INDs, IDEs, & IRBs

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Drugs & Devices

- Definitions/Applicability
- IND Exemptions
- Devices
- Hot Topics

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Key Definitions

Drug *means:*

(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and

(B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and

(C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and

(D) articles intended for use as a component of any article specified in clause (A), (B), or (C). (FD&C Act)

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Key Definitions

Device *means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is-*

1) *recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,*

2) *intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or*

3) *intended to affect the structure or any function of the body of man or other animals, and*

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. (FD&C Act)

Key Definitions

- **Clinical Investigation** *means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice*. (21 CFR 312.3(b))

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- **Investigation** *means a clinical investigation or research involving one or more subjects to determining the safety or effectiveness of a device.* (21 CFR 812.3(h))

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Key Definitions

- **Subject** *means a human who participates in an investigation, either as a recipient of the investigational drug or as control. A subject may be a healthy human or a patient with a disease*. (21 CFR 312.3(b))

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- **Subject** *means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.* (21 CFR 812.3(p))

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No Commercial Intent

Some believe that the IND regulations do not apply to clinical investigations that are not intended to investigate a drug's potential for commercial sale. Whether the IND regulations apply to a planned clinical investigation does not depend on whether the intent of the clinical investigation is commercial or noncommercial. Therefore, these types of studies would require an IND under part 312, unless they meet the criteria for an exemption…

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Part 312 Exempt

- Marketed drugs
- IVD Biologics
- Placebo
- Bioavailability/Bioequivalence (BA/BE)
- Radioactive Drug/Biologic
- Cold Isotopes (enforcement discretion)

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Part 312 Exemptions

21 CFR 312.2(b)(1): The drug being used in the research is lawfully marketed in the United States and **all** of the following requirements are met:

- The research is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug;
- In the case of a prescription drug, the research is not intended to support a significant change in the advertising for the product;
- The research does not involve a route of administration, dose, subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
- The research is conducted in compliance with the requirements of 21 CFR 312.7 (i.e., the research is not intended to promote or commercialize the drug product); and
- The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].

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FDA Guidance

Consider the risk implications of any conditions of use in the study that deviate from the conditions of use described in the drug's labeling, with particular attention to the following:

- Route of Administration
- Dose
- Patient Population

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Part 312 Exemptions

- 21 CFR 312.2(b)(2): For clinical investigations involving defined (blood grouping serum, reagent red blood cells, and anti-human globulin) IVD biological products, an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 312.160.

- 21 CFR 312.2(b)(5): A clinical investigation involving use of a placebo is exempt from the requirements of part 312 if the investigation does not otherwise require submission of an IND.

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Part 312 Exemptions

- 21 CFR 320.31(b) and (d): Bioavailability or Bioequivalence (BA/BE) studies if all of the following conditions are met:
  - The drug product does not contain a new chemical entity [21 CFR 314.108], is not radioactively labeled, and is not cytotoxic;
  - The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product;
  - The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and
  - The sponsor meets the requirements for retention of test article samples [21 CFR 320.31(d)(1)] and safety reporting [21 CFR 320.31(d)(3)].

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Part 312 Exemptions

- 21 CFR 361.1: Research using a radioactive drug or biological product if all of the following conditions are met:
  - It involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the product;
  - The use in humans is approved by a Radioactive Drug Research Committee (RDRC) that is composed and approved by FDA;
  - The dose to be administered is known not to cause any clinically detectable pharmacological effect in humans, and
  - The total amount of radiation to be administered as part of the study is the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study and is within specified limits.

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Part 312 Exemptions

- FDA practices enforcement discretion for research using cold isotopes of unapproved drugs if all of the following conditions are met:
  - The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry;
  - The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject;
  - The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies;
  - The quality of the cold isotope meets relevant quality standards; and
  - The investigation is conducted in compliance with the requirements for IRB review and informed consent. [21 CFR parts 56 and 50, respectively]

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Devices

- 812 Exempt
- Significant Risk
- Nonsignificant Risk

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Part 812 Exempt

Investigations of the following categories of devices:

- Devices, other than transitional devices, in commercial distribution prior to May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time
- Devices, other than transitional devices, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent (510k) to a device in commercial distribution prior to May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed in determining substantial equivalence

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Part 812 Exempt

- A diagnostic device, if the sponsor complies with applicable requirements in §809.10(c) and if the testing:
  - i. Is noninvasive,
  - ii. Does not require an invasive sampling procedure that presents significant risk,
  - iii. Does not by design or intention introduce energy into a subject, and
  - iv. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

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Part 812 Exempt

- A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, **if** the testing is not for the purpose of determining safety or effectiveness **and** does not put subjects at risk.
- A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

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Significant Risk (SR)

Significant risk device *means an investigational device that:*

1) *Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;*

2) *Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;*

3) *Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or*

4) *Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.*

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Nonsignificant Risk (NSR)

A **Nonsignificant risk device** study is one that is not part 812 exempt and does not meet the definition for an Significant Risk device study.

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Nonsignificant Risk (NSR)

- Importantly, NSR device studies do not require prior approval by the FDA nor are progress reports to the FDA required. The IRB functions as the FDA's surrogate with the IRB approval serving as the IDE approval and continuing review substituting for progress reports.
- FDA requires the NSR vs. SR determination to be made by the convened IRB. A part 812 exempt determination does not need to be made by the convened IRB, so long as the study otherwise qualifies for expedited review.
- NSR studies are subject to the abbreviated requirements at 812.2(b).

IRB

- IRB Procedures
- FDA Guidance

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IRB Procedures

- If the FDA has not made a determination:
  - Evaluating the sponsor or investigator's determination of whether an IND or IDE is required for the proposed study and the basis for this determination
  - Evaluating the sponsor or investigator's initial determination of whether the proposed study is 812-exempt, Nonsignificant Risk, or Significant Risk, and making and documenting the IRB's determination
- Reviewing the qualifications of the investigator(s), and the adequacy of the site(s) where the research will be conducted

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FDA Guidance

- IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed
- Determining Whether Human Research Studies Can Be Conducted Without an IND
- Frequently Asked Questions About Medical Devices
- Significant Risk and Nonsignificant Risk Medical Device Studies
- Off-Label and Investigational Use of Marketed Drugs, Biologics, and Medical Devices

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FDA Guidance

- Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of the Study Subject
- IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer
- IVD Device Studies – FAQs
- Informed Consent for IVD Device Studies Using Leftover Human Specimens that are Not Individually Identifiable

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Hot Topics

- HCT/Ps
- Medical Software

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Hot Topic – HCT/P

Human cells, tissues, or cellular or tissue-based products (HCT/Ps) means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/Ps include, but are not limited to, bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue.

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Hot Topic – HCT/P

The following articles **are not** considered HCT/Ps:

- Vascularized human organs for transplantation;
- Whole blood or blood components or blood derivative products subject to listing under parts 607 and 207, respectively;
- Secreted or extracted human products, such as milk, collagen, and cell factors; except that semen is considered an HCT/P;
- Minimally manipulated bone marrow for homologous use and not combined with another article (except for water, crystalloids, or a sterilizing, preserving, or storage agent, if the addition of the agent does not raise new clinical safety concerns with respect to the bone marrow);
- Ancillary products used in the manufacture of HCT/P;
- Cells, tissues, and organs derived from animals other than humans;
- In vitro diagnostic products as defined in 809.3(a);
- Blood vessels recovered with an organ, as defined in 42 CFR 121.2, that are intended for use in organ transplantation and labeled "For use in organ transplantation only. (21 CFR 1271.3(d))

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Stem Cells

- August 2017 FDA Statement
  - Stem cells and regenerative medicine as areas of focus for FDA for enforcement and for improved FDA procedures
- November 2017 FDA Announcement
  - Policy framework “to more clearly describe what products are regulated as drugs, devices, and/or biological products” and to ensure safety and effectiveness.
  - Risk-based enforcement discretion for 36 months

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Enforcement

- **August 2017** – Warning letter to US Stem Cell Clinic for marketing stem cell products derived from body fat without FDA approval and for significant GMP deviations
- **August 2017** – seizure of vials of vaccinia vaccine in California after finding that the vaccine was used in combination with stem cells derived from body fat to create an unapproved stem cell product which was being injected into cancer patients
- **May 2018** – FDA filed complaint against both clinics for permanent injunction
- **Nov 2018** – Warning letter to StemGenex for marketing stem cell products derived from body fat without FDA approval and for significant GMP deviations
- **Dec 2018** – Warning letter to Genentech – contaminated umbilical cord stem cell products

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Stem Cells

- **Dec 2018** – FDA sent letter to providers, clinics, and manufacturers around the nation reminding them of the policy framework, that the 36 month grace period of risk-based enforcement discretion would end in Nov 2020, and encouraging them to contact FDA *"well in advance of November 2020, to determine whether their products are subject to the agency's premarket approval requirements."*

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21 CFR 1271

- General Provisions (scope, definitions, exceptions)
- Registration and Listing
- Donor Eligibility
- Good Tissue Practice
- Reporting
- Labeling
- Inspection & Enforcement

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Applicability

- Establishments that manufacture human cells, tissues, and cellular and tissue-based products (HCT/P's) unless the establishment qualifies for an exception.

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Key Terms

- **Establishment** *means a place of business under one management, at one general physical location, that engages in the manufacture of human cells, tissues, and cellular and tissue-based products. "Establishment" includes:*

  (1) Any individual, partnership, corporation, association, or other legal entity engaged in the manufacture of human cells, tissues, and cellular and tissue-based products; and

  (2) Facilities that engage in contract manufacturing services for a manufacturer of human cells, tissues, and cellular and tissue-based products.

- **Manufacture** *means, but is not limited to, any or all steps in the recovery, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and the screening or testing of the cell or tissue donor.*

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FDA's Policy Framework

- Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use
- Same Surgical Procedure Exception: Questions and Answers Regarding the Scope of the Exception
- Expedited Programs for Regenerative Medicine Therapies for Serious Conditions
- Evaluation of Devices Used with Regenerative Medicine Advanced Therapies

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Regulatory Buckets

- Establishments that qualify for an exception from 21 CFR 1271
- HCT/Ps that do not require premarket review but are subject to regulatory controls to *"prevent the introduction, transmission, and spread of communicable disease*"
- HCT/Ps that are regulated as drugs, devices, and/or biological products

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Bucket 1 – Establishment Exceptions

1) Establishment that uses HCT/Ps solely for nonclinical scientific or educational purposes.
2) Establishment that removes HCT/Ps from an individual and implants such HCT/Ps into the same individual during the same surgical procedures
3) Carrier who accepts, receives, carries, or delivers HCT/Ps in the usual course of business as a carrier
4) Establishment that does not recover, screen, test, process, label, package, or distribute, but only receives or stores HCT/Ps solely for implantation, transplantation, infusion, or transfer within it's facility.
5) Establishment that only recovers reproductive cells or tissue and immediately transfers them into a sexually intimate partner of the cell or tissue donor.
6) Limited exception (from registration and list submission requirements): Individuals under contract, agreement, or other arrangement with a registered establishment and engaged solely in recovering cells or tissues and sending the recovered cells or tissues to the registered establishment (21 CFR 1271.15)

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Same Surgical Procedure

The "Same Surgical Procedure" exception from part 1271 applies when a single establishment:

- Removes and implants the HCT/Ps into the same individual from whom they were removed (autologous use);
- Implants the HCT/Ps within the same surgical procedure; **AND**
- The HCT/Ps remain in their original form (i.e., the only processing steps that may occur are rinsing, cleansing, sizing, and shaping*)

**Note that this is a different standard than "minimally manipulated" – FDA intends the SSP exception to be a very narrow exception.*

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Bucket 2 – Limited Rules

HCT/Ps that meet all of the criteria at 21 CFR 1271.10(a):

1) The HCT/P is minimally manipulated;
2) The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
3) The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; **AND**
4) Either:
   i. The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
   ii. The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and: a) Is for autologous use; b) Is for allogeneic use in a first-degree or second-degree blood relative; or c) Is for reproductive use.

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Minimal Manipulation

Minimal manipulation means:

1) For structural tissue, processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement;

2) For cells or nonstructural tissues, processing that does not alter the relevant biological characteristics of cells or tissues.

21 CFR 1271.3(f)

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Minimal Manipulation

FDA's default position:

"Please note that if information does not exist to show that the processing meets the definition of minimal manipulation, FDA considers the processing of an HCT/P to be "more than minimal manipulation" that cannot qualify for regulation solely under section 361 of the PHS Act and 21 CFR Part 1271."

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Homologous Use

Homologous Use means:

- the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor.

21 CFR 1271.3(c)

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Homologous Use

FDA generally considers an HCT/P to be for homologous use when it is used to repair, reconstruct, replace, or supplement:

- Recipient cells or tissues that are identical (e.g., skin for skin) to the donor cells or tissues, and perform one or more of the same basic functions in the recipient as the cells or tissues performed in the donor; or,

- Recipient cells or tissues that may not be identical to the donor's cells or tissues, but that perform one or more of the same basic functions in the recipient as the cells or tissues performed in the donor.

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Bucket 2 – Regulatory Controls

Abbreviated FDA Regulations, including:

- **Section 361 of PHS Act** *(regulations to control communicable diseases)*
- **Under Part 1271, must:**
  - Register establishment with FDA
  - Submit and maintain a list of HCT/Ps
  - Comply with Subparts C – F, as applicable (Donor Eligibility, Current Good Tissue Practice (CGTP)), Reporting, Labeling, Inspection & Enforcement)

*For Manufacturer/individuals/facilities who don't qualify for an establishment exception

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Bucket 3

- Establishments that manufacture HCT/Ps; and
- Do not qualify for an establishment exceptions; and
- The HCT/Ps do not meet all of the criteria at 1271(a)

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Bucket 3 - Regulatory Controls

Regulated as drug, device, and/or biological products under section 351 of PHS Act and subject to all applicable FDA regulations, including:

- Registration and listing of HCT/Ps as drugs/biologics/devices
- Premarket review
- Part 1271, Subparts C & D (Donor Eligibility, CGTP)
- Good Clinical Practice (GCP) and Clinical Trials
- Good Manufacturing Practice (GMP)

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IRB Implications

- Recognize HCT/Ps vs. tissues/cells not considered HCT/Ps
- Refer to FDA as needed, for example:
  - When no IND or IDE is presented for the investigational use of an HCT/P
- Apply FDA regulations (parts 50, 56, and 312 or 812 when applicable)

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Hot Topic – Medical Software

- The 21st Century Cures Act amended the FD&C Act to specifically exclude certain software functions from the definition of medical device. Summarized, these include exclusions for software functions intended:
  - For administrative support of a health care facility
  - For maintaining or encouraging a healthy lifestyle
  - To serve as electronic patient records
  - For transferring, storing, converting formats, or displaying clinical laboratory tests or other device data and results and related information
  - With limitations – for displaying, analyzing, or printing medical information; for supporting or providing recommendations to a health care professional; and enabling the health care professional to independently review the basis for such recommendations

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General Wellness

The term device, as defined in section 321(h) of this title, shall not include a software function that is intended…

> *for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;…*

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General Wellness

Categories of General Wellness Products:

1. An intended use that relates to maintaining or encouraging a general state of health or a healthy activity; or

2. An intended use that relates the role of healthy lifestyle with helping to reduce the risk or impact of certain chronic diseases or conditions and where it is well understood and accepted that healthy lifestyle choices may play an important role in health outcomes for the disease or condition.

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General Wellness

Category One: An intended use that relates to maintaining or encouraging a general state of health or a healthy activity

- **Excluded** from definition of medical device *"so long as its claims are unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition"*
- Software with "*healthy lifestyle claims, such as weight management, physical fitness, relaxation or stress management, mental acuity, self-esteem, sleep management, or sexual function, are not devices when not related to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.*"

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General Wellness

Category One Examples:

Mobile Apps that:

- play music to “soothe and relax” an individual and to “manage stress”
- monitors and records daily energy expenditure and cardiovascular workout activities to “allow awareness of one’s exercise activities to improve or maintain good cardiovascular health”
- monitors and records food consumption to “manage dietary activity for weight management and alert the user, healthcare provider, or family member of unhealthy dietary activity”
- are intended for individuals to log, record, track, evaluate, or make decisions or behavioral suggestions related to developing or maintaining general fitness, health or wellness

General Wellness

Category Two: An intended use that relates the role of healthy lifestyle with helping to reduce the risk or impact of certain chronic diseases or conditions and where it is well understood and accepted that healthy lifestyle choices may play an important role in health outcomes for the disease or condition.

- **Not Excluded** from definition of medical device because the intended uses relate to the mitigation or prevention of a disease or condition
- FDA will practice enforcement discretion so long as the software function "*presents a low risk to the safety or users and other persons*"

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Decision Support Software

Must meet all 4 of the following criteria to be excluded from the definition of device:

(1) not intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system;

(2) intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);

(3) intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; **and**

(4) intended for the purpose of enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient

FDA Guidance

1. **Not intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system**

Software functions that do acquire, process, or analyze images, signals, or other information fall within the above and **remain devices**.

Examples:

- in vitro diagnostic tests
- technologies that measure and assess electrical activity in the body (e.g., ECG, EEG)
- medical imaging technologies
- algorithms that process physiologic data to generate new data points (such as ST-segment measurements from ECG signals), analyze information within the original data (such as feature identification in image analysis), or analyze and interpret genomic data (such as genetic variations to determine a patient's risk for a particular disease)

FDA Guidance

2. **Intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information**

FDA interprets this to include *software functions that display, analyze, or print patient-specific information, such demographic information, symptoms, and test results, and/or medical information, such as clinical practice guidelines, peer-reviewed clinical studies, textbooks, approved drug labeling, and government agency recommendations. In general, this is the kind of information that health care professionals may use to make decisions about prevention, diagnosis, or treatment of a disease or condition for an individual patient.*

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FDA Guidance

3. **Intended for the purpose of supporting or providing recommendations to a health care professional (HCP) about prevention, diagnosis, or treatment of a disease or condition**

Specific to software that is directed at HCPs, not patients, caregivers, or other consumers. However, FDA intends to practice enforcement discretion for products that provide comparable support to non-healthcare professionals.

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FDA Guidance

4. **Intended for the purpose of enabling such HCP to independently review the basis for such recommendations that such software presents so that it is not the intent that such HCP rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient**

The function must be intended to enable HCPs to independently review the basis for the recommendations presented by the software so that they do not rely primarily on such recommendations, but rather on their own judgment, to make clinical decisions for individual patients…

The sources supporting the recommendation or underlying the rationale for the recommendation should be identified and easily accessible to the intended user, understandable by the intended user (e.g., data points whose meaning is well understood by the intended user), and publicly available (e.g., clinical practice guidelines, published literature)...

Examples

Not Devices	Remain Devices
Software that uses a patient's diagnosis to provide a HCP with current practice treatment guidelines, and provides the source of the guidelines	Software that manipulates or analyzes images and other data obtained from a radiological device to create 3D models of the region intended to be used in planning surgical treatments.
Software that helps to identify drug-drug interaction and drug-allergy contraindication alerts, based on FDA-approved drug labeling and patient-specific information	Software that analyzes CT images to compute and/or approximate fractional flow reserve. In this case the software performs and provides the user an image analysis that the user could not independently derive.
Software that suggests an intervention or test, consistent with clinical guidelines and/or drug labeling, based on or in response to a physician's order	Software that analyzes a patient's laboratory results using a proprietary algorithm to recommend a specific radiation treatment, for which the basis of the recommendation is unavailable for the HCP to review.
Software that provides HCPs with a report based on arterial blood gas results that includes a calculated anion gap and recommends possible next steps, based on practice guidelines.	Software that calculates the fractal dimension of a lesion and surrounding skin image and builds a structural map to provide diagnosis or identify whether the lesion is malignant or benign

FDA Guidance

- Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act
- Clinical and Patient Decision Support Software
- General Wellness: Policy for Low Risk Devices
- Mobile Medical Applications

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IRB Implications

- Recognize when software/apps are excluded from the definition of medical device and when they are not
- Refer to FDA as needed (e.g., when it is unclear whether a product falls within the definition of device)
- Apply FDA regulations (parts 50, 56, and 812 when applicable) to studies evaluating the safety or effectiveness of products that fall within the definition of device
- Apply standard IRB review criteria to research studying products that fall outside of the definition of a medical device

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