

**The University of Michigan Medical School  
Institutional Review Board for Human Subject Research**

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**<http://www.med.umich.edu/irbmed>**

**HOW TO REQUEST REVIEW OF A  
PREVIOUSLY-APPROVED PROJECT**

This document has an **information section** (General Information & Specific Information), and an **application template section**. When you have completed the template section, please delete the information section, and **submit to the IRBMED one printed copy and one electronic copy (saved in RTF format) of only the completed template and required supporting documents on CD or disk.**

**GENERAL INFORMATION**

See [http://www.med.umich.edu/irbmed/forms/whatsnew\\_app.htm](http://www.med.umich.edu/irbmed/forms/whatsnew_app.htm) for a summary of IRBMED Application Form changes. The footer at the bottom of each application page provides the date the form was last updated.

Sections of the template that are not relevant to the application type may be deleted, as indicated in each section heading. Otherwise, please do not change or delete any of the text already embedded in the template. To complete the template, place the cursor in the blank spaces under each query and any information which follows it, and enter the appropriate text. Save a copy of the completed application to your computer's hard disk.

Please submit all documents relevant to this application to the IRBMED office (address above). **Submit the documents, which have been prepared by the investigators, as one printed copy and one electronic copy (on a diskette)** (e.g. this application; informed consent documents). Documents prepared by a sponsor of the research (e.g. study protocol; Investigator's Brochure...) may be submitted as paper copy only; however, if available, please include an electronic copy. **The electronic documents should be saved to the diskette in Interchange "Rich Text Format" (RTF), so that they can be opened using any text-processing application in any computer operating system environment** (if you have difficulty with this process, please consult the user's manual or help facility of your application). The electronic documents will be posted in the restricted-access section of the IRBMED Internet Web site, for the review of IRBMED members, as required by the US Government. The documents will be handled as confidential.

Upon completion of the review process, the IRBMED will issue a "**Notice of Outcome of Review**", a printed copy of which will be sent to the Principal Investigator (usually within 6-8 weeks from the date of receipt of the complete application package).

Each Notice of Outcome of Review will inform the Principal Investigator of two important dates: "**Approval Date of Most Recent Version of Consent Document**" (if applicable), and "**Expiration Date of Project Approval**". These dates will be requested by the IRBMED at all subsequent interactions related to a previously approved project. Federal regulations require that both dates appear on all written informed consent instruments in use in conjunction with the research project. Whenever a consent document is revised and approved by the IRBMED, the newly assigned "Approval Date of Most Recent Version of Consent Document" should appear on all subsequent copies of the document. Whenever a project receives scheduled-continuation approval, the newly assigned "Expiration Date of Project Approval" should appear on all subsequent copies of the consent document.

For further information on IRBMED procedures, please consult the Federal and institutional documents posted at the IRBMED Internet Web site: <http://www.med.umich.edu/irbmed/>

## **SPECIFIC INFORMATION**

This is a multi-purpose application template for use in conjunction with all types of **Previously Approved Projects**. Sections 1–3 are to be completed for all types of applications. One or more of the remaining sections (Sections 4–11) are to be completed optionally, depending upon the type of application. You are encouraged to delete those sections not relevant to your request. A single application may have more than one purpose. When submitting an application for approval of an amendment or adverse event report, investigators may include a request for scheduled-continuation approval, even if the expiration date of project approval is several months away.

### **Section 1: Project Identification**

Completion of this section provides certain identifiers related to the project, which the IRBMED needs for “tracking” purposes.

### **Section 2: Reasons for Requesting this Review (Application Type)**

Completion of this section will help to determine which of the remaining sections will be required to complete the submission.

### **Section 3: Information on the Research Project**

Informed consent process is a critical element in protecting the rights of human research subjects. This section allows the Investigators to report to the IRBMED the consent process utilized with the project, so that concordance with the IRBMED records on the project can be ascertained. Submission of copies of the most recent version of the previously-approved informed consent instrument is mandatory.

All copies of project-specific informed consent instruments are to show the following information: [1] Project Title. [2] Names of all investigators. [3] IRBMED archive number. [4] Approval date of most recent version of consent document. [5] Expiration date of project approval.

For further information, please consult the Informed Consent Guidelines posted at the IRBMED Web site.

As mandated by Federal regulations, the IRBMED closely monitors vulnerable subject populations to ascertain that special precautions are in effect to minimize risks which may cause harm.

Incomplete submission of supporting documents is a common cause for delays in completion of the review process. The document list in this section is intended to serve as a reminder to investigators, and those preparing submissions.

### **Section 4: Report on Termination of Project**

Federal regulations require that Institutional Review Boards are notified by the investigators of the completion or termination of all research projects involving human subjects. Termination of a research project means that any and all involvement of research subjects in the study has come to an end. Section 4 provides the format in which the final summary report is to be presented. If a summary report has been prepared by the sponsor of the research, a copy of that report should be appended as well.

The records of a terminated project will be removed from the current IRBMED archives, and kept in storage at a separate location for the Federally-required period of three years.

### **Section 5: Scheduled-Continuation Renewal**

Federal regulations require that Institutional Review Boards review all research projects involving human subjects at least once every twelve months (the higher the risks of the study, the more frequent are the continuation reviews). Following satisfactory review, approval is processed. At the time of the initial review and approval of a new research project, in the “Notice of Outcome” sent to the Principal Investigator, the IRBMED also notifies the investigator of the **“Expiration Date of Project Approval”**. The expiration date is the date before which the investigators are expected to review the events and progress made in the project since the initial or most recent scheduled-continuation approval.

If IRBMED approval for continuation has not been received prior to the “Expiration Date of Project Approval,” the investigators are required to suspend recruitment of subjects into the study, and cease any experimental procedures on subjects already enrolled in the study, except to eliminate immediate hazard to subjects, until approval to continue is received.

Applications to the IRBMED, which may have been submitted to request approval of interim amendments, adverse events or progress are not substitutes for the comprehensive scheduled review and approval of continuation of a

project; *i.e.*, approvals received at the time of such unscheduled reviews do not change the “Expiration Date of Project Approval” of the initial or most recent continuation approval. Section 5 is designed to facilitate submission of complete information which is necessary for the IRBMED to renew the status of the project, prior to the expiration of the approval.

## **Section 6. Adverse Events Not Reported Previously**

Follow the AE guidance posted at the IRBMED website: [http://www.med.umich.edu/irbmed/ae\\_orio/](http://www.med.umich.edu/irbmed/ae_orio/). The information below provides details on filling out the application; it does not provide the reporting guidance available at the AE website.

Use section 10 when submitting follow-up reports.

**6.1:** The number of related events plus the number of unrelated events must equal the number of events included in 6.2.

This ratio of adverse events to number of persons affected by the events provides a brief but helpful overview. For example, a report could state “10 related AEs affecting 1 person” or “10 related AEs affecting 10 persons.” Even though both reports are of 10 related AEs, the context of the two reports is quite different.

**6.2** Review is facilitated by providing all requested information and following the format and order indicated in the application. Single-space each event and double-space between events. The type of event, seriousness, relatedness, and expectedness can be put in one line, separated by commas.

List events in the order of importance (in the context of the IRBMED obligation to assess the risk/benefit ratio, and subject safety and autonomy). For example: Serious, unexpected, and definitely related events first, followed by serious, unexpected, and possibly related, then serious, expected, definitely related, then non-serious, unexpected, related, and so on.

Number events for each submission (1, 2, 3, etc.). Relying on date or subject number slows processing. Write the event number on any supporting documents (1,2 3, etc.) and place in the same order as listed in the submission.

~~**6.3** The number of related events plus the number of unrelated events must equal the number of events included in 6.4.~~

~~If the number of persons affected is not known, put “unknown.” List the external adverse events that constitute an ‘unanticipated problem involving risks to subjects or others’ (UaP).~~

~~**6.4** Review the guidance for reporting External Adverse Events. The PI is required to submit the report to the IRB only when one of following criteria applies:~~

- ~~• The event or information in the report constitutes an ‘unanticipated problem’\* (Report in 6.3)~~
- ~~• The report requires a change in the research (Report in 6.4)~~
- ~~• The report is an analysis, safety, or statistical report from an oversight entity (e.g. FDA letter, Periodic Sponsor Report of all AEs, Data and Safety Monitoring Board Report). (Report in section 10)~~

~~Review is facilitated by providing all requested information indicated in the application including a justification for any non-required reports.~~

~~WHEN LISTING EVENTS IN THE APPLICATION: Single-space each event and double-space between events. The type of event, seriousness, relatedness, and expectedness can be put in one line, separated by commas.~~

~~List events in the order of importance (in the context of the IRBMED obligation to assess the risk/benefit ratio, and subject safety and autonomy). For example: Serious, unexpected, and definitely related events first, followed by serious, unexpected, and possibly related, then serious, expected, definitely related, then non-serious, unexpected, related, and so on.~~

~~Number events for each submission (1, 2, 3, etc.). Relying on date or subject number slows processing. Write the event number on any supporting documents (1,2 3, etc.) and place in the same order as listed in the submission.~~

~~**WHEN ATTACHING A SUMMARY REPORT:** Provide an overview assessment or narrative description of the attached report (applications that do not provide a description may be returned) at 6.4 in the application. The summary should include the same information at that noted above, and follow the same type of order (important events first).~~

**Example 1--** Events that occurred at other sites: 250 adverse events. 10 serious, related ,and unexpected; the informed consent document has been modified to include them (cardiac arrest and sepsis) in the risk section. 40 related and expected. 200 MedWatch reports with an attribution of possibly related. These are either included in the currently approved consent document (expected) or occurred in a significantly different study population and indication, and as such, are unrelated to this research study.

**Example 2--** Adverse Events Elsewhere: 20. Study is closed to accrual. Event 1: Kidney transplant rejection, nephropathy toxic. Serious, unexpected, possibly related. Investigator could not exclude study-drug-name as a contributing factor. 19 other events, serious, expected. No changes in the protocol or consent required.

### **Sections 7–11. Amendments Not Reported Previously**

Investigators of a previously-approved project are required to request IRBMED approval to make changes (amendments) in any aspect of the project, which has a bearing upon the human research subjects. Amendments may not be implemented prior to obtaining the approval of the IRBMED including those perceived to reduce risk (except for changes to eliminate apparent **immediate hazards** to the subject, implement the change and report by a formal ORIO or amendment submission within 7 days after the action is taken). Sections 7–11 are designed to facilitate submission of complete information on the amendments, for review and approval by the IRBMED, prior to or in conjunction with the project’s next regularly scheduled-continuation review. If *waiver of consent or waiver of documentation or alteration of consent* has been previously granted by IRBMED for any aspect of this project, then the [HIPAA-compliant Request Form](#) must also be submitted with this application if the project is being changed or amended. The waiver request form is not required to request a text change in an informed consent document.

Amendments, which may be requested by the sponsor of the research, or by the investigators themselves, include, but are not limited to the following:

**Section 7:** Amendments in the investigatorship. The IRBMED recognizes the Principal Investigator of a project as the person responsible for the protection of rights and welfare of human research subjects. In situations necessitating a change in the Principal Investigatorship, the IRBMED intends to facilitate an orderly change-over. As part of the process, the outgoing Principal Investigator affirms the suitability of the successor to assume the responsibilities, and the incoming Principal Investigator gives assurances to protect the rights and welfare of the subjects.

**Section 8:** Amendments in research or study protocol, which may include changes in experimental design, the addition of new information or the correction of errors in the text, change in title, change in or institution of advertisements or survey instruments. The IRBMED reviews protocol changes from the standpoint of risks of harm to the research subjects.

**Section 9:** Amendments in Investigator’s Brochure, if the study involves a test article (investigational drug, biologic or device). Sponsors of research involving FDA-exempted investigational drugs, biologics or devices will periodically update their brochures, which are to be reviewed and approved by IRBs, to assure that the risks of harm to human subjects have not increased.

**Section 10:** Amendments in any other aspect of the study, not approved previously by the IRBMED, or progress in a current or terminated study. This section is also to be used when reporting any adverse event which occurred elsewhere, after the termination of a research project at this site.

**Section 11:** Amendments in informed consent instruments.

IRBMED approval of an interim amendment request will not change the “Expiration Date of Project Approval”, before which a scheduled-continuation review of a project needs to occur.

The template that follows is to be used in conjunction with a project previously-approved by the IRBMED, to apply to the IRBMED for any purpose, including Termination, Scheduled-Continuation, Adverse Events, and Amendments. A single application may be submitted for more than one purpose (e.g. adverse events and amendments, scheduled-continuation approval and amendments, etc.) Sections 1–3 are to be completed for any type of application. One or more of the remaining sections (Sections 4–11) are to be completed optionally, depending on the type of application. • Section 1 is to identify the project for tracking purposes. • Section 2 is to determine the application type, and the respective sections of the application to be completed. • Section 3 is to define the status of the project, in regards to human subjects and consent process, and to identify documents being submitted. • Section 4 is to report Project Termination & cessation of all human subject involvement. • Section 5 is to request Scheduled-Continuation approval, prior to previously designated expiration of approval date. • Section 6 is to report Adverse Events and request approval to continue. • Section 7 is to request approval of amendment in Investigatorship. • Section 8 is to request approval of amendments in study protocol, advertisements, survey instruments. • Section 9 is to request approval of amendment in Investigator’s Brochure. • Section 10 is to request approval of amendments or progress in any other aspect of a project. • Section 11 is to request approval of amendment in Informed Consent Process. In finalizing an application using this template, you may delete any of Sections 4–11, if they are not relevant to your request.

***Please note: Do not submit the preceding text to the IRBMED. Only submit a completed version of the template, which follows.***

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**REQUEST FOR REVIEW OF A  
PREVIOUSLY-APPROVED PROJECT**

See [http://www.med.umich.edu/irbmed/forms/whatsnew\\_app.htm](http://www.med.umich.edu/irbmed/forms/whatsnew_app.htm) for a summary of any IRBMED Application Form changes.

See [http://www.med.umich.edu/irbmed/ict/ict\\_new.htm](http://www.med.umich.edu/irbmed/ict/ict_new.htm) for a summary of informed consent template changes.

**Submit to the IRBMED one printed copy and one electronic copy (saved in RTF format) on a CD or Disk.**

**1. PROJECT IDENTIFICATION**

Do not delete this section. Completion of this section is required for all types of projects.

*(Please note: In the near future, this section will be completed on-line at the IRBMED Internet Web site. Information will be transferred electronically to the IRBMED electronic database. A printed copy to be produced by the Investigator at that time will be part of this application.)*

**1.1 Principal Investigator, who remains responsible for or will take over the responsibility of this project; enter last name, followed by first name:**

If this is a new PI taking over the responsibility from a PI previously-approved by the IRBMED, please provide the name & signature of the old PI in Section 7.

**1.2 Principal Investigator's signature:**

If a new PI is taking over the responsibility, the new PI signs here, and the old PI signs in Section 7.

Signature of the PI is required on the printed copy of this application document. By signing, the PI assures that he/she will protect the rights and welfare of human research subjects to the best of his/her ability.

**1.3 IRBMED Archive Number:**

Enter the previously assigned number.

**1.4 Title of research project:**

Enter the title previously-approved by the IRBMED, if there will be no change. If there will be a new title, please enter the new title here, and provide the old title in Section 8.

Do not include any identifier codes in the title (enter such codes under 1.5 & 1.6).

**1.5 Name of extramural company or agency sponsoring the research:**

Enter "NA", if there is no extramural support (A Company outside of the University of Michigan).

**1.6 Extramural research sponsor's identifier code:**

Enter "NA", if not applicable or not necessary.

**1.7 Research project local/institutional identifier code, if any:**

Enter the same code used in the initial application, or "NA". (DRDA, UMCC or CRC Number, etc)

**1.8 Principal Investigator's fax number:**

If a new PI is taking over the responsibility, please enter the new PI's fax number.

IRBMED will fax official documents to this number rather than sending by campus mail. If you wish the Notice of Approval to be faxed to another number, such as the Study Coordinator or Research Lab, please indicate that number as well.

**1.9 Date of submission of this application:**

Please use the format YYYY/MM/DD.

**1.10 Date of receipt of complete application by IRBMED office:**

Leave blank; for office use only.

**1.11 Project Type: PREVIOUSLY APPROVED PROJECT**

Leave one or more of the choices listed below; delete those not applicable.

- DIRECT INVOLVEMENT OF HUMAN SUBJECTS: Research using invasive treatments, procedures, or experimentation.
- DIRECT INVOLVEMENT OF HUMAN SUBJECTS: Research solely using surveys, interviews, focus groups, observations, or other similar methods.
- NO DIRECT INVOLVEMENT OF HUMAN SUBJECTS: RESEARCH solely using human data or biological specimens.
- NO DIRECT INVOLVEMENT OF HUMAN SUBJECTS: INSTITUTIONAL research project, training, program or center, solely to provide support to other human subject research.

**1.12 Approval Date of Most Recent Version(s) of Consent Document(s):**

Transcribe the date shown in the IRBMED Notice of Outcome of Review letter of the most recent review. **If informed consent process has been waived, or if subject involvement has ceased, enter that information instead of a date.**

Please use the format YYYY/MM/DD.

**1.13 Expiration Date of Project Approval:**

Transcribe the date shown in the IRBMED Notice of Outcome of Review letter of the most recent review.

Please use the format YYYY/MM/DD.

**1.14 Are FDA-regulated test articles, namely investigational drugs, biologics or devices in use in this project?**

Please delete those entries listed below that are not applicable to this project. For an investigational drug or biologic, please enter the FDA-assigned “IND” (Investigational New Drug) archive number and trial phase. For an investigational device, please enter FDA-assigned “IDE” (Investigational Device Exemption) archive number and risk level. If more than one test article is involved, provide the same information for each, together with the respective generic or code name. **Please refer to your new project application to the IRBMED for initial review.** If you are providing this information for the first time, Please refer to [1] the IRBMED guidelines document “Test Articles in Research” for comprehensive information on FDA-regulated test articles and FDA-compiled lists of significant and nonsignificant risk devices, and [2] Federal regulatory documents 21 CFR 312 & 314. These documents are available at the IRBMED Internet Web site.

- No test article used
- Drug or Biologic used  
IND#: \_\_\_\_\_  
Trial Phase: \_\_\_\_\_
- Device used  
IDE#: \_\_\_\_\_  
Risk Level (significant or nonsignificant): \_\_\_\_\_

**1.15 Information on the Principal Investigator, who will be responsible for this project:**

Please enter the requested information. If a new PI is taking over the responsibility, please give the information for the new PI.

- Name and Academic degree:
- University (or company) title:
- Administrative unit:
- Campus (or company) mail address & code:
- Telephone number:
- Fax number:
- Electronic-mail address/Pager Number:

**1.16 Information on the Study Coordinator or Office Assistant who may be contacted in reference to this project:**

- Name and Academic degree:
- University (or company) title:
- Administrative unit:
- Campus (or company) mail address & code:

- Telephone number:
- Fax number:
- Electronic-mail address:

**1.17 Co-investigators' last names followed by first names, and academic degrees:**

**1.18 Co-investigators' signatures:**

**Required ONLY if the application involves ADDING a Co-Investigator.**

By signing, each Co-investigator acknowledges that he/she is familiar with the contents of this research, and pledges to assist the PI in protecting the rights and welfare of human research subjects.

\*\*\*\*\* End of Section \*\*\*\*\*

## **2. REASONS FOR REQUESTING THIS REVIEW (APPLICATION TYPE)**

Do not delete this section. Completion of this section is required for all types of projects.

**2.1 Is this a report of Termination of the research project?**

Please answer "Yes" or "No". **If yes, please complete Sections 1, 2, 3 & 4.**

**2.2 Is this a request for Scheduled-Continuation approval of a project approaching its "Expiration Date of Project Approval"?**

Please answer "Yes" or "No". **If yes, please complete Sections 1, 2, 3 & 5.** (Also include **Sections 6 and 10** if any AEs (6) and ORIOs (10) are due to be reported at scheduled-continuation. See the IRBMED AE & ORIO Timetables at [http://www.med.umich.edu/irbmed/ae\\_orio/index.htm](http://www.med.umich.edu/irbmed/ae_orio/index.htm))

**2.3 Is this a report of Adverse Events or Unanticipated Problem not previously reported?**

Please answer "Yes" or "No" and indicate the IRBMED AE Reporting Timetable used for this study. **If yes, please complete Sections 1, 2, 3 & 6.**

(Delete bullet that does not apply.)

- Standard AE Timetable ([http://www.med.umich.edu/irbmed/ae\\_orio/ae\\_report\\_standard.htm](http://www.med.umich.edu/irbmed/ae_orio/ae_report_standard.htm))
- Study-Specific AE Timetable ([http://www.med.umich.edu/irbmed/ae\\_orio/ae\\_report\\_specific.htm](http://www.med.umich.edu/irbmed/ae_orio/ae_report_specific.htm))

**2.4 Is this a request for approval of Amendments in Investigatorship, not previously approved by the IRBMED?**

Please answer "Yes" or "No". **If yes, please complete Sections 1, 2, 3 & 7.**

**2.5 Is this a request for approval of Amendments in Study Protocol, not previously approved by the IRBMED?**

Please answer “Yes” or “No”. **If yes, please complete Sections 1, 2, 3 & 8.** ]. If the IRBMED previously approved a *waiver or alteration of the informed consent process* for any aspect of this project, or if *documentation of informed consent* has been waived, then the [HIPAA-compliant Request Form](#) for waiver or alteration of consent must also be submitted when approval of changes or amendments in the study protocol are requested. **The waiver request form is not required to request a text change in an informed consent document.** It is only needed if waiver of the written informed consent process is being used in this study.

**2.6 Is this a request for approval of Amendments in Investigator’s Brochure, not previously approved by the IRBMED?**

Please answer “Yes” or “No”. **If yes, please complete Sections 1, 2, 3 & 9.**

**2.7 Is this a request for approval of Amendments in any other aspect of the study (excluding amendments noted in 2.4, 2.5, 2.6 or 2.8), not previously approved by the IRBMED, or Progress in a current or terminated study, or Other Reportable Information or Occurrences (ORIOs)?**

Please answer “Yes” or “No”. **If yes, please complete Sections 1, 2, 3 & 10.**

**2.8 Is this a request for approval of Amendments in Informed Consent Process, not previously approved by the IRBMED?**

Please answer “Yes” or “No”. If yes, please complete Sections 1, 2, 3 & 11. If the IRBMED previously approved a *waiver or alteration of the informed consent process* for any aspect of this project, or if *documentation of informed consent* has been waived, then the [HIPAA-compliant Request Form](#) for waiver or alteration of consent must also be submitted when approval of changes or amendments in the study protocol are requested. **The waiver request form is not required to request a text change in an informed consent document.** It is only needed if waiver of the written informed consent process is being used in this study.

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\*\*\*\*\* End of Section \*\*\*\*\*

### **3. INFORMATION ON THE RESEARCH PROJECT**

Do not delete this section. Completion of this section is required for all types of projects.

**3.1 What documents are you submitting together with this application in conjunction with termination, scheduled continuation, adverse events or amendments in this previously-approved project?**

Please submit all documents prepared “in house” in one printed and one electronic copy.

Please ascertain that the consent instruments show [1] Title of Project as it appears in this application and in the study protocol, [2] names of the Principal Investigator and all Co-investigators, [3] “IRBMED Archive Number”, [4] “Approval Date of Most Recent Version of Consent Document”, [5] “Expiration Date of Project Approval”, and [6] date document was prepared.

Please delete those entries listed below that have not been appended. Please indicate the number of documents of each kind being submitted.

- Informed consent instrument (if applicable) with previously-approved content (**mandatory as long as subject interactions continue—including after recruitment has closed**)
- Informed consent instrument amended
- Adverse event reports
- Letter to previously recruited subjects about adverse events or protocol changes
- Study Protocol amendment texts or notices/memoranda
- Solicitation materials for subject recruitment (*e.g.* Advertisement) newly instituted or amended
- Survey Instruments newly instituted or amended
- Investigator's Brochure amended
- [HIPAA-compliant Request Form](#) for *waiver or alteration of consent* or *waiver of documentation of consent*
- Other (please specify)

**3.2 Are “vulnerable populations” among the research subjects?**

Please delete those entries listed below that are not applicable to this project.

- Not applicable: no direct involvement of human subjects
- None
- Children (age <18 years)
- Mentally disabled (decisionally impaired) persons
- Women with child-bearing (reproductive) potential
- Pregnant or lactating women
- Fetuses (*ex utero*)
- *in vitro* Fertilization
- Prisoners

**3.3 What type of informed consent process is in use in this project, as previously approved by the IRBMED?**

Among the entries listed below, leave intact the process(es) in effect, and delete the rest.

- Comprehensive written informed consent document [project-specific].
- Assent of children (may be documentation within the main consent document, or a separate document) [project-specific].
- Written information without documentation of consent [project-specific].
- Written short information & separate documentation, plus third-party witness [project-specific].
- Informed consent requirement waived entirely.

**3.4 Is more than one informed consent instrument in use in this project?**

Please answer “Yes” or “No”. If yes, please indicate what each instrument is being used for.

**3.5 Who may act on behalf of the subject in giving consent to participate in this research?**

Among the entries listed below, leave those applicable, and delete the rest.

- Not applicable
- Adult subject himself/herself
- Legal guardian
- One parent of a child
- Both parents of a child
- Assent of a child
- Next-of-kin of an adult (spouse; adult son or daughter; either parent; adult brother or sister; legal guardian; any other explicitly authorized person)

\*\*\*\*\* End of Section \*\*\*\*\*

## **4. REPORT ON TERMINATION OF PROJECT**

Please complete this section, if answer to Question 2.1 was “Yes”.

If not relevant, please delete this section.

**4.1 Has the involvement of human subjects or use of human data or biological specimens in this project come to an end in every respect at this site?**

Please answer “Yes” or “No”. A “Yes” answer would mean that the involvement of all subjects in this research project has come to an end, no research subject is still being followed or contacted, and no new subject will be recruited.

**4.2 All together, how many research subjects were recruited, or how many cases of human data or biological specimens were used at this site since the initiation of this project?**

Please specify number and type of unit (subjects, specimens, cases, tissue samples, etc.)

**4.3 What was the ethnic, racial and gender composition of the subjects recruited at this site since the initiation of this project?**

Please skip this question, if study did not involve human subjects directly.

To permit monitoring for equity, please enter below the numbers in each category of subjects listed:

- American Indian or Alaskan native:
- Asian or Pacific Islander:
- Black, not of Hispanic origin:
- Hispanic:
- White, not of Hispanic origin:
- Other, unknown or otherwise not reported:

- 
- Female:
  - Male:

**4.4 How many of the recruited research subjects at this site withdrew from the study since the initiation of this project?**

Please skip this question, if study did not involve human subjects directly.

Please indicate the total number and reasons for withdrawal.

**4.5 How many of the recruited research subjects at this site complained about any aspect of the study since the initiation of this project?**

Please skip this question, if study did not involve human subjects directly.

Please indicate the total number, the nature and resolution of the complaints.

**4.6 How many adverse events involving research subjects at this site occurred since the initiation of this project?**

Please skip this question, if study did not involve human subjects directly.

Please indicate the total number, the nature and outcome of these adverse events.

**4.7 All together, how many adverse events involving research subjects at this site, or elsewhere were reported to the IRBMED?**

Please skip this question if study did not involve human subjects directly.

Please answer “None” or indicate the total number.

\*\*\*\*\* End of Section \*\*\*\*\*

## **5. SCHEDULED-CONTINUATION REVIEW**

Please complete this section, if answer to Question 2.2 was “Yes”.

If not relevant, please delete this section.

For a previously approved project approaching its “Expiration Date of Project Approval”, an interval report is to be provided. The interval corresponds to the period that elapsed since the project’s initiation in its first year, or since the most recent scheduled-continuation application for a project in its second year or beyond. To request approval of any new changes in any aspect of the project conjunction with this scheduled review, please use Sections 7–11.

**5.1 Does this research meet all of the following three criteria at this site? [1] Research is permanently closed to enrollment of new subjects. [2] All research-related interventions in previously recruited subjects have come to an end. [3] Research remains active only for long-term observation of subjects or for data analysis.**

Please respond with a “Yes”, only if all criteria are met. Otherwise, respond with a “No”. Enter “NA”, if there is no direct involvement of subjects in the research.

**5.2 All together, how many research subjects were recruited, or how many cases of human data or biological specimens were used at this site since the initiation of this project?**

Please specify number and type of unit (subjects, specimens, cases, tissue samples, etc.)

**5.3 What was the ethnic, racial and gender composition of the subjects recruited at this site since the initiation of this project?**

Please skip this question, if study did not involve human subjects directly.

To permit monitoring for equity, please enter below the numbers in each category of subjects listed:

- American Indian or Alaskan native:
- Asian or Pacific Islander:
- Black, not of Hispanic origin:
- Hispanic:
- White, not of Hispanic origin:
- Other, unknown or otherwise not reported:

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- Female:
- Male:

Please double check the above noted numbers and verify content and total.

**5.4 During the most recent interval, how many new research subjects were recruited, or how many new cases of human data, or new biological specimens were used at this site?**

**5.5 At the present time, how many research subjects are undergoing research-related interventions, or are under long-term observation at this site?**

**5.6 How many more research subjects will be recruited, or how many more cases of human data or biological specimens will be used at this site, until the completion of this project?**

Enter the estimated number. If subject recruitment is closed, enter "0".

**5.7 Did any of the recruited research subjects at this site withdraw from the study during the interval?**

Please skip this question, if study did not involve human subjects directly.

Please answer "Yes" or "No". If yes, please indicate the number and reasons for withdrawal.

**5.8 Did any of the recruited research subjects at this site complain about any aspect of the study during the interval?**

Please skip this question, if study did not involve human subjects directly.

Please answer "Yes" or "No". If yes, please indicate the number, the nature of the complaints, and resolution of the complaints.

**5.9 Did any adverse events occur during the interval?**

Answer “Yes” or “No”. If yes, please complete this section. (Note: a follow-up report is not an event; submit follow-up reports using section 10)

[a] Total number of UM adverse events (events involving subjects or others under the oversight of the UM investigator(s) and IRBMED)

Previously reported \_\_\_\_\_ + new events in section 6 \_\_\_\_\_ = Total for interval \_\_\_\_\_

[b] Total number of adverse events that occurred at other sites (events involving subjects or others who are under the oversight of non-UM investigator(s) and institution(s)):

Previously Reported \_\_\_\_\_ + new events in section 6 \_\_\_\_\_ = Total for interval \_\_\_\_\_

**5.10 Do you wish to provide follow-up information on any of the adverse events previously reported to the IRBMED?**

Please skip this question, if study did not involve human subjects directly.

Please answer “Yes” or “No”. If yes, please enter here the information.

**5.11 Did you implement amendments in any aspect of this research project during the interval, and receive IRBMED approval?**

Please answer “Yes” or “No”. If yes, please provide information on types of amendments and IRBMED-approval dates (*e.g.* study protocol 1997/10/08).

**5.12 Please submit an unsigned copy of each project-specific informed consent instrument currently in use in this project, unless subject involvement has ended permanently.**

Among the entries listed below, leave those applicable, and delete the rest.

- Consent instruments appended
- Subject involvement/interactions ended permanently
- Consent process waived

\*\*\*\*\* End of Section \*\*\*\*\*

## 6. ADVERSE EVENTS (AEs) NOT REPORTED PREVIOUSLY

Please complete this section, if answer to Question 2.3 was “Yes”.

If not relevant, please delete this section.

Refer to the IRBMED web-posted guidance at

[http://www.med.umich.edu/irbmed/ae\\_orio/index.htm](http://www.med.umich.edu/irbmed/ae_orio/index.htm) ~~[http://www.med.umich.edu/irbmed/ae\\_orio/ae\\_report.htm](http://www.med.umich.edu/irbmed/ae_orio/ae_report.htm)~~ for AE reporting guidance and time schedules. [Click here for more details regarding filling out this form.](#)

**Unexpected:** An event that has not been addressed or described in one or more of the following:

- Informed consent document(s) for this study
- IRB application for this study
- Grant application or study agreement
- Protocol or procedures for this study
- Investigators’ brochure or equivalent (for FDA regulated drugs or devices)

- DSMB/DSC Reports
- Published literature
- Characteristics of the study population
- Other (provide documentation to the IRBMED if not previously submitted)

At this site **UM Events:** Events involving subjects or others under the oversight of the UM investigator(s) and IRBMED.

At other sites **External AEs:** Events involving subjects or others who are under the oversight of non-UM investigator(s), IRBs, and institution(s)

**6.1 For reports of NEW (not previously reported) AEs that occurred at this site provide the following information:**

# \_\_\_\_\_ related AEs affecting # \_\_\_\_\_ persons (definitely, possibly, or probably related)

# \_\_\_\_\_ unrelated AEs affecting # \_\_\_\_\_ persons (probably not related or unrelated)

**6.2 What were the new adverse events that occurred at this site?** Provide the requested information for each event. Number events (1, 2, 3, etc), list them in order of importance to risk/benefit assessment, and correlate numbers (1, 2, 3 etc.) with any appended reports ([click here for more details](#)). *For reports due at scheduled-continuation you may submit a summary in paper and electronic formats (Excel, Microsoft Word, PDF, or RTF) and indicate "see attached."* WHEN ATTACHING A SUMMARY provide an overview description [here](#) (see 6.4 instructions in introduction for examples).

**Event 1:**

Subject identifier code, date

Type of event (single phrase description—if considered an 'unanticipated problem involving risks to subjects or others' add 'UaP' to the descriptor)

Seriousness

Relatedness--presumed association with the test article/procedure (*i.e.* definite, probable or possible association, or unrelated)

Expectedness

Any information on the incidence of the adverse event, particularly for multicenter studies (how many cases observed among the cumulative subject pool?).

Supporting report (indicate ATTACHED or NONE)

**Event 2:**

~~Subject identifier code, date~~

~~Type of event (single phrase description)~~

~~Seriousness~~

~~Relatedness--presumed association with the test article/procedure (*i.e.* definite, probable or possible association, or unrelated)~~

~~Expectedness~~

~~Any information on the incidence of the adverse event, particularly for multicenter studies (how many cases observed among the cumulative subject pool?).~~

Repeat as needed

Supporting report (indicate ATTACHED or NONE)

6.3 For reports of NEW (not previously reported) List all external AEs that constitute an 'unanticipated problem involving risks to subjects or others' (UaP) as defined in IRBMED guidance. Provide all indicated information. that occurred at other sites provide the following information: A supporting report must also be attached.

# \_\_\_\_\_ related AEs affecting # \_\_\_\_\_ persons (definitely, possibly, or probably related)

# \_\_\_\_\_ unrelated AEs affecting # \_\_\_\_\_ persons (probably not related or unrelated)

**UaP# 1:**

Subject identifier code, date

Type of event (single phrase description)

Seriousness

Relatedness—explain to what aspect of the research the event is attributable

Provide a concise explanation of why this event is considered unanticipated and in what way it indicates a greater risk than was previously known or recognized.

Repeat as needed

6.4 What were the new adverse events that occurred at other sites? Other external AEs (those that are not UaPs)—Answer both A and B

A. Are the AEs listed in B being submitted as support for an amendment in the research (as noted in one or more of sections 7-11)? YES/NO If no, provide a justification for submitting a non-required report.

B. List all external adverse events. Provide the requested information for each event. Number events (1, 2, 3, etc), list them in order of importance to risk/benefit assessment, and correlate numbers (1, 2, 3 etc.) with any appended reports (click here for more details)-or attach a summary: Provide an overview description here and indicate, "see attached." (click here for more details). The summary report must be submitted in paper and electronic formats (Excel, Microsoft Word, PDF, or RTF).

**Event 1:**

Subject identifier code, date

Type of event (single phrase description)

Seriousness

Relatedness--presumed association with the test article/procedure (i.e. definite, probable or possible association, or unrelated)

Expectedness

Any information on the incidence of the adverse event, particularly for multicenter studies (how many cases observed among the cumulative subject pool?).

Supporting report (indicate NONE or ATTACHED)

6.5 **What is the total number of serious or unexpected adverse events that have occurred at this site and at other sites over the entire history of the study?**

[1] At this site.

[2] At other sites.

**6.6** Please submit copies of supporting reports for each AE (e.g. IND Safety Report, MedWatch, DSMB report).

Please indicate total number of supporting reports included in this submission. Number reports according to the event numbers (not the subject identifier codes or dates) used in 6.2, 6.3 and 6.4 above.

**6.7** Will any changes/amendments be made to the research because of information included in this report (including informing currently enrolled subjects and/or those who have completed the study)? (Delete the items from the least below that will not be changed and leave those that will change. Correlate answers below with section 2.)

- Risk Assessment (also note if risk level is increased even if not enough to adjust the overall risk assessment)
- Informed Consent Document (Indicate which subjects, if any, will be re-consented. Also, if reporting any related and unexpected AEs that are not being added to the risk section of the informed consent, provide the reasons for not revising the consent document.)
- Intervention or investigational agents
- Protocol
- Investigator's Brochure
- Other (indicate)

~~Did the risks of harm to the subjects increase because of the newly observed adverse events?~~

~~Please answer "Yes" or "No". If yes, please indicate whether or not the benefits of the study still outweigh the risks, and the study protocol should be changed to reduce the risks of harm to the subjects. If study protocol needs to be revised, please report in Section 8.~~

~~**6.8** Has the informed consent instrument been revised to include any of the new adverse events?~~

~~If any of the adverse events were unexpected and considered to be related to the project, the "Risks" section of the consent documents will have to be revised.~~

~~Please answer "Yes" or "No". If yes, report in Section 11. If no, please indicate the reasons for not revising the consent documents (e.g. already included under risks; causally not related to the study; consent document no longer in use, because subject involvement has ended; consent requirement waived)~~

**6.89** Will the subjects who are currently in the study be informed about any of this new safety information, and how will it be done?

Please answer "Yes" or "No". If yes, please indicate how and how soon the information will be conveyed to the subjects. **Please submit content or text of any verbal or written information for approval.**

\*\*\*\*\* End of Section \*\*\*\*\*

## **7. AMENDMENTS IN INVESTIGATORSHIP NOT REPORTED PREVIOUSLY**

Please complete this section, if answer to Question 2.4 was "Yes".

If not relevant, please delete this section.

- 7.1 Does the change involve the Principal Investigator?**  
If yes, please enter the last name, followed by first name of the old PI. If no, enter “Not Applicable”.
- 7.2 If there is a change in Principal Investigator, the old Principal Investigator, please sign here:**  
By signing, the old PI assures that he/she affirms that the new PI is capable of assuming the responsibility of the project.
- 7.3 Are any of the previously approved Co-investigators leaving the project?**  
Please answer “Yes” or “No”. If yes, enter last names followed by first names.
- 7.4 Are any new Co-investigators joining the project?**  
Please answer “Yes” or “No”. If yes, enter last names followed by first names, academic degrees, University (or company) titles and administrative units.
- 7.5 Please revise the current informed consent instrument(s) to reflect the changes in investigatorship, and submit revised instrument(s) for approval.**  
Revise & report in Section 11.

\*\*\*\*\* End of Section \*\*\*\*\*

## **8. AMENDMENTS IN STUDY PROTOCOL NOT PREVIOUSLY REPORTED**

Please complete this section, if answer to Question 2.5 was “Yes”.  
If not relevant, please delete this section.

**Any amendments in advertisements or survey instruments are also to be reported in this section, as extensions of the study protocol.**

- 8.1 Is a separate document describing the amendments to the study protocol being submitted?**  
Please answer “Yes” or “No”. If yes, please **ascertain that the amended protocol document carries a title matching that shown in Section 1 of this application, the date on which it was prepared, and optionally sponsor’s identifier code(s)**, and enter below any identifiers which you wish to appear on the “Notice of Outcome of Review” document.
- 8.2 Was a new title identified for this project in Section 1 of this application?**  
Please answer “Yes” or “No”. If yes, please enter the previously-approved (old) title below, itemize in 8.3, and revise **the informed consent instruments to show the new title, and report it in Section 11.**
- 8.3 What are the specific changes in the study protocol?**  
Please itemize the protocol changes, and include a concise description of each change.

**8.4 Will the protocol changes involve the use of investigational devices, radioisotopes, or gene-transfer material?**

Please delete those entries, which do not apply. Please arrange review and acknowledgment/approval by the relevant units of the University, as specified below, and submit the respective acknowledgment / approval documents with this application.

Please indicate below, if any of the documents listed below are appended. If review by the involved committees is taking place concurrently, indicate so below; make sure that the document is sent to the IRBMED by fax (763-9603).

- None of the above.
- Investigational devices: Biomedical Engineering Unit of the University of Michigan Hospitals approval appended or is forthcoming.
- Radioisotopes: Subcommittee for Human Use of Radioisotopes of the University of Michigan appended or is forthcoming.
- Gene-transfer material: Institutional Biosafety Committee (IBC) of the University of Michigan appended or is forthcoming.

**8.5 Will the protocol changes affect the research subjects directly, in such a way as to impose greater risks of harm upon them?**

Please answer “Yes” or “No”. If yes, please clearly define what the nature and magnitude of the additional risks are, and whether or not the benefits of this study would still outweigh the risks.

**8.6 Is a revised version(s) of the informed consent instrument(s) being submitted, so that future subjects are informed of the protocol, as amended?**

If the risks were deemed increased, or the benefits decreased as a result of the protocol changes, the respective sections of consent instruments will have to be revised.

Please answer “Yes” or “No”. **If yes, report in Section 11.** If no, please indicate the reasons for not revising the consent instruments (*e.g.* administrative changes not affecting subjects directly; consent document no longer in use, because subject involvement has ended; consent requirement waived)

**8.7 Should subjects currently in the study be informed about the protocol changes?**

Please answer “Yes” or “No”. If yes, please indicate how and how soon the information will be conveyed to the subjects. **Please submit content or text of any oral or written information for approval.** Please indicate below, whether it is appended or not.

**8.8 Is there a new advertisement about the study, or is an existing advertisement being revised?**

Please answer “Yes” or “No”. **If yes, please submit the text of the advertisement for approval.** Please indicate below, whether it is appended or not.

- 8.9 Is a new survey instrument for use in the study being introduced, or an existing one revised?**  
Please answer “Yes” or “No”. **If yes, please submit the text of the survey instrument for approval.**  
Please indicate below, whether it is appended or not.

\*\*\*\*\* End of Section \*\*\*\*\*

## **9. AMENDMENTS IN INVESTIGATOR’S BROCHURE NOT REPORTED PREVIOUSLY**

Please complete this section, if answer to Question 2.6 was “Yes”.  
If not relevant, please delete this section.

- 9.1 Please submit a copy of the revised investigator’s brochure document.**  
Please enter below any identifiers for the Investigator’s Brochure, which you wish to appear on the “Notice of Outcome of Review” document. Please indicate below, that it is appended.
- 9.2 Please concisely summarize the new information provided in the amended brochure that may have relevance to the subjects of this research.**
- 9.3 Does the new information provided in the amended brochure suggest that the use of the test article may impose greater risks of harm on the subjects than originally estimated?**  
Please answer “Yes” or “No”. If yes, please clearly define what the nature and magnitude of the additional risks are, and whether or not the benefits of this study would still outweigh the risks.
- 9.4 Is a revised version(s) of informed consent instrument(s) being submitted to include any of the new information provided in the amended brochure?**  
Please answer “Yes” or “No”. **If yes, report in Section 11.** If no, please indicate the reasons for not revising the consent document.
- 9.5 Should subjects currently in the study be informed about the new information provided in the amended brochure?**  
Please answer “Yes” or “No”. If yes, please indicate how and how soon the information will be conveyed to the subjects. **Please submit content or text of any oral or written information for approval.** Please indicate below, whether it is appended or not.

\*\*\*\*\* End of Section \*\*\*\*\*

**10. AMENDMENTS IN ANY OTHER ASPECT OF THE STUDY NOT REPORTED PREVIOUSLY, OR PROGRESS IN A CURRENT OR TERMINATED STUDY, OR OTHER REPORTABLE INFORMATION OR OCCURRENCES (ORIOs)**

Please complete this section, if answer to Question 2.7 was “Yes”.  
If not relevant, please delete this section.

Please provide sufficient information and documentation on the unclassified amendments, sufficient for the IRBMED to judge their impact on human subjects of research. For ORIOs, refer to the IRBMED web-posted guidance at [http://www.med.umich.edu/irbmed/ae\\_orio/orio\\_report.htm](http://www.med.umich.edu/irbmed/ae_orio/orio_report.htm).

**10.1 Is this a progress report related to a research project previously acknowledged by the IRBMED as terminated (completed)?**

Please answer “Yes” or “No”. If yes, please provide the date of IRBMED acknowledgment of termination of the project (Expiration Date of Project Approval).

**10.2 What is the type or nature of amendment or progress is being reported?**

(*e.g.* Follow-up information on a previously reported adverse event. Memorandum dated 1997/01/01 received from the sponsor. Follow-up of a subject being transferred to another site.)

Please summarize the content. **Please append to this document any supporting materials, and indicate here what is being appended.**

**10.3 If the information provided is related to an active research project, does it impose greater risks of harm on the subjects than originally estimated?**

Please answer “Yes” or “No”. If yes, please clearly define what the nature and magnitude of the additional risks are, and whether or not the benefits of this study would still outweigh the risks (**current informed consent document may have to be revised**).

**10.4 If the information provided is related to an active research project, has a revised version(s) of informed consent instrument(s) been submitted to include any of the new information provided in this progress report?**

Please answer “Yes” or “No”. **If yes, report in Section 11.**

\*\*\*\*\* End of Section \*\*\*\*\*

## **11. AMENDMENTS IN INFORMED CONSENT PROCESS NOT REPORTED PREVIOUSLY**

Please complete this section, if answer to Question 2.8 was “Yes”, or if any of the preceding sections indicated that consent process should be amended. If not relevant, please delete this section.

**11.1 What are the reasons for making changes in informed consent instruments?**

If the changes are being made to accommodate adverse events or other amendments, please refer to the respective Section Number. (*e.g.* to accommodate adverse events in Section 6; to improve clarity of information given; to correct typographical errors)

**11.2 What specific changes will occur in the consent instruments?**

Please itemize.

**11.3 Please submit for approval printed & electronic copies of amended consent instrument's to replace previously approved version(s) or any newly introduced consent instrument(s).**

Please make sure that the revised versions display the date they were prepared, to distinguish them from previous versions. On printed copies, please highlight the changes for quick recognition. Please ascertain that the consent instruments show [1] Title of Project as it appears in this application and in the study protocol, [2] names of the Principal Investigator and all Coinvestigators, [3] “IRBMED Archive Number”, [4] “Approval Date of Most Recent Version of Consent Document”, [5] “Expiration Date of Project Approval”, and [6] date document was prepared.

Please indicate below, whether it is appended or not.