2024 Regulatory Update – CDRH Trends and Key Developments

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Founded in 2004, Boston MedTech Advisors has worked with more than 400 medical technologies and life sciences companies.

Celebrating 20

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About Boston MedTech Advisors

Our Mission

We assist medical technology companies and healthcare providers to achieve their business goals, offering ethical, result-oriented insights that recognize the multi-faceted aspects of today's healthcare markets and the client's unique business needs.

Our Business

We support our clients to commercialize new products and services and increase their market adoption, by addressing their unique and inter-dependent regulatory, clinical evidence, reimbursement, and marketing and requirements and strategies.

Our Operating Principles

Provide optimal solutions. Recognize the multi-faceted aspects of today's healthcare markets and the client's unique business needs.

Maximize value. Deliver high quality services at a reasonable cost.

Establish ongoing relationships. Align our incentives with those of our clients and partners.

Driving Value to Our Clients

Our Expertise

Principals of Boston MedTech Advisors are entrepreneurs, founding their own medtech and healthcare service companies, leveraging their extensive management, product development, marketing, reimbursement, regulatory, clinical affairs and business development capabilities.

Our diverse Clients

We support **start-ups, private and public companies, not-for-profit organizations, investors and multi-nationals**.

Our extensive network

We provide access to an extensive network of industry, healthcare providers, academia, investors and business partners.

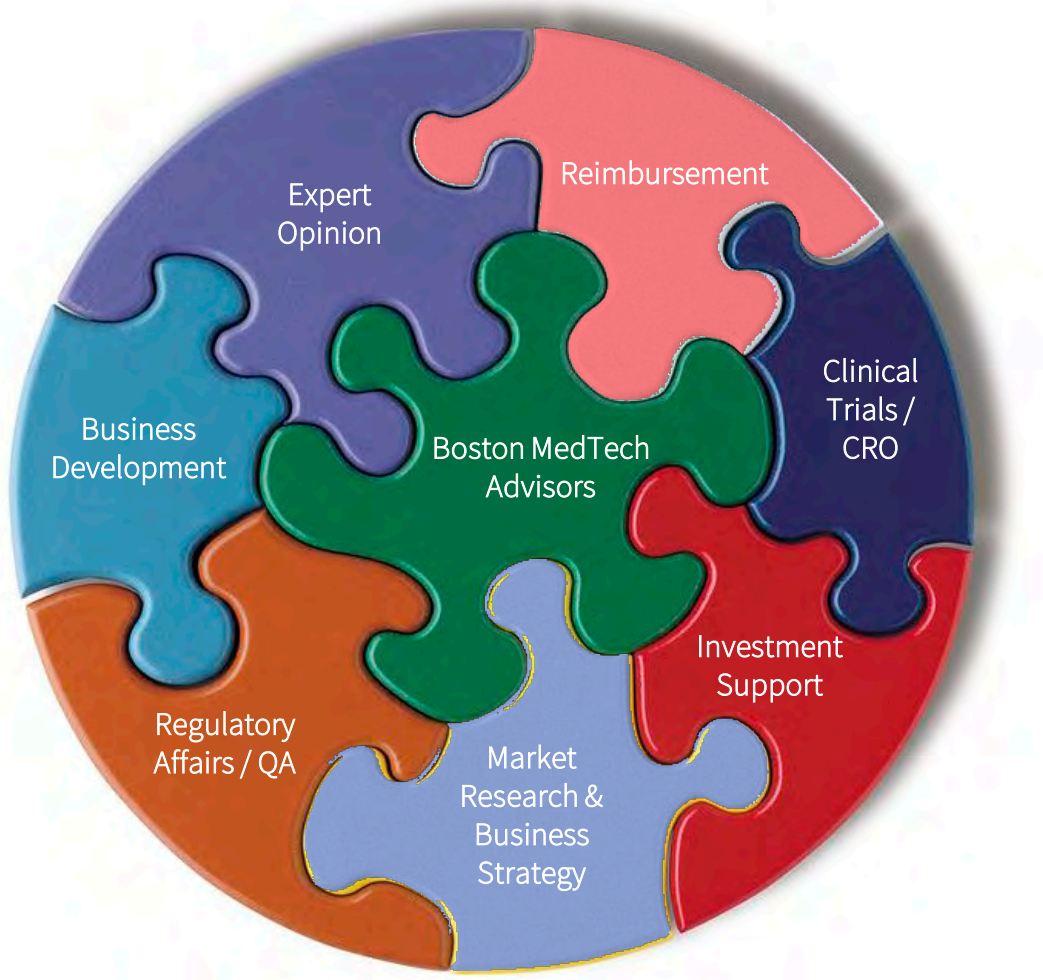
Our Hands-On Experience

We have hands-on working experience within the US and European healthcare systems.

- Broad industry experience, spanning diverse medical specialties.
- Excellent submission and communication history with the FDA and other regulatory agencies.
- Successful record of strategizing and implementing reimbursement solutions.
- Developing and executing marketing and business plans for new technologies and clinical services.
- Financing of early-stage companies.

The Benefits of Working with Boston MedTech Advisors

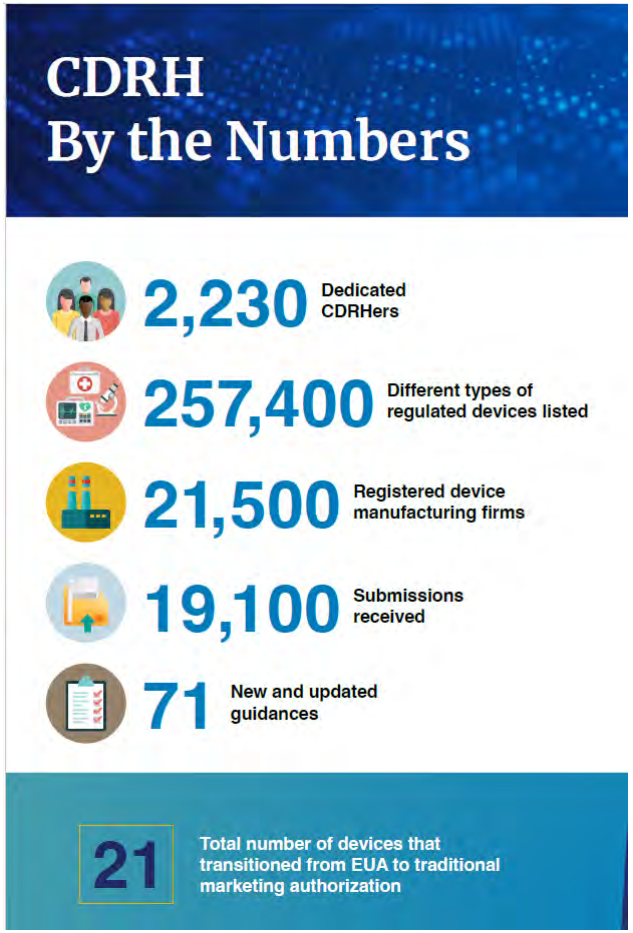
- Active involvement by an experienced team, dedicated to helping your company successfully develop and execute its plans.
- Receiving comprehensive support, tailored to the specific needs of each organization, whether an early-stage or an established company.
- Recognizing significant efficiencies by working with a single entity offering integrated strategy development, planning and execution services.



Experiences *(partial list)*

Aesthetic Medicine	Allergy	Ambulatory Monitoring	Anesthesiology	Biologics	Biomarkers	Brain / Neurosurgery	Cancer Therapies
Cardiology	Cellular Therapies	Critical Care	Cryosurgery	Dermatology	Diabetes	Digital Health	Drug Delivery
Drug / Device Combinations	Durable Medical Equipment	Emergency Medicine	Endoscopy	Gastroenterology	General Surgery	Health IT	Healthcare Services
Hematology	Hepatology	Home Care	Hypertension	Hyperthermia	Interventional Cardiology	In-Vitro Diagnosis	Interventional Radiology
Light-Based Therapies	Neurology	NICU	Ophthalmology	Orthopedic	Pain	Patient Monitoring	Pathology
Pulmonary	Radiology / Imaging	Rehabilitation Medicine	Renal	Robotics / Navigation Systems	Sleep Medicine	Speech Therapy	Spine Surgery
Surgical Simulation	Telemedicine	Transfusion Medicine	Urology	Vascular Medicine	Wearable Devices	Wellness / mHealth	Wound Care

2023 for FDA's CDRH



Device Innovation

15 STeP requests enrolled	29 Submissions designated as Breakthrough Devices received marketing authorization
124 Novel devices received marketing authorization	167 Submissions designated as Breakthrough Devices

[2023 CDRH Annual Report](https://www.fda.gov/media/175479/download?attachment)
https://www.fda.gov/media/175479/download?attachment

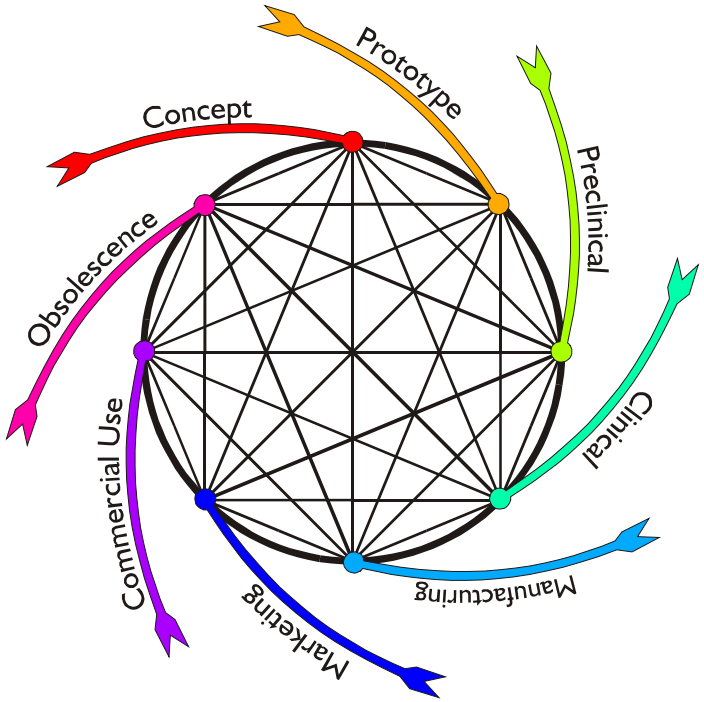
Key Accomplishments – 2023

- Transformative year – Public Health Emergency (PHE) ended May 2023
  - From pandemic era operation to:
    - Sustainable workload
    - Normal review times for all incoming premarket submissions
- Authorizing the highest number of novel devices on record (excluding EUAs) in CDRH's more than 40-year history
  - First over the counter (OTC) fentanyl test – **cleared in 16 days**!
- Total Life Cycle Advisory Pilot (TAP) – Foster innovation in medical devices
  - Improve predictability
  - Reduce time and cost of "valley of death" from concept to commercialization
  - Improve patient access to safe, high-quality, transformative medical devices
  - Spur greater investment in innovative device development
  - Maintain FDA's rigorous standards for device safety and effectiveness
- Expanded Breakthrough Devices Program
  - Technology involving artificial intelligence and machine learning (AI/ML)
- Patient safety / Risk mitigation
  - Cybersecurity
    - 10-year anniversary of CDRH's Cybersecurity Program
    - New authority from Congress in FY2023 Omnibus legislation
- Strategic priorities 2022 – 2025
  - Prioritized diversity, equity, inclusion and belonging in hiring
  - Enhanced employee engagement and wellness programs

Medical Device User Fee Amendments (MDUFA) V

- Review Timelines
  - Exceeded by 20% pre-submission goal of providing written feedback to an applicant within 70 calendar days or five days prior to a meeting 75% of the time.
  - In spite of having the highest volume in a decade of premarket submissions
- 510(k) Electronic submissions
  - Electronic submissions template (eSTAR)
- Expanded submissions progress tracking
  - Now includes Pre-Sub Packages
- Total Product Life Cycle (**TPLC**) Advisory Program (TAP) Pilot
  - Earlier and more frequent interaction with industry
    - 15 Breakthrough-designated devices from Office of Cardiovascular Devices
    - Expanded to devices reviewed by Office of Neurological and Physical Medicine Devices

TPLC



From FDA Presentation by David Feigal, MD May 23, 2001

Device Shortages

- Resilient Supply Chain Program (RSCP)
  - Assures patient access to critical life-saving life-supporting medical devices
  - Established during COVID-19 PHE
  - Works with manufacturers, distributors, healthcare providers
  - Prevent and mitigate shortages and improve resiliency of US medical device supply chain
- Information sharing
  - Public shortages list
  - Public-private partnerships / device manufacturers and trusted third party
  - Guidances
    - Notifying FDA of permanent discontinuance or interruption in manufacturing
    - Updates of devices affected during PHEs
- Currently (post-PHE) – voluntary program(!)

https://www.fda.gov/medical-devices/medical-device-supply-chain-and-shortages/medical-device-shortages-list

Category	Product Code (Description)	Availability and Estimated Shortage Duration[2]	Additional Information	Reason for Interruption (per 506J)	Date (YYYY/MM/DD)[3]
Cardiovascular - Circulatory Support, Structural and Vascular Devices	**BYS** (Oxygenator, Long Term Support Greater Than 6 Hours)	• Estimated through summer of 2024.	Oxygenator devices intended for extracorporeal circulation are in shortage.	• Shortage or discontinuance of a component, part or accessory of the device.	2023/09/11 Initial
Cardiovascular - Circulatory Support, Structural and Vascular Devices	**DTZ** (Oxygenator, Cardiopulmonary Bypass)	• Estimated through summer of 2024.	Oxygenator devices intended for extracorporeal circulation are in shortage.	• Shortage or discontinuance of a component, part or accessory of the device.	2023/09/11 Initial
Cardiovascular - Circulatory Support, Structural and Vascular Devices	**DSP** (Intra-aortic Balloon and Control System)	• Data not available to estimate duration at this time.[5]	To provide recommendations to health care providers and facilities who use these devices, the FDA is providing IABP Shortage - Letter to Health Care Providers	• Demand increase for the device • Shortage or discontinuance of a component, part or accessory of the device	2022/12/02 Initial 2023/01/20 Reverified

Modernizing 510(k) Program

- Limitations of 510(k) program
  - The concept of ‘substantially equivalent’
  - Introduction of new technologies
  - Obsolescence of ‘old’ predicates
- New draft guidance documents, including:
  - Use of clinical data in premarket submissions
    - https://bmtadvisors.com/fda-draft-guidance-issued-on-the-use-of-clinical-data-in-premarket-notification-510k-submissions/
  - Selecting predicate device to support premarket notification
    - https://bmtadvisors.com/new-draft-guidance-document-on-selecting-a-predicate-device-to-support-a-premarket-notification-510k-submission/
  - Biocompatibility / contact with skin
    - https://bmtadvisors.com/final-biocompatibility-guidance-update-on-devices-in-contact-with-intact-skin/
  - Evidentiary expectations for implant devices
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/evidentiary-expectations-510k-implant-devices

Novel Devices

- Novel = benefit to patients
  - Unmet need / Safer / More effective
- 124 novel devices received marketing authorization
- X5 increase compared to 2009

23andMe Granted New FDA Clearance to Report Additional BRCA Variants

August 31, 2023

510(k) clearance will allow 23andMe to report an additional 41 genetic variants in the BRCA1 and BRCA2 genes that increase risk for breast, ovarian, prostate and pancreatic cancer

Breaking News: Snoo is FDA De Novo Authorized!

All Test – Fentanyl Urine Test Cassette – CLIA Waived

Owlet – FDA-cleared BabySat, FDA-cleared Dream Sock

Endolumik – Illuminating Possibilities

1st STeP (Safer Technologies Program) authorized for marketing

Expediting Premarket Submissions

Breakthrough Devices

"…provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions."

Eligibility – First Criterion and at least one of Second Criterion

Criteria	Description
First Criterion	The device provides for **more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions**
Second Criterion	The device also meets **at least one** of the following:
	a) Represents Breakthrough Technology
	b) No Approved or Cleared Alternatives Exist
	c) Offers Significant Advantages over Existing Approved or Cleared Alternatives
	d) Device Availability is in the Best Interest of Patients

https://bmtadvisors.com/fda-updates-on-the-breakthrough-devices-program/

Safer Technologies (STeP)

"…reasonably expected to significantly improve the safety of currently available treatments or diagnostics that target an underlying disease or condition associated with morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program"

Eligibility – First Eligibility Factor and at least one of Second Eligibility Factor

Criteria	Description
First Eligibility Factor	**Not eligible for the Breakthrough Devices Program** due to the less serious nature of the disease or condition treated, diagnosed, or prevented by the device
Second Eligibility Factor	Should be reasonably expected to significantly improve the benefit-risk profile of a treatment or diagnostic through substantial safety innovations that provide for at least one of the following:
	a) A reduction in the occurrence of a known serious adverse event
	b) A reduction in the occurrence of a known device failure mode
	c) A reduction in the occurrence of a known use-related hazard or use error
	d) An improvement in the safety of another device or intervention

Expedited Review Programs

- 167 devices granted Breakthrough Device designations (2023)
  - 921 devices received designation (total)
- 29 Breakthrough devices received marketing authorizations (2023)
- Updated guidance
  - Devices that benefit populations impacted by health and/or healthcare disparities
  - Non-addictive medical products to treat pain or addiction

- Safer Technologies Program (STeP)
  - Safer devices not qualifying for Breakthrough designation
  - Faster/better interaction with FDA reviewers
  - 15 devices enrolled in program (2023)
    - Total – 35 devices in program

Digital Health Revolution Update

- Digital health: mHealth apps, telemedicine, electronic health records (EHRs), wearable devices, remote patient monitoring systems, healthcare analytics, and artificial intelligence (AI) applications.
- 77% of US adults have smartphones (>250M users)[1]
- 2023 – 40% of US adults use healthcare-related apps, and 35% use wearable healthcare devices[2]
  - Up by 6% and 8%, respectively since 2018
- >350,000 mHealth apps available[3]; >90,00 new introduced in 2021
- 77% of young adults (18-29) used smartphone to look up health conditions
- 2023 – global mHealth app market reached $49.2B[4]
- 2030 (expected) >$105B market[4]

1. https://www.bankmycell.com/blog/how-many-phones-are-in-the-world
2. Morning Consult survey data
3. According to numbers cited by IQVIA in a Medical Device Network article from 2021
4. Home » Healthcare IT » Global mHealth Apps Market Size & Trends Report, 2030 https://www.grandviewresearch.com/industry-analysis/mhealth-app-market#

Digital Health Innovation (2023)

- Challenges of artificial intelligence (AI) / machine learning (ML) devices
- To date CDRH authorized 692 AI/ML-enabled devices (>100 devices in 2023 alone)[1] and 38 Augmented Reality (AR) / Virtual Reality (VR) devices[2]
- FDA established specialized center and committee to explore DHTs such as AI/ML, AU/VR, digital therapeutics, wearables, remote patient monitoring and software.
  - Digital Health Center of Excellence (DHCoE) (9/2020)
  - Digital Health Advisory Committee (10/2023; should be fully operational in 2024)
- 2023
  - DHCoE responded to over 900 inquiries
  - Guidance Documents
    - Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions (4/3/2023)
    - Content of Premarket Submissions for Device Software Functions (6/14//2023)

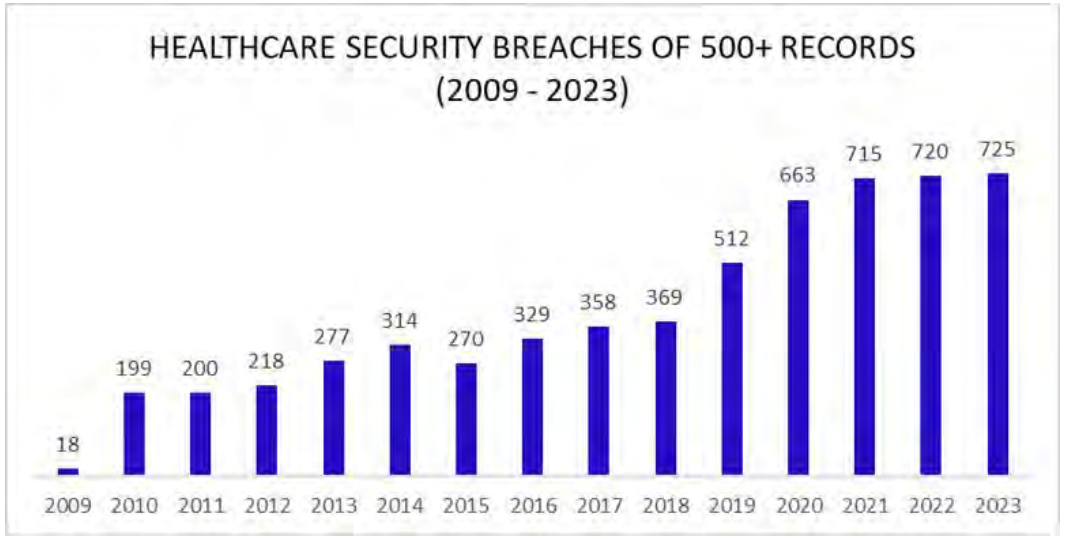
1. https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices
2. https://www.fda.gov/medical-devices/digital-health-center-excellence/augmented-reality-and-virtual-reality-medical-devices

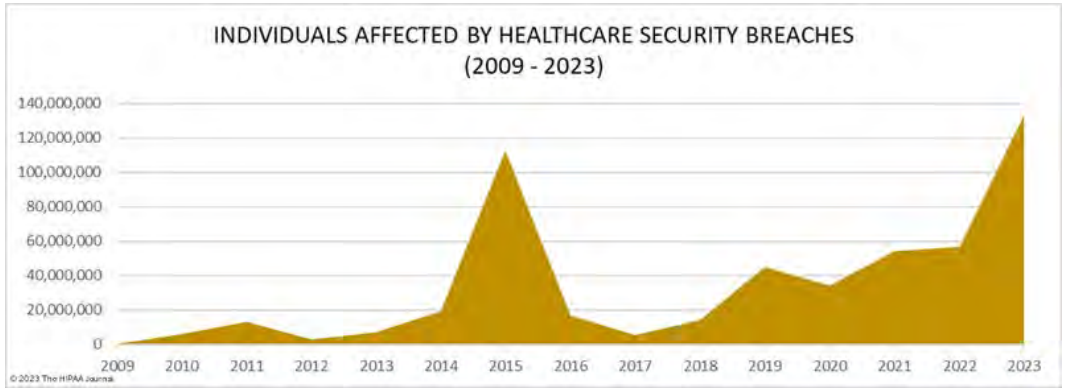
Laboratory Developed Tests (LDT)

- In vitro diagnostic products (IVDs), including LDTs, used to measure or detect substances, analytes or markers in the body
  - Proteins, glucose, cholesterol or DNA
  - Provide information about a patient's health
    - Detect, monitor, or determine treatment for diseases and conditions.
- Testing devices vs. LDTs
- Challenges presented by increasingly complex LDTs
- Proposed rule aimed at helping to ensure the safety and effectiveness of LDTs, used in a growing number of health care decisions and for which the FDA's concerns have increased in recent years (October 2023)
  - https://bmtadvisors.com/fdas-proposed-new-rule-on-laboratory-developed-tests-ldts/
- The proposed rule would amend FDA's existing regulations to make explicit that
  - IVDs are devices under the FD&C Act, including when the manufacturer is a laboratory
  - Includes a phaseout of the general enforcement discretion approach for most LDTs

This proposed rule is an important step in the FDA's work to address LDTs

Cybersecurity Breaches – 2023





https://www.hipaajournal.com/wp-content/uploads/2024/01/Security_Breaches_In_Healthcare_in_2023_by_The_HIPAA_Journal.pdf

https://www.hipaajournal.com/2023-healthcare-ransomware-attacks/#:~:text=At%20Least%20141%20Were%20Hospitals%20Directly%20Affected%20by%20Ransomware%20Attacks%20in%202023,-Posted%20By%20Steve&text=Last%20year%20was%20a%20particularly,2022%20and%2027%20in%202021.

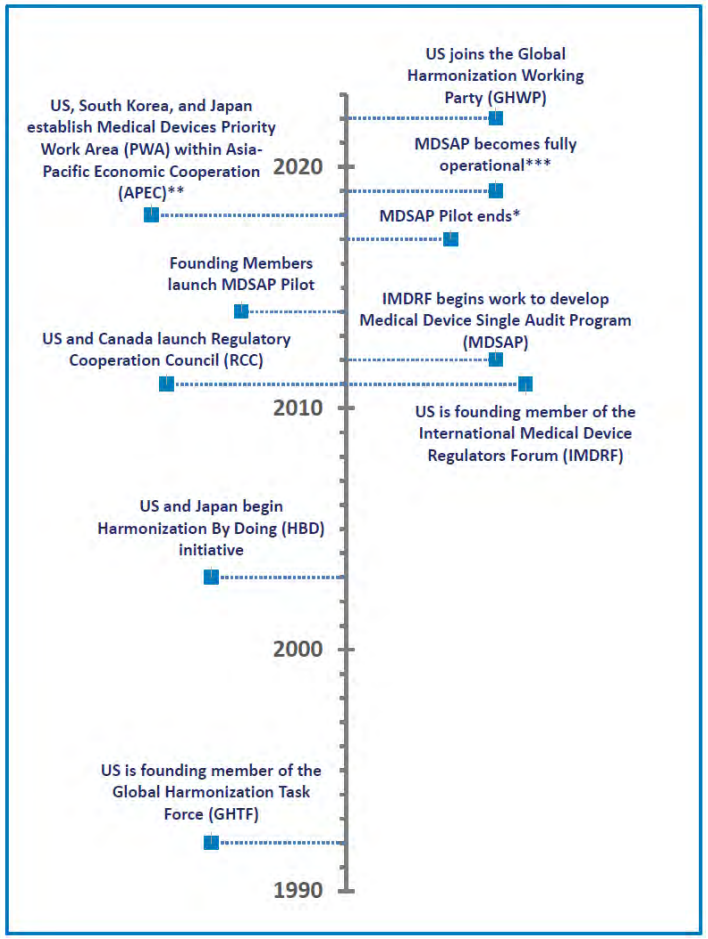
Cybersecurity

- 10th anniversary of CDRH's cybersecurity program
- Spearheaded international medical device cybersecurity risk management efforts through the co-chairing of the International Medical Device Regulators Forum (IMDRF) Cybersecurity Working Group
- Published two final guidances this year on key cybersecurity topics
  - https://bmtadvisors.com/cybersecurity-in-medical-devices-final-fda-guidance-document/

2023 CDRH Annual Report
https://www.fda.gov/media/175479/download?attachment

Promoting International Alignment of Regulations and Standards

- Engagement with international regulatory agencies
- Promote alignment in
  - Regulations
  - Standards
- International harmonization
  - Reduce barriers
  - Important public health impact
- Draft International Harmonization Strategic Plan
  - Encourage harmonization, convergence, reliance among medical device regulatory authorities



CDRH International Harmonization Draft Strategic Plan, 2023

Thank You!

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