A First Look at the FDA's Proposed Regulatory Framework for Modifications to AI-Based Software as a Medical Device (SaMD): IP Review and Strategy Guide

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Introduction

Software has become an integral part of our society. Virtually every aspect of life could incorporate software at some level (e.g., smart toothbrushes, digital currency, app-controlled thermostats, etc.). When applied to health, mobile devices already track steps and heart rate and will call 911 if the wearer is immobile after a hard fall.[2] Products within the medical field from hospitals to pharmaceutical and medical device companies are being improved through software to give patients more knowledge and control over their diagnosis and treatment. It is when software is intended to diagnose or treat that software qualifies as a medical device in and of itself and therefore necessitates its own approval from the Food and Drug Administration (FDA).

The FDA has adopted the definition of Software as a Medical Device (SaMD) from the International Medical Device Regulators Forum (IMDRF) as software intended to be used for one or more medical purpose that performs such purpose without being part of hardware for a medical device.[3] To clarify, software is *not* SaMD, for example, if its intended purpose is to drive hardware for a medical device (e.g., firmware on a powered injector). However, SaMD does include software that may be interfaced with medical devices or software present on a mobile device or other products. Generally, SaMD is a medical device and includes in-vitro diagnostic medical devices. In addition, SaMD is capable of running on general purpose computing platforms. It is the function of the software that determines whether it qualifies as SaMD.

[2] *Use fall detection with Apple Watch*, Apple Inc., https://support.apple.com/en-us/HT208944 (last visited Sept. 8, 2021).
[3] *"Software as a Medical Device": Possible Framework for Risk Categorization and Corresponding Considerations*, International Medical Device Regulators Forum (IMDRF) (Sept. 18, 2014), http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf.

The IMDRF further explains that SaMD may also:

- providing means and suggestions for mitigation of a disease;
- providing information for determining compatibility, detecting, diagnosing, monitoring or treating physiological conditions, states of health, illness or congenital deformities; or
- aiding diagnosis, screening, monitoring, determination of predisposition; prognosis, prediction, determination of physiological status.[4]

To further illustrate, consider some of the software utilized during image acquisition in radiology. The software utilized to assist a radiologist in arriving at a patient diagnosis based on an acquired image after a CT scan, for example, by calculating the measurements of various images present on the scan, is SaMD.[5] Other examples of SaMD include patient image processing software, biometric signal processing software, clinical outcome predictive software, etc.

The FDA has recognized that its traditional review processes and procedures have not been well suited for the faster iterative design and type of validation used for software-based medical technologies. To that end, the FDA announced a Digital Health Innovation Action Plan in 2017[6], issued guidance to clarify FDA's oversight of device software functions[7] and launched a software pre-certification pilot program.[8]

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[4] *Id.*
[5] FDA recently further clarified several types of software to no longer qualify as a medical device. *See* Medical Devices; Medical Device Classification Regulations To Conform to Medical Software Provisions in the 21st Century Cures Act, 86 Fed. Reg. 20,278 (April 19, 2021), https://www.govinfo.gov/content/pkg/FR-2021-04-19/pdf/2021-07860.pdf.
[6] *Digital Health Innovation Action Plan*, United States Food and Drug Administration (July 27, 2017), https://www.fda.gov/media/106331/download.
[7] *Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act*, United States Food and Drug Administration (Sept. 27, 2019), https://www.fda.gov/media/109622/download.
[8] *Digital Health Software Precertification (Pre-Cert) Program*, United States Food and Drug Administration https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-software-precertification-pre-cert-program (last visited Sept. 8, 2021).

Additionally, use of artificial intelligence (AI) in software, particularly in healthcare-related software, is increasing. In the healthcare context, AI includes software models (e.g., machine learning (ML) models, deep learning (DL) models, etc.) trained and tested based on available data to analyze healthcare data and draw a conclusion, identify a correlation, make a prediction, etc. AI can be used in diagnostic software, such as to detect the presence or absence of certain features or characteristics (e.g., identify a lesion, a tumor, a pneumothorax, etc.). Diagnostic AI can also be used to correlate features to predict a condition or problem in a patient. AI can also be used for treatment, such as to predict an outcome for a particular patient to undergo a particular procedure, other personalized medicine, etc. AI can also be used to drive natural language processing for speech recognition, document and/or data classification, etc. According to a 2020 report by the United State Patent and Trademark Office (USPTO), 16% of filed patent applications included AI and 12% of the AI-related applications involved life and medical sciences (second only to telecom).[9]

The growth of ML and other AI are providing numerous opportunities within health care for improvements in patient care. For example, SubtlePET™ by Subtle Medical, Inc. analyzes images acquired during positron emission tomography (PET) and can reduce the noise surrounding the image from scans conducted in 1/4th the time.[10] By reducing the scan time per patient, the patient experience may be more pleasant, and the scan room workflow efficiency may be improved. The product utilizes an AI algorithm developed with ML to recognize noise in an image scan as the image is being acquired and then "scrubs" the image to provide the doctor with a final image for diagnosing the patient.

[9] *Inventing AI: Tracing the diffusion of artificial intelligence with U.S. patents*, U.S. Patent and Trademark Office, Office of the Chief Economist, IP DATA HIGHLIGHTS, Number 5, October 2020.
[10] https://subtlemedical.com/usa/subtlepet/.

Although the FDA approved an AI algorithm as early as 2008, only 15 additional AI algorithms were approved over the next 9 years.[11] FDA has proposed a framework for AI/ML-enabled products. It is the intent of this paper to review FDA's Proposed Regulatory Framework publications from 2019 to 2021 and to discuss associated intellectual property issues that medical device companies should consider while seeking FDA approval for their AI/ML products.

Overview: The FDA's Proposed Regulatory Framework for AI/ML

A 510(k) is a premarket submission made to the FDA to demonstrate that a medical device to be marketed is as safe and effective, that is, substantially equivalent, to a legally marketed device.[12] In response to medical device innovations that utilize AI/ML-enabled technologies, the FDA has proposed a framework for 510(k) premarket clearance of AI/ML-based SaMD's, which may involve modifications, in two, recent publications: (1) *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)* [13] published in 2019, and (2) *Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan*[14] published in 2021. Although these two publications provide an informative perspective for making modifications to AI/ML-based SaMD's, it is important to note that these publications describe "innovative approaches that may require additional statutory authority to implement fully and ***are not a draft guidance***."[15] Furthermore, these documents are "not intended to communicate FDA's proposed (or final)

[11] 110 additional AI algorithms have been cleared since the start of 2018.
[12] Section 513(i)(1)(A) FD&C Act.
[13] *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning-Based Software as a Medical Device*, United States Food and Drug Administration (April 2019), https://www.fda.gov/media/122535/download (herein "2019 FDA publication").
[14] *Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan*, United States Food and Drug Administration (January 2021), https://www.fda.gov/media/145022/download (herein "2021 FDA publication").
[15] *Id.* at 4–5 (emphasis added).

regulatory expectations but [are] instead meant to seek early input from groups and individuals outside the Agency prior to development of a draft guidance."[16] Notwithstanding the preliminary status of the framework proposed in these publications, the framework can provide useful insights into future regulatory expectations and intellectual property (IP) issues that may arise from such regulatory expectations.

This section analyzes potential regulatory requirements that may arise from the proposed framework, while later sections of this paper analyze potential IP considerations of such requirements. The more recent 2021 FDA publication proposed five, future FDA actions in response to stakeholder input generated from the 2019 FDA publication. The first of these five actions proposed to "[d]evelop an update to the proposed regulatory framework presented in the AI/ML-based SaMD discussion paper, including through the issuance of a Draft Guidance on the Predetermined Change Control Plan."[17] Central to the FDA's proposed regulatory approach to AI/ML is the Predetermined Change Control Plan (PCCP), which allows manufacturers to specify the types of anticipated modifications for the software and the associated methodology being used to implement those changes.[18] Under the proposed regulatory approach, a manufacturer can define and submit a Predetermined Change Control Plan to the FDA in a premarket submission. Following input and authorization from the FDA on the Predetermined Change Control Plan, the manufacturer can use the Predetermined Change Control Plan to make modifications that are within the bounds of the Predetermined Change Control Plan.

[16] *Id.*
[17] *Id.* at 7.
[18] 2019 FDA Publication, *supra* at 10.

Predetermined Change Control Plan

To provide initial premarket assurance of safety and effectiveness, the FDA proposes the use of a Predetermined Change Control Plan as a framework for modifications to AI/ML-based SaMD.[19] FDA premarket review of a Predetermined Change Control Plan is intended to "provide reasonable assurance of safety and effectiveness and would include review of the SaMD's performance, the manufacturer's plan for modifications, and the ability of the manufacturer to manage and control resultant risks of the modifications."[20] By pre-defining and agreeing upon a Predetermined Change Control Plan with the FDA, manufacturers can determine in advance whether later modifications to SaMDs will require additional FDA premarket review or simply documenting those modifications. Accordingly, this framework is intended to address the self-learning behavior of an AI/ML-based SaMD, which may modify its models and operations frequently in response to new data. In addition to providing greater certainty to manufacturers for regulatory review, the use of a Predetermined Change Control Plan may reduce the number of regulatory submissions that would otherwise be required for each modification to a SaMD under conventional FDA premarket review frameworks.

SaMD Pre-Specifications (SPS) and Algorithm Change Protocol (ACP)

A Predetermined Change Control Plan includes two primary components: SaMD Pre-Specifications ("SPS") and Algorithm Change Protocol ("ACP").[21] As described in the 2019 Proposed Regulatory Framework, the SPS should describe the manufacturer's "anticipated modifications to 'performance' or 'inputs,' or changes related to the 'intended use' of AI/ML-

[19] *Id*.
[20] *Id.* at 7–8.
[21] *Id.* at 10–11.

based SaMD."[22] In other words, the SPS should describe "the types of changes the manufacturer plans to achieve when the SaMD is in use."[23] By drawing a "region of potential changes" around the initial specifications and labeling of the original device, the SPS defines "what" the manufacturer intends the algorithm to become as it learns.[24]

In addition to the SPS, the Predetermined Change Control Plan also includes the ACP, which specifies the "methods that a manufacturer has in place to achieve and appropriately control the risks of the anticipated types of modifications delineated in the SPS."[25] As described in the 2019 Proposed Regulatory Framework, "[t]he ACP is a step-by-step delineation of the data and procedures to be followed so that the modification achieves its goals and the device remains safe and effective after the modification."[26] This step-by-step delineation requires the SaMD manufacturers to include specificity on data and procedures in four core areas: Data Management, Re-training, Performance Evaluation, and Update Procedures.[27] For each of the four core areas of the ACP, the 2019 Proposed Regulatory Framework provides additional specificity on example submission information.

Once the ACP and SPS have been agreed upon by the FDA and manufacturer in a Predetermined Change Control Plan, "manufacturers are expected to evaluate the modifications based on risk to patients as outlined in the software modifications guidance."[28] The 2019 Proposed Regulatory Framework illustrates this process as follows:[29]

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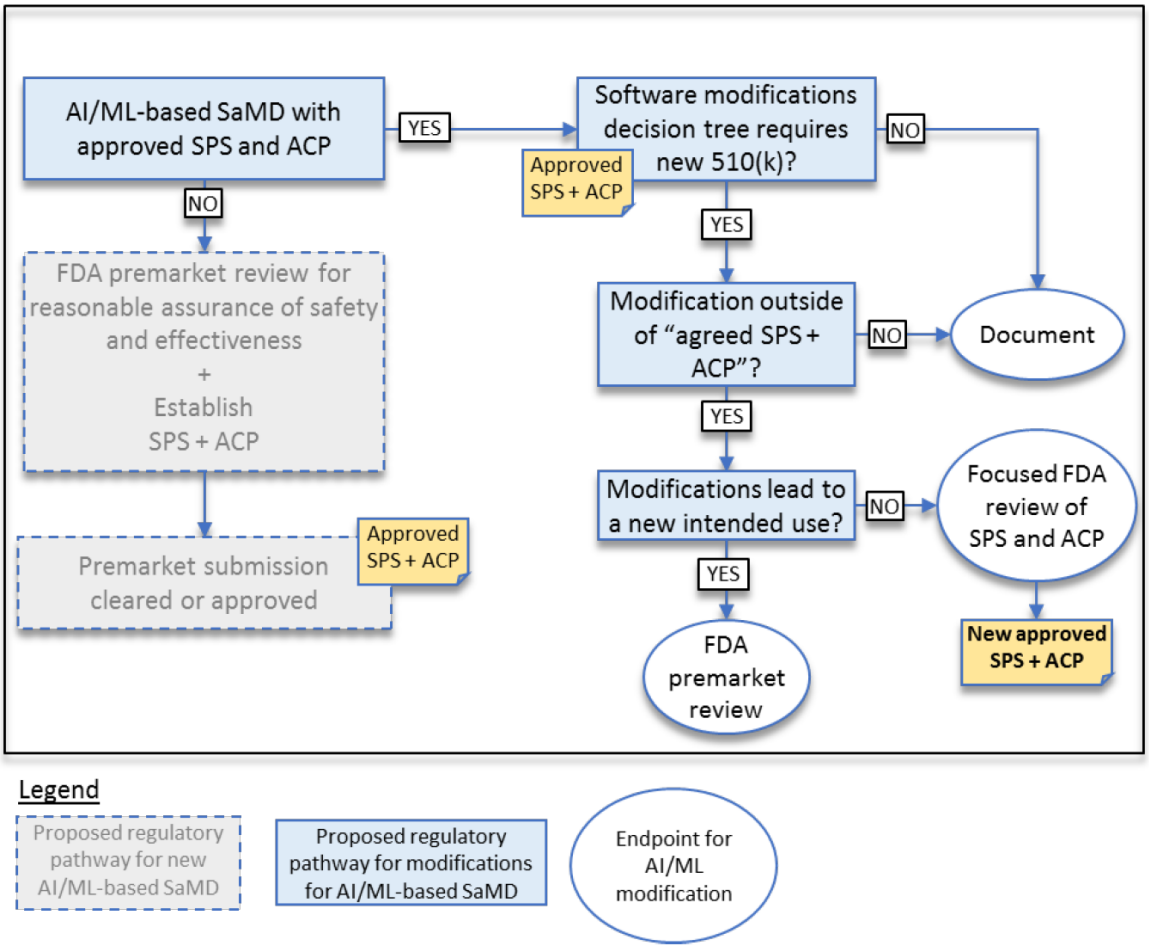
[22] *Id.*
[23] *Id.*
[24] *Id.*
[25] *Id.*
[26] *Id.*
[27] *Id.*
[28] *Id.*
[29] *Id.* at 13.



As shown above, "[i]f, for AI/ML SaMD with an approved SPS and ACP, modifications are within the bounds of the SPS and the ACP, … manufacturers would document the change in their change history and other appropriate records, and file for reference."[30] On the other hand, "if the modification is beyond the intended use for which the SaMD was previously authorized, manufacturers are expected to submit a new premarket submission."[31] Under this framework, modifications to SaMD implementations that are within the bounds of the SPS and the ACP can be delivered to the market quickly, while more significant changes are subjected to additional FDA premarket review to ensure appropriate regulatory review and patient safety. The FDA has also

[30] *Id.*
[31] *Id.*

noted that the SCS and ACP may not be static, and "there may be cases where the SPS or ACP can be refined based on the real-world learning and training for the same intended use of AI/ML SaMD model. In those scenarios, FDA may conduct a 'focused review' of the proposed SPS and ACP for a particular SaMD."[32] In such instances, the FDA has suggested that manufacturers engage with the FDA for further discussions and modifications to the SPS and ACP.[33]

Implications of the Proposed Regulatory Framework

The Predetermined Change Control Plan, including its primary components, the SPS and ACP, provide a flexible approach to ensure the safety and effectiveness of SaMDs, and particularly those SaMDs that continuously modify their operation based on new data or changing conditions. With this new regulatory approach, SaMD manufacturers and their legal counsel must carefully consider IP issues that arise from the requirements of the SPS and ACP. For example, SaMD manufacturers should evaluate with the FDA and discuss the appropriate level of technical detail that is necessary to include in the SPS or ACP. In some instances, disclosing functional descriptions of systems and algorithms might be considered for a Change Control Program, while in other examples, pseudocode or detailed designs for the SaMD may be more appropriate. Similar considerations apply to data sets that are used to train or test AI/ML models used with SaMDs. In some instances, providing descriptions of the data (e.g., data set size, data set collection period, patient population attributes, etc.) used to train or test AI/ML models and the results of the model (e.g., classification accuracy) might be considered without sharing actual data sets with the FDA. Appendix A of the 2019 FDA publication provide several helpful examples that illustrate when

[32] *Id.*
[33] *Id.*

disclosure to the FDA may be necessary and what updated information may be needed in a disclosure.[34]

Although submissions from SaMD manufacturers to the FDA are entitled to confidentiality protections, various IP risks may still exist in the form of Freedom of Information Act (FOIA) requests, unplanned public disclosures of inventions, inadequate levels of protection for trade secrets, and data privacy regulations. The next section of this paper analyzes several IP considerations that may accompany the Predetermined Change Control Plan and ways to mitigate various risks. Finally, the 2021 FDA publication indicated that the FDA "will leverage docket input received on the AI/ML-based SaMD discussion paper as well as recent submission experience" to publish additional draft guidance in 2021 bringing further clarity to the proposed framework and potential IP considerations that may arise.[35]

Patent Considerations

The requirements for FDA submission may conflict with desires to protect the associated IP. According to current FDA regulation and guidance, SaMD manufactures are required to make a new 510(k) submission for certain improvements to authorized devices. For example, the FDA's publication entitled *Deciding When to Submit a 510(k) for a Software Change to an Existing Device*[36] states that a new 510(k) submission is likely needed if the change "could significantly affect clinical functionality or performance specification that are directly associated with the intended use of the device."[37] The FDA anticipates that many modifications to AI/ML-based SaMD will involve algorithm and architecture modifications and re-training with new data sets,

[34] *Id. at 15–18.*
[35] 2021 FDA Publication, *supra* at 3.
[36] *Deciding When to Submit a 510(k) for a Software Change to an Existing Device*, United States Food and Drug Administration (Oct. 25, 2017), https://www.fda.gov/media/99812/download.
[37] *Id*. at 10.

which the FDA states that, under the software modifications guidance, would be subject to premarket review.[38] The FDA classifies these modifications into three groups: as changes in (1) performance, (2) inputs used by the algorithm, and (3) intended use of the SaMD.[39]

Such modifications can reasonably be expected when using a continuously learning algorithm that keeps improving when more training data becomes available. Using continuous learning algorithms with AI/ML-based SaMD allows the algorithms to adapt or otherwise change after the SaMD is deployed and distributed in the "real world."[40] Following approval and commercial use, such continuous learning, adaptive AI/ML algorithms, once deployed, may begin generating an output that is different from the output initially cleared for a given set of inputs. Examples include optimizing algorithm performance based on a new or better-defined patient population, specific users (e.g., a specific physician), and improving algorithm performance based on additional data collected (e.g., expanding the algorithm training set with real-world data).

In the AI/ML space, SaMD improvements based on changes in performance, inputs, or intended use, may also merit a patent filing on the improvement. A SaMD manufacturer must balance FDA and USPTO requirements to ensure that FDA obligations are being met while also securing patent protection for SaMD innovation and related improvements. This obligation extends to the drafting and filing of a new patent application, as well as submission of references and responding to Office Actions during the prosecution of the patent application, which may be proceeding concurrently with the 510(k) submission for the SaMD.

[38] Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning-Based Software as a Medical Device, United States Food and Drug Administration (April 2019), https://www.fda.gov/media/122535/download (herein "2019 FDA publication") at 6.
[39] *Id*.
[40] *Id*.

A 510(k) submission is a premarket submission made to the FDA to demonstrate that the new device to be marketed is "substantially equivalent" to a legally marketed device which is not subject to premarket approval (PMA)[41]. As opposed to a *de novo* submission, in which an applicant must provide information to support a new classification into Class I or Class II for a new product not previously reviewed, manufacturers in a 501(k) submission must compare their new device to a similar legally marketed device (referred to as a predicate) to support their claims of substantial equivalence.[42] The FDA will clear the device if the device is determined to be "substantially equivalent" to a predicate device. However, making assertions of "substantial equivalence" to the FDA may be in tension with seeking patent protection for the improvement.

As an initial matter, "substantial equivalence" is not the same as the legal standard for showing obviousness (pursuant to 35 U.S.C. § 103) or anticipation (pursuant to 35 U.S.C. § 102) of an invention. "Substantial equivalence" is also not the standard for showing that an invention is conventional, which can be relevant to a patent eligible subject matter inquiry under 35 U.S.C. § 101 and the Supreme Court's *Alice* decision. As such, the patent application can draw this distinction when challenged on whether a) an assertion that product X is "substantially equivalent" to product Y is also b) an admission that the claimed invention related to product X is obvious in view of product Y. Moreover, a patent applicant may possess evidence of improvements, which can be used to support patentability of the improvement.

Accused infringers, on the other hand, may attempt to get information about patentee's FDA filings to argue unpatentability and/or inequitable conduct. *Belcher Pharm. LLC v. Hospira, Inc.*[43] is a recent Federal Circuit case that illustrates the risk of making seemingly inconsistent

[41] 21 U.S.C. §§ 360(k), 360(n), 360c(f)(1) & 360c(i); 21 CFR 807.92(a)(3).
[42] 21 U.S.C. § 360(c)(i); 21 CFR 807.92(a)(3).
[43] *Belcher Pharm. LLC v. Hospira, Inc.* Appeal No. 2020-1799 (Fed. Cir. Sept. 1, 2021).

statements to the FDA and USPTO. Patentee Belcher switched to the claimed pH range of an epinephrine formulation to expedite FDA approval of its product because the new pH range matched the pH range of two FDA-approved products. As summarized by the Federal Circuit, Belcher told the FDA that the pH range in its product was "old," but told the USPTO that the same range was "critical" and yielded "unexpected results" when seeking a patent for its product. Furthermore, Belcher failed to submit references describing the approved products it relied on to make its case to the FDA to the USPTO. The district court found that Belcher had committed inequitable conduct, including a finding of intent to deceive the USPTO, and the Federal Circuit affirmed.

The Federal Circuit's opinion has caught attention of Congress, and Sens. Leahy and Tillis, co-chairs of the Senate Judiciary Intellectual Property Subcommittee sent a letter to the USPTO on Sep. 9, 2021, requesting that "the PTO take steps to reduce patent applicants' making inappropriate conflicting statements in submissions to the PTO and other federal agencies."[44] If a 510(k) submission is submitted and patent protection on the improvement is sought, patent applicants will need to think carefully what information to submit to the USPTO to satisfy their duty of disclosure. While further developments from Congress and the USPTO can be expected, submission of certain redacted FDA submissions to the USPTO on an Information Disclosure Statement might be a good place to start. A step further might include reaching out the Examiner about these submissions and address any concerns the Examiner might have.

Thus, a SaMD manufacturer's use of the Predetermined Change Control Plan, if not redacted or designated as confidential, may not only help ensure more efficient modification of authorized SaMD while still ensuring safety and effectiveness, it may avoid headaches if patent

[44] https://www.leahy.senate.gov/imo/media/doc/20210909%20Letter%20to%20PTO%20on%20FDA%20submissions.pdf.

protection for the improvement is also requested. As discussed below in connection with trade secrets, patent protection for SaMD may be particularly favored over trade secret protection when (1) the market demonstrates the need for "explainable AI," which may be particularly important in healthcare, and (2) when there is uncertainty about the ability to protect trade secrets from disclosure.

However, if a patent application filing is to be pursued, applicants must keep in mind 35 U.S.C. § 101 subject matter and 35 U.S.C. § 112 written description concerns to ensure that they provide sufficient detail regarding the AI and its use in the SaMD to satisfy the patent examiner (and the courts). Filing a patent application at a high level with insufficient detail may only serve to further alert and educate the competition without providing the right to exclude in return. Patent filings related to AI-based SaMD should be mindful of divided infringement issues (e.g., one party trains and tests an AI model and another uses the deployed model in an application). Further, to address the "black box" nature of some AI models, patent applications can focus on inputs, outputs, improvement to medical device functionality, particular context, and/or particular approaches to training and/or testing an AI model. For example, Manual of Patent Examining Procedure (MPEP) provides example claims that do not recite an abstract idea, including:

> A method of training a neural network for facial detection comprising:
>
> collecting a set of digital facial images, applying one or more transformations to the digital images, creating a first training set including the modified set of digital facial images;
>
> training the neural network in a first stage using the first training set, creating a second training set including digital non-facial images that are incorrectly detected as facial images in the first stage of training; and

training the neural network in a second stage using the second training set.[45]

As such, an applicant must carefully consider how a patent application aligns or conflicts with an FDA regulatory submission.

Trade Secret Considerations

As discussed above, the FDA's proposed regulatory framework includes the Predetermined Change Control Plan, which includes the SPS and ACP. The SPS describes what aspects of the SaMD may change through learning and the ACP describes how the algorithm learns and changes while remaining safe and effective.[46] Additionally, the FDA has promoted transparency as a key aspect to engender user trust in AI/ML-based SaMDs. The final shape of these disclosures remains to be seen and will likely be subject to change.

However, manufacturers may have competing IP-related interests in maintaining some aspects of an AI/ML-based SaMD secret. Long overshadowed by other forms of intellectual property, trade secrets have recently gained prominence. In some cases, trade secrets may be an attractive form of intellectual property protection for aspects of the AI/ML components of an SaMD.

Trade secrets do not require registration or fees, may, in theory, extend indefinitely, and cover a wide range of subject matter. On the other hand, patents require fees, expire after a defined period of time, and are subject to the uncertainties of an examination process. In particular, AI/ML inventions may require artful drafting to avoid being deemed an abstract idea, such as a mathematical formula or akin to a mental process, in view of *Alice Corp. Pty. Ltd. v. CLS Bank*

[45] Manual of Patent Examining Procedure 2106.04(a)(1) (9th edition, June 2020), https://www.uspto.gov/web/offices/pac/mpep/s2106.html#ch2100_d29a1b_13b3e_21; *see* USPTO Subject Matter Eligibility Example 39, https://www.uspto.gov/sites/default/files/documents/101_examples_37to42_20190107.pdf.
[46] *Id.*

International, 134 S. Ct. 2347 (2014), although, as discussed above, the MPEP provides at least one example of a patent eligible claim that recites machine learning processes. Additionally, many machine learning architectures comprise different combinations of known primitives and many architectures are public or open sourced, which may be considerations with respect to novelty and obviousness.

Consider also that AI/ML is a quickly evolving field. A manufacturer may iterate AI/ML aspects of an SaMD at a rate that is difficult or expensive for a patent strategy to protect. Additionally, qualified candidates in hot fields such as AI/ML are highly sought after, and the risk of trade secret leaks, intentional or not, is high. AI/ML-based SaMD manufacturers may be able to mitigate harms caused by misappropriation via trade secret protection more expeditiously than via patent enforcement. AI/ML aspects of an SaMD may function as a black box, opaque to users. Thus, infringement may be difficult to detect, and lack of detectability may factor negatively in the cost-benefit analysis of a patent.

Weighing the costs, risks, and benefits associated with the patenting and, thus, disclosing, of an AI/ML-based SaMD against the costs, risks, and benefits associated with maintaining aspects of the AI/ML-based SaMD as trade secrets, a holder of AI/ML intellectual property would be well-served to consider trade secret protection.

The Defend Trade Secrets Act (DTSA) defines trade secrets as:[47]

> "[A]ll forms and types of financial, business, scientific, technical, economic, or engineering information, including patterns, plans, compilations, program devices, formulas, designs, prototypes, methods, techniques, processes, procedures, programs, or codes, whether tangible or intangible, and whether or how stored, compiled, or memorialized physically, electronically, graphically, photographically, or in writing if—
>
> (A) the owner thereof has taken reasonable measures to keep such information secret; and

[47] 18 U.S.C. § 1839(3).

> (B) the information derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable through proper means by, another person who can obtain economic value from the disclosure or use of the information."

The Uniform Trade Secrets Act, which forms the basis of most state causes of action for trade secret misappropriation, includes a similar definition.

Accordingly, some aspects of an AI/ML-based SaMD that may rise to the level of trade secrets include, for example, aspects related to training data, model weights, and hyperparameters. Training data and procedures for collecting such data may be valuable because data directly affects development and training of an AI/ML model and thus affects the utility and effectiveness of the SaMD. Model weights, which are derived during the training process, also are valuable because they control the inner transformations of data within the AI/ML model. Given that many popular model architectures are known for various use cases (e.g., AlexNet or ResNet 50 convolutional neural network), the unique and proprietary aspects of a particular AI/ML heart of an SaMD may thus be the learned model weights. Hyperparameters control the learning process and are a critical part of the machine learning process. Hyperparameters directly impact the performance of the model and tuning of hyperparameters may take place over a large solution space either by manual labor and expertise or by automated means. While the foregoing focuses on keeping successful aspects of an AI/ML-based SaMD secret, it should be noted that knowledge of aspects that did not work during development also may be valuable trade secrets, since access to such information may allow a competitor to avoid costly trial and error.

Theoretically, if some or all of these foregoing aspects were made known or "readily ascertainable," a competitor may conceivably develop a similar competitive product using such information, where it would otherwise not be possible to reverse engineer an AI/ML-based SaMD. Thus, taking "reasonable measures" to keep some or all of such information secret is vital to

maintaining trade secret protection. Typical measures include restricting access to trade secrets (e.g., including cybersecurity controls), proper labeling of sensitive information, non-disclosure agreements, employee training, and employee onboarding and exit procedures.

In view of these considerations, questions arise regarding the extent of disclosure necessary to navigate a successful FDA approval and ensuring transparency for patients (whether in an initial premarket submission, in a Predetermined Change Control Plan, or under any transparency guidance) while also maintaining secrecy for intellectual property protection of the fullest extent. Initially, confidential commercial or financial information and trade secrets submitted to the FDA may be unavailable for public disclosure.[48] Procedures are provided to designate submitted information as exempt under exemption 4 of the Freedom of Information Act (which will expire after 10 years), and further procedures to object to an independent decision by the FDA that disclosure is required.[49] The FDA defines trade secrets under 21 C.F.R. § 20.61(a) as "any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort" and "[t]here must be a direct relationship between the trade secret and the productive process." Although this definition differs slightly from the DTSA, the potential AI/ML trade secrets described above may reasonably satisfy the "direct relationship" requirement if they are related to the functionality of the SaMD.

However, rather than solely relying on disclosure exemptions, a manufacturer should consider carefully to what extent trade secrets need to be disclosed to satisfy regulatory requirements, or whether trade secret functionality can be described in more general, higher level

[48] 21 C.F.R. §§ 20.21, 20.61(c). *See also* Douglas Nemec, William Casey and Tara Melillo, *Protecting Trade Secrets Disclosed To The FDA*, Portfolio Media, Inc. (Feb. 13, 2018), https://www.skadden.com/-/media/files/publications/2018/02/protecting_trade_secrets_disclosed_to_the_fda.pdf.
[49] 21 C.F.R. § 20.61(d),(e),(f).

terms. While subject matter eligibility issues under 35 U.S.C. § 101 may have previously resulted in owners keeping AI/ML functionality a trade secret, FDA disclosure obligations may now tilt the scales back in favor of a patent application filing. Aside from FDA disclosure obligations, the burden, and risk, of not properly keeping information secret may lead some companies to pursue patent, rather than trade secret, protection for some innovations. Manufacturers may also consider using explainability and/or interpretability techniques to characterize the trustworthiness of the AI/ML aspects of an SaMD in terms of accuracy, reliability, robustness, fairness, and transparency metrics, for example. Thus, manufacturers are encouraged to take advantage of the FDA's Pre-Submission process to receive feedback on a submission strategy that avoids disclosing trade secret information altogether.

FOIA Request Considerations

The Freedom of Information Act (FOIA) permits third parties to request recorded information generated during pre-market and postmarked investigations by the FDA. It is already common practice for third parties to make FOIA requests to receive non-public information for drug approvals, facility inspections, etc. This section analyzes potential considerations for a manufacturer undergoing an FDA reviewal process for a SaMD.

According to the *2021 FDA publication*, the FDA is planning to implement a regulatory framework for investigating artificial intelligence (AI) and machine learning (ML) software as medical devices (SaMD) through a software's entire lifecycle. The *2021 FDA publication* does not provide guidance as to what documentation will need to be provided for the review of a SaMD. However, the FDA's Predetermined Change Control Plan provides some guidance on the content necessary for a review of a change to a SaMD. Changes to a SaMD include modification to clinical

and analytical performance, modifications to inputs used by an algorithm and their clinical association to the output, and modification to the intended use of the SaMD including the output of the SaMD. Changes to any of these aspects of a SaMD could cause a manufacturer to provide documents describing state of the SaMD prior to the change and the state of the SaMD after the change. These documents could be discoverable by a third party under the FOIA.

To protect their intellectual property, manufacturers may need to consider identifying certain aspects of an FDA approval filing as confidential information or a trade secret. The FDA's definition of a trade secret includes "any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to the end product of either innovation or substantial effort.[50] Information that is submitted and qualifies as a trade secret, must be protected by the FDA and may not be subject to disclosure in response to an FOIA request.

Yet, submission of trade secrets to the FDA carries some risk of disclosure. Under FOIA, an agency can withhold from production any documents that are "trade secrets and commercial or financial information obtained from a person [that is] privileged or confidential."[51] FDA has a process of notifying submitters who have designated submissions as trade secrets of FOIA requests, which is outlined in 21 C.F.R. § 20.61. If the FDA has decided to disclose the information, it will notify the trade secret submitter in writing, after which the submitter will have five working days to object to the disclosure.[52] This is a short time period that does not leave much room for error. Moreover, if the FDA must notify a large number of submitters, notification may be done "by posting or publishing a notice in a place where the submitters are reasonably likely to

[50] 21 C.F.R.§ 20.61(a).
[51] 5 U.S.C. § 552(b)(4).
[52] 21 .C.F.R. § 20.61(e)(2).

become aware of it."[53] Lack of direct notice to the trade secret submitter further increases the risk of trade secret disclosure. The FDA's stated goal of increased transparency, safety, performance, and elimination of data bias suggests that the FDA is likely to lean towards disclosing more, as opposed to less, information about AI/ML based SaMDs to the public, further increasing the risk of trade secret disclosure.

As such, an unexpected FOIA request may come at a point in time at which is too late for an applicant to pivot from trade secret protection to a patent application filing. If the product is out on the market or has otherwise been publicly disclosed, a subsequent reveal of trade secret material in response to a FOIA request may come after any grace period allowed for patent application filing has already passed. As such, the trade secret may be disclosed, and the owner may no longer have the ability to apply for patent protection, potentially leaving the information available in the public domain. For at least these reasons, careful thought and consideration should go into a company's strategy for harmonizing FDA clearance and IP protection.

Without further guidance as to the granularity of the information that the FDA will require manufactures to produce, it can be difficult to ascertain how much information would be disclosed pursuant to an FOIA request. Therefore, manufacturers should think carefully about maintaining flexibility and options, where possible, to protect their confidential information. Sometimes, however, commercial reasons may override the benefit of protecting trade secrets. If, for example, physicians request access to more information regarding the rationale of the AI/ML model and generated conclusions, how important will trade secret protection be for a device that is not succeeding in the market? In such a case, releasing more information to the public may be commercially more important than the risk of disclosing trade secrets related to the device. The

[53] 21 C.F.R. § 20.61(e)(1).

need for a customer to understand how the AI works before adopting it is often referred to as "explainable AI," and is perhaps more important in healthcare industry than in certain other industries where AI is commonly used.

Finally, it should be noted that trade secret protection does not protect from independent development of the same technology by a competitor. If the competitor has access to similar training data and suitable AI training methods are known or can readily be worked out, what is the likelihood that a competitor will be able to develop the same technology? If the likelihood is significant, patent protection may better suit a SaMD manufacturer's goals.

Disclosure Questions for AI/ML Patents and FDA Processes

U.S. patent law requires that the claims of a patent application: (1) have a proper "written description" disclosure, and (2) have enablement support. *See* 35 U.S.C. § 112(a). The written description requirement requires a patent specification to describe the claimed invention in sufficient detail to establish that the applicant had "possession" of the claimed invention as of the application filing date. The enablement requirement requires a determination of whether the patent specification contains sufficient information regarding the subject matter of the claims so as to "enable" a person skilled in the art to make and use the claimed invention.

Thus, an applicant for a SaMD-related patent must describe their invention such that someone of ordinary skill, such as a computer scientist or computer engineer skilled with medical device hardware, in the art could read the application to make and use the invention, and the description must show that the applicant had possession of the material as claimed. Although a manufacturer is not required to concurrently file an application for patent protection along with

filing for FDA approval of a SaMD, it may be prudent to do so. This section discusses how those manufacturers that choose to pursue a patent may find support by the FDA process.

Documents provided by a manufacturer to the FDA can be presented to the U.S. Patent and Trademark Office to show that disclosure requirement pursuant to U.S.C. § 112(a) has been met. As stated in the MPEP, an applicant may submit factual affidavits under 37 CFR § 1.132 or cite references to show what one skilled in the art knew at the time of filing the application.[54] The MPEP specifically mentions that in chemical and biotechnical applications, evidence submitted to the FDA to obtain approval for clinical trials may be submitted, to demonstrate enablement, but is not required. Although, the MPEP passage is directed towards chemical and biotechnical cases, an argument can be made that the clinical trials are analogous to a training and inferencing phase for an AI/ML-based SaMD. Therefore, if an applicant for a SaMD patent application is confronted by a rejection for lack of adequate disclosure (e.g., with respect to enablement or written description), the patent practitioner should consult with the attorney handling a concurrent FDA review process and determine whether any information in the FDA process is germane to establishing such written description.

Information useful for demonstrating written description for SaMD invention can include information regarding an "algorithm" as executed by the underlying hardware upon which the SaMD invention operates. For example, the USPTO published, in the Federal Register, guidance regarding (and titled): "Examining Computer-Implemented Functional Claim Limitations for Compliance With 35 U.S.C. 112" See 84 Fed. Reg. 4 at 57-63 (Jan. 7, 2019) (referred to as "the Section 112 Guidance" herein). The Section 112 Guidance is intended for use by U.S. patent examiners for examining software-related inventions, which would presumably cover SaMD. For

[54] Manual of Patent Examining Procedure § 2164.05.

software-related inventions, the Section 112 Guidance provides an overarching solution to meeting both the written description and enablement requirements. That is, the Section 112 Guidance informs that disclosure of a software "algorithm" can meet both the written description and enablement requirements.

According to the Section 112 Guidance, an algorithm is defined as "a finite sequence of steps for solving a logical or mathematical problem or performing a task."[55] More importantly, the Section 112 Guidance defines an "algorithm" in the manner described by the Federal Circuit, which provides a flexible approach for expressing an algorithm in a patent application. That is, according to the Federal Circuit, a patent application may define an "algorithm in any understandable terms including as **a mathematical formula, in prose, or as a flow chart, or in any other manner that provides sufficient structure**."[56]

Accordingly, for any software-related invention, such as a SaMD invention, an applicant should include an algorithm that meets one or more of these definitions, especially if such algorithm is already identifiable in a concurrent FDA review process. Typically, a flow chart, included as part of a figure of a patent application, provides a practical approach to illustrating an algorithm, as the flow chart is easily identifiable to the examiner or district court when the patent is reviewed. For AI/ML related inventions, such algorithm could include a description of the type of training data used to train a respective model, an example of the weight(s) of the model, and/or the hyper-parameters used during the training process.

[55] Section 112 Guidance at 61-61 (citing Microsoft Computer Dictionary (5th ed., 2002)).
[56] *Id*. (citing *Finisar Corp. v. DirecTV Grp., Inc.*, 523 F.3d 1323, 1340 (Fed. Cir. 2008).

Device Labeling for Medical Devices

Software that qualifies as a medical device is subject to the FDA's regulations on medical device labeling. Labels are written, printed, or otherwise graphical matter on a medical device or its packaging. The FDA's labeling requirements for software do not differ substantially from the requirements for tangible medical devices. In general, the FDA requires that labels conspicuously placed on a medical device include information name and place of business of the manufacturer, intended use, and instructions. AI/ML-based SaMD offers unique challenges that are not present in conventional software, such as in implementations where the algorithm may be locked into place. For AI/ML-based SaMDs, the training data used to train a medical algorithm can change throughout the device's lifecycle. Additionally, based on feedback data or new training data sets, AI/ML-based SaMD can manipulate its own output. According to the *2021 FDA publication*, the FDA has heard from various parties regarding the challenges of labelling an AI/ML-based SaMD and using the labelling to provide transparency of the device to users. Among the issues, the FDA identified the need for manufacturers to describe the training data, the relevance of the inputs, the logic the device employs, the role of the output, and evidence of the performance. To address these issues, the FDA's plan is to hold a public workshop to disseminate information and gather input from form the community as to how labelling promotes transparency.

One challenge in particular that the FDA should address is that information initially provided on the label of an AI/ML-based SaMD may need to contemplate the SaMD's behavior throughout the device's lifecycle. The FDA has not yet addressed the unique demands of labeling an AI/ML-based SaMD. However, FDA's publication entitled *Deciding When to Submit a 510(k) for a Change to an Existing Device* may be instructive.[57] According to the guidance, relevant

[57] *Deciding When to Submit a 510(k) for a Change to an Existing Device*, United States Food and Drug Administration (Oct. 25, 2017), https://www.fda.gov/media/99812/download.

considerations for determining whether to change a label include: is there a change in the indications for use, does the change describe a new population that the device is intended to be used for, and does the change identify any new risks or significantly modified risks. For an AI/ML-based SaMD, changes to the medical algorithm can certainly impact these considerations and necessitate a label change. For example, changing training data sets to include or remove new populations segments could certainly affect to which population segment a device is intended for. Therefore, as the content of a label changes during the device's lifecycle, the label may need to be changed to include the accurate information. As the AI/ML-based SaMD changes throughout its lifecycle, manufacturers will also need to monitor the changes and determine whether the changes trigger a need for a labeling change. In some instances, electronic labeling may improve transparency and accuracy as changes occur in software-based devices.

Data: Ownership, Sharing with the FDA, Tension in Legal Doctrines

AI/ML-based SaMDs rely on data sets to train the medical algorithms to reach the correct results. In many instances, larger training data sets may lead to more robust algorithms for providing accurate predictions and avoiding issues such as overfitting. In the health care space, companies may not be able to share training data for a multitude of reasons. Privacy laws may prohibit the sharing of data that can identify an individual, a process to unencrypt data that has been encrypted to protect confidential information may be cost prohibitive, data received from a foreign jurisdiction may be subject to strict control requirements, or a company's training data may be a strategic advantage over its competitors.

The *2021 FDA publication* does not appear to provide any resolution or plan for addressing issues related to data ownership. Helpfully, the *2021 FDA publication* does, however, describe

different, example scenarios in which a manufacturer may need to produce training data. Among the scenarios described, the FDA may need to inspect the training data sets to determine whether the AI/ML-based SaMD are subject to biases that mirror biases in the training data sets. Additionally, as part of its quality control, the FDA may need to inspect the data to evaluate a manufacturer's data management practices. To promote transparency and reassure the public, the FDA may inspect the manufacturer's training data. Each of the goals are reasonable and important to protect the public health. The 2021 FDA publication does not describe a methodology for inspecting the data to protect the public's interest, while maintaining the manufacturer's interests in complying with the rules by which it obtained the data and protecting itself from disclosure of the data. However, conflict between these various interests is likely an issue that will need to be resolved.

Brief Discussion of Some SaMD Examples from the FDA

In conjunction with their Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan, the FDA provided three hypothetical examples for public comment. These examples may or may not be permitted under the FDA's proposed framework but are intended to be illustrative of types of AI-related SaMD. They can be instructive to evaluate how such SaMD might fit into a regulatory and IP protection strategy.

Intensive Care Unit (ICU) SaMD

In this example, the medical software includes a ML model that 1) receives electrocardiogram, blood pressure, and pulse oximetry signals from a patient monitor and 2) detects patterns in the signals that indicate instability. When instability is predicted by the model,

the software triggers an alarm for urgent care for the patient. As the software is used, the algorithm and associated ML model can be modified based on feedback and analysis across various sub-populations to improve model performance. Validation data set(s) are collected for ongoing validation of the model and possible modification and regeneration of a new model if the validation does not satisfy a threshold.

From an IP perspective, while the ML model itself is likely not patentable, the overall system including the ML model, various signal inputs, and actionable output alarm could be patentable. The applicant may have to focus on the output alarm and what it triggers in another system to show a practical application from a 35 U.S.C. § 101 subject matter perspective. How the ML model is trained on patient data and updated based on sub-population analysis may be interesting from a subject matter eligibility perspective. Additionally, the validation process by which data sets and model performance are analyzed and compared to a threshold to trigger regeneration of a new model may also be interesting from a patent perspective. Conversely, some of the details around the ML model may be undetectable (and/or insufficiently describable under 35 U.S.C. § 112) such that the applicant chooses to protect that IP as a trade secret instead.

From an FDA perspective, the original ML model and associated software can be documented for premarket 510(k) clearance by the FDA. A PCCP can be developed around the ongoing validation and regeneration of the ML model to allow for continuing approval of the ML model-based SaMD as the ML model continues to evolve based on exposure to more and more patient sub-populations. Such FDA 510(k) submissions may be able to focus on the overall software process and without focus on the specific ML model details that the applicant might wish to protect as a trade secret.

Skin Lesion Mobile Medical App

In this example, the medical software includes a ML model that analyzes smartphone camera images including a skin lesion to determine characteristics of the lesion to aid a dermatologist in labeling the lesion. The software performs a quality review of the smartphone images and compares image quality across multiple devices to accept or reject images for further analysis. Physical characteristics of the lesion are analyzed by applying the image(s) to a ML model that has been trained using real-world data to generate a characterization of the lesion.

From an IP perspective, as above, the ML model itself, may be difficult to patent. However, image processing using an AI/ML model has been shown to be patent eligible and even featured in USPTO examples. The interaction with a single smartphone as well as across multiple smartphones to accept or reject images, and potentially provide some adjustment or feedback, could be patent eligible as well. If the characterization of the legion drives a next action in another device, that may also be an aspect to consider for patentability.

From an FDA perspective, the ML model and associated smartphone software can be documented for premarket 510(k) clearance by the FDA. The ML model here may not necessarily evolve, but a PCCP can be developed to anticipate and address that aspect of the software.

X-ray Feeding Tube Misplacement SaMD

In this example, the medical software analyzes chest x-rays to detect a misplaced feeding tube, which triggers a notification. X-ray detection uses an AI model trained on real-world image data to detect tube misplacement. An algorithm prioritizes images identified as having a misplaced tube in a radiologist's queue and notifies a nurse.

From an IP perspective, while the ML model itself is likely not patentable, the image processing using the AI model is an accepted avenue to subject matter eligibility. The associated algorithm to prioritize images and adjust images in a queue is also likely patent eligible. One aspect to consider is the nature of the notification – is it purely a notification or is it a trigger for another system (rather than the human nurse) to also take some action. If the latter, the automated triggering of an action at a second system based on an analysis at the first system can also be evidence of subject matter eligibility.

From an FDA perspective, the AI model and associated prioritization software can be documented for premarket 510(k) clearance by the FDA. The ML model here may not necessarily evolve, but a PCCP can be developed to anticipate and address that aspect of the software as well.

Conclusion

While AI-driven SaMD can leverage learnings and adaption from real-world usage and observation, such software also raises unique considerations for regulatory bodies, such as the FDA and the USPTO, due to the complex, iterative, and data-driven nature of their development. The USPTO and courts continue to grapple with suitable mechanisms for protection of AI/ML-based SaMD. The FDA continues its evaluation of how to provide appropriately tailored regulatory oversight over such subject matter as well. Software developers, medical device manufacturers, and intellectual property practitioners also continue to evolve how best to protect innovation in this area, while helping to ensure that such innovation is also regulated and available like other, more traditional, medical devices.

On October 27, 2021, Guiding Principles for Good Machine Learning Practice (GMLP) for Medical Device Development were published by the FDA in collaboration with Health

Canada and the UK's Medicines and Healthcare products Regulatory Agency (MHRA).[58] These guiding principles are intended to "help promote safe, effective, and high-quality medical devices that use AI/ML."[59] The ten guiding principles are intended to help promote good software engineering, multi-disciplinary expertise, monitoring, testing in clinically relevant conditions, and robust data sets based on best practices, diverse populations, and intended use of the device. The FDA's hope is that the guiding principles will help lay the foundation for development of GMLP for AI/ML-based devices.

At the same time, the Federal Circuit and other courts continue to struggle with the eligibility of medically-related software subject matter. Recent cases focus on whether the medical software improves a machine (e.g., a medical device or other healthcare system) itself or merely applies basic processing to data generated by another machine. Given a high degree of uncertainty at the USPTO and in the courts, a decision on patent application filing and its associated disclosure should be weighed carefully against the reality that the technology may then be described in a patent application yet ultimately found unpatentable.

As such, inventions directed to SaMD, SiMD, and other medical device-related software can be patented, but such inventions must address a unique combination of challenges faced by software, diagnostic methods, treatment methods, and biologics to help ensure patentability in the eyes of the USPTO and the courts while also meeting a company's regulatory obligations in the eyes of the FDA. Additional evolutionary unique considerations posed by AI-related inventions and corresponding FDA requirements for ongoing submission further complicate these efforts.

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[58] *Good Machine Learning Practice for Medical Device Development: Guiding Principles*, United States Food and Drug Administration (Oct. 14, 2021), https://www.fda.gov/media/153486/download.
[59] *Id*.

Efforts to balance FDA approval with IP protection in this area are in their infancy, and the FDA is just now exploring how to advance the FDA's oversight for AI-based SaMD through their AI Action Plan for SaMD and associated Predetermined Change Control Plan. The USPTO has also been alerted to potential friction in this area only recently. As more and more companies are active in this area, more patent applications, 510(k) submissions, issued patents, and associated decisions will arise. As more companies seek FDA approval of AI/ML-based SaMD and disclose AI/ML and other software functionality as part of that process, such companies may seek patent protection since they can no longer keep such functionality as a trade secret. Avenues for complementary 510(k) clearance and IP protection exist, but practitioners must be aware of the tensions between these regulatory regimes to provide the best counsel to their clients. Careful consideration should be given to an applicant's IP strategy in this area, and it is advisable for IP and regulatory counsel to work together on a more comprehensive plan rather than a siloed approach that separately focuses on each of these areas of concern.