University of Kentucky Office of Research Integrity

FDA Guidance for Unusual Products That May Be Investigational Test Articles Depending On Use In Research

Product	FDA Guidance/ Discussion Paper	Link	Summary
Artificial Intelligence/Machine Learning used in Drug/Biologic Development	Food and Drug Administration (FDA) Using Artificial Intelligence & Machine Learning in the Development of Drug & Biological Product 2023	https://www.fda.gov/media/167973/download	Artificial Intelligence (AI) and Machine Learning (ML) can be described as a branch of computer science, statistics, and engineering that uses algorithms or models to perform tasks and exhibit behaviors such as learning, making decisions, and making predictions. ML is considered a subset of AI that allows models to be developed by training algorithms through analysis of data, without models being explicitly programmed. This white paper includes an overview of the current and potential future uses for AI/ML in therapeutic development. It also discusses the possible concerns and risks associated with these innovations and ways to address them. For instance, the paper describes the importance of having human involvement, which will vary depending on how the technologies will be used. The paper also emphasizes adopting a risk-based approach to evaluate and manage AI/ML in facilitating innovations and protecting public health.
Artificial Intelligence/Machine Learning Software & Medical Devices	Artificial Intelligence/Machine Learning (AI/ML) in Software as a Medical Device (SaMD) 2021	https://www.fda.gov/media/145022/download	considers a total product lifecycle-based regulatory framework for these technologies that would allow for modifications to be made from real-world learning and adaptation, while ensuring that the safety and effectiveness of the software as a medical device are maintained.
Artificial Intelligence/Machine Learning Software & Medical Devices	Proposed Regulatory Framework for Modifications to AI/ML Based SaMD 2019	https://www.fda.gov/media/122535/download	Proposes a framework for modifications to AI/ML-based SaMD that is based on the internationally harmonized International Medical Device Regulators Forum (IMDRF) risk categorization principles, FDA's benefit-risk framework, risk management principles in the software modifications guidance. Considers

			when modifications related to performance, inputs, or intended use warrant 510(k) review during the Total Product Life Cycle (TPLC). Presents strategies for real-world monitoring and transparency.
Conventional Food, Dietary Supplement, or Cosmetic	Investigational New Drug Applications; Exemptions for Clinical Investigations to Evaluate a Drug Use of a Product Lawfully Marketed as a Conventional Food, Dietary Supplement, or Cosmetic 2022	https://www.fda.gov/media/164101/download?attachment	Proposes to amend IND exemption regulations for certain clinical investigations of lawfully marketed foods, dietary supplements, and cosmetics being evaluated as a drug. Must not be intended to support a drug development plan (drug claim), labeling change, or present significant risk to health, safety, or welfare of subjects. Includes provision for self-determination or FDA-determined exemption.
Cannabis	Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research 2023	https://www.fda.gov/media/164690/download	Describes FDA's recommendations regarding sources of cannabis for clinical research and resources for information on quality and control status considerations.
Cannabis	FDA and Cannabis: Research and Drug Approval Process 2023	https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process#main-content	Provides information on the specific requirements needed to develop a human drug that is derived from a plant such as cannabis. Links to botanical drug development and quality of products used in clinical trials. Encourages pre-IND meetings with FDA.
Cellular Tissue Based Products	(Final) Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2020	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/regulatory-considerations-human-cells-tissues-and-cellular-and-tissue-based-products-minimal	Provides guidance on minimal manipulation and homologous use criteria for determining if product qualifies for regulation solely under section 361 of the PHS Act (and not FDA). FDA intends to extend enforcement discretion under limited conditions with respect to the Investigational New Drug (IND) application and premarket approval (Biologics License Application (BLA)) requirements, for certain HCT/Ps, through May 2021.

In Vitro Diagnostics (IVDs) Used in Clinical Investigations of Therapeutic Products	IVDs considered investigational when used to guide management of subjects in therapeutic trials (e.g., drug trials), EVEN IF NOT BEING TESTED 2017	https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM589083.pdf	Provides guidance for In-vitro investigational devices (IVD) used to guide management of subjects in therapeutic product trials including drug trials. Outlines considerations on whether IVDs would be investigational, and if so, provides characteristics for studies that are significant risk, non-significant risk, or exempt from Investigational Device Exemption (IDE) requirements.
Lab Developed Tests (LDTs)	Medical Devices; Laboratory Developed Tests 2023	https://www.reginfo.gov/public/do/eAgendaViewRule?pubId=202304&RIN=0910-AI85	This proposed rule would propose to amend the Food and Drug Administration's regulations to make explicit that laboratory developed tests (LDTs) are devices under the Federal Food, Drug, and Cosmetic Act.
Studies Involving Administration of Unauthorized Tobacco Products	Use of Investigational Tobacco Products 2019	https://www.fda.gov/media/94052/download	Describes FDA's current thinking regarding the definition of investigational tobacco product and discuss the kind of information FDA intends to consider in making enforcement decisions regarding the use of investigational tobacco products until regulations are issued. This guidance document is intended to help researchers who may seek to study tobacco products that do not have marketing authorization.
Tobacco	Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products 2017	https://www.federalregister.gov/documents/2017/01/09/2016-31950/clarification-of-when-products-made-or-derived-from-tobacco-are-regulated-as-drugs-devices-or	FDA will consider whether the product is being used in a clinical investigation for an intended use that would meet the definition of "investigational new drug". Note that studies performed to meet statutory requirements in chapter IX of the FD&C Act relating to the impact of tobacco products on cessation behavior are not required to be designed as clinical investigations subject to the investigational new drug application requirements in part 312.

Fecal Transplant	(Draft) FDA Draft Enforcement Policy Regarding Investigational New Drug Requirements for Use of Fecal Microbiota for Transplantation To Treat Clostridium difficile Infection Not Responsive to Standard Therapies 2016	https://www.federalregister.gov/documents/2016/03/01/2016-04372/enforcement-policy-regarding-investigational-new-drug-requirements-for-use-of-fecal-microbiota-for	FDA plans to continue to exercise enforcement discretion if Fecal Microbiota for Transplantation (FMT) is used to treat C. difficile infection not responding to other therapies, provided that: A licensed healthcare provider obtains consent; donor and stool are qualified by screening; and FMT product is not obtained from a stool bank. The federal register notice added that FDA wants comments on the requirement for IRB review when the FMT is provided by a stool bank.
Other Products (Generally Recognized As Safe, isotopes, organisms, etc.)	(Final) Investigational New Drug Applications (INDs) - Determining Whether Human Research Studies Can Be Conducted Without an IND 2013	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-new-drug-applications-inds-determining-whether-human-research-studies-can-be	Final represents FDA's current thinking regarding when an Investigational New Drug (IND) application is needed. Includes information on (1) clinical investigations using marketed drugs, (2) bioequivalence/ bioavailability studies, (3) studies using radio labeled or cold isotopes, (4) studies using dietary supplements, foods, cosmetics (5) studies using endogenous compounds, (6) pathogenesis studies using modified organisms, (7) studies using wild-type organisms in challenge models, and (8) studies that do not have a commercial purpose. Also provides information on IND exempt studies and a process for seeking advice from FDA.
Virtual Reality & Augmented Reality	Primarily provides clinicians and patients considerations for use of AR or VR in healthcare	https://www.fda.gov/medical-devices/digital-health-center-excellence/augmented-reality-and-virtual-reality-medical-devices#how https://www.fda.gov/medical-devices/digital-health-center-excellence/augmented-reality-and-virtual-reality-medical-	List of Augmented Reality and Virtual Reality Marketed products Questions to Consider

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