number: CPT1800705

Dear Mr. Dayan:

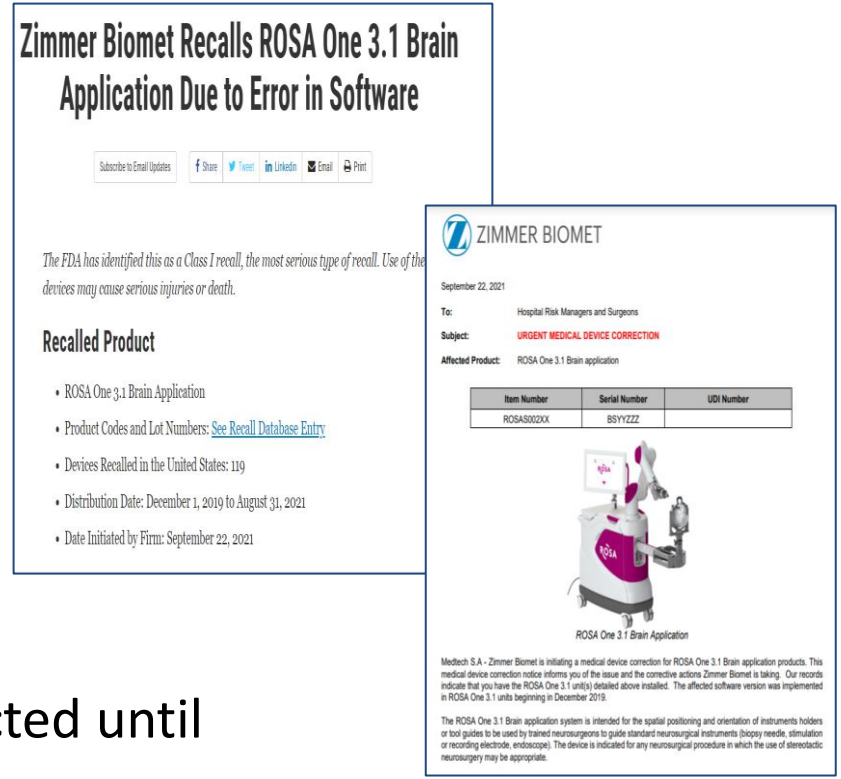
It has come to our attention that you may be marketing the Alma Lasers Pixel CO_2 Laser System (FemiLift), which meet the definition of a device as that term is defined in section 201(h) of the Federal Food Drug and Cosmetic Act (FD&C Act), in a manner that potentially violates the FD&C Act.

Specifically, the Alma Lasers Pixel CO_2 Laser System (FemiLift) was cleared (K103501) for use in surgical applications requiring the ablation, vaporization, excision, incision, and coagulation of soft tissue in medical specialties including: aesthetic surgery (dermatology and plastic surgery), podiat1y, gynecology, neurosurgery, orthopedics (soft tissue), arthroscopy (knee). However, we have conducted a review of our files and are unable to identify an additional Food and Drug Administration (FDA) clearance or approval supporting the use of the claims located on http://www.almalasers.com/us/feminine-health/ such as the following:

- "FEMILIFT is a laser assisted procedure designed to improve vaginal irregularities through vaporization and thermal effect using a CO_2 laser."
- "The Alma FemiLift is a breakthrough technology using an Alma CO_2 laser to deliver fractionated light and thermal energy to assist in vaginal mucosa revitalization."

Recalls

- Recalls are generally conducted voluntarily by the device manufacturer.
- They are required to be reported to FDA under 21 C.F.R. s. 806.
- Filing an “806 report” will trigger discussions with FDA regarding a recall plan.
- Usually, a communication to providers will be part of that plan.
- Status updates to FDA will be expected until recall is terminated.



Zimmer Biomet Recalls ROSA One 3.1 Brain Application Due to Error in Software

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The FDA has identified this as a Class I recall, the most serious type of recall. Use of the devices may cause serious injuries or death.

Recalled Product

- ROSA One 3.1 Brain Application
- Product Codes and Lot Numbers: See Recall Database Entry
- Devices Recalled in the United States: 119
- Distribution Date: December 1, 2019 to August 31, 2021
- Date Initiated by Firm: September 22, 2021

ZIMMER BIOMET

September 22, 2021

To: Hospital Risk Managers and Surgeons

Subject: URGENT MEDICAL DEVICE CORRECTION

Affected Product: ROSA One 3.1 Brain application

Item Number	Serial Number	UDI Number
ROSAS002XX	BSYYZZZ	

ROSA One 3.1 Brain Application

Medtech S.A - Zimmer Biomet is initiating a medical device correction for ROSA One 3.1 Brain application products. This medical device correction notice informs you of the issue and the corrective actions Zimmer Biomet is taking. Our records indicate that you have the ROSA One 3.1 unit(s) detailed above installed. The affected software version was implemented in ROSA One 3.1 units beginning in December 2019.

The ROSA One 3.1 Brain application system is intended for the spatial positioning and orientation of instruments holders or tool guides to be used by trained neurosurgeons to guide standard neurosurgical instruments (biopsy needle, stimulation or recording electrode, endoscope). The device is indicated for any neurosurgical procedure in which the use of stereotactic neurosurgery may be appropriate.

Recalls

If a manufacturer fails to recall a device voluntarily, FDA may:

- Issue a cease distribution notification. *21 C.F.R. § 810.10(a)*
  - FDA must find a "reasonable probability" that the device would cause serious, adverse health consequences or death
  - Notification requires a person to cease distribution and instruct health professionals and device user facilities to cease use of the device
- Require a mandatory recall by the device manufacturer or importer. *21 C.F.R. § 810.13*
  - Recall order may specify the extent of and timetable for the recall and may require the manufacturer or importer to submit a proposed recall strategy and provide periodic status reports

Administrative Detention

- If during an authorized FDA inspection, the FDA investigator has reason to believe a device is adulterated or misbranded, FDA can order the administrative detention of the device for up to 30 days. FDCA. *Sec. 304(h)*
- During the detention period the device may not be used, moved, altered or tampered with. *Sec. 304(h)*

Import Alerts and Refusal

- Notification that an imported product and/or firm is in violation of the FDCA and permits FDA to detain the products at the border without physical examination

- FDA may refuse shipments in violation of the FDCA, and such shipments must either be destroyed or exported. *FDCA Sec. 801(a)*

Banned Devices

- If a device intended for human use presents substantial deception or an unreasonable and substantial risk of illness or injury, which cannot be corrected by a labeling change, FDA can issue a ban for the device. *FDCA Sec. 516(a)*
- FDA has issued or proposed a ban on three medial devices:
  - Issued ban on prosthetic hair fibers in 1983
  - Issued ban on powdered patient examination gloves, powdered surgeon's gloves, and absorbable powder for lubricating a surgeon's gloves in 2017
  - Issued a ban on electrical stimulation devices (ESDs), intended to reduce aggressive or self-injurious behaviors in 2020.
    - The US Court of Appeals for the D.C. Circuit overturned the ban on July 6, 2021.
    - In September, the FDA petitioned the Court for an en banc rehearing of the case.

Use of Publicity

- FDA required to publish "reports summarizing all judgments, decrees, and court orders," and information regarding devices that involve "imminent danger to health, or gross deception of the consumer" *FDCA Sec. 705(a)-(b)*
- FDA frequently publishes safety communications and enforcement reports
- FDA routinely publishes warning letters and some other advisory notices
  - Example: Due to a rise in needle-free devices for injection of facial fillers, the FDA published a safety communication in October 2021, to alert the public that these devices have not been approved and can result in serious and permanent injury


FDA

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← Safety Communications

Do Not Use Needle-Free Devices for Injection of Dermal Fillers - FDA Safety Communication

Share Tweet LinkedIn Email Print

Date Issued: October 8, 2021

The U.S. Food and Drug Administration (FDA) is warning the public and health care professionals not to use needle-free devices such as hyaluron pens for injection of hyaluronic acid (HA) or other lip and facial fillers, collectively and commonly referred to as dermal fillers or fillers.

The FDA is aware of serious injuries and in some cases, permanent harm to the skin, lips, or eyes with the use of needle-free devices for injection of lip and facial fillers.

Judicial Enforcement Tools

- Seizure
- Civil Money Penalties
- Injunction
- Criminal Prosecution/Fines

Seizure

- Action taken to remove a device from commerce that is found to be in violation of the law. *FDCA Sec. 304(a)*
- FDA files complaint with U.S. District Court where the product is located to initiate the seizure
- Court directs US Marshall to take possession of the goods until the matter is resolved
  - Lot-specific seizure – all units in a specific lot or batch of a product
  - Open-ended seizure – all units of a certain product
  - Mass seizure – all products and equipment at an establishment/facility
  - Multiple seizures – same product in more than one district court

Civil Money Penalties

Civil Money Penalties

- Civil money penalty complaint used to initiate administrative legal action for violations of the FDCA relating to devices, hearing with CDRH
- May result in entry of a consent decree and civil penalty of up to $15,000 for each such violation, and up to $1,000,000 for all such violations adjudicated in a single proceeding. *FDCA Sec. 303(f)(1)(A)*

CMP Example: Globus Medical

- Device manufacturer Globus Medical submitted 510(k) for its NuBone Osteoinductive Bone Graft product
- FDA declined to grant 510(k) clearance, finding the product was not substantially equivalent to identified predicate devices, but the manufacturer continued distribution of the device
- FDA filed complaint for civil money penalties against the Company and its CEO for distributing an unapproved medical device
- In 2012, the company agreed to pay penalty of $550,000 and the CEO agreed to pay $450,000, for a total of $1 million

Injunction

- Judicial action taken against an individual or firm to stop continued production or distribution of a violative device. *FDCA Sec. 302*
- FDA files complaint, which alleges specific violations against firm or individuals and identifies the relevant history of noncompliance and continuing violations
- Complaint seeks to restrain and enjoin the firm and individual from continuing to manufacture and distribute device unless and until certain remedial actions are taken

Injunction

- Consent decree of permanent injunction may be entered
- Consent decree generally will:
  - Require company to cease violative activity
  - Require company to remedy violations (hiring of consultants to assist is often necessary)
  - Require company to come into compliance prior to resuming operations and distribution of device, as confirmed through FDA inspection
  - Require Company to pay fees to FDA for continued FDA supervision and inspection
- Generally, five years of continuous compliance required before consent decree will be vacated

Injunction Example: Philips

- In October 2017, DOJ filed a complaint against Philips, an automated external defibrillator manufacturer, alleging cGMP violations, including issues with design verification and validation controls
- Philips entered into a consent decree which permits the company to continue manufacture and distribution of certain models, and does not require a recall of AEDs currently in use
- Consent decree requires Philips to suspend the manufacture and distribution of AEDs manufactured at certain facilities, until FDA certifies compliance of the facility's Quality System Regulation
- Decree also requires Philips to pay 30% of net revenue from the sale of certain devices to the US Treasury

Criminal Prosecution

- Criminal proceedings can be initiated against any person who violates any provision listed in section 301 of the FDCA. *FDCA Sec. 303(a)*
- Person includes any individual or corporation. *Sec. 201(e)*
- Any violation of section 301 of the FDCA can result in a misdemeanor charge, regardless of intent. If the violation is committed with the "intent to defraud or mislead," a 3 year felony violation can be charged
- DOJ has the authority to initiate criminal proceedings on its own initiative, without a referral from FDA

Criminal Fines

- While the FDCA lists applicable fines in Section 303, fines are more typically imposed under 18 U.S. Code § 3571:
  - up to $250,000 for individuals for a felony or for a misdemeanor resulting in death
  - up to $100,000 for an individual for a misdemeanor that does not result in death
  - up to $500,000 for an organization for a felony or for a misdemeanor resulting in death
  - up to $200,000 for a misdemeanor that does not result in death
- Fines can also be based on gain or loss
  - A defendant can be fined not more than the greater of twice the gross gain or loss unless such a fine would unduly complicate sentencing

Criminal Proceedings Example: Pentax

U.S. v. Pentax of America, Inc. (April 2020)

- Pentax charged with distributing devices misbranded within the meaning of 21 U.S.C. § 352(f) (Sec. 502(f) of FDCA in connection with alleged deliberate decision not to use revised FDA-cleared instructions for cleaning endoscopes because of a fear that longer cleaning process would upset customers.
- Pentax also charged with distributing devices that were misbranded within the meaning of 21 U.S.C. 352(t)(2) (Sec. 502(t)(2) of FDCA) due to company's failure to report known infection incidents associated with its endoscope.
- Company enters into three-year Deferred Prosecution Agreement that allows it to avoid conviction if it complies with enhanced compliance requirements. Also agrees to pay a $40 million criminal fine and to forfeit $3 million.

Criminal Proceedings Example: Acell

U.S. v. Acell Inc. (June 2019)

- Acell enters into $15 million settlement to resolve criminal and civil FCA charges.
- “Silent recall” case: ACell allegedly removed its wound dressing powder MicroMatrix from the market, but did not report it to the FDA or providers in violation of 21 U.S.C. § 331(q)(1)(b) (Sec. 301(q)(1)(b)) .
- Admitted that more than 30,000 MicroMatrix devices were contaminated with endotoxin levels and due to health risk, initiated removal but concealed the reason for the product removal from doctors, hospitals, and the company’s own sales force, and did not notify doctors who had already used MicroMatrix devices from the lots subject to removal of the elevated endotoxin levels.
- Civil FCA settlement involves allegations of misleading marketing of MicroMatrix as safe and effective for internal use when indicated for topical use only, among other allegations.

Criminal Proceedings Example: Facteau

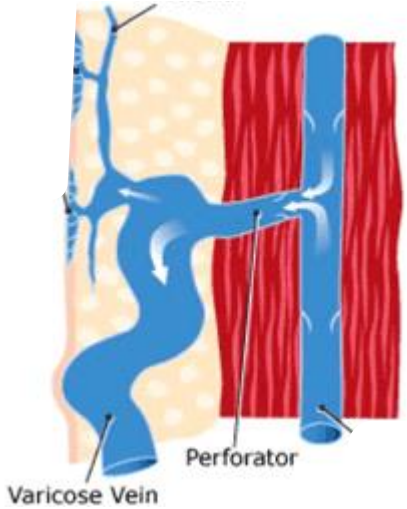
U.S. v. Facteau et al. (2016)

- Facteau and Fabian, two former Acclarent executives, were charged with distributing devices that were misbranded and adulterated because, among other reasons, the devices were distributed solely for an uncleared and unapproved use (the delivery of steroid drugs) rather than for the cleared use as a sinus spacer that could also elute saline to moisten the area following sinus surgery
- Executives were also indicted for conspiracy, securities fraud, wire fraud, and both felony and misdemeanor counts of introducing an adulterated and misbranded device into interstate commerce under the FDCA
- Executive were **convicted** in July 2016 of 10 misdemeanor FDCA adulteration and misbranding counts but were **acquitted** of 14 felony counts of fraud
- Convictions currently on appeal to 1st Circuit.

Criminal Proceedings Example: VSI

U.S. v. Vascular Solutions, Inc. (2016)

- Device manufacturer, Vascular Solutions, and CEO were charged with distributing devices that were misbranded because no 510(k) notification had been submitted for one of its marketed off-label uses, the treatment of perforator veins (device cleared to treat superficial varicose veins)
- District court charged the jury that "solely truthful and not misleading" speech could not be the basis for misbranding conviction
- Jury acquitted manufacturer and CEO of all charges in Feb. 2016.



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- Other Enforcement/Remedial Possibilities

Authority to Conduct Inspections

- FDCA Sec. 704 expressly authorizes FDA inspections
- FDA Reauthorization Act of 2017
  - Requires FDA to conduct establishment inspections using a risk-based approach that considers the establishment's compliance and recall history, FDA inspection frequency and history, and the inherent risk of devices manufactured at the establishment
  - Requires FDA to establish uniform processes and standards for routine inspections of both domestic and foreign device establishments, which must include providing notification of the type and nature of the inspection within a reasonable time before such inspection occurs

Authority to Conduct Inspections

FDA permitted to:

- Enter at reasonable times. *FDCA Sec. 704(a)(1)*
- Inspect within reasonable limits and in a reasonable manner upon presenting appropriate credentials and written notice to the owner (Form 482). *Sec. 704(a)(1)*
- Access, copy, and verify any FDA-required records or documentation. *Sec. 704(a)(3)*
  - GMP records must be readily available for review and copying by FDA. *21 C.F.R. § 820.180*

Scope of Inspections

- Under FDCA Sec. 704(a), FDA may inspect:
  - Any factory, warehouse, or establishment where a product is manufactured, processed, packaged, or held. Any vehicle used for transport of product. All pertinent equipment, finished and unfinished (in process) materials, containers, and labeling.
  - All records that must be maintained under the regulations.
- However, FDA may not inspect:
  - Financial, sales, or pricing data; personnel data, other than job qualifications; research data, except data subject to FDA review for product license approval.

Scope of Inspections

Other Inspection issues:

- The status of privileged documents in the context of FDA inspections has not been tested in litigation
- By policy, FDA does not demand access to internal audit reports as part of routine inspections
- Companies may consent to broader FDA inspections than authorized by the FDCA
- Photographs

Types of Inspections

- Routine GMP inspection
- PMA preapproval and post-market inspections
- "For cause" inspection
  - Previous violative inspection
  - Recall
  - Consumer complaints
  - Competitor complaints

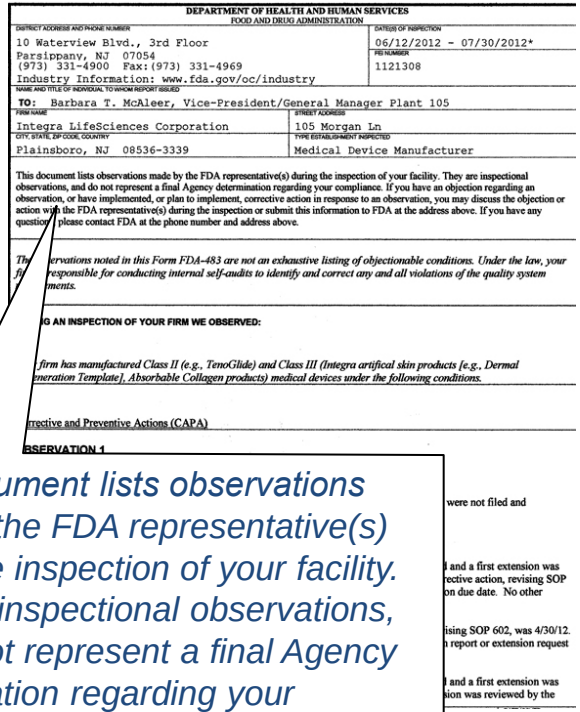
Typical GMP/QSR Inspection Activities

- Presentation of FDA Form 482 (Notice of Inspection)
- Document review, employee interviews, questions and answers
- Observations of operations
- Daily/periodic investigator debriefs
- Efforts to resolve potential observations
- Presentation of Form 483 (Notice of Inspectional Observations), if applicable, and “discussion with management”
  - After each FDA inspection, FDA investigators prepare an establishment inspection report (EIR), which contains a narrative of inspectional observation, and will release the report once the inspection is “closed” under 21 C.F.R. § 20.61(d)(3)

FDA Actions for Findings of Non-Compliance

- 483 Response and follow-up correspondence
  - Following issuance of a 483, FDA requires firms to provide a response to the 483 observations within 15 business days
- Warning Letter
  - May be immediately issued or issued after FDA receives and reviews the firm's 483 response (if FDA finds the firm's corrective actions are inadequate)
- Recall
- Injunction or Product Seizure
- Consent Decree of Permanent Injunction

483 vs. Warning Letter: A Distinction with a Difference



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054
(973) 331-4900 Fax:(973) 331-4969
Industry Information: www.fda.gov/oc/industry

DATE(S) OF INSPECTION
06/12/2012 - 07/30/2012*

FEI NUMBER
1121308

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: Barbara T. McAleer, Vice-President/General Manager Plant 105

FIRM NAME
Integra LifeSciences Corporation

STREET ADDRESS
105 Morgan Ln

CITY, STATE, ZIP CODE, COUNTRY
Plainsboro, NJ 08536-3339

TYPE ESTABLISHMENT INSPECTED
Medical Device 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.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

...G AN INSPECTION OF YOUR FIRM WE OBSERVED:

...firm has manufactured Class II (e.g., TenoGlide) and Class III (Integra artifical skin products [e.g., Dermal ...neration Template], Absorbable Collagen products) medical devices under the following conditions.

...rrective and Preventive Actions (CAPA)

...BSERVATION 1

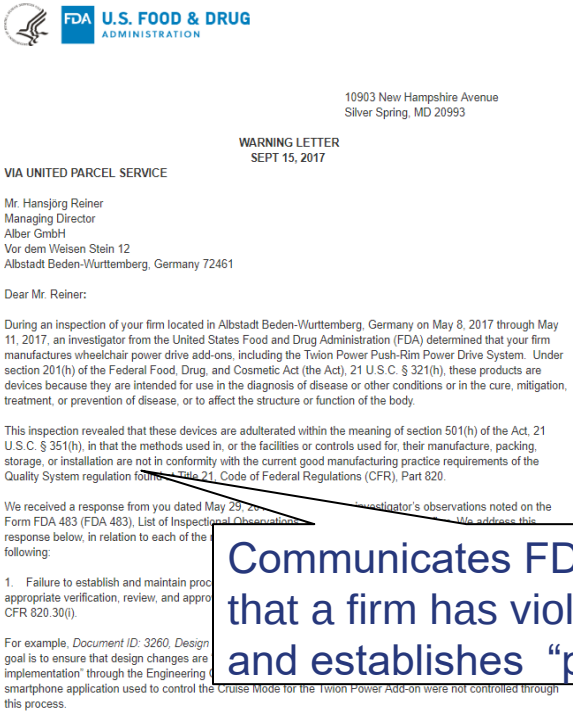
...were not filed and

...d and a first extension was ...rective action, revising SOP ...on due date. No other

...ising SOP 602, was 4/30/12. ...report or extension request

...d and a first extension was ...sion was reviewed by the

"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."



U.S. FOOD & DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER
SEPT 15, 2017

VIA UNITED PARCEL SERVICE

Mr. Hansjörg Reiner
Managing Director
Alber GmbH
Vor dem Weisen Stein 12
Albstadt Beden-Wurttemberg, Germany 72461

Dear Mr. Reiner:

During an inspection of your firm located in Albstadt Beden-Wurttemberg, Germany on May 8, 2017 through May 11, 2017, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures wheelchair power drive add-ons, including the Twion Power Push-Rim Power Drive System. 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 function of the body.

This inspection revealed that these 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, their manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation found in Title 21, Code of Federal Regulations (CFR), Part 820.

We received a response from you dated May 29, 2... ...investigator's observations noted on the Form FDA 483 (FDA 483), List of Inspectional Observations... ...We address this response below, in relation to each of the ... following:

1. Failure to establish and maintain proc... appropriate verification, review, and appro... CFR 820.30(i).

For example, *Document ID: 3260, Design* goal is to ensure that design changes are ... implementation" through the Engineering ... smartphone application used to control the Cruise Mode for the Twion Power Add-on were not controlled through this process.

Communicates FDA's position that a firm has violated the law and establishes "prior notice"

Inspection Classifications

- **NAI** – “No action indicated”
  - No objectionable conditions or practices were found during the inspection (or the objectionable conditions found do not justify further regulatory action)
- **VAI** - “Voluntary action indicated”
  - Objectionable conditions or practices were found, but FDA is not prepared to take or recommend any administrative or regulatory action
- **OAI** – “Official action indicated”
  - Objectionable conditions or practices found and regulatory and/or administrative actions will be recommended

FDA Inspections Are Not Optional

- Under Sec. 301(f), it is a prohibited act to refuse to permit entry or inspection as authorized by Section 704

Agenda

- FDA Jurisdiction: Prohibited Acts
- FDA Enforcement Tools
- FDA Inspections
- **Relevant Actors at FDA/DOJ**
- Other Enforcement/Remedial Possibilities

Relevant Actors at FDA/DOJ

FDA/HHS

Product Center Review Divisions

Compliance Personnel

Office of Regulatory Affairs (ORA)

Office of Chief Counsel (OCC)

Office of Criminal Investigations (OCI)

HHS-Office of Counsel of Inspector General (OCIG)

DOJ

Consumer Protection Branch

U.S. Attorneys' Offices

Civil Frauds Section

Criminal Frauds Section

Other Investigators

Other Investigative Agencies

FBI, HHS-OIG, VA-OIG, DCIS…

Agenda

- FDA Jurisdiction: Prohibited Acts
- FDA Enforcement Tools
- FDA Inspections
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- **Other Enforcement/Remedial Possibilities**

Other Enforcement/Remedial Possibilities

- DOJ criminal enforcement under Title 18 provisions, *e.g*. mail fraud, wire fraud, conspiracy
- Injunctions against fraud under 18 USC § 1345
- False Claims Act Actions
- Office of Inspector General
- Federal Trade Commission
- Securities and Exchange Commission
- State enforcement, *e.g.* state FDCA statutes, consumer protection laws
- Tort liability

Fraud Injunction Example: Tatum

- In August 2020, the U.S. District Court for the Western District of Texas ordered a permanent injunction to prevent Living Health Holistic Healing Center and its owner from advertising or performing COVID-19 tests.
- The clinic and Tatum misled the public into believing that they were qualified to administer COVID-19 tests and to interpret the results of such tests
- Additionally, the tests Tatum sold were not authorized by the FDA
- Entered a consent decree of permanent injunction, which enjoined defendants from committing mail or wire fraud, ordering or receiving any device purported to perform COVID-19 testing, and performing COVID-19 testing or any services related to COVID-19 testing.

Securities Fraud Examples:

- **U.S. v. Mark Schena (June 2020):** DOJ filed a criminal complaint against the president of a medical technology company charging one count of securities fraud and one count of conspiracy to commit health care fraud based on allegations that the executive made false claims about the company's ability to provide accurate, fast, reliable and cheap COVID-19 testing with its finger-prick blood allergy test technology, despite notice from FDA that the test did not perform at an acceptable level.
- **U.S. v. Keith Berman (Dec. 2020):** A federal grand jury indicted the CEO of a medical device company for his participation in an alleged scheme to defraud investors regarding a purported COVID-19 finger-stick test.
  - The executive allegedly made numerous false and misleading statements to investors, including falsely claiming that the company had developed a 15- second test to detect COVID-19, when, in fact, the test had never been properly validated.
  - The executive also allegedly told investors that FDA would soon approve a request for an emergency use authorization for the test, despite knowing that FDA would not authorize the test without reviewing results from required clinical testing that the company had not performed.

Questions?

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