FDA Issues Guiding Principles for Good Machine Learning Practice for Medical Device Development

On October 27, 2021, the U.S. Food and Drug Administration (FDA), Health Canada and the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) **issued** a set of ten guiding principles meant to aid the development of Good Machine Learning Practice (GMLP).

Artificial intelligence and machine learning (AI/ML) offers the potential to analyze the vast amount of real-world data generated from health care every day to provide transformative insights. These insights can not only help improve individual product design and performance, but also hold the promise of transforming health care.

However, AI/ML technology has unique complexities and considerations. The goal of these guiding principles is to help promote safe, effective, and high-quality medical devices that use AI/ML to best cultivate the future of this rapidly progressing field.

Although not formal or binding, as companies continue to leverage AI/ML in their medical devices, they should remain mindful of each of the ten guiding principles:

1. **Leveraging Multi-Disciplinary Expertise Throughout the Total Product Life Cycle**

   Companies should leverage internal and external multi-disciplinary expertise to ensure they have a thorough understanding of the model's integration into the clinical workflow, and the desired benefits and associated patient risks, to ensure the safety and effectiveness of the device while serving clinically meaningful needs throughout the product lifecycle.

2. **Implementing Good Software Engineering and Security Practices**

   Companies should implement as part of model design data quality assurance, data management, good software engineering practices, and robust cybersecurity practices.

3. **Utilizing Clinical Study Participants and Data Sets that Are Representative of the Intended Patient Population**

   Companies should ensure that their data collection protocols have sufficient representation of relevant characteristics of the intended patient population, use, and measurement inputs in an adequate sample size in their clinical study and training and test datasets so that results can reasonably be generalized to the population of interest. Data collection protocols appropriate for the intended patient population may help to

identify where the model may underperform and may mitigate bias.

4. **Keeping Training Sets and Test Sets Independent**

   Companies should consider and address all sources of dependence between the training and test datasets, including patient, data acquisition, and site factors to guarantee independence.

5. **Selecting Reference Datasets Based Upon Best Available Methods**

   Companies should use accepted, best available methods for developing a reference dataset, *i.e.*, a reference standard, to ensure clinically relevant and well characterized data are collected (and that the reference's limitations are understood). Where available, companies should use accepted reference datasets in model development and testing that promote and demonstrate model robustness and generalizability across the target population.

6. **Tailoring Model Design to the Available Data and Reflecting the Intended Use of the Device**

   Companies should have a solid understanding of the clinical benefits and risks related to the product and utilize this understanding to create clinically meaningful performance goals. Additionally, companies should ensure the model design is suited to the available data and supports active mitigation of the known risks.

7. **Focusing on the Performance of the Human-AI Team**

   Where the model has a human element, companies should consider human factors and human interpretability of the model outputs.

8. **Testing Demonstrates Device Performance during Clinically Relevant Conditions**

   Companies should develop statistically sound tests and execute them to assess device performance data independent of the training data set. Such assessment should be conducted in clinically relevant conditions with consideration given to the intended use population, important subgroups, clinical environment and use by the Human AI-Team, measurement inputs, and potential confounding factors.

9. **Providing Users Clear, Essential Information**

   Companies should provide users ready access to clear, contextually relevant information that is appropriate for the target audience. Such information includes not only information pertaining to the product's intended use and indications for use, performance of the model for appropriate subgroups, characteristics of the data used to train and test the model, acceptable inputs, known limitations, user interface interpretation, and clinical workflow integration of the model, but also users should be made aware of device modifications, updates from real-world performance monitoring, the basis for decision-making (when available), and a way to communicate product concerns to the company.

10. **Monitoring Deployed Models for Performance and Managing Re-Training Risks**

    Companies should deploy models that are capable of being monitored in real-world usage

with a focus on maintaining or improving safety and performance. Further, when models are trained after deployment, companies should ensure there are appropriate controls in place to manage risks that may impact the safety and performance of the model.

FDA's expectations with respect to GMLP will continue to advance and become more granular as additional stakeholder input is considered. The docket for FDA's GMLP Guiding Principles, **FDA-2019-N-1185**, is open for public comment.

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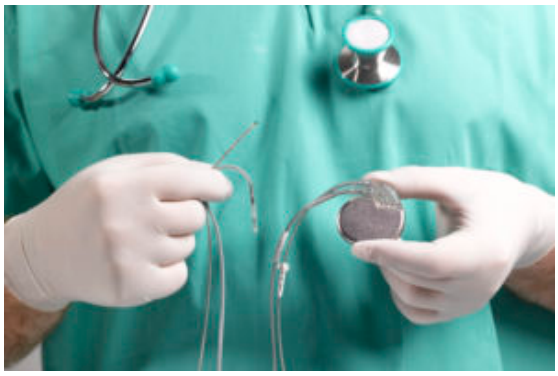
Exactly One Year Later, CMS Reverses Course on Covering Innovative MedTech



In September 2020, the Centers for Medicare & Medicaid Services (CMS) **proposed** a new rule that would expedite Medicare coverage for medical technology approved through the Food & Drug Administration's (FDA's) "Breakthrough Devices Program." CMS's proposal – the Medicare Coverage of Innovative Technology, or MCIT, Pathway – was groundbreaking in that innovative medical technology would be afforded a new, expedited coverage avenue that would significantly reduce the time it takes for Medicare beneficiaries to gain access to and benefit from innovative technology. It published the **final rule** on January 14, 2021.

But, just one year later on September 15, 2021, CMS plans to rescind the MCIT pathway altogether. As a result, the medical technology industry, providers, and patients, which had looked favorably upon the agency's MCIT proposal, will continue to face the uphill climb of traditional Medicare coverage for medical devices.

Medicare Coverage of Medical Technology

Prior to CMS's proposal, FDA marketing authorization of a breakthrough device did not mean immediate access for Medicare beneficiaries. Instead, Medicare rules required even greater effort on the part of manufacturers and providers for Medicare to actually pay for the technology.

Under traditional Medicare coverage rules, even if the FDA granted a particular product marketing authorization, CMS separately determines if the device should be considered "reasonable and necessary" for patient diagnosis and treatment via a National Coverage Determination (NCD) from CMS or via a Local Coverage Determination (LCD), made by one or more Medicare Administrative

Contractors, or MACs. This process, which includes evidence-based reviews, is lengthy and – in the case of an LCD – may even result in different standards in different geographies, based on the location of the MAC. And, as the medical technology industry has repeatedly emphasized, the result is that America's seniors and others dependent upon Medicare coverage, would have to wait – in some cases for years – to access the most innovative technology.

MCIT Proposal – An Expedited Avenue to Coverage for Innovation

Under the original 2020 proposal's MCIT coverage path, CMS would offer a four-year period after FDA marketing authorization for breakthrough status medical technology to be reimbursed by Medicare, thereby bypassing the NCD or LCD process. If the technology did not have an existing Medicare benefit category or was excluded from Medicare coverage by statute, MCIT would not be available. During the MCIT path's four-year period, medical device makers would be encouraged (not required) to develop additional clinical evidence and to collect additional data. And at the end of the four years, the device would be subject to an NCD that either grants or denies Medicare coverage or offers MACs the discretion to conduct claim-by-claim adjudication or an LCD.

Put another way, the MCIT path would significantly abbreviate what has become a lengthy coverage process and would provide Medicare beneficiaries with quicker access to advanced, innovative technology.

In promulgating the MCIT coverage path, then-CMS Administrator Seema Verma **emphasized** its goal of expediting the delivery of advanced, innovative technology to Medicare beneficiaries, and diminishing administrative burdens on that hamper or slow this process. Verma noted, "Government processes have slowed beneficiaries' access to innovative treatments. Despite being deemed safe and effective by the FDA, Medicare beneficiaries have not had predictable, immediate access to innovative breakthrough devices . . . [t]he MCIT rule will eliminate this lag time for both seniors and innovators."

MCIT Proposal's "Reasonable and Necessary" Definition

The MCIT rule also addressed another critical issue for the Medicare program: defining the term "reasonable and necessary." Under the **current regulatory framework**, Medicare may only cover items and services that are classified as "reasonable and necessary" for the diagnosis or treatment of an illness or injury. Notably, this term – despite its clear significance – is not defined in the statute or regulations. The term is defined only in informal guidance (i.e., the **Medicare Program Integrity Manual**).

The **MCIT Final Rule** sought to codify and expand the definition of "reasonable and necessary" as laid out in the Medicare Program Integrity Manual. In expanding the definition, the **MCIT Final Rule** stated that, in addition to meeting any of the qualifications outlined in the **Medicare Program Integrity Manual**, items and services may be deemed "reasonable and necessary" based on CMS review of commercial insurer coverage decisions and policies. At the time of the **MCIT Final Rule**, CMS stated that it would publish a draft methodology for determining when commercial insurers' policies could be considered to meet the definition of "reasonable and necessary." Most notably, Verma **emphasized** that this portion of the rule would help give innovators a clearer understanding of CMS standards.

A New Administration, a New Approach

Despite the clarity provided by the MCIT rule, despite the certainty offered Medicare beneficiaries to accessing innovative technology, and despite the release of a final rule in January 2021, the Biden

Administration now plans to kill the MCIT path outright, citing the following reasons for its decision to rescind what had promised to get seniors better access to advanced technology:

- **Lack of Adequate Studies**: There is no FDA requirement that Medicare beneficiaries be included in clinical studies needed for market authorization. CMS, not FDA, typically requires and reviews evidence specific to medical devices for the Medicare population. By automatically granting national Medicare coverage to devices that receive FDA market authorization, the MCIT path would have eliminated CMS's ability to ensure whether medical device makers have generated adequate evidence that the breakthrough device would be reasonable and necessary for the Medicare patients that have the particular disease or condition that the device is intended to treat or diagnose.

- **Limited Ability to Revoke Coverage**: Traditionally, CMS reserves the right to deny coverage if it learns that particular devices may be harmful to Medicare beneficiaries. The MCIT path limited such rights for breakthrough medical devices with FDA market authorization. Under the MCIT path, CMS would only be able to expeditiously remove a Breakthrough Device from MCIT coverage for limited reasons, such as if FDA issued a warning letter or removed marketing authorization for the device.

- **Disincentivizing Development**: According to CMS, by incentivizing devices eligible for FDA breakthrough device designation, the MCIT path may have the unintended consequence of disincentivizing development of innovative second-to market devices and subsequent technologies of the same type that would not be eligible for breakthrough device designation.

CMS also plans to return to the drawing board on the definition of "reasonable and necessary," noting the following:

- **The Definition Removes Flexibility for the Agency**: Suggestions to codify or expand the definition of "reasonable and necessary" to include commercial insurer policies may remove existing flexibility and could even impact CMS's ability to ensure equitable health care access.

- **Need for a Separate Rule**. Given the implications the definition has for Medicare policy above and beyond just the coverage of innovative medical technology, the agency notes that the definition should be included in a separate rule.

Conclusions

While CMS's decision to rescind the MCIT Pathway appears to be a *fait accompli*, **comments to the agency's proposed rule are due on or before October 15, 2021.** If finalized, it is unclear whether the agency will revisit the concept in the future or whether the industry will continue to face lengthy delays between the time a medical device is authorized and the time America's seniors will benefit. CMS will continue to require and review evidence specific to the Medicare population to cover medical devices– a lengthy process that is above and beyond any clinical evidence produced as a result of any clinical studies required for FDA authorization.

Further, stakeholders will continue to face uncertainty. This includes **providers** (who will not be certain that their claims for procedures or products will be paid, especially if handled on a claim-by-claim basis or if subject to varied and differentiated local decisions from contractors); **patients** (who may or may not be able to access innovative technology), and **medical device makers** (who may be required to undergo significant evidence collection processes, not to mention delays in recouping

the funds invested into developing and building the medical technology in the first place).

We will continue to monitor and provide updates on this important issue for the medical technology industry. If you have any questions or would like to submit comments, please reach out to Matt Wetzel (**mwetzel@goodwinlaw.com**).

Alere Pays $198.75 Million to Settle False Claims for Allegedly Billing Medicare for Defective POC Devices, Not Charging Copays, and Sending Supplies to Deceased Patients

Alere Inc. and Alere San Diego Inc. (collectively "Alere") have come under fire recently by the U.S. Department of Justice ("DOJ") and other government agencies, agreeing to settle several rounds of accusations of False Claims Act violations for a total of $198.75 million.

The first series of settlements was **announced** by DOJ on July 8, 2021 and cost the company approximately $38.75 million in fines and penalties. Here, the medical device manufacturer was alleged to have billed Medicare for rapid point-of-care testing devices that Alere knew were defective. More specifically, the government alleged that the INRatio blood coagulation monitors (manufactured by Alere) were defective. The monitors were used by Medicare beneficiaries taking anticoagulant drugs to monitor their blood coagulation. Anticoagulants drugs can cause major bleeding when used in access or blood clots and strokes can develop when not enough medication is taken. DOJ alleged that Alere concealed the fact that the device was producing inaccurate results for some patients, resulting in several deaths and hundreds of injured beneficiaries. This practice was ongoing for a total of eight years, according to DOJ.

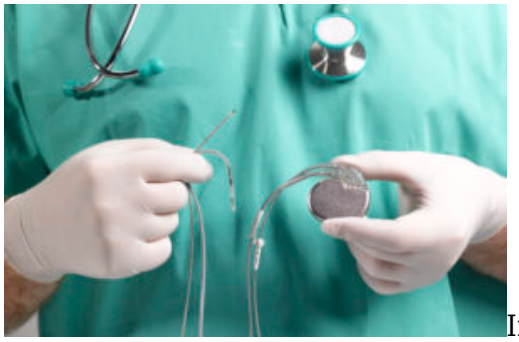
One month after this first massive settlement was announced, the DOJ **announced** an even more sizable settlement with Alere Inc.'s subsidiary, Arriva Medical ("Arriva"), a diabetes testing equipment supplier, totaling an additional $160 million to settle false claims related to an alleged kickback scheme. The DOJ purported that, from April 2010 through December 2016 – immediately prior to Abbott's $5.3 billion acquisition of Alere in 2017 – Arriva (1) regularly waived and failed to collect Medicare beneficiaries' cost-sharing amounts (i.e. copays); (2) sent glucose meters at no cost to patients; and (3) sent diabetic testing equipment to deceased patients.

Medical device makers, durable medical equipment suppliers, and Medicare providers of all sorts should take heed of these recent settlements and implement regular third party compliance and billing audits as part of their Compliance Program to help ensure that practices are aligned with

government expectations and rules. In addition, companies acquiring, merging with, or investing in healthcare entities should incorporate complete third party billing and compliance testing as part of their due diligence in connection with these types of transactions to identify billing-related risks.

If you have any questions, please contact Anne Brendel (**abrendel@goodwinlaw.com**; 415-733-6047) or Matt Wetzel (**mwetzel@goodwinlaw.com**; 202-346-4208).

Patient Stakeholder Group Zeroes in on Medical Device Industry



In recent months, the Kaiser Health Network (part of the Kaiser Family Foundation) has issued three reports scrutinizing the orthopedic industry and its practices. Each report articulates the stakeholder group's concerns over relationships among orthopedic and spinal surgeons, orthopedic implant manufacturers, and their sales representatives. Medical device manufacturers, especially those in the orthopedic space, should pay careful attention.

- **The first report** (June 2021) dives deeply into payments made by medical device makers to orthopedic surgeons who use their products. Kaiser highlights government allegations against orthopedic medical device makers (focusing specifically on the recent **SpineFrontier matter**) that they pay "sham consulting fees" to spinal surgeons for "doing little or not work." Kaiser identifies what it considers to be troublesome payments from medical device makers to surgeons that implant their products, including royalty payments (for "helping to design implants"), speakers' fees ("for promoting devices at medical meetings"), to stock ownership provided in exchange for consulting. Kaiser notes that, from 2013 through 2019, the orthopedic industry has paid $3.1 billion to its surgeon consultants, highlighting the potential to "corrupt medical judgment and tempt surgeons to perform unnecessary and wasteful operations." The patient stakeholder group also spotlights what it considers to be a "startling array of schemes to influence surgeons," including compensation for joining a medical society created by a medical device company; purchasing billboard space to advertise medical practitioners; providing employment to surgeon's relatives, and entertainment/sporting activities. The patient stakeholder group also emphasizes that "more than 600,000 American doctors lap up industry largesse . . . [mostly] through small payments that cover the cost of food, drinks, and travel to industry-sponsored events."

- **A second report** (August 2021) highlights the relationships between orthopedic makers and their sales reps, who are often called upon to provide technical support to surgeons in the operating room during surgeries. Device makers assert that having sales representatives must be present for certain procedures to ensure the proper functioning of highly complicated

surgical equipment and to make sure that the right scope of surgical tools and equipment are available. Critics, however, argue that the practice demonstrates the coziness between sales reps and physicians. The Kaiser report states that it is like "the relationship of a caddy and an avid golfer" and that "[d]uties can include lugging 20-pound sets of surgical hardware to the operating room, assuring it is sterile and knowing its specifications," even though – according to Kaiser – reps are not required to be trained medically. Critics further assert that companies are spending excessively for top sales talent, and the amount of money creates bad incentives, including failures to track injuries and pushing for unneeded surgeries. The result, according to Kaiser, is an increase in patient injuries and harm, which the stakeholder group asserts often go unreported.

- **A third report** (August 2021) places a spotlight on the issue of orthopedic surgeons taking ownership interests in private medical device companies, often referred to as PODs, including highly lucrative payments for selling and using products and as a result of larger medtech companies purchasing privately held medical device makers. Kaiser highlights the potential for incentivizing unnecessary surgeries and the negative consequences on patients. CMS has, in fact, **recently proposed updates to its Open Payments (Sunshine Act) program** to clarify requirements for physician-owned distributors to help ensure all of these payments are appropriately captured, reported, and publicly disclosed.

Should medical device makers pay attention to the Kaiser reports? Yes, especially makers of orthopedic devices. Increased interest from key patient stakeholder groups like Kaiser can only mean that others are also watching. We have not seen any let-up in the continued enforcement of the federal fraud and abuse laws against medical device companies. And as the government keeps the heat on the orthopedic industry, **companies should consider undertaking an independent, third-party compliance assessment** that addresses the following:

- Policies and practices on engaging health care providers to serve as consultants, including selection criteria, evaluation of payments, controls to limit influence, and documentation of services provided, focusing on royalties, speaker fees (see **OIG's November 2020 Special Fraud Alert on Speaker Programs**), and payments for technical training, among others.

- Policies and practices on physician ownership, including whether there are appropriate controls and measures for assessing when it is appropriate to provide ownership interests to physicians, especially given CMS's recent ramp-up of interest in physician-owned distributorships.

- Policies and practices relating to sales representatives in the operating room to support procedures, including identifying the extent to which videoconferencing and other virtual technologies might be used instead of permitting a rep's in-person presence in the operating room.

- Policies and practices on disclosure of payments and transfers of value made to physicians and other healthcare practitioners (as required under the Sunshine Act) and conflicts of interest, as these concerns are central to the criticisms lobbed by Kaiser and by the government in its enforcement actions.

A periodic, independent review of compliance practices helps ensure better alignment not only with federal healthcare fraud and abuse laws but also with compliance best practices and ethical principles that prioritize and protect patients. If you have any questions, please contact Matt Wetzel

(**mwetzel@goodwinlaw.com**) or (202-346-4208).

Is Prescription Support Software Classified as a Regulated Medical Device in Europe?

...the essential criterion for being classified as a medical device is the software's medical objective...

Background

Relying on an unregulated app or piece of standalone software to provide a diagnosis or recommend treatment could have potentially life-threatening consequences. In June 2020, the UK's medical devices regulator, the Medicines and Healthcare Products Regulatory Agency (MHRA) updated its **guidance** to help software and app developers in the medical field identify whether their products should be regulated as medical devices.

In particular, the MHRA endorsed the European Court of Justice (CJEU) ruling of **Snitem v Philips France C-329/16** from December 2017. This case considered whether prescription support software which used patient-specific data to detect drug interactions and excessive doses, constituted a medical device.

The CJEU's Judgment

The CJEU held that the prescription support software was a medical device under EU law for the following reasons:

- the software cross-referenced patient-specific data with the medicines that the prescriber had contemplated prescribing;
- the software automatically provided the prescriber with an analysis intended to detect possible drug interactions and excessive dosages; and
- the manufacturer intended the software to be used for one of more medical objectives specified in Article 1(2)(a) of the **Medical Devices Directive 93/42/EEC** (MDD), which include the diagnosis, prevention, monitoring, treatment or alleviation of a disease.

The CJEU further held that it is irrelevant whether the software acts directly or indirectly on the human body. According to the court, the essential criterion for being classified as a medical device is the software's medical objective, examples of which are mentioned above.

Practical Implications

The MHRA guidance provides further certainty that prescription support software and other decision support software in the medical field may be classified as medical devices and thus need to comply with the requirements under the MDD.

As a final point, the MDD is due to be replaced by the Medical Devices Regulation on 26 May 2021. A key implication is that the risk classification of a significant proportion of existing medical device software could change which would mean manufacturers will soon need to obtain regulatory approval to market such software in the EU.