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| **FDA – IND REVIEWER CHECKLIST** |

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| **HRPP USE ONLY** | |
| **IRB Application Number:** |  |

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| **PURPOSE** |

This checklist is a supplement to the non-Exempt reviewer checklist. It should be used as a tool for providing information and support for individuals assessing whether an FDA-regulated study needs an IND approval from the FDA before conducting the research.

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| **FDA GUIDANCE** |

The FDA guidance, [*Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can be Conducted Without an IND*](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-new-drug-applications-inds-determining-whether-human-research-studies-can-be) describes how to obtain consultation from the FDA about whether an IND is required. It also includes guidance about when an IND is required for studies involving:

* Use of endogenous compounds
* Administration of live organisms (e.g., modified or wild-type virus) to subjects
* Dietary supplements, complementary or alternative medicines including organic materials from botanical sources

Per further FDA guidance, [IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed](https://www.fda.gov/media/85294/download), reviewers should pay particular attention to an investigator’s qualifications to conduct a study submitted for approval to the IRB if the study involves one or more of the following:

* A sponsor- investigator
* A study that is outside the investigator’s area of expertise; or
* Any study design features of other characteristic(s) that may significantly increase potential risks to participants

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| **RELATED MATERIALS & REGULATORY REFERENCES** |

* [IRB Manual](https://irb.wsu.edu/documents/2022/09/hrpp-manual.pdf) – Section 7, “FDA Regulated Research”
* [21 CFR 56](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56)
* [21 CFR 312](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312)
* [21 CFR 320](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-320)
* [21 CFR 361](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-361)
* The FDA draft guidance, “[*Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can be Conducted Without an IND*](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-new-drug-applications-inds-determining-whether-human-research-studies-can-be)” Sep, 2013
* FDA Guidance, “[*IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed*](https://www.fda.gov/media/85294/download)”, August 2013

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| **SECTION 1: IS THE USE EXEMPT FROM THE IND REQUIREMENT?** |

**The use of the drug for a specific research study is IND exempt and does not require IND approval from the FDA if** ***all aspects are met within one category listed below (every box should be checked as “Met” in order to qualify)***.

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| **IND Not Required** | **Met** |
| The project does not qualify for any of the FDA exemption categories (please proceed to evaluation of the PI qualifications and research site) |  |

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| **Category 1 – Exemption for Marketed Drugs** [21 CFR 312.2(b)(1)] | **Met** |
| The drug is lawfully marketed in the United States. |  |
| The research is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use nor is it intended to be used to support any significant change in the drug labeling.   * *FDA guidance.*“Certain investigator-initiated research in an academic setting has the potential to influence labeling or promotion, notwithstanding the investigator’s intent (e.g., a controlled trial with an endpoint representing improvement of a serious disease)… Similarly, certain studies of effectiveness conducted by government agencies (e.g., NIH) have the potential to influence labeling. FDA strongly encourages submission of IND submissions for these types of studies.” |  |
| For research involving a prescription drug: it is not intended to support a significant change in the advertising of the drug.   * If this is not applicable because the drug is not a prescription drug, check the box. |  |
| The research does not involve a route of administration, dose, patient population, or other factor that significantly increases the risk (or decreases the acceptability of the risk) associated with the use of the drug.   * *FDA guidance.*FDA comments made with the publication of the IND regulations, “This exemption was not intended to require an investigator to use the drug in exactly the same dosage form, dosage levels, and patient populations described in the marketed labeling for the product, but rather to permit changes to the lawfully marketed drug product that do not increase risks… over the risk presented by use of the product in conformance with its marking labeling” 52 Federal Register 8798 at 8801, March 19, 1987. |  |
| The research is conducted in compliance with all of the marketing limitations described in 21 CFR 312.7 (the research is not intended to promote or commercialize the drug). |  |
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| **Category 2 – In Vitro Diagnostic Biological Products** [21 CFR 312.2(b)(2)] | **Met** |
| The study is an investigation for an in vitro diagnostic biological product that involves one or more of the following: **(1)** blood grouping serum; **(2)** reagent red blood cells; or **(3)** anti-human globulin. |  |
| The diagnostic product is intended to be used in a diagnostic procedure that confirms diagnosis made by another, medically established, diagnostic product or procedure. |  |
| * The product will be shipped only if it is labeled as follows: “CAUTION: Contains a biological product for investigational in vitro diagnostic test only.” |  |
| * The shipper of the product will use due diligence to assure that the recipient is regularly engaged in conducting tests and that the shipment of the product will actually be used for tests in vitro. |  |
| * The shipper of the product will maintain adequate records showing the name and post office address of the expert to whom the product is shipped and the date, quantity, and batch or code mark of each shipment and delivery. Shipment records will be maintained for 2 years after the shipment and will be available for copying/verification by any properly authorized officer of employee of the FDA. |  |
| * The shipper of the product will assure the return of all unused supplies of the product from individual investigators whenever the investigation discontinues, or the investigation is terminated. This may include authorization in writing of alternative dispositions, provided this alternative does not expose humans to risks from the product, either directly or indirectly (e.g., through food producing animals) and provided that the shipper maintains records of any alternative disposition. |  |
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| **Category 3 – Placebos** [21 CFR 312.2(b)(5)] | **Met** |
| The investigation involves the use of a placebo but otherwise does not require an IND. |  |
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| **Category 4 – Bioavailability/Bioequivalence Studies** [21 CFR 312.2(c); 21 CFR 320.31] | **Met** |
| The active ingredient is chemically identical to the active ingredient in an FDA approved drug. |  |
| The drug is not radioactively labeled. |  |
| The drug 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. |  |
| For multiple dose studies of an extended-release drug: a single dose study has already been completed. |  |
| The sponsor will meet the requirements for retention of drug samples, as described in 21 CFR 320.31(d)(1). |  |
| The sponsor (or contact research organization) will notify the FDA and all participating investigators of any serious adverse event as soon as possible but in no case later than 15 calendar days after becoming aware of its occurrence, as described in 21 CFR 320.31(d)(3). |  |
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| **Category 5 – Radioactive Drugs for Research Use** [21 CFR 361.1]  *Drugs meeting the criteria below are considered “safe and effective” and therefore IND requirements do not apply. This applies to radioactive versions of both approved and unapproved drugs.* | **Met** |
| The drug has been approved by the Radioactive Drug Research Committee as a radioactive drug for certain research uses, per the criteria described in 21 CFR 361.1(b). |  |
| The amount of active ingredient or combination of active ingredients to be administered shall be known to not cause any clinically detectable pharmacological effects in humans. |  |
| The amount of radioactive material to be administered shall be such that the subject receives the smallest radiation dose with which it is practical to perform the study without jeopardizing the benefits to be obtained from the study. |  |
| The radiation dose to an adult research subject from a single study or cumulatively from a number of studies conducted within 1 year will not exceed the limits described in 21 CFR 361.1(b)(3). |  |
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| **Category 6 – Cold Isotopes for Research Use**  *The FDA has expressed its intention to exercise enforcement discretion when research using cold isotopes under the following circumstances is conducted without an IND.* | **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 subject. |  |
| The dose to be administered is known to not cause any clinically detectable pharmacological 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. |  |
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| **Category 7 – FDA Determination** | **Met** |
| The FDA has provided a documented determination that an IND is not required for the use of this drug. |  |

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| **SECTION 2: IS THE INVESTIGATOR QUALIFIED TO CONDUCT FDA-REGULATED RESEARCH?** |

The regulations at [21 CFR 56.107(a)](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56/subpart-B/section-56.107#p-56.107(a)) require that an IRB "...be able to ascertain the acceptability of the proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice..." In addition, the regulations at [21 CFR 56.111](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56/subpart-C/section-56.111) require that an IRB determine that the proposed research satisfies the criteria for approval, including that "...risks to subjects are minimized...[and] reasonable in relation to anticipated benefits, if any, to subjects..." In order to fulfill these responsibilities, the IRB needs information about the qualifications of the investigator(s) to conduct and supervise the proposed research.

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| **PI Qualification** | **Yes** | **No** | **N/A** |
| The PI is qualified to conduct the proposed research. Verification of this has been provided via   * Previous WSU IRB approvals, or * a statement from the department chair has been provided, or * the curriculum vitae of the PI (or other sub-investigators or study staff) has been included with the submission, or * for vulnerable participant populations, previous specific experience as shown by recent presentations, or publications, and prior clinical experience with the test article or study-related procedures. |  |  |  |
| The FDA’s website has been checked to determine whether a clinical investigator has been the subject of an inspection by the agency and the results have been reviewed.   * [FDA Warning Letters](https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters) * [Clinical Investigator List](https://www.fda.gov/vaccines-blood-biologics/compliance-actions-biologics/clinical-investigator-status-biologics)  [Clinical Investigator-Disqualification Proceedings](https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/clinical-investigators-disqualification-proceedings)[Bioresearch Monitoring Information System File (BMIS)](https://www.fda.gov/drugs/drug-approvals-and-databases/bioresearch-monitoring-information-system-bmis): contains information on clinical investigators (CIs), contract research organizations (CROs), and institutional review boards (IRBs) involved in the conduct of clinical studies conducted under an Investigational New Drug (IND) application with human investigational drugs and therapeutic biologics[Investigational Human Drugs Clinical Investigator Inspection List](http://www.accessdata.fda.gov/scripts/cder/cliil/index.cfm): maintained by the Center for Drug Evaluation and Research and contains the names, addresses and other information obtained during FDA inspections of clinical investigators who have performed studies with human investigational drugs. The list contains information on clinical investigator inspections conducted since October 1, 2008, and that have a final classification.  * Investigators who conducted a device study from 2009 to present are included in * the [Inspection Classification Database](https://datadashboard.fda.gov/ora/index.htm) maintained by FDA’s Office of Regulatory Affairs * [FDA Debarment List](https://www.fda.gov/fda-debarment-list) |  |  |  |

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| **SECTION 3: IS THE RESEARCH SITE ADEQUATE?** |

FDA’s regulations require that before an IRB can approve research covered by the regulations at [21 CFR 56.107(a)](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56/subpart-B/section-56.107#p-56.107(a)), the IRB must "...be able to ascertain the acceptability of the proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice..." The regulations also require that each IRB have sufficient information to determine that the proposed research satisfies the criteria for approval at [21 CFR 56.111](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56/subpart-C/section-56.111).

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| **Site Adequacy – WSU or a major medical institution** | **Yes** | **No** | **N/A** |
| The site is in a WSU facility that is appropriate for the study or the site is part of a major medical institution. |  |  |  |
| **Site Adequacy – Research outside of WSU or a major medical institution** | **Yes** | **No** | **N/A** |
| A statement has been provided from an appropriate person or persons at the site or institution stating that the facilities are adequate |  |  |  |
| The PI has provided a description of the facility where the research will take place, including it’s staffing and resources relevant to the research under review. |  |  |  |

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| **DETERMINATION** | | | |
| Reviewer notes/Comments:  **Please note: THESE WILL NOT BE SENT TO THE PI. Add required changes to the Non-Exempt Review Checklist.** |  | | |
| Qualifications of the investigator: | The PI is qualified to oversee and conduct this research.  The PI is not qualified to oversee and conduct this research. | | |
| Research site adequacy: | The research site(s) **is/are** adequate for the needs of the study.  The research site(s) **is/are** **not** adequate for the needs of the study. | | |
| Exemption Determination: | This study is exempt from an IND. All criteria in the appropriate category for this study have been met.  Please specify which category applies to this research:  Category 1 – Exemption for Marketed Drugs [21 CFR 312.2(b)(1)]  Category 2 – In Vitro Diagnostic Biological Products [21 CFR 312.2(b)(2)]  Category 3 – Placebos [21 CFR 312.2(b)(5)]  Category 4 – Bioavailability/Bioequivalence Studies [21 CFR 312.2(c); 21 CFR 320.31]  Category 5 – Radioactive Drugs for Research Use [21 CFR 361.1]  Category 6 – Cold Isotopes for Research Use  This study does not qualify for an IND exemption. The sponsor/PI must submit an IND application to the FDA. | | |
| **Reviewer name:** |  | **Date:** |  |