AdventHealth Orlando

WORKSHEET: Drugs

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This worksheet is used to determine whether requirements for FDA-regulated drug research are met. (see Footnote 1)

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1. Special issues where 21 CFR §312 does not apply

1.1	☒	The research involves one or more of the following being used to affect the structure or any function of the body, and not being used for the diagnosis, cure, mitigation, treatment, or prevention of disease
		○ Food
		◉ Dietary supplement
		○ Infant formula
		○ Substance Generally Recognized As Safe (GRAS) for use in food
1.2	☐	The clinical investigation will be conducted outside the US and the sponsor does not intend to submit the data to FDA

2. IND requirements (One of the following must be true)

2.1	☐			The protocol will be conducted under a valid IND number provided by the sponsor, CRO, or FDA (Investigator Brochure is not protocol-specific)
2.2	☐			The protocol is IND exempt under one of the following categories:
		2.2.1	☐	21 CFR §312.2(b)(1) Marketed drug with no change in risk (see Footnote 2)
			2.2.1.1 ☐	The drug is lawfully marketed in the United States
			2.2.1.2 ☐	The investigation does not involve a route, dosage level, or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product
		2.2.2	☐	21 CFR §312.2(b)(2) *In vitro* diagnostic biologic product (see Footnote 3)
			2.2.2.1 ☐	The drug is an in vitro diagnostic biologic product (see Footnote 4)
			2.2.2.2 ☐	The drug is a blood grouping serum, reagent red blood cells, or anti-human globulin
			2.2.2.3 ☐	The drug is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure
		2.2.3	☐	21 CFR §312.2(b)(5) Placebos (see Footnote 5)
			2.2.3.1 ☐	A clinical investigation involves the use of a placebo and does not otherwise require submission of an IND
		2.2.4	☐	21 CFR §312.120(a)(1) Non-US studies
			2.2.4.1 ☐	The clinical investigation will be conducted outside the US and sponsor intends to submit the data to FDA
			2.2.4.2 ☐	The study will be conducted in accordance with good clinical practice (GCP) (see Footnote 6)
		2.2.5	☐	21 CFR §361 Radioactive drugs being used to assess physiology
			2.2.5.1 ☐	The drug is a radioactive drug approved by a Radioactive Drug Research Committee under 21 CFR §361.1
		2.2.6	☐	21 CFR §320.31 Bioequivalence studies (see Footnote 7)
			2.2.6.1 ☐	The clinical investigation is an in vivo bioavailability or bioequivalence study
			2.2.6.2 ☐	The drug is the same as an FDA-approved drug
			2.2.6.3 ☐	The drug is not a radioactively labeled and not cytotoxic
			2.2.6.4 ☐	The maximum single and total daily dose do not exceed that specified in the labeling of the approved drug product
			2.2.6.5 ☐	For a multiple-dose study on an extended release product a single-dose study has been completed
		2.2.7	☐	FDA Guidance - Determining Whether Human Research Studies Can Be Conducted Without an IND - Cold Isotopes
			2.2.7.1 ☐	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
			2.2.7.2 ☐	The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject
			2.2.7.3 ☐	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
			2.2.7.4 ☐	The quality of the cold isotope meets relevant quality standards
		2.2.8	☐	21 CFR §1271.10 Human cells, tissues, and cellular and tissue-based products (HCT/P) (see Footnote 8)
			2.2.8.1 ☐	The product is an HCT/P (see Footnote 9) that is minimally manipulated (see Footnote 10)
			2.2.8.2 ☐	The HCT/P is intended for homologous use only (see Footnote 11), as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent
			2.2.8.3 ☐	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
			2.2.8.4 ☐	The manufacturer is registered with FDA and has submitted this HCT/P to FDA
			2.2.8.5 ☐	The HCT/P: (select one)
				○ Does not have a systemic effect and is not dependent upon metabolic activity of living cells for its primary function
				○ Is for autologous use
				○ Is for allogeneic use in a first-degree or second-degree blood relative
				○ Is for reproductive use

3. Notes

4.	Footnotes
4.1	*Drug* means an article that is: *FDC Sec. 201(g)* (1) Recognized by the FDA as an approved drug; (2) Intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; or (3) Not a food or dietary supplement but is intended to affect the structure or any function of the body.
4.2	Additional FDA criteria for sponsors: • The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug. • The investigation is not intended to support a significant change in the advertising for the product. • The sponsor or person acting on behalf of a sponsor will not represent the drug as safe or effective for the purposes for which it is under investigation, or promote, commercially distribute, or test market the drug.
4.3	Additional FDA criterion for sponsors: The person shipping the drug will follow FDA requirements for labelling and records (Label the drug "CAUTION: Contains a biological product for investigational in vitro diagnostic tests only." Use due diligence to assure that the consignee is regularly engaged in conducting such tests and that the shipment of the new drug will actually be used for tests in vitro or in animals used only for laboratory research. Maintain adequate records showing the name and post office address of the expert to whom the drug is shipped and the date, quantity, and batch or code mark of each shipment and delivery.)
4.4	*In vitro diagnostic (IVD) products* are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. IVD products are devices and may also be biological products.
4.5	Additional FDA criterion for sponsors: FDA will be able to validate the data from the study through an on-site inspection.
4.6	*GCP* means as a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials in a way that provides assurance that the data and reported results are credible and accurate and that the rights, safety, and well-being of trial subjects are protected. GCP includes review and approval (or provision of a favorable opinion) by an independent ethics committee (IEC) before initiating a study, continuing review of an ongoing study by an IEC, and obtaining and documenting the freely given informed consent of the subject (or a subject's legally authorized representative, if the subject is unable to provide informed consent) before initiating a study. GCP does not require informed consent in life-threatening situations when the IEC reviewing the study finds, before initiation of the study, that informed consent is not feasible and either that the conditions present are consistent with those described in 21 CFR §50.23 or §50.24(a), or that the measures described in the study protocol or elsewhere will protect the rights, safety, and well-being of subjects.
4.7	Additional FDA criterion for sponsors: The sponsor will retain reserve samples of any test article and reference standard per 21 CFR §320.38.
4.8	*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. 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 of this chapter, 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; and • In vitro diagnostic products as defined in 809.3(a) of this chapter. • 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."
4.9	Additional FDA criterion for sponsors: The manufacturer will comply with the other requirements in 21 CFR §1271.
4.10	*Minimal manipulation* means: • 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; and • For cells or non-structural tissues, processing that does not alter the relevant biological characteristics of cells or tissues.
4.11	*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. The limitation to homologous use should be reflected by the labeling, advertising, or other indications of the manufacturer's objective intent.