**Please note that all Duke-sponsored regulatory submissions to the FDA (or other federal regulatory agency) must be reviewed and submitted by the Duke Office of Regulatory Affairs and Quality (ORAQ).**

**Overview – IDE supplements, Reports and amendments**

# What is the difference between a supplement, a report and an amendment?

**Supplement** - is a written submission from the Sponsor-Investigator while the IDE is under review or approved (trial is ongoing) regarding changes to the protocol or the device. Supplements are intended to seek FDA’s approval for something new or different.

**Report** – is a written submission from the Sponsor-Investigator while the IDE is approved regarding study progress and unanticipated events. Reports are intended to provide notification or updates for FDA’s routine monitoring of a clinical investigation.

**Amendment** - is a written submission from the Sponsor-Investigator in response to the FDA’s request for more information regarding a previous supplement, report, or original IDE.

# What kinds of submissions fall into each category?

**Supplements:** The FDA tracks requests for a new protocol, changes to the approved protocol, or changes to the device, such as device design or manufacturing change, as supplements.

Submissions tracked as Supplements include:

* Change in correspondent, manufacturer, or sponsor
* Request for approval of changes in design or manufacturing
* Request for approval of a change in informed consent or protocol
* 5-day notices- Notification that changes not requiring prior approval have been made
* Request for compassionate use, live case demonstration, or other deviation from approved protocol
* Request for approval of expansion of the study (patients and/or sites)
* Request an extension of time to respond to FDA letter
* Request for waiver
* Institutional Review Board (IRB) certification
* Request for Centers for Medicare and Medicaid Services (CMS) re-categorization
* Notification of study suspended or resumed
* Acknowledgement and response to clinical hold
* Request for approval to terminate the study without final report
* Request for approval of a new study or protocol

**Timeline requirements for supplements:**

**Changes requiring prior approval** – most of the time, changes that are made in the Investigational Plan, need to be pre-approved by FDA. Examples of these changes are:

* **Changes in the Investigational Plan or Protocol**

-Affecting the validity of data/information,

-Patient risk to benefit relationship,

-Scientific soundness of investigational plan,

-Right, safety or welfare of subjects.

* **Developmental Changes** in the device (including manufacturing changes) that present a significant change in design or basic principle of operation

**Changes requiring 5-day notice -** these changes do not require prior approval, but notice must be provided to FDA within 5 working days of making the change:

* **Changes Effected for Emergency Use**-are considered to be changes in the investigational plan to protect the life or well-being of the subject in the case of emergency. However, these changes must be reported to the FDA **within 5- working days**.
* **Non-significant changes in design or manufacturing** - those changes should also be reported to the FDA within **5-working days**.
* **Certain changes to the clinical protocol –** for changes that do not fit the criteria for prior approval such as:
  + Modification to inclusion/exclusion criteria to better define the target patient population
  + Increasing the frequency at which data or information is gathered
  + Inclusion of additional patient observations or measurements
  + Modifying secondary endpoints

Other minor changes can be submitted in the annual progress report including minor changes in the following areas: the purpose of the study, risk analysis, monitoring procedures, labeling, informed consent materials, and IRB information.

**Reports:** Reports to IDEs are submitted for several reasons. Submissions tracked as reports include:

* Unanticipated Adverse Device Effect
* Final Report
* Annual Progress Report
* Interim Progress Report, if requested by FDA
* Biannual Investigator List
* Failure to Obtain Informed Consent
* Compassionate Use Follow-Up
* Emergency Use
* Live Case Follow-Up
* Completion of enrollment
* Completion of study (including all patient follow-up)
* Withdrawal of IRB approval

The timelines for a sponsor or sponsor-investigator sending reports to the FDA, reviewing IRB(s), and/or participating investigators per 21 CFR 812 are summarized in the table below. However, individual IRBs may have more stringent timelines. You must follow your reviewing IRB’s policies as long as they are not in conflict with the FDA regulations. Please refer to the Duke University Health System (DUHS) IRB [policy](https://irb.duhs.duke.edu/sites/irb.duhs.duke.edu/files/PROMPT%20REPORTING%20TO%20THE%20IRB_merged%20policy_8-9-2019.pdf) for reporting unanticipated problems involving risks to subjects or others. Please keep in mind that if you are running a multi-center trial, timelines for reporting to other reviewing IRB’s should be followed as well.

Table : Reporting Timelines to FDA, IRBs, and/or Participating Investigators per §812.150

| **Type of report** | **Timeline** | **FDA** | **IRB(s)** | **Participating**  **Investigators** |
| --- | --- | --- | --- | --- |
| Unanticipated Adverse Device Effects | 10 working days from sponsor becoming aware of the effect | X | X | X |
| Withdrawal of IRB approval | 5 working days from sponsor being notified | X | X | X |
| Withdrawal of FDA approval | 5 working days from sponsor being notified |  | X | X |
| Current Investigators list | Every 6 months | X |  |  |
| Progress report | At least annually | X | X |  |
| Recall and device disposition | 30 working days after the request is made | X | X |  |
| Deviation from the investigational plan[[1]](#footnote-1) | Within 5 working days of the event |  | X |  |
| Failure to Obtain Informed Consent[[2]](#footnote-2) | Within 5 working days of the occurrence |  | X |  |
| Within 5 working days from sponsor being notified of the occurrence | X |  |  |
| Significant risk device determination by a reviewing IRB | Within 5 working days from sponsor being notified | X |  |  |
| Final report | Notification of completion- 30 working days | X | X |  |
| Report- 6 months | X | X | X |
| Other | As requested by FDA or IRB | X | X |  |

**Amendments:** Amendments are any response to FDA’s request for more information regarding a previously submitted supplement or report or original IDE. The FDA tracks any IDE submission sent as a response to deficiencies communicated in an FDA disapproval, approval with conditions, or deficient report letter as an IDE Amendment to that submission. For example, if you receive an “approval with conditions” letter after you submit your original IDE, your response intended to address deficiencies in that letter will be logged in as an Amendment. Amendments may be submitted to supplements and reports, as well as to the Original IDE.

Submissions tracked as Amendments:

* Response to Disapproval
* Response to Approval with Conditions
* Response to Refuse to Accept
* Response to Report Deficient
* Voluntary Withdrawal by Sponsor

# Can I include information that should be reported under different submission types in one submission?

No, this is not recommend. Your IDE submission cover letter should identify the reason for the submission and you may use the submission reasons in the bulleted lists above.

The following examples illustrate the challenges that arise when one submission includes more than one submission reason (for example, a request to modify the study protocol, a deficiency letter response, and an adverse event report are three different submission reasons):

* A submission contains both a response to deficiencies from a disapproval letter and a request for a design change. The FDA finds the deficiency responses acceptable, but finds that the design change raises new safety concerns. Because FDA makes only one decision per submission, the FDA would disapprove the entire submission and the proposed study would remain disapproved. Therefore, separate submissions for responses to deficiencies and unrelated change requests may result in more timely study initiation or progress.
* A submission intended to report the progress of a study also includes a request to change the study protocol. Because changes to the study protocol require FDA approval prior to implementation and would be deemed approved if a decision is not made within the 30-day review period, the FDA will prioritize review of the change request over review of the report. As such, FDA will consider the submission to be a Supplement. In this case, the reporting requirement would not have been met and a separate report would be required. Therefore, separate initial submissions for reports and requests to change the device or study will result in more timely IDE submission review.

While it is not recommend to combine submission types, FDA will work interactively with submitters to address any submissions that mistakenly contain multiple submission reasons, such as those described in the examples above.

# To whom do I address supplements, reports and amendments?

All IDE submissions should be sent to the person identified by the FDA in your initial notification letter.

# Where can I get more information on IDE Submissions?

More information regarding the recent IDE tracking improvements made by CDRH can be found here:

<https://www.fda.gov/medical-devices/investigational-device-exemption-ide/ide-tracking-improvements>

More information on IDE Reports can be found here:

<https://www.fda.gov/medical-devices/investigational-device-exemption-ide/ide-reports>

More information on IDE Supplements for changes or modifications during the conduct of a clinical investigation can be found here:

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-or-modifications-during-conduct-clinical-investigation-final-guidance-industry-and-cdrh>

More information on FDA decisions for IDEs

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-decisions-investigational-device-exemption-clinical-investigations>

If additional information is needed, the CDRH IDE Staff can help answer any questions at 301-796-5640.

For questions specific to devices reviewed by the Center for Biologics Evaluation and Research (CBER), please contact CBER’s Office of Communication, Outreach and Development (OCOD) at 301-827-1800.

1. Deviations from the Investigational Plan Reports are submitted by Investigators and Sponsor-Investigators to the reviewing IRB. These reports are not required to be submitted to the FDA unless the change or deviation may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects in accordance with § 812.35(a).

   2 Failure to Obtain Informed Consent reports are submitted by Investigators and Sponsor-Investigators to the reviewing IRB. Sponsors and Sponsor-Investigators must submit these reports to the FDA. [↑](#footnote-ref-1)
2. [↑](#footnote-ref-2)