# Device Advice for AI and Machine Learning Algorithms In Medical Imaging

Here is a document of links pointing to FDA guidance documents and other forms of communication. It was compiled by googling CDRH regulatory buzz words. We hope this document is useful. You might also refer to Figure 2 of this paper: Marble et al. (2020). A regulatory science initiative …" J Pathol Info, 11(1), 22. https://doi.org/10.4103/jpi.jpi_27_20

Caveat to all: You won't know what's required for your submission until you ask in a Q-sub.

## Pre-submission meeting

In CDRH, the best advice is to know about pre-submission meetings.

- Slides: Pre-Submissions and Meetings with FDA Staff
- Guidance document: Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff

## IFU: Indications for Use

Part of the definition of your medical device are the indications for use.

- Webpage: Indications For Use.

It's never to early to start thinking about, researching, and crafting an IFU for your device.

## Comprehensive Regulatory Assistance

- Webpage: Comprehensive Regulatory Assistance

## 510k program

- Guidance Document: The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications 510(k)
- 510(k) Premarket Notification Database

A Premarket Notification, 510(k), is a submission made to FDA to demonstrate that the device to be marketed is safe and effective by proving substantial equivalence (SE) to a legally marketed device (predicate device).

- Guidance Document: Deciding When to Submit a 510(k) for a change to an Existing Device.
- Guidance Document: Deciding When to Submit a 510(k) for a Software Change to an Existing Device.

## de Novos

- Special controls accompany all de Novo classifications.
- Special controls outline submission requirements for medical devices with similar IFU.
- Special controls are defined for a device type that can be broad or narrow.
- Webpage: Special Controls
- De Novo Database

If you can't find a de Novo or existing 510k that is a perfect predicate for your device type: Then find and learn about the closest one or two. It's a way to start.

## PMA

Pursuing a pre-market authorization (**PMA**) is a regulatory pathway for medical devices that have a higher risk profile than a 510(k). PMAs are not covered here but information can be found by searching for "FDA CDRH PMA" from any internet search engine.

## Software as a Medical Device (SAMD)

- Digital Health Center of Excellence
  - Software as a medical device
  - AI/ML in SAMD
  - List of AI/ML enabled devices
- Computer aided detection (CADe) guidance – Radiology
  - Webpage: Non-clinical=Stand-alone=No human in the loop:
  - Webpage: Clinical=Reader Study=Human in the loop:
- Guidance on Off-The-Shelf Software Use in Medical Devices

## Quantitative Imaging

Guidance Technical Performance Assessment of Quantitative Imaging in Device Premarket Submissions

## Adaptive Algorithms, continuous learning

- Webpage, Artificial Intelligence and Machine Learning in Software as a Medical Device
- White paper, Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

## Digital Pathology

- Device type Whole Slide Imaging System
  - Philips IntelliSite Pathology Solution (DEN160056: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN160056.pdf).
  - Classification Product Code: PSY
  - Record includes special controls
- Device type Whole Slide Imaging System
  - Guidance for industry and FDA staff – technical performance assessment of digital pathology whole slide imaging devices

## CAD Examples

- Device type: Medical image analyzer (including breast cancer detection)
  - Secondlook (P010038: http://www.accessdata.fda.gov/cdrh_docs/pdf/P010038B.pdf)
  - Originally a PMA. Downclassified to 510k on 01/22/2020 (FR LINK)
  - Classification Product Code: MYN

- Device type: Radiological computer-assisted diagnostic (CADx) software for lesions suspicious for cancer.
  - QuantX (DEN170022: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN170022.pdf)
  - Classification Product Code: POK

- Device type: Radiological Computer Assisted Detection and Diagnosis Software" (CADe + CADx).
  - Imagen OsteoDetect (DEN180005: https://www.accessdata.fda.gov/cdrh_docs/pdf18/DEN180005.pdf)
  - Classification Product Code: QBS

- Device type: Radiological computer aided triage and notification software.
  - Viz.AI ContaCT (DEN170073: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN170073.pdf)
  - Classification Product Code: QAS

- Device type: Retinal diagnostic software device
  - IDx IDx-DR (DEN180001: https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180001.pdf)
  - Classification Product Code: PIB

- Device type: Image acquisition and/or optimization guided by artificial intelligence
  - Bay Labs Caption Guidance (DEN190040: http://www.accessdata.fda.gov/cdrh_docs/pdf19/DEN190040.pdf)
  - Classification Product Code: QJU

- Device type: Software algorithm device to assist users in digital pathology
    - Paige.AI Paige Prostate (DEN200080: https://www.accessdata.fda.gov/cdrh_docs/pdf20/DEN200080.pdf)
    - Classification Product Code: QPN
    - Presentation and discussion about the Paige.AI decision summary convened by the Pathology Innovation Collaborative Community (June 2022): LINK

## Presentations in this space

- "Tutorial on Reader Study Designs and MRMC Analysis"
    - FDA internal training, April 8, 2022
    - Pathology Innovation Collaborative Community Webinar, August 5, 2022
    - Brandon Gallas, Research Mathematical Statistician, Division of Imaging, Diagnostics, and Software Reliability OSEL, CDRH, FDA
    - 20220805-PIcc-MRMCstudyDesigns-Gallas.pdf (14 MB, uploaded by Brandon D. Gallas 1 year 7 months ago)
    - Video MRMC tutorial: 1 hour 20 seconds

- "ROC curves: Receiver Operating Characteristic Curves"
    - FDA internal training, April 8, 2022
    - Pathology Innovation Collaborative Community Webinar, August 5, 2022
    - Brandon Gallas, Research Mathematical Statistician, Division of Imaging, Diagnostics, and Software Reliability OSEL, CDRH, FDA
    - 20220805-PIcc-ShortROCtutorial.pdf (737 KB, uploaded by Brandon D. Gallas 1 year 7 months ago)
    - Video ROC tutorial: 6 minutes 17 seconds

- "Regulatory Considerations and Assessment of AI/ML Devices"
    - Yale, January 29, 2020, New Haven, Connecticut
    - Nicholas Petrick, Deputy Division Director, Division of Imaging, Diagnostics, and Software Reliability OSEL, CDRH, FDA
    - Petrick_RegulatoryConsiderationsAssessmentAI2020-01-29.pdf (2 MB, uploaded by Brandon D. Gallas 4 years 2 months ago)

- "AI and Digital Pathology: Regulatory Perspective"
    - Pathology Visions, October 8, 2019, Orlando, FL.
    - Shyam Kalavar, Senior Scientific Reviewer, Division of Molecular Genetics and Pathology
    - S.Kalavar.PathVision2019.pdf (2 MB, uploaded by Brandon D. Gallas 4 years 5 months ago)

- "Evaluating Artificial Intelligence Devices at the FDA and Related Collaborations and Initiatives"
    - ACR Informatics Summit, October 5-6, 2019, Washington, DC.
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    - Brandon Gallas, PhD, Research Mathematical Statistician, Division of Imaging,

Diagnostics, and Software Reliability OSEL, CDRH, FDA
    - 20191005ACRinformaticsSummit_BDG-6-FINAL.pdf (5 MB, uploaded by Brandon D. Gallas 4 years 6 months ago)
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    - Jennifer Segui, Lead Medical Device Reviewer, Division of Radiological Health, FDA
    - J.A.Segui.ACR.Informatics.2019.Slides.FINAL.pdf (3 MB, uploaded by Brandon D. Gallas 4 years 6 months ago)
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- "Evaluation and Regulatory Considerations for AI Methods in Medical Imaging"
    - Society for Imaging Informatics in Medicine Annual Meeting, June 26, 2019, Aurora, Co
    - Berkman Sahiner, Senior Scientist, Division of Imaging, Diagnostics, and Software Reliability OSEL, CDRH, FDA
    - Sahiner_EvaluationRegulatoryConsiderationsAIinMedicalImaging20200626.pdf (779 KB, uploaded by Brandon D. Gallas 4 years 2 months ago)

- "Digital Pathology Regulatory Considerations"
    - Pathology Informatics Summit 5/9/19
    - Cheng Cui, Senior Scientific Reviewer, Division of Molecular Genetics and Pathology,
    - PathologySummit2019_Pittsburgh_ChengCui_FDA.pdf (421 KB, uploaded by Brandon D. Gallas 4 years 11 months ago)

## Medical Device Development Tools (MDDT) program

The FDA's Medical Device Development Tools (MDDT) program is a way for the FDA to qualify tools that medical device sponsors can use in the development and evaluation of medical devices. It is a way for the broader community (academia, health providers, and government scientists, not just industry) can impact the regulatory process.

- Webpage: FDA page, "Medical Device Development Tools (MDDT)"

## Catalog of Regulatory Science Tools to Help Assess New Medical Devices

- Link to catalog

## Mock Submission

- Webpage: MDICx webinar that includes **a presentation on mock submissions to FDA/CDRH.**
- Slides: Mock Submissions to FDA/CDRH: History and Lessons Learned: by Kyle Myers, Director DIDSR/OSEL/CDRH/FDA. This presentation was made as the agency was working with MDIC to pursue a mock submission about, "Augmenting a Clinical Study

with Virtual Patient Models."
    - Webpage: All the **mock submission documents** to and from the MDIC team and FDA. Actually, this cached web link seems to now point to the updated Virtual Patient Page at MDIC which is missing the FDA submission feedback.
    - The mock submission was followed quickly by actual submissions.
    - Slides, Mock Submissions updated 20190412-HTTMockSubmissions.pdf (1 MB, uploaded by Brandon D. Gallas 4 years 11 months ago)
    - Updated Virtual Patient Page at MDIC
- The virtual patients mock submission was preceded by "Protein-Based Multiplex Assays: Mock Presubmissions to the US Food and Drug Administration" , Regnier et al.
    - Supplementary Materials