Compass Life Science Solutions LLC

SaMD within the Life Sciences Industry

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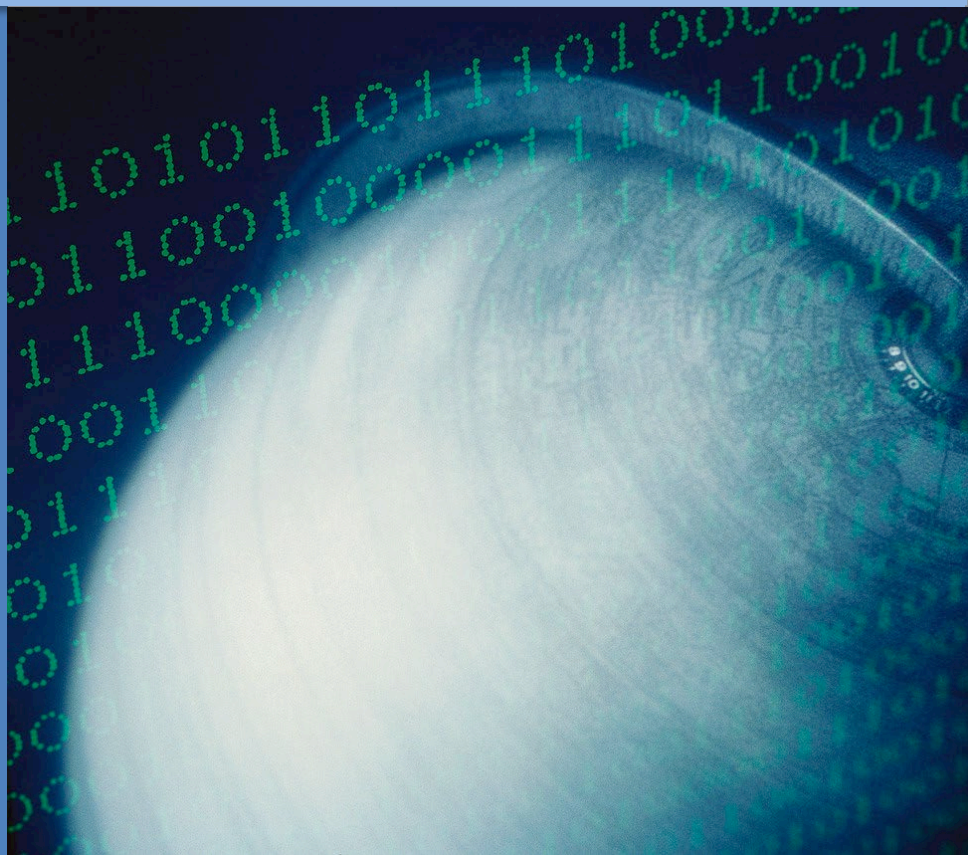

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Presentation Overview

- Challenges related to the use of these new technologies
- Applicable regulations and guidance documents
- Classifying Software as a Medical Device (SaMD) based on U.S. and international guidance
- Impacts of how a company's use of a software product impacts the classification of SaMD
- How a Life Sciences company can unintendedly become a specification owner for a SaMD after purchasing software
- Software development and validation practices for different types of SaMD

Background

- FDA – “Use of Software as a Medical Device is continuing to increase. It can be used across a broad range of technology platforms, including medical device platforms, commercial "off-the-shelf" platforms, and virtual networks, to name a few. Such software was previously referred to by industry, international regulators, and health care providers as "standalone software," "medical device software," and/or "health software," and can sometimes be confused with other types of software.

Background

- MDR – “It is necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of a medical device, qualifies as a medical device, while software for general purposes, even when used in a healthcare setting, or software intended for life-style and well-being purposes is not a medical device.”

Background

- IVDR – “It is necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of an in vitro diagnostic medical device, qualifies as an in vitro diagnostic medical device, while software for general purposes, even when used in a healthcare setting, or software intended for well-being purposes is not an in vitro diagnostic medical device.”

Background

- Life Science Industry Challenges with SaMD
  - Tremendous change has made it challenging for regulators to provide guidance
  - Regulatory agencies have taken different views of the risks related to SaMD
  - Many of the new SaMD manufacturers are struggling with the compliance requirements
  - Pharma companies face a new type of combination product
  - Drug and treatment efficacy claims are based on SaMD used in clinical trials
  - Significant technological advancements are coming from non-regulated companies

Background

- Mounting evidence is showing that software helps patients and improves treatment
- Software innovations are being used by Life Science companies in ways not intended by the original manufacturer
- SaMD manufacturers want device approval, control, and monitoring methods that better fit the agile and rapid development methodologies used for software development
- Trying to find the right balance between patient safety and innovation

Background

- Compliance Issues
  - Software vendors unexpectedly pursue product registration impacting Pharmaceutical clients and their studies
  - Approved SaMDs evolve without being reclassified
  - Companies make medical claims without proper filings
    - Lumosity $2 Million Settlement to FTC; Deceptive Advertising Brain Training
  - Companies do FDA filings, but do not comply with registration or other regulatory requirements due to lack of enforcement
    - Overall quality system missing
    - Complaint history files missing
    - Some class 1 SaMD companies in US not planning for compliance to UDI
    - SaMDs being used as part of clinical trials in Europe with no CE marking; no evidence of compliance to ISO 14971 or to ISO 13485 or IEC 62304

Background

- Unaddressed Regulatory Issues
  - Data integrity issues where SaMDs are used to improve or ensure drug efficacy. Drugs can be approved with clinical results that may not be maintainable without the SaMD.
  - SaMDs making medical claims or advertising medical benefits of their products prior to their approval
  - SaMDs drawing equivalency to “physical” class 1 medical devices, but complexity is much higher and not accurate comparisons
  - Limited distribution controls
    - SaMDs can be acquired online without medical oversite
    - Patients can be using SaMDs that are not in a country’s boarders
  - SaMD components swapped out interchangeably

Background

- Many SaMD companies do not make the entire product. SaMD companies buy and integrate software from nonregulated SaMD component manufacturers (i.e. facial recognition), which are not complying with regulatory requirements.
- Patient support when SaMD or SaMD component companies go out of business
- When dealing with combination products, pharmacovigilance processes are currently not robust enough to properly identify if seizures, migraines, insomnia, etc. are properly linked to SaMD use instead of the drugs
- Infrastructure and database software are components of the SaMD and need to be controlled as part of technical and design files

Background

- Missing combination product regulations related to SaMD products supporting efficacy claims related to drug efficacy
  - Drug sponsors should be required to maintain software licenses and system access for patients
  - Software licenses should be required to be included as part of drug pricing and kiting
  - Sponsors need to be able to take on technical support responsibilities if SaMD providers go out of business
  - SaMD should be bound to the same record retention requirements as traditional device manufacturers
  - SaMDs should be not interchangeable without evidence of equivalency
  - If SaMD approved as a combination product, drug sponsors should be required to maintain and support code to ensure patient use and efficacy of the drug

Important Terms and Definitions

- Artificial Intelligence (AI) – the theory and development of computer systems able to perform tasks that normally require human intelligence, such as visual perception, speech recognition, decision-making, and language translation
- Combination Product per FDA – is a product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product
- Design History File (DHF) – The collection of documents from the design and development process

Important Terms and Definitions

- Device Master Record (DMR) – The instructions, drawings and other records, that must be used to produce a product
- Device History Record (DHR) – is the production history of the device
- Digital Health - is the use of digital technologies (hardware & software) to enhance the efficiency of healthcare delivery and to help address the health problems and challenges faced by patients.
- Digital Therapeutics – are the digital technologies utilized to treat a medical or psychological condition

Important Terms and Definitions

- Learning, Machine – is the scientific study of algorithms and statistical models that computer systems use to effectively perform a specific task without using explicit instructions, relying on models and inference instead
- Learning, Reinforcement – is an area of machine learning concerned with how software takes actions to maximize success (i.e. robot was able to get out of a maze)
- Learning, Semi-supervised – algorithms are trained on a combination of labeled and unlabeled data

Important Terms and Definitions

- Learning, Supervised – the machine learning task of learning a function that maps an input to an output based on example input-output pairs. It infers a function from labeled training data consisting of a set of training examples
- Learning, Unsupervised – is a branch of machine learning that learns from test data that has not been labeled, classified or categorized. Unsupervised learning identifies commonalities in the data and reacts based on the presence or absence of such commonalities in each new piece of data

Important Terms and Definitions

- Software as a Medical Device (SaMD) per IMDRF – software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device
- Software in a Medical Device (SiMD) per FDA – software that is considered an accessory to hardware medical devices
- Technical File – a set of documents that describes a product and can prove that the product was designed according to the requirements of a quality management system and that the product conforms with EU regulations for CE-marked products

Traditional Regulatory References

- 21 CFR Part 11 – FDA regulation related to electronic records and electronic signatures
- 21 CFR 812 - Investigational Device Exemptions – covers the procedures for the conduct of clinical studies with medical devices including application, responsibilities of sponsors and investigators, labeling, records, and reports
- 21 CFR Part 820 – Quality System Regulation – FDA regulation on the current good manufacturing practices for the methods, facilities, and controls used for the design, manufacture, packaging, labeling, storage, installation, and servicing of medical devices intended for human use

Traditional Regulatory References

- Evaluation of Automatic Class III Designation (De Novo) – a FDA pathway to classify novel medical devices for which there is no legally marketed predicate device
- General Principles of Software Validation – outlines validation principles that the FDA considers applicable to the validation of medical device software or the validation of software used to design, develop, or manufacture medical devices
- IEC 62304:2006 – Medical Device Software Development – Software Life Cycle Processes – defines the requirements and framework for a medical device software life cycle

Traditional Regulatory References

- ISO 14971:2007 – Medical Devices – Application of Risk Management to Medical Devices – specifies a process for a manufacturer to
  - identify the hazards associated with medical devices, including *in vitro* diagnostic (IVD) medical devices
  - estimate and evaluate the associated risks, to control these risks, and to monitor the effectiveness of the controls

Regulatory Developments

- 21st Century Cures Act (12/13/2016) – amended the definition of “device” in the Food, Drug and Cosmetic Act to exclude certain software functions
- Breakthrough Device Program – FDA program which supersedes the Expedited Access Pathway (EAP) and the Priority Review Program for devices
- Digital Health Innovation Action Plan - defines the CDRH’s vision for fostering digital health innovation while continuing to protect and promote the public health

Regulatory Developments

- FDA Digital Health Software Precertification Program – a pilot program initiated to develop a regulatory model that will provide more streamlined and efficient regulatory oversight of software-based medical devices developed by manufacturers who have demonstrated a robust culture of quality and organizational excellence, and who are committed to monitoring real-world performance of their products once they reach the U.S.

Regulatory Developments

- FDA Draft Guidance on Clinical and Patient Decision Support Software
  - Clinical Decision Support (CDS) Software - software intended for healthcare professionals
  - Patient Decision Support (PDS) Software - software intended for patients and caregivers who are not healthcare professionals
- FDA Guidance - Distribution of In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only
- Food and Drug Administration Safety and Innovation Act (FDASIA) – updated July 9th, 2012 and expanded "custom device" exemptions

Regulatory Developments

- IEC 82304-1:2016 – Health Software – Part 1: General Requirements for Product Safety – covers the
  - manufacturer requirements for the safety and security of health software products designed to operate on general computing platforms and intended to be placed on the market without dedicated hardware
  - entire lifecycle including design, development, validation, installation, maintenance, and disposal of health software products
- In Vitro Diagnostic Regulation (IVDR) – the EU regulation replacing the existing In Vitro Diagnostic Device Directive (98/79/EC)

Regulatory Developments

- International Medical Device Regulators Forum (IMDRF) – a working group focused on international medical device regulatory harmonization and convergence
  - SaMD related regulations
    - IMDRF/SaMD WG/N10FINAL:2013 – SaMD: Key Definitions
    - IMDRF/SaMD WG/N12FINAL:2014 – SaMD: Possible Framework for Risk Categorization and Corresponding Considerations
    - IMDRF/SaMD WG/N23 FINAL:2015 – SaMD: Application of Quality Management System (QMS)
    - IMDRF/SaMD WG/N41FINAL:2017 – SaMD: Clinical Evaluation
    - IMDRF/GRRP WG/N47 FINAL:2018 – Essential Principles of Safety and Performance of Medical Devices & IVD Medical Devices

Regulatory Developments

- Took over for Global Harmonization Task Force (GHTF) which disbanded in 2012; and includes:
  - Australia, Therapeutic Goods Administration
  - Brazil, National Health Surveillance Agency (ANVISA)
  - Canada, Health Canada
  - China, China Food and Drug Administration
  - European Union, European Commission Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs
  - Japan, Pharmaceuticals and Medical Devices Agency and the Ministry of Health, Labour and Welfare
  - Russia, Russian Ministry of Health
  - Singapore, Health Sciences Authority
  - South Korea, Ministry of Food and Drug Safety
  - United States of America, US Food and Drug Administration

Regulatory Developments

- ISO 13485:2016 – Medical Devices -- Quality Management Systems -- Requirements for Regulatory Purposes – a QMS for medical device organizations that need to meet customer and applicable regulatory requirements. Covers organizations involved in design and development, production, storage and distribution, installation, or servicing of a medical device (e.g. technical support)

Regulatory Developments

- MEDDEV 2.1/6 - Guidance document Medical Devices - Scope, field of application, definition - Qualification and Classification of stand alone software – EU guidance to define the criteria for the qualification and classification of standalone software used in a healthcare setting as a medical device or in vitro diagnostic (IVD)
- Medical Device Development Tools (MDDT) – a program managed by the FDA for any tool developer to qualify tools that medical device sponsors can use in the development and evaluation of medical devices

Regulatory Developments

- Medical Device Regulation (MDR) – the EU regulation implemented to replace the EU's current Medical Device Directive (93/42/EEC) and the EU's Directive on active implantable medical devices (90/385/EEC)
- Proposed De Novo Updates – intended to provide structure, clarity and transparency on the De Novo classification process, as well as processes and criteria for accepting, granting, declining and withdrawing De Novo requests

Regulatory Developments

- National Evaluation System for Health Technology (NEST) – a 2016-2017 CDRH priority to:
  - Establish a National Evaluation System for medical devices to address the high costs and inefficiencies of data generation in clinical trials that have created disincentives for innovators to study their technologies and bring products to the U.S.
  - Address limitations of current post-market surveillance tools, and to help CDRH rapidly address safety concerns.
  - Utilize the real-world evidence to help strike the right balance between premarket and post-market data collection to facilitate patient device access and more quickly identify safety signals by assuring timely and robust post-market data collection.

Important Notes – Regulatory Developments

- Kisor v. Wilkie - Could over turn 1997 Auer v. Robbins where Supreme Court set precedent that requires courts to defer to federal agencies' interpretations of their regulations

Investigation Device Exemption Details

- Investigation Device Exemption (IDE) – Applicability
  - This should only be used when appropriate
  - The intent
    - An IDE allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data
    - Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices
    - All clinical evaluations of investigational devices, unless exempt, must have an approved IDE **before** the study is initiated

Investigation Device Exemption Details

- Clinical evaluations of devices that have not been cleared for marketing require:
  - an investigational plan approved by an institutional review board (IRB). If the study involves a significant risk device, the IDE must also be approved by FDA;
  - informed consent from all patients;
  - labeling stating that the device is for investigational use only;
  - monitoring of the study and required records and reports.
- An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements of the Food, Drug, and Cosmetic Act that would apply to devices in commercial distribution. Sponsors need not submit a PMA or Premarket Notification 510(k), register their establishment, or list the device while the device is under investigation. Sponsors of IDE's are also exempt from the Quality System (QS) Regulation except for the requirements for design controls (21 CFR 820.30).

Investigation Device Exemption Details

- When using IDE all the following apply for the clinical trial:
  - 21 CFR 812, *Investigational Device Exemptions*, covers the procedures for the conduct of clinical studies with medical devices including application, responsibilities of sponsors and investigators, labeling, records, and reports.
  - 21 CFR 50, *Protection of Human Subjects*, provides the requirements and general elements of informed consent;
  - 21 CFR 56, *Institutional Review Boards*, covers the procedures and responsibilities for institutional review boards (IRBs) that approve clinical investigations protocols;
  - 21 CFR 54, *Financial Disclosure by Clinical Investigators*, covers the disclosure of financial compensation to clinical investigators which is part of FDA's assessment of the reliability of the clinical data.
  - 21 CFR 820 Subpart C, *Design Controls of the Quality System Regulation*, provides the requirement for procedures to control the design of the device in order to ensure that the specified design requirements are met.

Breakthrough Device Program Details

- The device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions and,
- The device also meets **at least one** of the following:
  - Represents Breakthrough Technology
  - No Approved or Cleared Alternatives Exist
  - Offers Significant Advantages over Existing Approved or Cleared Alternatives
  - Device Availability is in the Best Interest of Patients

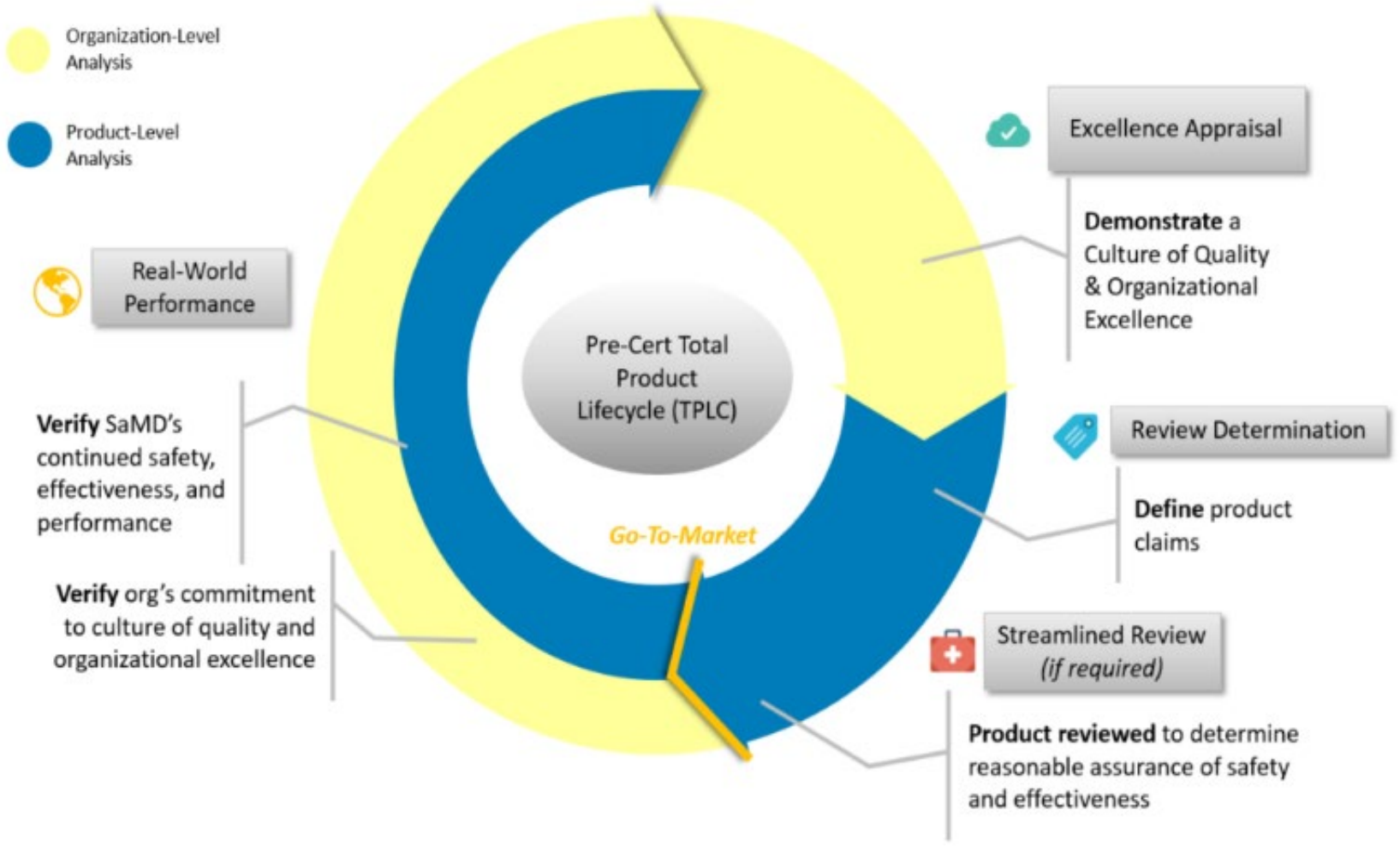
FDA Precertification Process Details

- The goal of the program is to have tailored, pragmatic, and least burdensome regulatory oversight that assesses organizations to establish ***trust*** that they have a culture of quality and organizational excellence such that they can develop high quality SaMD products, leverages ***transparency*** of organizational excellence and product performance across the entire lifecycle of SaMD, utilizes a tailored streamlined premarket review, and leverages unique post-market opportunities available in software to ***verify*** the continued safety, effectiveness, and performance of SaMD in the real-world

FDA Precertification Process Details

- The Software Precertification (Pre-Cert) Pilot Program, is outlined in the FDA's Digital Health Innovation Action Plan
- Pre-Cert 1.0, the first version of the program that will be available for pilot testing within the FDA's current authorities in 2019, is limited to SaMD Pre-Cert pilot participants

FDA Precertification Process Details



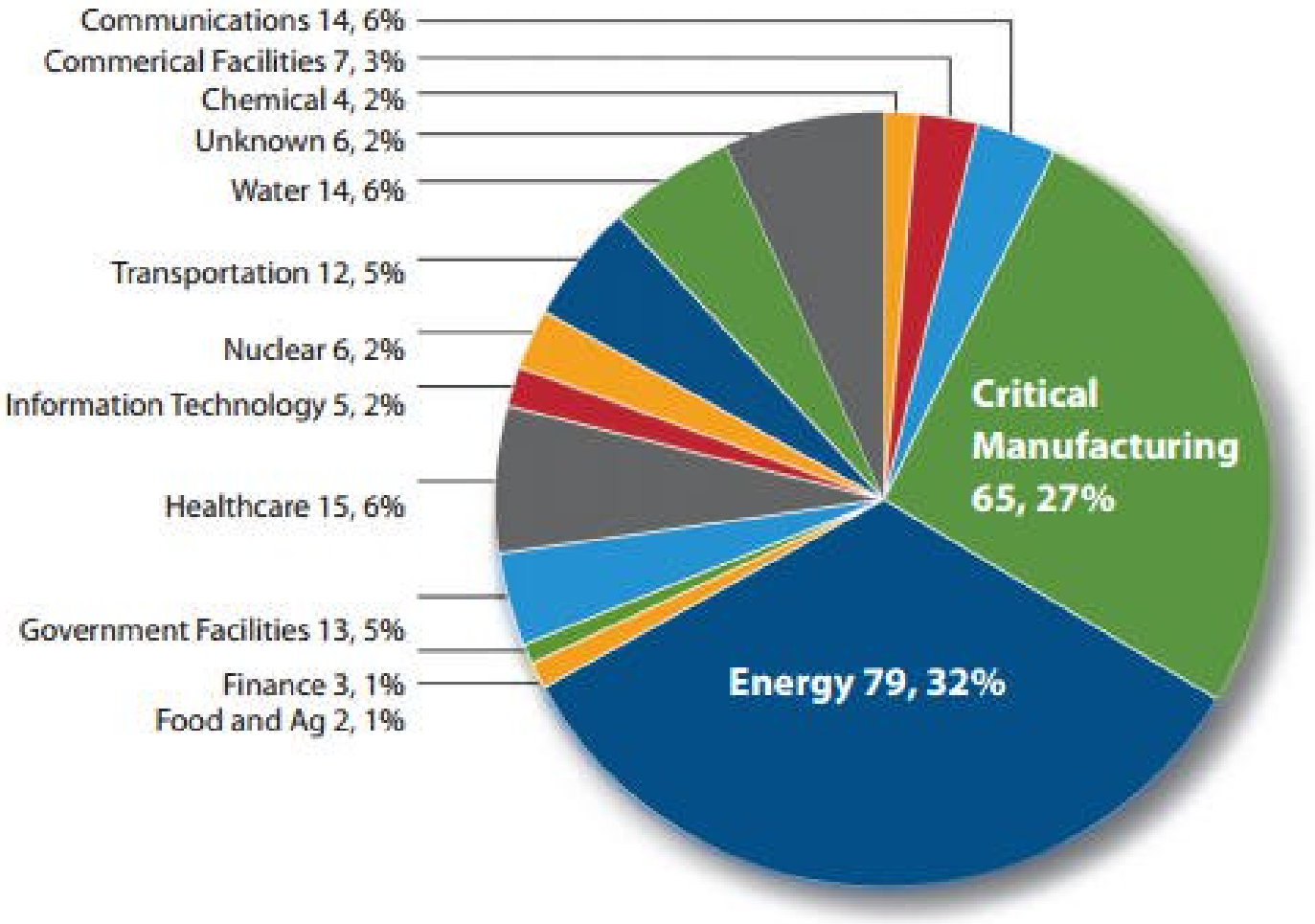
Important Notes - Digital Health Innovation Action Plan

- FDA Digital Health Plan specifically states FDA oversight
  - For mobile medical apps is to only those that present higher risk to patients, while choosing not to enforce compliance for lower risk mobile apps
  - Is not focused on technologies that receive, transmit, store or display data from medical devices
  - Is not focused on products that only promote general wellness
- Some SaMD manufacturers view this as meaning they can file registrations with the FDA, but not comply with the exemption rules (i.e. not being exempt from 21 CFR 820.198) or other regulatory requirements

Important Notes - Digital Health Innovation Action Plan

- Example of how under-reported incidents and lack of oversite can lead to inaccurate metrics
  - In 2014, the Industrial Control Systems Cyber Emergency Response Team (ICS-CERT) received and responded to 245 incidents reported by asset owners and industry partners
  - ICS-CERT is part of the National Cybersecurity and Communications Integration Center's (NCCIC)
  - Reported Cyber-Security Incidents by Industry Sector

Important Notes - Digital Health Innovation Action Plan



SaMD Assessment Process

- Developing your own SaMD
  - Make sure you know the device definitions; know if your product is a medical device or IVD
  - Define intended use and risk of device
  - Then determine your device classification
    - US FDA –
      - Combination product
      - Utilize the classification database and search for a part of the device name, or leverage the device panel (medical specialty) to which your device belongs
      - Best option might be De Novo process
    - EU MDR – Use MDR Rule 11

SaMD Assessment Process

- 21st Century Cure Act states, the term device, shall not include a software function that is intended
  - (A) for administrative support of a health care facility;
  - (B) for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;
  - (C) to serve as electronic patient records, so long as
    - (i) such records were created, stored, transferred, or reviewed by health care professionals;
    - (ii) such records are part of health information technology that is certified under section 3001(c)(5) of the Public Health Service Act; and

SaMD Assessment Process

- (iii) such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

– (D) for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings; or

SaMD Assessment Process

- (E) unless the function is intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system, for the purpose of
  - (i) displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);
  - (ii) supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; and
  - (iii) enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient

SaMD Assessment Process

- In the case of a product with multiple functions, and that otherwise meets the definition of a device, the Secretary shall not regulate the software functions that are now excluded as a device. Notwithstanding the preceding sentence, when assessing the safety and effectiveness of the device function or functions of such product the Secretary may assess the impact that the non-device software function or functions have on such device function or functions

SaMD Assessment Process

- Notwithstanding, a software function described in subparagraph (C), (D), or (E) shall not be excluded from the definition of device if
  - the Secretary makes a finding that use of such software function would be reasonably likely to have serious adverse health consequences
  - In making such a finding under with respect to a software function, the Secretary shall consider
    - the likelihood and severity of patient harm if the software function were to not perform as intended;
    - the extent to which the software function is intended to support the clinical judgment of a health care professional;
    - whether there is a reasonable opportunity for a health care professional to review the basis of the information or treatment recommendation provided by the software function; and
    - the intended user and user environment, such as whether a health care professional will use a software function of a type described in subparagraph (E)

SaMD Assessment Process

- US – FDA
  - **Class I General Controls (With and Without Exemptions)** – These devices present minimal potential for harm to the user and are often simpler in design than Class II or Class III devices. 47% of medical devices fall under this category and 95% of these are exempt from the regulatory process
  - **Class II General Controls and Special Controls (With and Without Exemptions)** – Devices in Class II are held to a higher level of assurance than Class I devices, and are designed to perform as indicated without causing injury or harm to patient or user. 43% of medical devices fall under this category

SaMD Assessment Process

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- **Class III General Controls and Premarket Approval** – These devices usually sustain or support life, are implanted, or present potential unreasonable risk of illness or injury. 10% of medical devices fall under this category
- Regulatory Controls (General, Special, and PMA)
- Exemption Details:
  - Exempt from the premarket notification, 510(k), requirements subject to the limitations on exemptions. These devices aren't exempt from other general controls
  - A few Class I devices are additionally exempt from the GMP requirements with the exception of complaint files and general record keeping requirements

SaMD Assessment Process

- All medical devices must be manufactured under a quality assurance program, be suitable for the intended use, be adequately packaged and properly labeled, and have establishment registration and device listing forms on file with the FDA
- Other Options:
  - Breakthrough Devices Program
  - Combination Product
  - De Novo
    - Avoids having to go Class III and PMA path
  - FDA pre-cert process if included in the pilot program
  - IDE

SaMD Assessment Process

- EU MEDDEV 2.1/6
  - Standalone software shall be qualified as an in vitro diagnostic (IVD) medical device or as an accessory to an IVD provided it satisfies the definition of an IVD, or that of an accessory to an IVD
  - Standalone software shall be treated an IVD device if it intended to be used together with an IVD medical device to enable that device to be used in accordance with its intended purpose
  - If the software does not perform an action on data, or performs an action limited to storage, archival, communication, “simple search” or lossless compression (i.e. using a compression procedure that allows the exact reconstruction of the original data) it is not a medical device

SaMD Assessment Process

- If the software is for the benefit of individual patients i.e. the software is intended to be used for the evaluation of patient data to support or influence the medical care provided to that patient and the manufacturer specifically intends the software to be used for any of the purposes listed in the MDR, then the software shall be qualified as a device
- If data are obtained from both IVD medical devices and from medical devices are analyzed together for the purpose of providing information according to the definition of an IVD medical device, this software is an IVD medical device

SaMD Assessment Process

- EU MDR
  - Under classification rules - Rule 11 - Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes is classified as class IIa, except if such decisions have an impact that may cause:
    - death or an irreversible deterioration of a person's state of health, in which case it is in class III; or
    - a serious deterioration of a person's state of health or a surgical intervention, in which case it is classified as class IIb.
    - Software intended to monitor physiological processes is classified as class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, in which case it is classified as class IIb
    - All other software is classified as class I

SaMD Assessment Process

- Software, which drives a device or influences the use of a device, shall fall within the same class as the device. If the software is independent of any other device, it shall be classified in its own right.
- Understand MDR Rule 11 and how its impacts your or your vendor's device class and quality system:
  - The same software could be in a higher risk class than FDA
  - All software must have a technical file
  - Leaves little scope for Class I software. Most software is assigned to Class IIa at the lowest.
  - In the case of Class IIa and higher, a Notified Body must be involved
  - No "grandfathering"

SaMD Assessment Process

- Purchased SaMD Assessment
  - Ask the vendor how the software is marketed (i.e. FTC vs. FDA)
  - If not a device
    - Ask the vendor if they are pursuing registration, and in what regions and what classifications
    - Assess if your use of the software impacts whether or not it is a device. Mistakes are being made not to have robust requirements gathering sessions.
    - Be careful of what a companies marketing department says, do your homework
  - If a device
    - Will you create any off label uses?
    - Will it used as part of a combination product?
    - Is the risk level of the device impacted based on your use?

SaMD Assessment Process

- If it is a combination product work with the following agencies
  - Office of Combination Products – FDA
  - Your designated notified body per Article 117 of the MDR - EU
- Per IMDRF/SaMD WG/N10FINAL:2013 – “Any person who changes the intended use of, or modifies, a medical device without acting on behalf of the original manufacturer and who makes it available for use under his own name, should be considered the manufacturer of the modified medical device.”
- Will your software be used in regions under the purview of other regulatory agencies?
  - Can be classified differently, not just the US rules apply
  - The sponsor may need to work with the vendor to get additional registrations
  - Clinical trials maybe required of the SaMD

Important Notes - SaMD Assessment Process

- If the SaMD (purchased or developed internally) was used to justify and provide evidence of efficacy claims then this is a combination product
  - Drug approval should be dependent on the SaMD

Validation Approaches

- Purchased SaMD
  - Ensure the vendor is following the appropriate regulations
  - Audit the vendor and verify their controls are in place and work
  - Verify software was validated and being kept validated to its intended use
    - If you are impacting the intended use there is a need as the sponsor to take on the additional regulatory and validation work
    - Avoid vendors that have a registered device, but do not comply with the device regulations
    - Gives you the chance to work on strategies to mitigate vendor issues
      - Only use software where you can control the version
      - Wait until device version of software
      - Document what version of the software going forward is and will be the device

Validation Approaches

- Allows a sponsor to document what version of the software or will be the device
- Gives you the chance to work on strategies to control versions or mitigate the impact of versions
  - Only use a software where you can control the version
  - Ensure all the same all hardware is the same model
  - Wait until device version of software

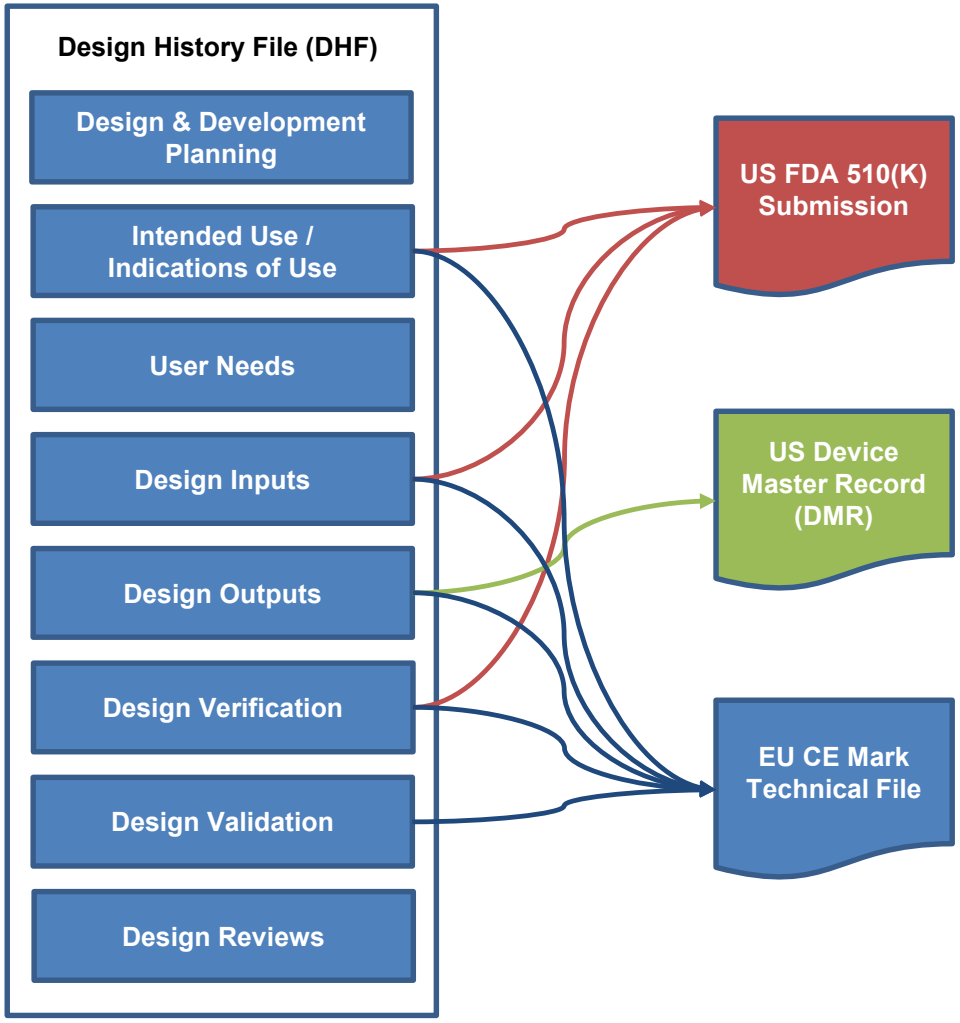
Validation Approaches

- Important Vendor Considerations and Mitigations
  - Know audit history
  - Know registration dates and countries (i.e. the device is registered OUS, but need time to register in US)
  - The device is registered, but your intended use is not supported
  - Use quality agreements to ensure the vendor is legally obligated to comply with device regulations
  - Pharma note: Ensure the SaMD vendor is not making efficacy claims based on your clinical trial that you are not aware of are able to support

Validation Approaches

- Developed SaMD
  - US Registration Specific Considerations
    - Ensure agreement with the FDA on the device classification, low risk applications won't face FDA oversite
    - A US specific regulatory approach for low risk devices could create remediation efforts OUS
    - Companies need to know their risk tolerance if for some reason classification is not approved by the FDA or if enforcement discretion changes
  - Recommendations
    - Follow IMDRF as the major SaMD regulatory bodies recognize this forum
    - Follow design controls, this allows for flexibility across regulated regions, is best practice, and minimizes impacts of any potential remediation efforts

Validation Approaches



Validation Approaches

- Validation approaches are very technology based
  - General Principles of Software Validation is still an excellent starting point, but more is needed
  - Clinical trails when applicable are critical to validate SaMD
    - Follow IMDRF requirements for clinical trails on SaMD
    - Combination product SaMD clinical trials should be coordinated and planned with the sponsor
  - AI tools need validation based on algorithm and data, but which is more important depends on the AI technology
    - Learning method is critical to managing AI change control
    - Supervised learning offers the most control, but creates significant limitations on future SaMD
    - AI's ability to assess and process data affects data integrity and accuracy of AI tool, how to learn something that was "bad"
    - Post-market surveillance vs. limiting changes

Validation Approaches

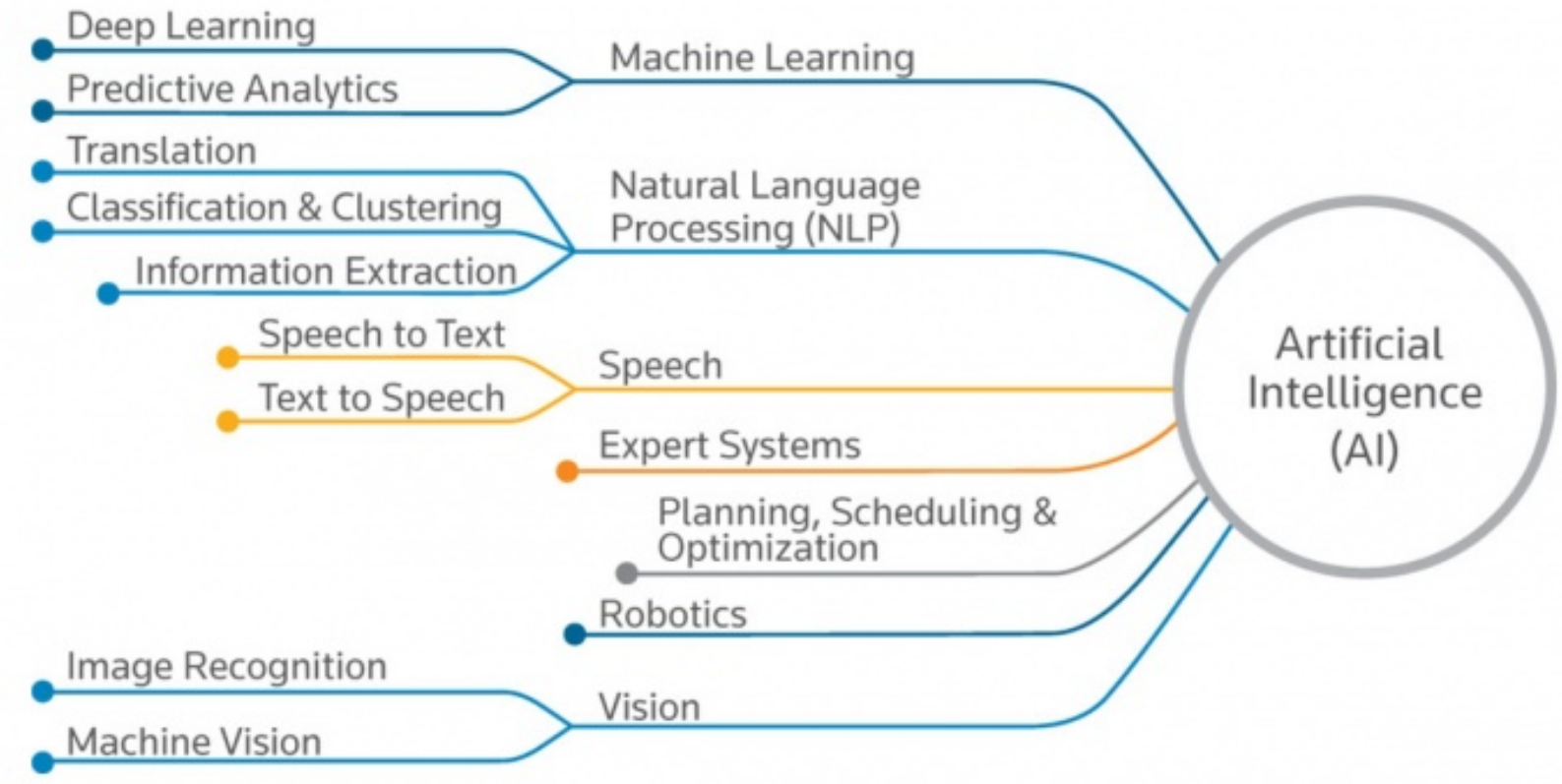


***diagram from https://mildaintrainings.com/blogs/artificial-intelligence/**

Questions