The following worksheet was developed to provide guidance for the completion, review, and maintenance of required essential regulatory documents and incorporates the requirements and guidelines referenced in ICH GCP Guidelines, DMID Regulatory File Document Guidelines, 45 CFR 46, 21 CFR 50 and 21 CFR 312.

According to ICH GCP 8.1: “Essential Documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of GCP and with all applicable regulatory requirements… Filing essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor, and monitor.”

The worksheet is intended for use by site staff conducting DMID supported studies, clinical site monitors and DMID contractors involved in the review and tracking of essential regulatory documents.

Documents grouped by Tier including Section and Page Number

Tier 1A:

|  |  |  |
| --- | --- | --- |
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| [Form FDA 1572](http://www.fda.gov/opacom/morechoices/fdaforms/FDA-1572.doc) (applicable for DMID-held IND studies) | |
| --- | --- |
| Yes No | * Current version of Form FDA 1572 is used. * All sections are completed. * Correction fluid is not used anywhere on the form. * There are no significant *(may impact the interpretation or intended use of the information)* typographical errors and there are no “write-overs”. * When addendum to the Form FDA 1572 is needed (e.g., additional space is needed to include all facilities listed in Section 3) include the following information at the top of the page *(for identification).*    + Protocol number and full DMID Protocol title   + Name of the Principal Investigator (PI)   + Section number   NOTE:  *The addendum information must correspond to the Form FDA 1572*. |
| Yes No | Section 1:   * The PI name is spelled correctly and corresponds (exact match not required) to the name on the CV. * Suffixes such as “Jr.” and “Sr.” (or “II” and “III”) for the PI are on the Form FDA 1572 if listed on the CV. * Credentials such as MD, PhD are on the CV if listed on the Form FDA 1572. * Complete mailing address is present (physical address is preferred; PO Box is acceptable). * The PI is not currently listed as Debarred, Disqualified or Restricted by the FDA   NOTE:  Each main site where the clinical investigation will be conducted (site listed in Section 1 of the 1572), must have an OHRP Federal Wide Assurance number (FWA #) assigned. |
| Yes No | Section 2:   * The appropriate box is checked (usually the CV box). |
| Yes No | Section 3:   * Name(s) and complete address(es) of all facilities where clinical investigation(s) will be conducted are listed. * Name(s) and complete address(es) for receiving shipments of study product and/or supplies are listed. * If the study is conducted at the address that is entered in Section 1, the name and address is also entered in Section 3. (*“Same as above” or “See Section 1” is not acceptable)* |
| Yes No | Section 4:   * Only clinical laboratory facilities need to be included. Do not include Research laboratories on the Form FDA 1572. Research laboratories must be identified in the Protocol. * Names and complete addresses of the clinical laboratories must be listed, as well as the names and addresses of laboratories that support the safety and efficacy data defined in the Protocol (e.g., Central EKG reader, imaging lab, central clinical lab). * If no clinical laboratories are used for the trial, “None” or “Not Applicable” is noted. *(This section cannot be left blank.)* |

| [Form FDA 1572](http://www.fda.gov/opacom/morechoices/fdaforms/FDA-1572.doc) (applicable for DMID-held IND studies) | |
| --- | --- |
| Yes No | Section 5:   * Name and complete address of all IRBs (e.g., local IRB, single IRB per NIH policy, and central IRB) utilized for the study are listed, see section VII. * The IRB must have an OHRP registered IRB number and linked to the main site’s FWA. * If the IRB is not linked to the main site’s FWA, a reliance between the main site and the IRB must be provided. |
| Yes No | Section 6:   * Names of all Sub-Investigators authorized by the PI to conduct significant subject assessments are listed. (Sub-Investigators are usually physicians or other professionals responsible for making Protocol decisions. The administrative site PI may be listed in this section.) * If there are no Sub-Investigators, “None” or “Not Applicable” is noted. * Sub-Investigators are not currently listed as Debarred, Disqualified or Restricted by the FDA |
| Yes No | Section 7:   * Must list full DMID Protocol title as listed in the most recent version of the Protocol; also list DMID Protocol number. (Protocol number only is not sufficient.) |
| Yes No | Section 8:   * The appropriate box is checked for the clinical trial. |
| Yes No | Section 10:   * The completed form must be dated by the PI listed in Section 1(either by hand or using acceptable electronic method). |
| Yes No | Section 11:   * The completed form must be signed by the PI listed in Section 1(either by hand or using acceptable electronic method). |

| [Investigator of Record Form (IoR)](https://www.dmidcroms.com/CRS/ERDG/EssentialRegulatory/DMID%20Investigator%20of%20Record%20Form.docx) (applicable for DMID IDE/Non-IND studies) | |
| --- | --- |
| Yes No | * All sections are complete. * Correction fluid is not used anywhere on the form. * There are no significant *(may impact the interpretation or intended use of the information)* typographical errors and there are no “write-overs”. * When addendum to the IoR Form is needed (e.g., additional space is needed to include all facilities listed in Section 4) include the following information at the top of the page *(for identification)*.   + Protocol number and Full DMID Protocol title   + Name of the Principal Investigator (PI)   + Section number   NOTE:  *The addendum information must correspond to the IoR*. |
| Yes No | Section 1:   * Must list full DMID Protocol title as listed in the most recent version of the Protocol; also list DMID Protocol number. (Protocol number only is not sufficient.) |

| [Investigator of Record Form (IoR)](https://www.dmidcroms.com/CRS/ERDG/EssentialRegulatory/DMID%20Investigator%20of%20Record%20Form.docx) (applicable for DMID IDE/Non-IND studies) | |
| --- | --- |
| Yes No | Section 2:   * The PI name is spelled correctly and corresponds (exact match not required) to the name listed on the CV. * Suffixes such as “Jr.” and “Sr.” (or “II” and “III”) for the PI are on the IoR if listed on the CV. * Credentials such as MD, PhD are on the CV if listed on the IoR. * Complete mailing address is present (physical address is preferred; PO Box is acceptable). * The PI is not currently listed as Debarred, Disqualified or Restricted by the FDA   NOTE:  Each main site where the clinical investigation will be conducted (site listed in Section 2 of the IoR), must have an OHRP Federal Wide Assurance number (FWA #) assigned*.* |
| Yes No | Section 3:   * The appropriate box is checked (usually the CV box). |
| Yes No | Section 4:   * Name(s) and address(es) of all facilities where clinical investigation(s) will be conducted are listed. * If the study is conducted at the address that is entered in Section 2, the name and address is also entered in Section 4. |
| Yes No | Section 5:   * Only clinical laboratory facilities need to be included. Research laboratories must be identified in the protocol, not on the IoR. * Names and addresses of the clinical laboratories must be listed, as well as the names and addresses of laboratories that support the safety and efficacy data defined in the Protocol (e.g. Central EKG reader, imaging lab, central clinical lab). * If clinical laboratories are not used for the trial, “None” or “Not Applicable” is noted. *(This section cannot be left blank.)* |
| Yes No | Section 6:   * Name and complete address of all of IRBs utilized for the study are listed. |
| Yes No | Section 7:   * Names of all Sub-Investigators authorized by the PI to conduct significant subject assessments are listed. (Sub-Investigators are usually physicians or other professionals responsible for making Protocol decisions.) * If an Administrative Site IoR is not collected, the administrative site PI may be listed as a Sub-Investigator in this section. * If there are no Sub-Investigators, “None” or “Not Applicable” is noted. * Sub-Investigators are not currently listed as Debarred, Disqualified or Restricted by the FDA |
| Yes No | Section 8:   * The PI must review the Commitments before signing. * The completed form must be signed and dated by the PI listed in Section 2 (either by hand or using acceptable electronic method). |

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| Investigator CVs (Sub-Investigator CVs applicable for DMID-held IND/IDE studies only) | |
| Yes No | CVs for all Investigators listed in section 1 and section 6 of the Form FDA 1572 and section 2 and section 7 of the IoR are present. |
| Yes No | Name of the Investigator is spelled correctly and corresponds to the name in Section 1 of the Form FDA 1572 or section 2 of the IoR (exact match not required). |
| Yes No | CV indicates an affiliation to a location where the study will be conducted (noted in Section 3 of the FDA 1572 or Section 4 of the IoR). |
| Yes No | CV shows the relevant education, experience and training that qualifies the investigator for the study. |
| Yes No | CV is within five years of the current date determined by date of CV, date of signature, date of most recent publication, or date of work position. |
| Yes No | There are no breaks in page numbering (if present). |

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| Principal Investigator Medical Licensure | |
| Yes No | As applicable, a photocopy of the current medical license or written confirmation from the state licensing board (information from a licensing board web site is acceptable) is present. *(Documentation of license number and expiration date on the CV is insufficient).*  NOTE:   * A physician working at a US military base may have a license issued from a state different than the state in which the military base is located. * For a US investigator practicing in a Veterans Administration (VA) facility: * The license may be issued from a state different than the state in which the VA facility is located * If a license is not provided (i.e., licensure is not required per VA policy), documentation of the VA policy provided by the investigator is present. |
| Yes No | Name on the license corresponds with the name in Section 1 of the Form FDA 1572 or Section 2 of the IoR. |
| Yes No    NA | For a PI that does not hold medical licensure, a copy of Sub-Investigator’s medical license must be present. |

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| [DMID Financial Disclosure Forms](https://www.dmidcroms.com/CRS/ERDG/EssentialRegulatory/DMID%20Financial%20Disclosure%20Form%20with%20Instructions.pdf) (applicable for DMID-held IND/IDE studies only) | |
| Yes No | The Financial Disclosure Form for all Investigators listed in Section 1 and Section 6 of the Form FDA 1572 and section 2 and section 7 of the IoR are present. |
| Yes No | The Financial Disclosure Form is completed in its entirety and signed and dated by the investigator (either by hand or using acceptable electronic method). |
| Yes No | Full DMID Protocol title and/or number correspond to the information in the DMID Protocol. |
| Yes No | If financial interest is indicated, a disclosure of the financial interest is required.  The Investigator must include a statement/memo specifying the disclosure statement date, investigator name, protocol number, nature and amount of the interest, and a description of the risk mitigation plan to minimize any potential bias. |
| NOTE:   * Original, signed Financial Disclosure forms will remain at the site; copies of signed and dated forms will be sent to DMID-CROMS ERDG as part of the required site essential documents. * If an investigator indicates a financial interest a statement/memo should be provided which specifies the statement date, Investigator name, protocol number, nature and amount of the financial interest, and a description of the risk mitigation plan.   Financial Disclosure forms will not be collected for Administrative Site. | |

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| Protocol Signature Page, including Amendments (applicable only if Protocol contains signature page). | |
| Yes No | The Protocol contains a Protocol Signature Page. |
| Yes No | The Protocol Signature Page is completed and includes the Principal Investigator’s signature and date. A handwritten signature or E-signature will be accepted. |
| Yes No | The Protocol version number and/or version date must be present and correct. The Protocol number must be present and correct. The Protocol title may or may not be present on the Signature Page; however, if present, it must also be correct. |
| Yes No | **Protocols developed prior to 01-Apr-2009:** The following Protocol Signature Page requirements must be met:  For Single Center Studies:   * The Protocol Signature Page is complete and signed by the site Principal Investigator for the study. The form should be placed in the site regulatory Binder and submitted to DMID CROMS.   For Multi-center Studies:   * Lead Principal Investigator - The Protocol Signature Page is complete and signed by the lead Principal Investigator for the study. The form should be placed in site regulatory binder and submitted to DMID CROMS. Copies should be submitted to all ancillary sites. * Ancillary Site Principal Investigator(s) - The Protocol Signature Page is complete and placed in site specific regulatory binder. |

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| VI. Protocol Signature Page, including Amendments (applicable only if Protocol contains signature page). | |
|  | After 01-Apr-2009: The following Protocol Signature Page requirements must be met:  For all DMID Studies:   * The Protocol Signature Page is complete and signed by each site Principal Investigator for the study. * The form should be placed in the site regulatory binder and submitted to DMID CROMS.   NOTE:  Questions regarding how to file Protocol Signature Pages should be directed to your monitor. |

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| IRB Approval Documentation |
| This section includes requirements for Local, Central and per NIH Policy Single IRBs, in accordance with NIH Policy <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-004.html>  **Note: All IRB approvals must meet ICH GCP 8.2.7 requirements to document that the trial has been subject to IRB/IEC review and given approval/favorable opinion. And to identify the version number and date of the document(s).**  Refer to IRB approval documentation requirements below grouped by the following sub-headings:   * All IRB Approvals, * Central IRB, and * Single IRB per NIH Policy. |

| All IRB Approvals | |
| --- | --- |
| Must comply with ICH GCP 8.2.7, necessitating the use of version control of all documents submitted for review by the IRB. | |
| Yes No | Approval documentation must list full Protocol title as listed in the Protocol; may also list the DMID Protocol number. (Protocol number only is not sufficient) |
| Yes No | Approval documentation is on IRB letterhead with identifiers (e.g., name [abbreviations are acceptable], address) that correspond with the Form FDA 1572 or IoR of at least one of the participating investigators or sites.  *E-mail correspondence stating approval is not sufficient.* |
| Yes No | Approval documentation specifies the study documents that were reviewed such as:   * DMID Protocol (identified with version number/date) * Protocol Amendment(s) (identified with version number/date) * Informed Consent Form (identified with version number/date) * If applicable, Informed Consent Form in foreign language with required English Informed Consent Form or English translation included (identified with version number and/or date) * Written information provided to the subject (identified with version number and/or date) * Recruiting materials (e.g., advertising) (identified with version number and/or date) |
| Yes No | All approval documentation must be dated and dates of approval and/or duration of approval must be included (e.g., approved on [date], approval expiration on [date] or approved on [date] and in 12 months must be renewed). If renewal date is not listed, IRB documentation (e.g., SOPs, Guidelines, Policies, or Memo) stating approval/renewal timeframe must be included. |
| Yes No | If the Protocol is dated, the date of approval is after the Protocol version date. |
| Yes No NA | For conditional approval, IRB-issued documentation is present to indicate that the stated conditions were met and final approval granted. |
| Yes No | Approval documentation is initialed or signed by the IRB Chairperson or authorized representative. IRB documentation generated from electronic submission and approval systems are mostly acceptable if all components listed above are present. (Electronic signatures are acceptable). |
| *IMPORTANT:* If the IRB approval letter does not list the version and/or date of the Protocol, Informed Consent Form (ICF), or other documents, the following are required: | |
| For DMID-held IND Studies, submit one of the following alternative methods of documentation:   1. Obtain a revised IRB/IEC approval letter including the version requirements listed above for all approved study documents 2. Generate a letter on institutional letterhead which includes the following:    * Full DMID Protocol title and Protocol number    * Version of the Protocol, ICF, or other document(s) approved by the IRB    * Signature of the Principal Investigator   NOTE: A stamped approved copy of the version of the Protocol, ICF, or other approved document is required. The page of the document including the IRB approval stamp is acceptable for documentation purposes; however, in addition, DMID CROMS must have a complete version of the protocol/document on file.   1. For electronic IRB systems (eIRB), obtain a view attachments or equivalent page listing the documents submitted for review by the IRB which includes the following information:    * Document name    * Version number and/or version date    * Version information must match the version information as it appears in the header/footer of the approved document   Example: Radio Advertisement document name: Radio Ad\_v2.0\_12Mar2008   1. Under certain circumstances, and with DMID ORA approval, a DMID IRB Approval Certification Form may be used. The form must include the following:    * List of documents submitted and approved by the IRB    * Signature of the Principal Investigator   NOTE: If there are any questions, please contact Janice Arega, Regulatory Affairs Specialist, in the DMID Office of Regulatory Affairs at 240-292-0928. | |
| For Non-IND Studies, submit one of the following alternative methods of documentation:   1. Obtain a revised IRB/IEC approval letter including the version requirements listed above for all approved study documents 2. For electronic IRB systems (eIRB), obtain a view attachments or equivalent page listing the documents submitted for review by the IRB which includes the following information:    1. Document name    2. Version number and/or version date    3. Version information must match the version information as it appears in the header/footer of the approved document   Example: Radio Advertisement document name: Radio Ad\_v2.0\_12Mar2008   1. Under certain circumstances, the DMID IRB Approval Certification Form may be used. The form must include the following:    1. List of documents submitted and approved by the IRB    2. Signature of the Principal Investigator   NOTE: Approval from the DMID ORA is not required for Non-IND studies. | |
| Federalwide Assurance (FWA) for the Protection of Human SubjectsAll institutions that are engaged in non-exempt human subject research are required (by 45-CFR-46) to:  1. Hold or obtain an active FWA from OHRP; 2. Expiration date of the FWA number should be listed on the OHRP website; and 3. Certify to the HHS agency conducting or supporting the research that the protocol has been reviewed/approved by the IRB designated in the FWA and will be subject to continuing review by an IRB. 4. IRB has an OHRP registered IRB number linked to the main site’s FWA.   If there are any questions, see link <http://www.hhs.gov/ohrp/policy/engage08.html> for full requirements. | |

| Central IRB | |
| --- | --- |
| Site or Institution utilizing a Central IRB (private/independent IRB). | |
| Yes No | Approval documentation must acknowledge the Agreement between the relying IRB and the central IRB of Record. Names of participating institutions and date(s) of agreement should be present on the IRB Approval Letter |
| Yes No | Approval documentation must include Site PI, Site’s documents and corresponding version number/date of the document(s) |

| Single IRB, per NIH Policy | |
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| NIH Single IRB Policy for Multi-Site Research (effective January 25, 2018):  This NIH policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research. Use of a Single IRB is selected on a study-by-study basis. The following requirements are specific to use of a Single IRB, refer to <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-004.html> | |
| Yes No | Approval documentation must be on letterhead of the IRB of Record |
| Yes No | Approval documentation must acknowledge the Reliance Agreement between the relying IRB and the IRB of Record |
| Yes No | Approval documentation must include the names of participating institutions/clinical sites and applicable agreement date(s) |
| Yes No | Approval documentation must include PI Name for each respective site named on the approval letter |
| Yes No | Approval documentation must contain site-specific documents and materials with corresponding version number/date for each respective site named on the approval letter  *IRB of Record may include language specifying documents that apply to all involved sites (i.e. Protocol Amendments)* |

| VIII. IRB-Approved Informed Consent Form (ICF) and Additional Approved Documents | |
| --- | --- |
| NOTE:  All IRB approved materials will be reviewed for compliance with ICH GCP 8.2.7, necessitating the use of version control of all documents submitted for review by the IRB. | |
| Yes No | All pages of the document are present. |
| Yes No | The DMID Protocol title is listed correctly, if present. |
| Yes No | The document is approved by the IRB.  The document should have an approval stamp somewhere on the document or a notation present to indicate the IRB approval and effective approval date(s).  If the document does not contain an approval stamp or other approval notation, the IRB approval letter must specifically identify the approval of the document and correctly match the version listed on the document. |
| Yes No    NA | For Informed Consent Forms:  If state-specific and/or IRB-specific documents are required to be given to subject during the informed consent process in addition to the study consent, these documents are present  For example, the state of California requires the California Bill of Rights to be included with the consent. |

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| IX. OHRP Federal Wide Assurance | |
| Yes No | Each facility listed in Section 1 of the Form FDA 1572 or Section 2 of the IoR must have an OHRP Federal Wide Assurance number (FWA#) assigned.  IRB name corresponds to the IRB name listed in Section 5 of the Form FDA 1572 or Section 6 of the IoR. |
| Yes No | The expiration date of the FWA number should be listed on the OHRP website. |
| Yes No | The IRB must have an OHRP registered IRB number and linked to the main site’s FWA.  *If the IRB is not linked to the main site’s FWA, a reliance between the main site and the IRB must be provided.* |

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| X. Laboratory Credentials/Certification (If Applicable) | |
| Yes No | If CLIA certification or equivalent is required, certification is present and current for each clinical laboratory listed in Section 4 of the Form FDA 1572 or Section 5 of the IoR.  CLIA certificates are not required for the following:   * Foreign (outside US) country labs * All labs in the state of Washington * All Hospital labs in the state of New York (NY private practices require a CLIA) * All Veteran Administration (VA) hospital labs   NOTE: State certifications or foreign country equivalent are required in lieu of CLIA certification |
| Yes No | As applicable, private inspection agency certificates (e.g. CAP, COLA) are present and current for each clinical laboratory listed in Section 4 of the Form FDA 1572 or Section 5 of the IoR.  NOTE: A private inspection agency certificate is needed for:   * CLIA Certificate of Accreditation   NOTE: A private inspection agency certificate is not needed for:   * CLIA Certificate of Compliance * CLIA Certificate of Registration * CLIA Certificate of Waiver * CLIA Certificate for Provider-Performed Microscopy Procedures |

| XI. Laboratory Reference Ranges | |
| --- | --- |
| Yes No | Reference ranges (as applicable) are present for each clinical laboratory in Section 4 of the Form FDA 1572 or Section 5 of the IoR. |
| Yes No | The name of the laboratory is indicated on the laboratory reference ranges. |
| Yes No | The current date is indicated on the laboratory reference ranges. |
| Yes No | If the laboratory address is indicated on the laboratory reference ranges, it corresponds to Section 4 of the Form FDA 1572 or Section 5 of the IoR. (exact match not required) |
| Yes No | The laboratory reference ranges required by the Protocol for the subject population under study are present. |
| *NOTE:*  Memos clarifying lab reference range issues are obtained from the site and are signed and dated by investigator staff or laboratory personnel. | |

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| Please comment on any “No” responses: |

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|  |  |
| Completed by (Print Name) | Date |