

St David's | **OFFICE OF RESEARCH**

**St. David's HealthCare
Institutional Review Board
(SDH IRB)**

Standard Operating Procedures Manual

March 13, 2020

Unless otherwise required by law or regulation to be updated to new regulations, research activity approved under legacy regulations maintain their approvals under those legacy manuals or regulations unless specified by the IRB that they transition those research activities to the newer standards.

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TITLE: Appointment, Training, Evaluation and Removal of IRB Members	SOP 01
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PURPOSE:

The purpose of this policy is to set forth the process for appointment, training, evaluation, and removal of IRB members of St. David’s HealthCare Institutional Review Board (SDH IRB).

PROCEDURE:

Appointment, Evaluation and Removal of Members

1. The chair, members and alternates will be appointed by the highest ranking executive officer or his/her designee.
2. Every nondiscriminatory effort will be made, as appropriate, to ensure that the IRB does not consist entirely of men or entirely of women, including the institution’s consideration of qualified persons of both sexes, so long as no selection is made to the IRB solely on the basis of gender.
3. IRB members will be appointed for term lengths as determined by the needs of the institution. There are no limits to the length of time or number of terms a person can serve in any capacity on the IRB.
4. Appointment letters should be generated for all appointees and should identify any term length if not intended to be indefinite.
5. The Institution may adjust the membership and composition of the IRB to meet regulatory and organizational requirements.
6. Members (including alternates and the chair) may be removed at any time at the discretion of the Institutional Official (or his/her designee) during their appointed term for reasons including but not limited to, failure to perform in their duties or based on the evolving needs of the IRB and/or Institution.

Changes to IRB Membership

1. Upon any change in membership, the following should occur:
 - a. Verification that the new IRB membership continues to meet the requirements set forth by federal regulations and this policy manual.
 - b. Obtain and file a copy of any new member’s curriculum vitae or resume or other summary of qualifications (unless otherwise kept elsewhere such as in Human Resources or Medical Affairs/Credentialing).
 - c. A newly dated roster will be generated and made accessible to all research sites.
 - d. Updates to the IRB membership roster must be registered with OHRP, if required (i.e. change of IRB Chair).

Training of IRB Members

1. Training shall be customized to the needs of the IRB. Those that have obtained Certified IRB Professional (CIP) designation by the *Council for Certification of IRB Professionals* need only produce their current certificate to demonstrate adequate training. For all others, any of the following will suffice:
 - a. Courses from HCA’s IRB Podcast Channel
 - b. Any IRB courses put forth by [Public Responsibility in Medicine and Research \(PRIM&R\)](#)
 - c. [National Institute of Health \(NIH’s\) Computer–Based Training for NIH IRB Members](#)
 - d. [NIH’s Protecting Human Research Participants](#)
 - e. [Collaborative Institutional Training Initiative \(CITI\)](#)
 - f. Other additional or substitute training in human subject protection deemed acceptable to the IRB Chair.
2. The institution may offer training during meetings either on a routine basis or on a “just in time” basis (for example, offering training on the difference between a Significant Risk Device and a Non-Significant Risk Device immediately prior to reviewing a device study, offering training on criteria for de-identification under HIPAA standards immediately prior to reviewing a data study etc.).
3. The institution shall document any training of IRB members in either member folders (i.e. if individually trained), or in meeting minutes (i.e. if training was performed/received or validated during the meeting).

REFERENCES:

N/A

TITLE: IRB Membership Requirements	SOP 02
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PURPOSE:

The purpose of this policy is to set forth the IRB membership requirements of St. David's HealthCare Institutional Review Board (SDH IRB).

PROCEDURES:

1. The IRB shall have at least five members, with varying backgrounds, to promote complete and adequate review of research activities commonly conducted by the Institution.
 - a. The IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), the diversity of its members (including consideration of race, gender, and cultural backgrounds) and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
 - b. The IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources), regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas.
 - c. If the IRB regularly reviews research that involves subjects that are categorically more vulnerable (e.g. children, prisoners, pregnant women, handicapped individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons), consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.
2. The IRB may not consist entirely of members of one profession.
3. The IRB shall include at least one member whose primary concerns are in a scientific area and at least one member whose primary concerns are in nonscientific areas.
4. The IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.
5. The IRB may not have a member participate in the review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.
6. An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

REFERENCES:

N/A

TITLE: Scope, Authority and Statement of Ethical Principles of the IRB	SOP 03
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PURPOSE:

The purpose of this policy is to set forth the scope, authority, and ethical principles of St. David’s HealthCare Institutional Review Board (SDH IRB).

PROCEDURES:

1. SDH IRB (“the IRB”, hereafter) has the authority to approve, require modifications in (to secure approval), or disapprove all research activities assigned to its oversight by the Institution. The jurisdiction of SDH IRB shall include the following:
 - a. All research involving St. David’s Healthcare hospitals or stand-alone medical centers.
 - b. All research involving or conducted by St. David’s Healthcare employees.
 - c. All research involving or conducted by providers (MDs, DOs, RNs, NPs, APNs, etc.) who are members of St. David’s Healthcare medical staff.
 - d. All research involving or conducted by Las Palmas Medical Center and Del Sol Medical Center in El Paso, Texas
 - e. All research involving or conducted by employees of or providers for Las Palmas Medical Center and Del Sol Medical Center in El Paso, Texas
2. The IRB may enter into a joint review arrangement with another qualified IRB, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.
3. Research granted approval by the IRB is subject to further appropriate review and approval or disapproval (e.g. a facility “Research Council”). However, the institutional officials may not approve the commencement of non-exempt activities of human subjects research until it has been approved by its assigned IRB.
4. The IRB may work in conjunction with other research review entities that must also offer a favorable opinion of the research such as (a) Data Safety Monitoring Boards (DSMBs); (b) Radioactive Drug Research Committees (RDRCs); (c) Institutional Biosafety Committees (IBCs) and (d) NIH’s Recombinant DNA Advisory Council (RAC). The IRB may not override the opinion of these committees just as these committees cannot override the opinion of the IRB (knowing that non-exempt activities of research with human subjects cannot commence until the IRB offers its favorable opinion). In an effort to avoid time delays and/or optimize the sequencing of approvals, an IRB may approve research contingent on the approval of one or more of these review entities when such review is required by regulation.
5. The IRB has the authority under federal law to observe or designate a third party to observe the consent process and the research. This can be done via record review, personal observation and/or other means.

6. The IRB will charge fair market value rates for IRB review. The amount and collection of charges must be independent of any decisions the IRB makes. Any charges to physicians/physician-owned-entities/referral sources that fall under legal compliance policies require approval by the Institution's Operations Counsel.
7. The IRB adopts the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research's 1979 report entitled "Ethical Principles and Guidelines for the Protection of Human Subjects of Research" (a.k.a. "The Belmont Report") as its document of guiding principles in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution.
8. The IRB operates under United States federal laws and regulations of the Food and Drug Administration (FDA) and the Department of Health and Human Services' Office for Human Research Protections (OHRP).
9. The IRB operates under the compliance policies put forth by the Hospital Corporation of America (HCA HealthCare).
10. The informed consent requirements in these policies are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.
11. Nothing in this policy manual is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local laws.

REFERENCES:

N/A

TITLE: Needs Validation and Exemption Determinations	SOP 04
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PURPOSE:

The purpose of this policy is to set forth the review process used by the St. David’s HealthCare Institutional Review Board (SDH IRB) in processing exemption determinations.

PROCEDURES:

1. The IRB Chair, as the designee of the Institutional Official, will be responsible for determining whether research is exempt from IRB oversight or does not need certification of IRB oversight. The Institutional Official or his/her designee (e.g. IRB Chair) may rely on materials submitted by the investigator and/or other valid opinions that research does not need IRB oversight or certification of IRB oversight. Principal Investigators or other SDH staff are not permitted to make this determination on their own.
2. The IRB will consider the factors below to determine if a proposed research activity requires IRB oversight:
 - a. IRB review and oversight is required if the activity meets all of the following criteria:
 - i. The activity commenced after July 27, 1981 and FDA has not otherwise specifically waived IRB review
 - ii. The activity is considered a “clinical investigation” as defined by federal law
 - iii. The activity is considered “research” as defined by federal regulations
 - iv. The activity involves “human subjects” as defined by federal regulations
 - v. The activity does not meet any of the statutorily Exempt categories put forth by FDA or OHRP law (21 CFR 56.104 or 45 CFR 46.104).

Even when the above criteria are not met and IRB oversight is not necessary, other laws may still apply (i.e. HIPAA, state laws, etc.).

- b. IRB review and oversight is also required for the following:
 - i. In some cases otherwise required by law or regulation, such as when Expanded Access products or Humanitarian Use Devices are being used. In these cases, federal regulations specific to these scenarios must be followed. Refer to the appropriate SOP for additional information.
 - ii. In cases of Emergency Use (non-research). When this occurs, the use of a test article may be excused from prospective IRB review in certain situations, but a follow-up report is required after the emergency administration of the investigational product. Refer to the Emergency Use (Non-Research) SOP for additional information.

3. Furthermore, if IRB oversight is required, the facility must determine if it is “engaged in the research”, as defined by guidance put forth by OHRP to see if it needs to certify IRB review.
 - a. If the facility is NOT “engaged in research”, then the facility may (at its option) certify review, but it is not required.
 - b. If it is “engaged in research”, then the facility must certify IRB review by either the Institutional Official or his/her designee (e.g. IRB Chair) determining that the IRB review it themselves (via convened board or via Expedited Review for those activities meeting that criteria) or by deferring oversight to another IRB (by following the procedures of the external IRB). If SDH IRB waives IRB jurisdiction of a study, this will be documented in a written communication to the investigator.

Note: Certain studies may require the use of a single IRB for multicenter studies whether by regulation (as in most federally funded studies) or as a condition of site selection (as in many industry funded studies).

REFERENCES:

21 CFR 56.104
45 CFR 46.104

TITLE: Initial and Continuing Review SOP	SOP 05
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PURPOSE:

The purpose of this policy is to set forth the submission requirements, approval criteria, and continuing review process of St. David’s HealthCare Institutional Review Board (SDH IRB) in compliance with state and federal regulations.

POLICY:

The IRB must review all its assigned non-exempt research involving human subjects as defined in the HCA IRB Related Definitions and Common Acronyms Policy, CSG.IRB.001. The IRB must assess whether its members have the knowledge, skill and experience to adequately review and approve the submitted research (and secure adequate consultation if they do not) or refer the protocol to a properly experienced IRB.

IRB Review of Research

The IRB (through either a convened board or Expedited Review process) shall review non-exempt research with human subjects under the criteria set forth by federal, state and local regulations as well as the IRB Criteria to Approve or Exempt Human Subject Research Policy, CSG.IRB.006.

1. Initial Review

The IRB must conduct initial review of all non-exempt research with human subjects at convened meetings at which a majority of the members are present, unless the research falls into one or more of the categories appropriate for expedited review. Note: the initial review of the treatment (*i.e.*, non-research) use of Humanitarian Use Devices (HUDs) as well as the treatment use of drugs/devices/biologics under an FDA Expanded Access Program (a.k.a. “Compassionate Use”) must, by federal law, be reviewed initially at a convened board meeting. All subsequent reviews of the treatment use of HUDs according to their labelling may be reviewed via Expedited Review, at the discretion of the IRB Chair.

2. Continuing Review

For studies reviewed by the convened board, unless otherwise meeting the criteria eligible for expedited review or meeting the criteria that continuing review is no longer necessary, the IRB shall conduct substantive and meaningful continuing review of non-exempt research with human subjects at intervals appropriate to the degree of risk, but no less than once per year. In these cases, each approval period for research may extend no more than one calendar year after the conditions of IRB review have been met.

Methods of Review

1. Convened Meeting

Initial and continuing review submissions requiring full board review must be conducted by the IRB at convened meetings at which a majority (defined as >50%) of the voting IRB members listed on the most current roster are present, including at least one member whose primary concerns are in non-scientific areas (*i.e.*, a quorum). Alternate IRB members may vote in the absence of a voting member or when reviewing projects for which they have specific expertise that would be beneficial for a particular review. Although alternate IRB members may replace a regular voting IRB member, the same board diversity and quorum rules explained above must be met in order to grant approval (e.g. at least one non-scientific member must be present and voting).

Approval of research is by a majority vote (>50%) of this quorum.¹ Should the quorum fail during a meeting (e.g., loss of a majority through recusal of members with conflicting interests or early departures, or absence of a non-scientific member), the IRB may not take further actions or votes unless the quorum can be restored. In order for research to be approved, it shall receive the approval (i.e. a “For” vote) of a majority (>50%) of those members present at the meeting.²

Loss Of or Failure To Obtain a Quorum: If at any point of the meeting a quorum is not met or lost (e.g. if a quorum is lost due to an IRB member leaving the room) then no further actions can be taken by the IRB unless a quorum can be reestablished (e.g. alternates from the roster are present and converted to a voting capacity for their missing members).³

- i) Initial Reviews (unless eligible for Expedited Review or IRB Exemption) will be placed on the agenda for the next IRB meeting or deferred to external IRBs.
- ii) Continuing Reviews (unless eligible for Expedited Review) shall be placed on the agenda for the next meeting. In the event the next meeting is not expected to be conducted until after the expiration date of a particular study, the Investigator must be notified of the expiration date and that no research activities can take place until the IRB approves the continuance through continuing review (i.e. the failure of an IRB to timely conduct a continuing review, even if due to the fault of the IRB for reasons such as inability to obtain or maintain a quorum, does not allow for any extensions or grace periods). (Please see the Closure, Expirations & Reinstatement SOP)

¹ Any live bi-directional means of communication (i.e. teleconference or videoconference) is acceptable for participation. Non-live or non-bidirectional communication (i.e. individual phone solicitations, emails, proxy voting etc.) is not allowed.

² Note that when alternate members are present, they are not counted towards the quorum unless they are substituting in for a voting member.

³ For counting votes, note the following example: An IRB with 9 voting members present needs 5 “For” votes to approve the protocol. A vote of 5 For, 3 Against and 1 Abstaining would pass where a vote of 4 For, 4 Against and 1 Abstaining would not. Also with 8 voting present, a vote of 4 For, 3 Against and 2 Abstaining would not pass as 8 voting members present requires 5 “For” votes to pass.

- iii) Interim reviews such as requests for changes, notification of deviations or UPIRSOs (unless eligible for Expedited Review) will be placed on the agenda for the next IRB meeting. This includes changes to previously approved research that does not constitute a minor change (e.g. (i) adding procedures categorized as allowable under Expedited Review but are determined to not be minimal risk or (ii) adding other procedures involving increased risk or discomfort), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented, an exception being a change necessary to eliminate apparent immediate hazards to the research subjects. The IRB must be informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

Voting Actions: the IRB may approve, conditionally approve, defer to a future meeting, or disapprove any component of the research plan.

2. Expedited Review

In lieu of a convened board meeting, the "Expedited Review" process allowed under federal regulations should be utilized for those certain circumstances permitted under federal regulations.

The IRB Chair or another Expedited Reviewer (who must be an IRB voting member) who is without a conflict of interest may review research through an expedited procedure if:

- a. Initial or Continuing Review- The research is not greater than minimal risk (as defined in "Definitions", CSG.IRB.001) and falls within the current categories of the published Department of Health and Human Services (DHHS) and Food and Drug Administration (FDA)'s list of research activities eligible for expedited review, as published in the *Federal Register*.
- b. Minor Changes to the Research- The research constitutes a minor change in previously approved research during the period for which approval is authorized. "Minor changes" are defined as not affecting the relationship of likely subject risk to benefit relied upon to approve the protocol; or the rights, safety, or welfare of the human subjects involved in the investigation.
- c. Continuing Review of the use of a Humanitarian Use Device (HUD) under an HDE (Humanitarian Device Exemption) may be reviewed and approved via Expedited Review during continuing review upon the discretion of the IRB Chair. However, the initial review of HUD use must undergo Full Board review in order to obtain approval (See Humanitarian Use Device (HUD) and Expanded Access SOPs).
- d. Research reviewed in accordance with the Limited IRB Review option as required for IRB Exempt Status; or

Approvals under the Expedited Review procedure must be communicated to the IRB members. Any documentable method of such communication is acceptable, but this is usually accomplished by having a standing agenda item for the meeting (and documentation of the list in the minutes) for all Expedited Reviews that occurred between meetings. Approvals under

Expedited Review shall also be communicated to the investigator just as communications on decisions by convened board reviews are.

The reviewer may exercise all the authorities of the IRB except that they may not disapprove the request on behalf of the IRB. If they are unable or unwilling to approve (or conditionally approve) the request, it must be forwarded to the convened board for consideration with one of the following justifications:

- a) not meet any of the Expedited Review categories; OR
- b) the request met one or more of the Expedited Review category(ies) BUT the reviewer determined the request put forth more than minimal risk (and the reviewer must document to the IRB how it was more than minimal risk).⁴

Upon completion of Expedited Review, the decision of the Expedited Reviewer shall be communicated to the investigator in writing.

3. Facilitated Review

SDH IRB does not currently use facilitated review. All initial reviews of protocols shall be reviewed by the Full Board unless otherwise eligible for Expedited Review.

PROCEDURE:

Initial Review

In conducting the initial review of proposed research, the Board (for full board review) or Expedited Reviewer (for Expedited Review) should receive, have available to them, and/or discuss at least the following documents:

- the full protocol;
- a proposed informed consent form or request for waiver or alteration of required elements of consent (or waiver of documentation of consent);
- HIPAA Authorization to Use/Disclose Protected Health Information (or request for its waiver) if using/disclosing identifiable Protected Health Information (PHI);
- the investigator's brochure or product labeling, as applicable;
- subject surveys/questionnaires, as applicable;
- any recruitment materials including advertising intended to be seen or heard by subjects, as applicable (Note: According to the FDA, IRB review and approval of listings of clinical trials on the internet is not required when the system format limits the information provided to basic trial information, such as the title, purpose of the study, protocol summary, basic eligibility criteria, study site location(s), and how to contact the site for further information); and
- any other material submitted to the IRB and/or determined to be necessary for the protection of human subjects.

⁴ Essentially the regulation infrastructure encourages the approval by Expedited Review whenever the research activity meets the required categories statutorily deemed as minimal risk and thus if an Expedited Reviewer chooses not to do such approval, they must justify why the deemed activity within the category is not minimal risk.

For submissions reviewed at a convened board meeting, a Primary Reviewer system will be used. All IRB members will receive a copy of the complete documentation. These materials will be received by members sufficiently in advance of the meeting to allow review of this material. The Primary Reviewer(s) will do an in-depth review of all pertinent documentation listed above. All other IRB members may review an abbreviated set of documents which should include a protocol summary (of sufficient detail to make the determinations required under federal regulations and IRB policy), the proposed informed consent document (if applicable), and any recruitment materials, including advertisements intended to be seen or heard by potential subjects. In addition, the complete documentation should be available to all members for review at their request prior to or during the meeting.

For submissions reviewed via Expedited Review, the Expedited Reviewer will receive a copy of the complete documentation listed above and will conduct an in-depth review to ensure compliance with federal regulations and IRB policy.

Approval Criteria

For research subject to OHRP or FDA regulations, determinations for approval must meet the following criteria to comply with federal regulations (45 CFR 46.111, 21 CFR 56.111). For research not governed by FDA or OHRP regulations, these same criteria should be considered as a guideline:

- An analysis of the potential sources of risk (*i.e.*, physical, psychological and social/economic), with special mention of additional risk posed to vulnerable populations. Note, the IRB shall not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility;
- A favorable opinion that the risks to subjects are minimized (*i.e.*, including the use of procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes);
- A favorable opinion that the risks to subjects are reasonable in relation to anticipated benefits to subjects and/or the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research, as distinguished from risks and benefits of therapies subjects would receive in the absence of the research. The IRB shall not consider payment to research subjects as a benefit for purposes of this evaluation;
- Selection of subjects is equitable. In making this assessment the IRB shall take into account the purposes of the research and the setting in which the research will be conducted, and shall be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. See the HCA Policy IRB Required Additional Protections For Vulnerable Subjects/Children Policy, CSG.IRB.009 and also SDH IRB Vulnerable Populations SOP. The inclusion/exclusion criteria for the study should impose fair and equitable burdens and benefits. Recruitment efforts should be unbiased towards any population or sub-population;

- Unless meeting such criteria for waiver or partial waiver, informed consent will be sought from each subject or the subject’s legally authorized representative, in accordance with, and to the extent required by statute. See the HCA Policy IRB Review of Research Informed Consent and Its Documentation Policy (CSG.IRB.008) and SDH IRB Informed Consent SOP;
- Unless meeting such criteria for waiver, informed consent will be appropriately documented in accordance with, and to the extent required by, statute. See HCA Policy CSG.IRB.008;
- When appropriate, the research plan makes adequate provision to protect the privacy of subjects and to maintain the confidentiality of data;
- When appropriate, there are adequate provisions for monitoring the data collected to ensure the safety of the subjects; and
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards shall be included in the study to protect the rights and welfare of these subjects (See Vulnerable Populations SOP).

OHRP regulations provide a process of “Limited IRB Review” that eliminates all but one of these criteria to make certain Exempt determinations.⁵

Other regulated criteria for special requests are to be considered. These include but are not limited to the following:

- Waiver or alteration of required elements of consent
- Waiver of documentation of consent
- Required elements of a HIPAA Authorization
- Waiver of HIPAA Authorization to Use/Disclose Protected Health Information
- Significant Risk/Non-Significant Risk Device Determinations
- De-identified data set
- Limited data set
- Any other decision in which regulations have specific criteria

Documentation of the above should be included in the meeting minutes.

Conditional Approvals

For minor clarifications or modifications, the IRB or Expedited Reviewer may provide Conditional Approval to the investigator accompanied by specific instructions provided:

- To the extent practical, the investigator is informed of the specific and unambiguous changes required for the research to be approved. For example: “Make the consent form meet all federal requirements” may not be specific enough to be a minor clarification, whereas instructing the investigator to “Add ‘a minor skin rash that lasts 3-7 days has been noted in approximately 10% of subjects’ in the risk section and change ‘if you withdraw from the study, it will not affect your care at this institution’ to ‘if you withdraw from the

⁵ While Limited IRB Review is also allowed for the OHRP concept of “broad consent”, HCA facilities do not engage in the activity of “broad consent” and offers its protections of information and biospecimens through the usual process.

study before it is over, you do not lose any rights or benefits to which you are otherwise entitled,” is more specific and unambiguous.

- The investigator is informed that he/she cannot begin this research (or requested change in research) until the conditioned changes have been made and verified in accordance with IRB instructions; and
- That the IRB (as a committee or through their designee) must validate that the conditioned changes were made prior to the investigator conducting the research (or implementing the requested change in research).

Generally, only when the IRB stipulates specific revisions requiring simple concurrence by the investigator should IRB support staff or a non-voting member validate the change. Otherwise, the IRB Chair or another voting IRB member designated by the Chair should be the one to subsequently validate the change was enacted on behalf of the IRB.

If the changes have been submitted after 30 days from initial IRB review, the IRB will re-review the submission to consider any new information that might alter their previous approval.

If and when the IRB requests substantive clarifications or modifications regarding the research, the approval of the proposed research shall be deferred to the next convened meeting upon receipt of all responsive material.

Continuing Review

In conducting continuing review of research, all IRB members (during full board review) or the expedited reviewer (during expedited review) should receive, have available to them, and/or discuss at least the following:

- A copy of the full protocol or protocol summary;
- A status report on the progress of the research that includes:
 - The number of subjects accrued locally (and, for multicenter studies, the number accrued across all sites if available);
 - A summary of any adverse events or unanticipated problems involving risks to subjects or others;
 - Any withdrawal of subjects from the research and reasons for withdrawal;
 - A summary of any complaints about the research from subjects or others since the last IRB review;
 - A summary of any relevant literature, findings obtained thus far;
 - Amendments or modifications to the research since the last review;
 - Any relevant multi-center trial reports;
 - Any other relevant information, especially information about risks associated with the research (e.g. DSMB reports);
 - A current copy of the informed consent document being used, if applicable; and
 - A copy of the site’s most recent monitoring report from the sponsor, if applicable

The Primary Reviewer or Expedited Reviewer will also receive a copy of the complete protocol, if applicable, including any modifications previously approved by the IRB. Furthermore, upon

request, any IRB member shall have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting.

The IRB will provide ongoing oversight of approved research to monitor the welfare of the participants and to determine that the risks and potential benefits remain unchanged. Ongoing oversight shall include reviewing and responding, when necessary, to unanticipated problems, changes to previously approved research, protocol deviations/violations, significant new findings, complaints, noncompliance, or site visit results. Based on findings from ongoing oversight, the IRB may approve, disapprove, or require modifications to approved research protocols, and may also suspend or terminate some or all aspects of its approval of ongoing (previously approved) research (For these cases, see Suspension or Termination of IRB Approval SOP).

When expedited review is being utilized for the continuing review, the Expedited Reviewer may approve the project or request modifications. However, they may not disapprove the research. If the Expedited Reviewer feels that disapproval is required, the submission will then be forwarded on to the full board for consideration.

Consideration for Approval (for both Initial and Continuing Review)

Upon the initial or continuing review of each study, the IRB will review the submission documents to assess the risk/benefit ratio and will set a renewal period proportionate to the risks of the research. For studies reviewed by the convened board, unless otherwise meeting the criteria eligible for Expedited Review or meeting the criteria that continuing review is no longer necessary, the IRB shall conduct continuing review at a full board meeting and may not to exceed one year after the approval/re-approval date. The IRB can re-review the research at any time, particularly in the presence of new information pertaining to the risk/benefit ratio. At the time continuing review is due, the IRB has the scheduled periodic opportunity to continue approval for a set time period not to exceed one calendar year, to request consent or study modifications or other actions to notify subjects of new findings, or to suspend or terminate some or all aspects the approval of the research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. The IRB may also use its discretion to limit the approval period to a shorter timeframe for any reason, including due to consideration of the risk/benefit ratio for the project, previous non-compliance issues, or due to the experience level of the investigator. Until the research activity reaches a point where continuing review is no longer needed (see criteria below), the IRB shall determine the length of the approval period for each study at an interval appropriate to the degree of risk, but not to exceed one year from the previous review. If the Board agrees that the study meets the criteria that continuing review is no longer necessary, this will be communicated in writing to the Principal Investigator.

During the assessment of the risk/benefit ratio, the Board will review the study submission documents provided at initial or continuing review to ensure that the current consent document, if applicable, is still accurate and complete. The Board may consider documents such as investigator's brochures/device information, safety reports, sponsor or regulatory body reports, or other information in order to make this assessment. The Board may update the consent form or request that the investigator submit an update to the consent form at its discretion in order to ensure that the information presented is accurate and complete.

Generally, unless given reason otherwise, the IRB can accept information from the investigator as accurate. The IRB may decide to seek or ask for additional verification from sources other than the investigator that no material changes have occurred since the previous IRB review. Common reasons the IRB may desire to seek such verification may include:

- (a) projects conducted by investigators who previously have failed to comply with regulations or requirements/determinations of the IRB,
- (b) projects where information provided in continuing review reports or from other sources indicate possible material changes occurring without IRB approval have occurred,
- (c) a novice or seemingly disengaged investigator or clinical research coordinator, or
- (d) excessive turnover or long gap in replacement of the PI or clinical research coordinator.

The re-approval deadlines run from the date when all conditions for approval have been met (*i.e.*, when the protocol was approved by the convened board or Expedited Reviewer and not when the investigator receives notification). If the IRB granted Conditional Approval, the time runs from the date the IRB verified that the conditions of approval were met, not the date of the meeting. When subject to a Conditional Approval, the investigator should be given a reasonable amount of time to make the necessary changes before they must resubmit as a new application (e.g. 30 days for minor changes, 90 days for major changes involving external collaborators but extended time may be appropriate as determined by the IRB).

For protocols that were deferred and later approved at a subsequent meeting, time runs from the date that approval was actually given and not the first meeting the protocol was presented and deferred.

In addition, the IRB's Institutional Official has the authority to disapprove any research project at his/her discretion at any given time. However, the Institutional Official may not make a decision to approve any research project. Approval can only be granted by the IRB, or by a member of the IRB when a project is eligible for Expedited Review.

Process for Reviewing Changes to Ongoing Research During the Approval Period

The IRB may use Expedited Review procedures to review minor changes (including but not limited to those activities listed approval under Expedited Review) in ongoing previously-approved research during the period for which approval is authorized. An Expedited Review may be carried out by the IRB Chair or one or more experienced reviewers designated by the Chair from among the voting IRB members (not by a member with a Conflict of Interest). "Minor changes" are defined as not affecting the relationship of likely subject risk to benefit relied upon to approve the protocol; or the rights, safety, or welfare of the human subjects involved in the investigation. Adding procedures categorized as activities allowable under Expedited Review are deemed as minor changes unless determined otherwise by the Expedited Reviewer

When a proposed change in a research study is not a minor change (e.g., (i) adding procedures categorized as allowable under Expedited Review but are determined to not be minimal risk or (ii) adding other procedures involving increased risk or discomfort), then the IRB shall review and approve the proposed change at a convened meeting before the change can be implemented, an exception being a change necessary to eliminate apparent immediate hazards to the research

subjects. In these cases, the IRB must be immediately informed of the change following its implementation and will review the change to determine that it is consistent with ensuring the subjects' continued welfare.

All document revisions should be incorporated into the current, IRB-approved version and the revision date/version must be prominently placed to appropriately allow for version control. This is to ensure that the most current set of documents is being utilized.

Documentation of Research Review

Review activities of the IRB will be documented in detail. Such documents (*e.g.*, meeting minutes) will have sufficient detail to demonstrate thorough protocol review, analysis, discussions, actions with rationales and the ultimate determinations by the IRB.

The IRB will notify the investigators and the institution in writing of its decision to approve, disapprove, conditionally approve, or table the research activity, or of modifications required to secure IRB approval of the research activity. Please refer to the "Investigator Communications" SOP for additional information. If the IRB decides to disapprove or table a research activity, it shall include in the written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing (Refer to SDH IRB Investigator Communications SOP).

If a research protocol that involves an exception to the informed consent process is submitted for initial IRB review and the IRB determines that the protocol does not meet the criteria contained within the regulations or because of other relevant ethical concerns, then the IRB shall promptly notify the investigator in writing. The written notification shall include a statement of the reasons for the IRB's determination.

Interaction with Other Research Related or Institutional Committees

- **St. David's Division Research Operations Council "Research Council"**
All research conducted at St. David's facilities, Del Sol Medical Center, or Las Palmas Medical Center must also obtain approval from the St. David's Division Research Council prior to beginning a research study.
- **Data Safety Monitoring Boards**
The IRB will recommend, as appropriate, that Sponsor-Investigators with a high volume of self-sponsored research projects establish an independent data monitoring committee for such self-sponsored protocols to exercise oversight of the clinical investigation and the informed consent process. The Sponsor-Investigator will submit information (*e.g.* periodic reports) from these committees to the IRB in order to perform continuing review.
- **Radioactive Drug Research Committee (RDRC)**
An accredited RDRC with membership and operational requirements as dictated in 21 CFR 361.1 will be responsible for the review of basic science research protocols using radioactive drugs in humans. Among other things, the IRB will rely on the RDRC to

evaluate the radiation dose and qualifications of the administrator of the radiopharmaceutical, proper licensure of the facility, and appropriate quality of the radiopharmaceutical. The IRB will work in conjunction with the RDRC and approval by BOTH boards is required for study commencement. Additionally, the IRB and RDRC must coordinate the review of adverse events (AEs) that may be caused by radiation to assure all AEs are reviewed and both boards may benefit from the other's knowledge, experience and role.

- Institutional Biosafety Committees (IBC) and Recombinant DNA Advisory Council (RAC)

For certain kinds of genetic research, BOTH IBC and IRB approval must be obtained to conduct the research. The IRB will rely on an accredited IBC to assure that Biosafety Levels are appropriate and maintained throughout the study (such as security, insect/rodent protection plan in physical locations where vectors are prepared), and the IRB will additionally ensure that NIH's RAC has reviewed and approved the protocol. Usually, IBC approval and IRB approval are applied for simultaneously to prevent delays in the research from starting; however, the IRB cannot approve research until it has received final approval from the IBC.

REFERENCES:

1. IRB Related Definition and Common Acronyms Policy, [CSG.IRB.001](#)
2. Clinical Services Group Research Policies in the CSG.IRB series (CSG.IRB.001 through CSG.IRB.011)
3. 21CFR56.108(a)(2); 45CFR46.108(a)(3)(ii)
4. 45 CFR 46.111 Criteria for approval
5. HCA's IRB Required Additional Protections For Vulnerable Subjects/Children Policy, CSG.IRB.009
6. HCA's IRB Review of Research Informed Consent and Its Documentation Policy (CSG.IRB.008)
7. 45 CFR 46.116
8. 45 CFR 46.117
9. 21 CFR 361.1

NOTES:

1. Much of this text comes from *HCA Policy CSG.IRB.007* and should be updated accordingly.

TITLE: Informed Consent	SOP 06
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POLICY

Informed Consent Requirements

1. **Structure Requirements of Informed Consent:** Unless specified otherwise, these structure requirements for Informed Consent apply whether the Informed Consent is written or oral. Note: While an IRB may alter or waive an element of Informed Consent based on such criteria, they may not alter or waive any of these structure requirements.
 - a) Unless otherwise waived in accordance with the criteria for such, an Informed Consent must contain all Required Elements of Consent as well as all Additional Elements of Consent when those Additional Elements apply.
 - b) An investigator shall seek Informed Consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and minimize the possibility of coercion or undue influence.
 - c) The information that will be given to the subject or the legally authorized representative shall be in language understandable to the subject or the legally authorized representative.
 - d) No Informed Consent may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
 - e) For Federally-Funded studies, pursuant to regulations at 45CFR46.116(a) the following structure requirements are in addition to the above:
 - i) The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
 - ii) Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the Informed Consent must be organized and presented in a way that facilitates comprehension.
 - iii) Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

2. **Basic Elements of Informed Consent:** Unless otherwise waived via the approved criteria, in seeking Informed Consent the following information shall be provided to each subject or the legally authorized representative:

- a) **Notification of Research:** The intent is to inform the patient that he or she is participating in research. Informed consent information must include all of the following:
- i) A statement that the study involves research;
 - ii) An explanation of the purposes of the research;
 - iii) An explanation of the expected duration of the subject's participation;
 - iv) A description of the procedures to be followed;
 - v) Identification of any procedures that are experimental; and
 - vi) For all applicable clinical investigations governed by the FDA initiated on or after March 7, 2012, this exact statement (no deviations or rewording allowed except for non-English translations) is now required by FDA regulation: *"A description of this clinical trial will be available on <http://www.clinicaltrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."*
[Note: this required element cannot be altered or waived by the IRB]
- b) **Reasonably Foreseeable Risks or Discomforts:** Informed consent elements must describe any reasonably foreseeable risks or discomforts associated with research. Risks or discomforts that an individual would have experienced absent the research are not risks associated with the research (i.e. risks from conventional care).
- c) **Reasonably Expected Benefits to Subjects or Others:** Informed consent information must describe any benefits to subjects or to others who may reasonably be expected to benefit from the research. However, care must be taken not to overstate the benefits and create an undue influence on subjects. Payment to a subject for his or her participation in a research project is not to be considered as a benefit of the research. When there is no intended benefit to the subject, the subject must be made aware of this.
- d) **Appropriate Alternatives:** Informed consent information must include a disclosure of any appropriate alternatives to participation in the research, such as procedures or courses of treatment, if any, that may be available to the subject.
- e) **Protection of Confidentiality:** Informed consent information must describe the extent, if any, to which confidentiality of records identifying the subject will be maintained and, for studies on FDA regulated products, specifically that the FDA may inspect records⁶. Consent information should describe any procedures that the research team will use to protect a subject's private records.
- f) **Compensation or Treatment for Injury:** Informed consent information for research involving more than minimal risk must include explanations regarding:
- i) Whether any compensation is provided if a research-related injury occurs and, if so, what it consists of or where more information about it is available; and
 - ii) An explanation as to whether any medical treatments are available if a research-related injury occurs and, if so, what they consist of or where more information about them is available.

⁶ Recommended consent language for FDA regulated research: "Because this research involves articles regulated by the Food and Drug Administration (FDA), the FDA may choose to inspect and copy medical or research records that may identify individual subjects."

- g) **Contact Information:** Informed consent information must include whom to contact for all three of the specific situations below (NOTE: The same contact person/role should not serve for all 3 situations):
 - i) For answers to questions about research: The principal investigator and other members of the research team are appropriate contacts for this information.
 - ii) For answers to questions about the subject's rights: The IRB or another office that advocates for patient rights (i.e. Ethics and Compliance) are appropriate contacts for this information.
 - iii) In the event a research-related injury occurs: Depending on the nature of the research, the research team, or the study sponsor may serve as appropriate contacts for this information.
- h) **Voluntary Participation Statement:** It is particularly important for subjects and prospective subjects to understand and have complete confidence that their participation is voluntary and without coercion or undue influence. Informed consent provisions must contain clear statements of the following:
 - i) Participation in the research is voluntary;
 - ii) Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled; and
 - iii) The subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.⁷
- i) *[Required only of all federally funded studies but optional for all others]* **One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:**
 - i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional Informed Consent from the subject or the legally authorized representative, if this might be a possibility; OR
 - ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

3. **Additional Elements of Informed Consent. Unless otherwise waived via the approved criteria,** the following elements shall also be provided to each subject or their legally authorized representative as appropriate to the research.

- a) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may be pregnant) which are currently unforeseeable.
- b) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

⁷ Use of that exact phrase "no penalty or loss of benefits to which [you] are otherwise entitled" is preferred as opposed to "not affect your treatment at this facility" or other phrase that may be interpreted to imply other limitations.

- c) Any additional costs to the subject that may result from participation by the subject.
 - d) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
 - e) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue to participate will be provided to the subject.
 - f) The approximate number of subjects expected to participate in the study overall and at the local site.
 - g) *[Required applicability to all federally funded studies and optional for all others]* A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
 - h) *[Required applicability to all federally funded studies and optional for all others]* A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
 - i) *[Required applicability to all federally funded studies and optional for all others]* For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).
4. For studies involving remuneration to subjects, BOTH the amount and schedule of remuneration should be included.
5. The IRB may require additional information be given to subjects when, in its judgment the information would meaningfully add to the protection of the rights and welfare of subjects as well as an informed decision (i.e. as part of a Financial Conflict of Interest mitigation plan).

6. Waiver or Alteration of Required Elements of Consent

Note: This includes the waiver or alteration of the assent of a child when the IRB has determined that children are capable of assent but wish to have such requirement waived.

- a) The IRB should note that Waiver or Alteration of Required *Elements* of Consent differs from a Waiver of *Documentation* of Consent and a Waiver of HIPAA Authorization to Use/Disclose Protected Health Information
 - i) This should be recognized to assure the IRB is applying the correct criteria.
 - ii) Waiver or Alteration of Required Elements of Consent **does not automatically imply** a Waiver of Documentation of Consent **nor does it imply** a Waiver of HIPAA Authorization to Use/Disclose Protected Health Information. **Each of these three waivers must be evaluated separately based on their respective criteria.**
 - iii) The IRB notes that, if all elements of consent are waived, then there would be no elements of consent to document however if one or more elements remain, the investigator must obtain documentation of the remaining consent unless the IRB also waives documentation of consent according to that policy/criteria.
- b) Unless otherwise specified, one, many or all Basic Elements or required Additional Elements of Consent may be waived or altered only in accordance with the criteria set forth in federal regulations as described below (also see "Waiver of Documentation of Consent" section of this SOP below and the HIPAA Elements and Waivers SOP). Note that while

an IRB may alter or waive an element of Informed Consent based on such criteria, they may not alter or waive any of the structure requirements as stated previously in this policy:

- i) No more than minimal risk to the subjects;
 - ii) Waiver or alteration will not adversely affect the rights and welfare of the subjects;
 - iii) The research could not be practicably be carried out without the waiver or alteration;
 - iv) The research involves using identifiable private information or identifiable biospecimens, biospecimens in an identifiable format [Note: this is also included in the criteria for a Waiver of HIPAA Authorization so can serve both purposes; AND
 - v) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- c) Such findings must be documented (preferably in the meeting minutes or in other IRB documents, such as Expedited Reviewer’s approval).
- d) Unless all elements of consent are waived, the remaining elements of consent still need to be documented as well as written authorization to release any protected health information for research purposes.

7. **Exception to Informed Consent for Screening, Recruiting, or Determining Eligibility.** An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject’s legally authorized representative, if either of the following conditions are met:

- a) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
- b) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

8. **Exception From Informed Consent Requirements For Planned Research In Emergency Settings**

- a) Note: this provision is for research planned to take place in emergency settings and is not to be confused with the emergency use of an investigational product without IRB approval, the latter of which is a treatment issue.
- b) The IRB will be responsible for the review, approval, and continuing review of clinical investigations taking place in emergency settings (i.e. first responders, trauma etc.) and may approve the investigation without requiring that informed consent of all research subjects be obtained if the IRB, with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation, finds and documents that each of the criteria set forth in the “Waiver of Consent For Planned Research In Emergency Settings” SOP.
- c) Such findings shall be documented and maintained by the IRB in meeting minutes or in the protocol files.
- d) The IRB shall promptly provide in writing to the sponsor of research involving an exception to informed consent (under this Planned Research In Emergency Settings policy) a copy of information that has been publicly disclosed as part of the requirement to waive

consent for this kind of research (See Waiver of Consent For Planned Research In Emergency Settings SOP).

- e) Should the IRB determine that it cannot approve this research request as it does not meet the criteria set forth by the federal regulations, the IRB shall promptly notify the investigator and sponsor of this decision and reasons thereof.

Documentation of Informed Consent and Waiver of Informed Consent

1. Documentation Requirements of Informed Consent/Assent

- a) Unless otherwise waived by the IRB, informed consent must be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent (in paper or electronic format).
- b) A copy/printout must be given to the person signing the consent form. If the subject is "admitted" (inpatient or outpatient) to an HCA facility, then a copy must be placed in the patient's medical record.
- c) It is a best practice to have a version number or date on the consent form.
- d) The consent form may be either of the following:
 - i) A written consent document that contains all non-waived required and additional elements of informed consent. This form may be either read to the subject or the subject's legally authorized representative, but in any event, the investigator must give either the subject or the legally authorized representative adequate opportunity to read it (or have it read to them) before it is signed.
 - ii) A short form written consent document stating all non-waived required and additional elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. If the research is federally funded, this short written form must also describe that the "key information summary" required structure was presented first before other information, if any, was provided. When this method is used, there must be a witness to the oral presentation. Also, the IRB must approve a written summary of what is to be said to the subject or representative. Only the short form itself is to be signed by the subject or their legally authorized representative. However, the witness must sign both the short form and the copy of the summary, and the person obtaining the consent must sign a copy of the summary. A copy of the summary must be given to the subject or their legally authorized representative in addition to a copy of the short form.
- e) For children, the parent(s)/guardian(s) sign the consent form. Any IRB requirements for documentation of assent of the child shall be determined for each study by the IRB.

2. Waivers of Documentation of Consent

- a) A Waiver of Documentation of Consent differs from Waiver or Alteration of Required Elements of Informed Consent as well as Waiver of HIPAA Authorization to Use/Disclose Protected Health Information.
 - i) The IRB shall assure it is applying the correct criteria as each of the three have their own separate and distinct criteria.

- ii) If documentation of consent is waived, the investigator must still obtain informed consent (i.e. verbally) from the participants on all required elements of consent that have not been otherwise waived according to that policy/criteria
 - iii) Waiver of Documentation of Consent **does not automatically imply** a Waiver of Required Elements of Consent, **nor does it imply** a Waiver of HIPAA Authorization to Use/Disclose Protected Health Information. **Each of these three waivers shall be evaluated separately based on their respective criteria.**
 - iv) Note that if all elements of consent are waived, there can be no documentation of consent but if one or more elements of consent are required, documentation of consent must be addressed.
- b) The IRB may waive the requirement to obtain documentation of consent only in accordance with the criteria set forth in federal regulations as required for a Waiver or Alteration of Required Elements of Consent, a Waiver of Documentation of Consent, or a Waiver of HIPAA Authorization to Use/Disclose Protected Health Information (See HIPAA Elements and Waivers SOP). For a Waiver of Documentation of Consent, at least one of the following criteria must be met (only #2 is allowed for FDA-governed Non-Emergency Settings studies):
- (1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
 - (2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside for the research context; or
 - (3) If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects AND provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
- c) Such findings must be documented in the meeting minutes or in other IRB documents (e.g. expedited reviewer's approval).
- d) In cases in which the documentation requirement is waived, the IRB may require the Principal Investigator to provide subjects with a written statement regarding the research.
- e) If not requested by the Investigator, the IRB should inquire/consider if the investigator also needs a Waiver or Alteration of Required Elements of Consent or a Waiver of HIPAA Authorization to Use/Disclose Protected Health Information. Waiver of Documentation Of Consent does not automatically imply Waiver or Alteration of Required Elements of Consent nor does it imply Waiver of HIPAA Authorization to Use/Disclose Protected Health Information. For example, the IRB may waive documentation of consent but still require the investigator to review all required elements orally with the subject or their legally authorized representative and sign a HIPAA Authorization to release PHI. Each of these three waivers must be evaluated separately based on their respective criteria.

TITLE: HIPAA Elements and Waivers	SOP 07
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1. The IRB shall ensure that the informed consent that is intended to include HIPAA authorization language includes the required elements under federal law for such Authorizations:
 - a) A description of the protected health information (PHI) to be used or disclosed;
 - b) The name or other specific identification of the person or class or persons authorized to make the requested use or disclosure (*e.g.*, hospital name, physician name);
 - c) The name or other specific identification of the person or class or persons to whom the facility may make the requested use or disclosure (*e.g.*, the researcher);
 - d) A description of the purpose of the requested use or disclosure;
 - e) An expiration date or event (*e.g.*, “end of research study” or “none”);
 - f) A statement that the individual has the right to revoke the authorization in writing and the exceptions to this right (*i.e.*, facility has already taken reliance on authorization);
 - g) A statement that if the patient refuses to sign the consent, including the authorization elements, that he/she will not be treated under the research protocol;
 - h) A statement that the PHI is subject to re-disclosure by the recipient and may no longer be protected; and
 - i) The extent to which a patient would be temporarily denied access to their PHI created or obtained in the course of research until the research project was completed. This requirement pertains only to research where patient treatment is involved.
2. Additionally, the IRB should assure or obtain assurance that if there are any federal/state/local-specific HIPAA preemptions, that the Authorization language is in compliance with both HIPAA and those additional federal/state/local requirements (*e.g.* certain substances use disorder treatment programs governed by 42 CFR 2 have additional requirements and restrictions for release of their identifiable substance use disorder treatment status).
3. The IRB may choose whether or not to review HIPAA Authorization language when presented separate from research consent forms (*i.e.* “Stand-Alone” HIPAA Authorizations) based on the individual circumstances of the research.

4. Waiver of HIPAA Authorization to Use/Disclose Protected Health Information

a) The IRB has the authority under federal regulations to waive some or all requirements of HIPAA Authorizations, even when presented in “Stand-Alone” format.

i) In order for the IRB to waive one, more, or all required elements of HIPAA Authorizations to Release PHI, the IRB will review the request to ensure it meets the federal regulated criteria (also see 45 CFR 46.512 and “Waiver or Alteration of Required Elements of Consent” or “Waiver of Documentation of Consent” sections of Informed Consent SOP):

1. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:

- a. an adequate plan to protect the identifiers from improper use and disclosure;
- b. an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
- c. adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;

2. The research could not practicably be conducted without the waiver or alteration; and

3. The research could not practicably be conducted without access to and use of the protected health information

ii) The IRB must provide the required documentation that criteria are met for approval of a Waiver or Alteration of Required Elements of Consent, a Waiver of Documentation of Consent, and a Waiver of HIPAA Authorization to Use/Disclose Protected Health Information. Documentation for the Waiver of HIPAA Authorization to Use/Disclose Protected Health Information includes, at a minimum:

- 1. The name of the IRB or Privacy Board (not the names of individual members of the board);
- 2. The date on which the waiver was approved;
- 3. The signature of the IRB or Privacy Board chair, or other member designated by the chair;
- 4. A statement that the IRB or Privacy Board has determined that the waiver satisfies the required criteria;
- 5. A brief description of the PHI that the IRB or Privacy Board has determined is necessary for research purposes; and,

6. A statement that the waiver has been reviewed and approved under either normal or Expedited Review procedures and that all applicable procedures were followed.
- iii) If not requested by the Investigator, the IRB should inquire/consider if the investigator also needs a Waiver of or Alteration of Required Elements of Consent or a Waiver of Documentation of Consent. A Waiver of HIPAA Authorization to Use/Disclose Protected Health Information **does not automatically imply** a Waiver or Alteration of Required Elements of Consent **nor does it imply** Waiver of Documentation of Consent. **Each of these three waivers must be evaluated separately based on their respective criteria.**

TITLE: Managing Conflicts of Interest	SOP 08
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PURPOSE:

The purpose of this policy is to set forth the process for identifying and managing conflicts of interest.

PROCEDURES:

Identifying Potential Conflicts of Interest

1. **IRB Member Conflicts:** IRB members are determined to be conflicted when:
 - a. they have a proprietary interest in the tested product, including, but not limited to, a patent, trademark, copyright or licensing agreement;
 - b. they are involved in the design, conduct, or reporting of the research;
 - c. they are in a subordinate role to the Investigator (*i.e.*, employee, student etc.) regardless of involvement in the research; or
 - d. they have any other interests that would impair their ability to make fair and impartial judgments about an application.

2. **Investigator Conflicts:** There are numerous stakeholders (*i.e.*, NIH, FDA, research sponsors, trade associations, institutions, etc.) that define and require reporting of potential investigator conflicts of interests for various reasons specific to the activity. The general process is that the investigator reports significant financial interests (defined with different thresholds by NIH and FDA) to their Institution (e.g. for NIH-funded studies) or the Sponsor (e.g. for FDA-governed clinical investigations) or both (e.g. for both NIH-funded and FDA-governed clinical investigations). The Institutional Official and/or Sponsor determines if the significant financial interest could affect the research (be it human subject protections or other aspects of the research) and if so, works to eliminate or manage that conflict and report it accordingly to the federal agencies. The role of the IRB is solely to assist the institution or sponsor in determining if any conflict of interest affects the protection of human subject in research and if so, assist in the management plan. The IRB only receives information pertaining to conflicts of interest as defined by these various stakeholders. It is not responsible for creating or reporting such information in regulatory required reports (*i.e.* FDA’s 21CFR54 or PHS reports) unless otherwise assigned to do so by the institution.

Determining A Potential Conflict Of Interest As Affecting Human Subject Protection

1. The IRB must consider whether the specific conflicts of interests (perceived or otherwise) may adversely affect the rights and welfare of subjects. The “reasonable person” test should be utilized in making this determination.
2. In the absence of an IRB opinion or a financial interest, individuals may self-determine that a conflict of interest exists that may adversely affect the rights and welfare of subjects. This may be in cases where they feel that their decision is being altered by other personal factors such as

loyalty to colleagues, business competition with investigators, personal agendas or fear of IRB decisions impacting their non-IRB work.

Eliminating or Managing the Conflict Of Interests Potentially Affecting Human Subject Protection

1. If a conflict of interest is eliminated, then further management is not necessary.
2. **Managing IRB member's conflicts of interest:** For a conflicted IRB member, the risk is eliminated by the following without exception:
 - a. The conflicted member(s) may not serve as the primary reviewer, Expedited Reviewer, determiner of exempt status or consultant for the given research activity.
 - b. During convened meetings, the conflicted member(s):
 - i. May provide information germane to the discussions but must leave the meeting room during deliberations and voting; and
 - ii. Are not counted towards a quorum, thus a quorum must be re-validated after they leave in order to vote; and
 - iii. Documentation of such absence must be in the minutes.
 - c. Other protections for Conflicts of Interests affecting IRB Members include:
 1. The institution forbids facility representatives from using their authority to unduly influence how individual IRB members vote and that any violation of this policy should be immediately reported to the Institutional Official, the Facility Ethics and Compliance Officer, the Corporate Responsible Executive for Clinical Research or the Ethics Line. Depending on the severity and circumstances, the outcome of such investigations could range from requiring education to disciplinary action.
3. **Managing Investigator Conflicts of Interest**
 - a. It is up to the Institutional Official, not the Clinical Investigator, to determine if an actual, potential or perceived significant financial Interest is related to the research and subsequently a Financial Conflict of Interest. The IRB may be designated to assist in this role.
 - b. In the event any determined Financial Conflict of Interest (FCOI) cannot be eliminated, in order for the study to be approvable, the Institutional Official must be assured that the Financial Conflict of Interest is appropriately managed. The IRB may assist in this role as the Institutional Official's designee or otherwise help assure potential effects to human subject protections are minimized. The circumstances of the protocol, the subjects and the nature of the conflict will determine the best management plan for the conflict, some examples include:
 - i. Disclosing the potential conflict of interest during the Informed Consent process.
 - ii. Having another non-conflicted person perform informed consent interviews or collect data.
 - iii. Establishment of a more sufficient monitoring plan.
 - c. The IRB should coordinate with any other FCOI policies the institution may have.
4. **Non-compliance/non-adherence to this policy**
 - a. The IRB (or designee) shall assist the Institution in any retrospective review they are required to do for DHHS or other funded studies when notified of any of the following:

- i. that an Investigator failed to disclose (or inaccurately disclosed) a significant financial interest that is determined by the Institution to constitute a financial conflict of interest;
 - ii. that the Institution (or IRB as assigned by Institution) failed to review or manage such a financial conflict of interest; or
 - iii. that the Investigator failed to comply with a financial conflict of interest management plan.
- b. The IRB shall be involved, as necessary, in the institution's drafting of any corrective and preventative action plans.

Confidentiality

To the extent permitted by law, all statements, letters, other records and information submitted will be maintained confidentially by the IRB and IRB members. Notwithstanding the above, information pertaining to conflicts of interest will be made available to any federal agency funding the research upon written request of the agency, and otherwise as required by law or regulation.

REFERENCES:

N/A

TITLE: Vulnerable Populations	SOP 09
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Informed Consent in Vulnerable Populations and Unique Situations

1. Informed Consent for Non-English Speakers

- a) Subjects who do not speak English should be presented with consent content (oral and written) in the subject’s preferred language whenever possible.
- b) The IRB maintains copies of each approved translation of written documents. If no IRB member is competent to review the translated forms, the IRB may consider the advice of a consultant or translating person/organization in approving/disapproving the foreign language consent form.
- c) **Use of Short Form Consent.** Alternatively, if an oral presentation of informed consent information is used with subjects who do not speak English in addition to the requirements described above, (i) the oral presentation and the short form written document should be in a language readily understandable to the subject; (ii) the English language informed consent document approved by the IRB may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject. When a translator assists the person obtaining consent, the translator may serve as the witness. The IRB must receive all foreign language versions of the short form document and any other translated documents presented to the subjects as a condition of approval. The IRB recognizes that while the planned enrollment of subjects that do not speak English should have prospectively translated subject-facing documents (i.e. consent forms), from time to time the Investigator may unexpectedly encounter an individual for whom there is not translated documents.
- d) Expedited Review of foreign language versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the IRB.

2. Informed Consent Illiterate Persons: Illiterate persons who understand English may have the consent form read to them in their native language and “make their mark” on the subject signature line. Signatures of both a witness to the consent process and the person conducting the consent interview are required in such situations.

3. Informed Consent in Studies That Involve Deception or Incomplete Disclosure.

- a) Research may include scientific design that require elements of deception or incomplete disclosure at the informed consent process. This likely occurs in psychology or education studies.
- b) Incomplete Disclosure is defined as withholding information about the true nature of the research. Incomplete disclosure is essentially withholding one or more elements of consent thus is adequately handled as part of Waiver or Alteration of Required Elements of Consent.
- c) Deception is fundamentally different from incomplete disclosure as instead of simply withholding information, the researcher is deliberately providing misleading

or false information as part of the informed consent process.⁸ Deception also follows the rules of Waiver or Alteration of Required Elements of Consent with specific consideration that (i) the misleading or false information does not add more than minimal risk AND (ii) that any debriefing afterward, as required by the IRB pursuant to the criteria under this Waiver, may need to be delayed until the end of the study to prevent disclosure to other current or prospective study participants.

- d) In either case of deception or incomplete disclosure, it is permissible to inform the subjects as part of the informed consent that is done that they will either be deceived or purposely receive incomplete information for scientific reasons.

4. **Staged Consent:**

- a) The IRB may allow or require the investigator to "stage" information in the consent process. This process may be useful for studies with separate and distinct, but linked, phases through which the subject may proceed. For example, if faced with a protocol where a subject must receive genetic testing first and then, based on the results, there are different risks, limitations, follow-up and/or implications to the subject in the next phase of the research; rather than a lengthy initial consent that contemplates all possible results, the consent can be "staged" to re-consent the subject prior to the next phase of the research beginning. If this technique is used, the initial consent should explain that subjects will be asked to participate in the additional phases. It should be clear whether the phases are steps in one study or separate but interrelated studies.
- b) Staging consent does not alleviate any requirements of consent, documentation of consent or the criteria for their respective waivers.

5. **Tiered Consent:**

- a) The IRB may allow or require the investigator to have multiple differentiated consent forms/requirements that are tiered to specific subject choices or trait categories. This may be combined in one consent/form or by using multiple different consent/forms. One example is having a single consent/form where the subject must choose an option to have no, all or only certain individual results returned to them, such as in genomic studies. Another example is a protocol in which the risks, limitations, follow-up and/or implications vastly differ between those with diabetes versus those without diabetes, instead of a single lengthy consent/form contemplating everything for both people with and without diabetes, there are separate but complete consent/forms for use based upon if the individual has diabetes.

- 6. Tiering of consent (whether combined in a single consent/form or using multiple consent/forms) does not alleviate any requirements of consent, documentation of consent or the criteria for their respective waivers.

⁸ Note that *blinding* is not deception when the participant knows they will be blinded and the possibilities of what they are blinded to (as in a placebo controlled study).

Vulnerable Populations Subject to Additional Regulated Protections: Pregnant Women, Fetuses and Human in Vitro Fertilization

1. Research involving pregnant women, fetuses, and human in-vitro fertilization may require additional considerations. The IRB will follow the specific federal (OHRP) laws located at 45 CFR 46 Subpart B pertaining to the following conditions:
 - a) Research involving pregnant women;
 - b) Research directed towards the fetus *in utero*;
 - c) Research involving the fetus *ex utero*; and
 - d) Research involving dead fetuses, fetus material, or placenta.
2. It is important to note that OHRP regulations serve as a guideline for all research as appropriate (and without reporting obligations to OHRP), except the regulations are legally required if the research is conducted or supported by DHHS or otherwise falls under the jurisdiction of the Common Rule (45 CFR 46) Subpart B.
3. Additionally, the IRB should be familiar with the following special considerations:
 - a) National Commission for the Protection of Human Subjects recommendations concerning abortions; and
 - b) The President's Council on Bioethics recommendations concerning Stem Cell Research.

Prisoners

1. St. David's HealthCare Institutional Review Board does not review research involving prisoners. Should prisoners need to be enrolled in a research study for any reason, the researcher would need to request a Waiver of IRB Jurisdiction and obtain approval from an external IRB. Any IRB conducting a review under 45CFR46 Subpart C must be knowledgeable of the Subpart C requirements regarding having a prisoner's representative as a voting member as well as how to submit a "Subpart C Certification" to HHS.

Children

1. For OHRP and FDA governed research, IRBs are required to classify (and document such classification in their minutes if not elsewhere) all non-exempt research with children as subjects into one of four categories. IRBs are then only permitted to approve three of those four categories. The three categories (for research as a whole or individual arms of the research) that IRBs can approve and their requirements are:
 - a) **Research not involving greater than minimal risk to the children.** To approve this category of research, the IRB must make the following additional determinations:
 - i) the research presents no greater than minimal risk to the children; and
 - ii) adequate provisions are made for soliciting the assent of the children and the permission of at least one parent/guardian.
 - b) **Research involving greater than minimal risk but presenting the prospect of direct benefit⁹ to the individual child subjects involved in the research.** To approve research in this category, the IRB must make the following additional determinations:
 - i) the risk is justified by the anticipated benefits to the subjects;

⁹ Note that placebo arms do not offer the prospect of direct benefit, thus this arm would usually not be categorized here.

- ii) the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; and
 - iii) adequate provisions are made for soliciting the assent of the children and the permission of at least one parent/guardian.
- c) **Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition¹⁰.** To approve research in this category, the IRB must make the following additional determinations:
- i) the risk of the research represents a minor increase over minimal risk;
 - ii) the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
 - iii) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and
 - iv) adequate provisions are made for soliciting the assent of the children and the permission of both parent/guardians unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent/guardian has legal responsibility for the care and custody of the child.
2. The fourth category of research (**Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children**) is research that the IRB believes does not meet the conditions of 1.a, 1.b or 1.c above, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. In this situation, the IRB shall refer the protocol to DHHS and/or FDA for review as appropriate to their jurisdiction over the research. The research may proceed only if the Secretary of DHHS/FDA, or his or her designee, approves the research.
3. **Assent of the Child.**
- a) The IRB shall determine that adequate provisions are made for soliciting the assent of the children when, in the judgment of the IRB, the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, certain defined classes of children or for each child, as the IRB deems appropriate.
 - b) If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the requirement for assent of the children may be waived..
 - c) Even where the IRB determines that the children are capable of assenting, the IRB may still waive the assent requirement under circumstances (using the same criteria for Waiver

¹⁰ Note that healthy control arms consist of those that do not have a disorder or condition to gain knowledge on thus this arm would usually not be categorized here.

or Alteration of Required Elements of Consent) in accordance with federal/state regulations and the relevant policy.

4. Waiver of Parent/Guardian Permission.

- a) The usual provisions and criteria for Waiver or Alteration of Required Elements of Consent, Waiver of Documentation of Consent, and Waiver of HIPAA Authorization to Use/Disclose Protected Health Information apply for waiver of Parent/Guardian permission.
- b) In addition to the usual provisions for the above waivers, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects, the IRB may waive parental or guardian permission. Examples may include research involving older adolescents and treatment for which they may, under applicable state law, consent on their own behalf (e.g., treatment for sexually transmitted diseases, pregnancy, drug abuse etc.). In other research (e.g., research on child abuse or neglect), there may be serious doubt as to whether the parent/guardian's interests adequately reflect the child's interests. The IRB may waive the permission requirements provided the IRB determines there is an appropriate mechanism for protecting the children who will participate as subjects in such research, and provided further that the waiver is not inconsistent with federal, state, or local law and adheres to the remaining criteria set by the respective policy. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

5. Documentation of Permission and Assent:

- a) Documentation of Parent/Guardian permission shall be done in accordance with the usual policy of documentation of consent as described in this manual. The only modifications is that the documented permission (i.e. informed consent document) may be tailored to the situation (e.g. may reference "your child" instead of "you").
- b) Documentation of Assent of the child may or may not be required by the IRB and should be determined based on the individual aspects of the research. Any special instructions the IRB desires concerning documentation of assent shall be communicated to the investigators.

6. Wards

- a) Children who are wards of the state or any other agency, institution, or entity can be included in OHRP or FDA governed research categorized incertain classes designated above (specifically either "Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition" or "Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children") only if such research is:
 - i) Related to their status as wards; or
 - ii) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

- b) In addition to the above, required for OHRP and FDA governed studies (and at the discretion of the IRB for all others) the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization. The advocate need not be present for nor are they required to cosign the informed consent. They only need to be knowledgeable of the child's participation in the study.

Research Involving Decision-Impaired Subjects

- 1) Decision-impaired individuals are those who have a diminished capacity for judgment and reasoning due to psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals who may be considered decision-impaired may include individuals under the influence of drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling mental handicaps.
- 2) There are no regulations specific to research involving decision-impaired persons. As with all subjects the IRBs must carefully consider whether additional safeguards should be added to the proposed research to provide additional protection for these subjects.
- 3) Numerous articles to assist an IRB in the efforts to protect human research subjects with decision-impairment are found in recent publications. Examples of these documents may be found at <http://bioethics.gov>.

TITLE: Utilizing the “Limited IRB Review” Process as Required for Certain Exemptions	SOP 10
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POLICY

- 1) A Limited IRB Review is a new class of IRB review that may be done by the convened board or via Expedited Review. It is “limited” in that the regulations allow for the waiver of most obligations of IRB review for specific classes of research activity.

- 2) Limited IRB Review For Certain Exempt Determinations:
 - a) Certain Exempt determinations require a Limited IRB Review to ensure that there are adequate privacy safeguards for identifiable private information and identifiable biospecimens. No other criteria to approve research apply.
 - b) Approvals via a Limited IRB Review are not subject to continuing review.

- 3) **Limited IRB Review For Research Done Or Planned Under “Broad Consent” Alternative to Informed Consent:** *At this time the Institution does NOT endorse the use of the “Broad Consent” alternative (as defined at 45CFR46.116(d)) and thus the IRB will not engage in the activity of the affiliated Limited IRB Review required of “Broad Consent” alternative. All consents and IRB review for the use of information and biospecimens will be done via conventional mechanisms.*

TITLE: Investigator Communications	SOP 11
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PURPOSE:

The purpose is to outline the IRB's policies and procedures for communicating to investigators any IRB actions taken regarding proposed research activities, and/or any modifications or clarifications required by the IRB as a condition for IRB approval of proposed research.

POLICY:

The St. David's HealthCare Institutional Review Board (SDH IRB) will maintain and follow written procedures for communicating with investigators that contain the required elements under Department of Health and Human Services (HHS) regulations for the protection of human subjects ([45 CFR Part 46](#)) and are also compliant with CSG IRB policies (CSG.IRB.001-011).

PROCEDURES:

IRB Submissions

All submissions to SDH IRB should be sent electronically utilizing IRBNet at www.IRBNet.org. See separate SDH IRB instructions for registering with IRBNet, affiliating with St. David's HealthCare.

Telephone Communications

Investigators or their designees may telephone SDH IRB (512-544-2626) to ascertain the status of a submitted protocol. The following information should be provided:

- The IRB number, if assigned
- The Principal Investigator's name
- Protocol title
- Date of submission
- Type of submission (i.e., new project for full board review, renewal, modification)

Electronic Communications of IRB Decisions

Investigators or their designees may email SDH IRB at sdhp.irb@stdavids.com to ascertain the status of a submitted protocol.

Formal decisions of SDH IRB will generally be communicated to Principal Investigators or their designees through an electronic letter, which will generally be issued through IRBNet, that will outline the approval status and/or significant any concerns, questions, and comments of the IRB. Decisions from a convened board meeting will be verbally available the next business day. **A research study may not begin until the notification letter of final approval from the IRB is received from the IRB.**

Decision letters uploaded through IRBNet should include an electronic signature. Entities who wish to verify the authenticity of the electronic letter should obtain access IRBNet, view the protocol history tab, and verify that the approval document has been uploaded by the IRB into the IRBNet system, and confirm the date of posting. The letter should clearly indicate the IRB's decision and should not imply a full facility approval. For clarification, the letter may refer to the fact that other institutional obligations may be necessary to conduct the research.

The decisions of the IRB will fall into one of the following categories:

- **Full Approval:** The Principal Investigator may initiate the study upon written notification of full approval of the research protocol and, if applicable, the informed consent document, from the IRB chairperson or his designee.
- **Conditional Approval:** This decision is conveyed when the protocol is recommended for approval by the IRB, pending the Investigator's response to IRB-directed changes or requests for clarifications. The IRB will issue a written letter to the Investigator, published via IRBNet, specifying in detail the conditions that must be satisfied prior to the IRB granting approval of the research, and how the IRB wishes to verify that the changes were made.

The Principal Investigator must provide a response to the Board's questions and/or recommendations in writing and include any supporting documentation required (e.g. a modified protocol or consent form) with the changes highlighted in tracked changes or a similar method. The response materials will be uploaded into IRBNet as a subsequent package under the existing protocol project, and the submission type should be labeled as "Response/Follow-Up".

Usually, the response package should not add any new items, or add any new language to the consent form beyond those items/changes that the board has requested per its review of the original submission. If non-requested items or consent language are added in addition to a response for modifications, the reason(s) for adding these should be justified and documented in the response submission and the submitted documents may require additional Board review at a convened meeting.

The Principal Investigator's response will be reviewed by the IRB Chair or designee. If the response is acceptable and/or the conditions are met, the Principal Investigator will receive (typically within 5 working days) a written letter of notification of IRB approval. **Research activities (including screening, consenting, etc.) may not begin until the notification letter of IRB approval is published through IRBNet.**

Note: For purposes of determining the continuing review date, the Board decision at the convened meeting constitutes approval. The continuing review approval date is therefore based on the date of the Board meeting and not the date the Investigator's response was submitted/reviewed. However, the Investigator cannot begin any research activities until the IRB Chair or designee agrees that all conditions for approval have been satisfied.

- **Tabled:** This decision is conveyed when the IRB has a number of significant questions and concerns regarding the research protocol that could not be resolved at the IRB meeting. The IRB will issue a written letter to the Principal Investigator via IRBNet, specifying the questions that need to be answered and/or modifications that must be made before the IRB will reconsider the proposed research at a subsequent convened board meeting; the reasons for the Board's questions and requested modifications will be included in the letter.

The Principal Investigator must provide a written response to the IRB's concerns/comments, recommendations and/or questions. Usually, the response package should not add any new items, or add any new changes to the consent form, beyond those items/changes that the Board has requested based on its review of the original submission. If non-requested items or consent language are added in addition to a response for modifications, the reason(s) for adding these must be justified and documented in the response submission, and the changes should be highlighted with tracked changes or a similar method. The response materials must be uploaded into IRBNet as a subsequent package under the existing protocol project, and the submission type should be labeled as "Response/Follow-Up". See SDH IRB's separate IRBNet instructions for submitting a subsequent package in an existing project.

The Principal Investigator's response will be reviewed next available board meeting following resubmission. **The Principal Investigator may not initiate the research until the response has been reviewed and approved and a notification letter of IRB approval is received through IRBNet.**

- **Disapproval:** The SDH IRB may disapprove a research protocol based on its identification of major scientific or ethical problems which, in the committee's opinion, cannot be readily resolved by the Principal Investigator. When a research protocol is disapproved by the IRB, the Principal Investigator is not authorized to initiate the study. The IRB will issue a letter to the investigator via IRBNet, specifying in detail the reasons for the disapproval. **The IRB will not waive jurisdiction to another external IRB to review a research protocol that was initially disapproved by the IRB.**

Upon disapproval, the Investigator will have the opportunity to appeal the Board's decision. A modified protocol that addresses IRB's reason(s) for the initial disapproval may be resubmitted for full board review. The revised protocol, consent, and any additional material must be uploaded into IRBNet as a subsequent package under the existing protocol project, and the submission type should be labeled "Response/Follow-Up". See SDH IRB's separate IRBNet instructions for submitting a subsequent package in an existing project.

When re-submitting the protocol, the Principal Investigator must include a written response to the IRB's concerns, comments, recommendations and/or questions. The Principal Investigator's response will be reviewed next available meeting following resubmission. **The Principal Investigator may not initiate the research unless the response has been re-reviewed and approved and a notification letter of IRB approval is received through IRBNet.**

Reporting to the Institution

The SDH IRB Institutional Official has access to all board actions and decisions through IRBNet. The SDH IRB Institutional Official is also provided copies of meeting minutes promptly after their approval by the Board.

External or Central IRBs

For information on submission requirements and investigator communications when an external or central IRB is used, please see the separate SDH IRB Waiver of IRB Jurisdiction SOP.

REFERENCES:

N/A

TITLE: Maintenance of Records	SOP 12
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PURPOSE:

The purpose of this policy is to set forth the process for maintenance of St. David’s HealthCare Institutional Review Board (SDH IRB) records.

PROCEDURES:

IRB Member Documentation

1. The IRB coordinator will maintain (electronically or on paper) or have immediate access to (e.g. if any of the below are kept elsewhere such as in Human Resources or Medical Affairs/Credentialing) the following for each IRB member:
 - a. Appointment Notification(s) (*i.e.*, Letter, email, etc.);
 - b. Curriculum Vitae or other summary of qualifications;
 - c. Documentation of any IRB related training/certificates.

IRB Roster

1. The written IRB rosters will be dated with month, date and year and include the following fields:
 - a. First and Last Name;
 - b. Earned degree(s) if any;
 - c. Representative capacities (*i.e.* in terms of the vulnerable populations, if any, each member is knowledgeable about or experienced in working with);
 - d. Scientific/non-scientific status;
 - e. Affiliation status (whether the member or an immediate family member of the member is affiliated with the organization);
 - f. Employment or other relationship between each IRB member and the organization.
 - g. Indications of experience (such as board certifications, licenses etc.) sufficient to describe each IRB member’s chief anticipated contributions;
 - h. Officer Status, if applicable (*i.e.*, Chair, Vice Chair, etc.);
 - i. Membership status (*i.e.*, voting member, alternate member, non-voting, etc.); and
 - j. The voting members or class of voting members for whom each alternate member can substitute.
2. The Roster will be promptly updated with any change of membership.
3. The Roster will clearly display the date of the most recent change with a month, date, year format.
4. It is suggested that the IRB Coordinator maintain a single location (with electronic and/or paper backups) with all rosters will be kept so that they are easily located for audits.

Meeting Minutes

1. IRB minutes will document the following:
 - a. Date of meeting;
 - b. Voting members in attendance at meeting;
 - c. When an alternate member replaces a primary member in a voting capacity;
 - d. A list of all fully processed expedited reviews since the last meeting (unless all members were notified via other means);
 - e. Separate deliberations, action and voting for each protocol (i.e. no “block voting” across multiple protocols);
 - f. Exactly what was discussed (*i.e.*, protocol, consent, advertisements etc. - all with version numbers and dates as applicable);
 - g. Unless documented in the IRB records, certain specific determinations required by the regulations and their protocol-specific findings justifying those determinations for:
 1. OHRP governed (i.e. federally-funded) research involving pregnant women, fetuses, and neonates.
 2. OHRP governed (i.e. federally-funded) research involving prisoners.
 3. FDA governed or OHRP governed (i.e. federally-funded) research involving children.
 4. Significant Risk (SR)/Non-Significant Risk (NSR) device determinations for initial reviews of clinical investigations of devices.
 5. Waiver or Alteration of Required Elements of Consent, Waiver of Documentation of Consent, Waiver of HIPAA Authorization to Use/Disclose Protected Health Information, etc.
 6. The required rationale for an Expedited Reviewer’s determination that research fitting in categories consistent with the HHS approved Expedited Review list deemed as minimal risk is actually no more than minimal risk.
 7. The required rationale for conducting continuing review of the research that otherwise would not require continuing review by regulation or this policy.
 - i. A written summary of the discussion of controversial issues and their resolution;
 - j. Actions taken by the IRB;
 - k. The basis for requiring changes in research;
 - l. The basis for disapproving research;
 - m. Unless otherwise discernable from other documentation for initial and continuing approvals, the approval period (up to one year);
 - n. Unless otherwise discernable from other documentation for conditional approvals, the reason(s) for conditional approval shall be stated along with a description of how the IRB wishes to verify that the changes were made. Examples include, but are not limited to the following:
 - a. For purely administrative or clerical matters, the IRB may delegate IRB staff or another designee (i.e. a privacy officer) to verify the changes;
 - b. For simple matters requiring judgment, the IRB may designate the Chair or other Expedited Reviewer to verify the changes;
 - c. For complex matters of judgment or major changes, the IRB may require discussion of the full Convened Board.

- o. The names of IRB members who left the meeting because of a conflict of interest along with the fact that a conflict of interest was the reason for the absence;
 - p. Votes for each protocol counted in a format sufficient to show “# for, # against, and # abstaining”; and
 - q. Any training or other activity that took place.
2. The IRB Coordinator should keep all minutes chronologically in a single location
 3. When kept electronically, the IRB Coordinator should have an electronic backup or other accessibility to others in their absence.

Protocol Records

1. IRB records for research protocols (including documentation pertaining to their initial, continuing, and ad-hoc reviews) will be stored in paper and/or electronically in a manner sufficient for easy archival and retrieval.
2. All protocol-related information will be available for review by IRB members and auditors. This may include as applicable, but is not limited to:
 - a. Protocols;
 - b. Informed Consent documents, including justifications for Waiver or Alteration of Required Elements of Consent and/or Waiver of Documentation of Consent;
 - c. All correspondence to and from the investigator (including applications/progress reports and approval/denial letters);
 - d. Any advertisements;
 - e. Any scientific evaluations;
 - f. Any reports of injuries to participants;
 - g. Any information pertaining to investigator conflicts of interest;
 - h. Any statements of significant new findings provided to participants;
 - i. For initial, continuing, and ad-hoc reviews of research performed by an Expedited Review or for determinations of IRB exemption:
 1. The specific permissible category for expedited review or exemption;
 2. Description of action taken by the reviewer; and
 3. Any other findings required under the regulations.
 - j. Unless documented in the IRB minutes, determinations required by the regulations and protocol-specific findings supporting those determinations for:
 1. OHRP governed (i.e. federally-funded) research involving pregnant women, fetuses, and neonates;
 2. OHRP governed (i.e. federally-funded) research involving prisoners; and
 3. FDA governed and/or OHRP governed (i.e. federally-funded) research involving children.
 4. Significant Risk (SR)/Non-Significant Risk (NSR) device determinations for initial reviews of clinical investigations of devices.
 5. Waiver or Alteration of Required Elements of Consent, Waiver of Documentation of Consent, Waiver of HIPAA Authorization to Use/Disclose Protected Health Information, etc.

6. The required rationale for an Expedited Reviewer's determination that research fitting in categories consistent with the HHS approved Expedited Review list deemed as minimal risk is actually more than minimal risk.
7. The required rationale for conducting continuing review of research that otherwise would not require continuing review by regulation or this policy.

Written Procedures

1. The IRB will maintain current and previous sets of written procedures.
2. The written procedures shall be dated (month, date and year) to easily determine which procedures were in place at any given point in time.
3. Updates are preferred to be presented in a "redline" format so that changes are easily identified.

Record Retention and Accessibility

1. IRB records should be retained in a central location accessible for inspection and copying/printing by authorized representatives of the research's governing federal agencies or departments if applicable (e.g. the FDA and/or OHRP) at reasonable times and in a reasonable manner. Records to be stored at this location include:
 - a. The current and previous rosters in paper and/or electronic formats.
 - b. Meeting minutes in paper and/or electronic formats.
 - c. All research records relating to a protocol will be retained for at least three years after completion of the research (even if no subjects were enrolled), including IRB meeting minutes and rosters even if those records must be retained in excess of three years.
2. Records will be stored in a way that maintains confidentiality.
3. IRB records should be well organized to allow reconstruction of a complete history of all IRB actions related to the review, approval, and oversight of each research protocol.

REFERENCES:

N/A

TITLE: Waiver of IRB Jurisdiction to an External IRB	SOP 13
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PURPOSE:

The purpose of this policy is to set forth the procedures for processing a Waiver of IRB Jurisdiction Request.

Background

All research activities that occur at St. David’s facilities (in the greater Austin, TX metro area), Del Sol Medical Center (El Paso, TX), and Las Palmas Medical Center (El Paso, TX) are under the jurisdiction of St. David’s HealthCare Institutional Review Board. There may be some situations in which a researcher or sponsor prefers to seek approval from an external IRB. In these cases, a request may be made to obtain approval for a Waiver of IRB Jurisdiction from St. David’s HealthCare Institutional Review Board. These requests will be considered on a case-by-case basis by the Chair. St. David’s facilities and HCA Division facilities.

PROCEDURES:

Investigator Responsibilities

In order to request a Waiver of IRB Jurisdiction, the Principal Investigator will be required to submit the following items to SDH IRB:

- Waiver of IRB Jurisdiction Request form
- IRB Authorization Agreement- the researcher should be able to obtain this document from the relying IRB. This does not have to be signed by both parties prior to an approval of the waiver being granted. Typically, the site will take the following steps:
 - Obtain the IRB Authorization Agreement/Reliance Agreement form from the relying IRB
 - Provide this form to SDH IRB. There should be one form per hospital. However, if the hospital shares an FWA with another hospital, the form may list multiple hospitals/facilities.
 - SDH IRB will obtain signatures from the appropriate facility signatory.
 - SDH IRB will review the waiver request and issue a letter regarding the board’s decision.
 - The Office of Research will provide the signed IRB Authorization Agreement/Reliance Agreement form to the researcher.
 - The researcher will be responsible for obtaining approval from both IRBs and providing copies to both the reviewing IRB and to SDH IRB.

If SDH IRB agrees, the Principal Investigator may proceed with seeking approval from another IRB outside of St. David’s HealthCare. If the request is not approved, the researcher will be required to seek approval from SDH IRB prior to initiating the project. In addition, the researcher must also obtain approval from the Research Council for any research taking place at St. David’s HealthCare facilities, Del Sol Medical Center, or Las Palmas Medical Center.

If SDH IRB approves the Request for Waiver of IRB Jurisdiction, the Principal Investigator will be asked to provide the following to SDH IRB:

- A copy of the fully executed IRB Authorization Agreement/IRB Reliance Agreement form
- Any additional information as requested by SDH IRB

In addition, the following items should be provided to the Research Council as they become available:

- Initial approval letter and approved ICF from the designated IRB
- Continuing review submissions and approval letters from designated IRB
- Notification of any changes to sites where research activity will take place. If you need to add a research site, you will need to submit a request. Please contact SDH IRB and we will instruct you on how to proceed.
- Final/close-out report and approval letter from designated IRB

IRB Responsibilities

Upon receipt, the IRB Chair will review the Waiver of IRB Jurisdiction Request and decide whether or not to allow IRB jurisdiction to be waived. The IRB staff will document the Chair's decision in writing and a letter will be provided to the Principal Investigator or his/her designee.

REFERENCES:

N/A

TITLE: Adverse Events (AEs), Serious Adverse Events (SAEs), Unanticipated Problems (UPs), and Unanticipated Device Effects (UDEs)	SOP 14
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PURPOSE:

The purpose of this policy is to set forth the requirements for investigator and IRB reporting of unanticipated problems and safety-related concerns and to fulfill the regulatory requirements (45 CFR 46.103(b)(5) and 21 CFR 56.108(b)), which require that IRBs have written procedures for ensuring prompt reporting to the IRB of any unanticipated problems involving risks to subjects or others.

DEFINITIONS:

An **Adverse Event (AE)** is any untoward occurrence in a patient or clinical investigation subject. Adverse drug experiences, and adverse drug reactions, abnormal lab findings, symptoms, or diseases concurring with the research may be Adverse Events (AEs). Adverse Events may also be non-medical in nature, such as economic or social harms. An Adverse Event does not necessarily have to have a causal relationship with the subject’s participation in the study.

A “**Serious**” **Adverse Event (SAE)** is any Adverse Event that:

- Is fatal (results in death)
- Is life-threatening
- Results in persistent or significant disability/incapacity
- Requires inpatient hospitalization
- Prolongs existing inpatient hospitalization
- Is a congenital anomaly/birth defect
- Is a persistent or significant disability/incapacity
- Is considered by the Investigator to be an important medical event. Such an event may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definitions above.

An “**Unanticipated Adverse Device Effect (UADE)**” is any Serious Adverse Event related to health or safety or any life-threatening problem or death caused by or associated with a device, if that event, problem, or death was not previously identified in nature, severity, or degree of incidence in the study protocol, device information, or informed consent form. This also includes any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

An “**Unanticipated Problem**” (**UPIRSO**) involving risks to subjects or others may include Serious Adverse Events, Unanticipated Adverse Device Effects, or other incidents that are not Adverse Events but that involve risks to subjects or others (i.e., the loss of a study laptop with

unencrypted Protected Health Information (PHI) on it, protocol deviations that could potentially cause harm to subjects). To be considered an unanticipated problem, the event must meet all three of the following criteria:

- It is **Unexpected¹¹**, meaning **not otherwise previously known to the IRB** (in terms of nature, severity, or frequency) given: (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol, informed consent document, or Investigator’s Brochure/product information; and (b) the characteristics of the subject population being studied; and
- **Related or possibly related to participation in the research.** *Possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the research (e.g. by procedures that are done in support of the research that would not have been done absent the research); and
- The event suggests that the research **places subjects or others at a greater risk of harm** (including physical, psychological, economic, or social harm) **than was previously known or recognized.** If the event is a Serious Adverse Event, this criteria is automatically deemed as being met.

PROCEDURE:

Investigator Responsibilities:

1. Once the Investigator or study staff becomes aware of the UPIRSO, the Investigator is responsible for submitting a report of the event to the IRB for review through IRBNet generally **within 5 business days**.
2. Investigators should determine whether any Serious Adverse Event, Unanticipated Adverse Device Effect or UPIRSO indicates that an immediate hazard exists to human subjects. In such situations, the Investigator must also notify the IRB Chairperson by telephone immediately in addition to the written report, which must be submitted to the IRB within 5 business days. The IRB Chair will immediately report the situation to the Institutional Official and Hospital Administration where the research is being conducted.

Investigators may submit follow-up reports to provide additional information as it is gathered about the resolution of an event, such as subject health outcome or updates on risk assessment. Follow-up UPIRSO reports should include the same information as listed above.

IRB Responsibilities:

1. Investigators should be educated (i.e., through approval letters, manuals, and/or other training opportunities) by the IRB of their regulatory obligation to report UPIRSOs promptly after they become aware of them.

¹¹ Note the difference between “unexpected” as defined consistent with federal guidance herein as essentially not previously known to the IRB versus “unexpected” as may be used in the vernacular to include something that was already known but was regarded as not likely to happen. The latter would not be considered “unexpected” for purposes of categorizing the event as an UPIRSO as the risk, albeit small, was already considered by the IRB.

2. Upon receipt of a report of a potential UPIRSO, the IRB staff, IRB Chair, and/or another board member should conduct a pre-review of the report to determine whether the event meets the definition of an UPIRSO. If the event is determined not to be a UPIRSO, the IRB Chair, IRB staff, or a member of the board will acknowledge the report from the Investigator. The IRB staff will provide written documentation of this acknowledgement to the Investigator.
3. If the person conducting the pre-review determines that the event is a UPIRSO, then the report will be provided to the full board for review at the next available meeting. The IRB Chair or their designee may, at his/her discretion, convene an ad-hoc board meeting if the next scheduled IRB meeting is not proximal. Promptness of review will depend on the severity and circumstances of the event.
4. The board may request additional information from the Investigator, sponsor, or IRB staff related to local patient events, safety data, safety monitoring reports, or other relevant information in order to assist with their assessment of the UPIRSO. The board may also request that the Investigator or a sponsor representative attend a meeting to provide additional information.

The IRB also reserves the right to conduct an audit in order to confirm details or obtain more information related to the research study or project or to observe research activities or the consenting process.

5. During review, the board will assess the UPIRSO event and determine what type of action should be taken. Actions may include, but are not limited to:
 - a. Request for modification of the protocol
 - b. Modification of inclusion or exclusion criteria to mitigate the newly identified risks
 - c. Implementation of additional procedures for monitoring subjects
 - d. Corrective and preventative action plans to prevent protocol/regulatory deviations
 - e. Suspension of enrollment of new subjects (if not voluntarily done by the Investigator)
 - f. Suspension of the specific risk-inducing research procedure(s) in currently enrolled subjects (if not voluntarily done by the Investigator)
 - g. Suspension of the research
 - h. Termination of the research
 - i. Provision of additional information about newly recognized risks to previously enrolled subjects
 - j. Request consultation from an individual with additional expertise
 - k. Other actions as determined by the board
 - l. No action required

6. Board decisions or other actions related to UPIRSOs reviewed at a convened board meeting will be documented in the meeting minutes.
7. After board review, the IRB Chair or IRB staff will inform the Investigator of the review and notify him/her of any changes to the IRB approval (i.e. changes to the consent form, additional conditions of approval, etc.) in writing along with a statement of the reasons for its decision. The Investigator will have the opportunity to respond to the Board's decision either in person or in writing.
8. If the Board has determined that the event meets the definition of a UPIRSO, the Institutional Official should be informed of the event in writing. This may be done through direct correspondence, or by providing copies of correspondence or meeting minutes either in paper format or electronically. The Institutional Official or their designee (typically the IRB Chair or an IRB staff member designated by the Chair) will be responsible for reporting the event in writing to the appropriate regulatory authority governing the research:
 - a. Report to OHRP and/or FDA if the activity is governed by them
 - b. Report to DHHS Agency Head (if the activity is part of a federal grant..)

To meet the reporting deadlines stated above, it may be necessary to provide staged reporting, such as an initial report within these timeframes and follow-up reports as new information is gathered.

If the board decides to suspend or terminate the research, the **Suspension and Termination SOP** will be followed.

REFERENCES:

1. 21 CFR 56.108(b)(1), 312.53(c)(1)(vii) and 312.66 requires Investigators to promptly report to the IRB all unanticipated problems involving risks to human subjects and others (UPIRSOs), including adverse events that should be considered unanticipated problems.
2. 21 CFR 812.150(a)(1) requires the investigator to submit a report of an unanticipated device effect (UADE) to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event.
3. 45 CFR 46.103(b)(5)
4. FDA Guidance for Clinical Investigators, Sponsors, and IRBs: <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>

TITLE: Non-Compliance	SOP 15
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PURPOSE:

The purpose of this policy is to set forth the definition and examples of Non-compliance, the requirements for investigator and IRB reporting of Non-compliance, and the procedures for the IRB’s review and management of Non-compliance. This policy fulfills the regulatory requirements of 21 CFR 56.108(b)(1 - 2) and 45 CFR 46.103 (b)(5), which require IRBs establish and follow written procedures for ensuring prompt reporting to the IRB of any changes in approved research activities, and the requirements of 45 CFR 46.109 and 21 CFR 56.109, which mandate IRB review of human research.

DEFINITIONS:

A **Protocol Deviation** is any change, divergence, or departure from the study design or procedures outlined in the research protocol currently approved by the IRB.

Non-compliance is the failure to comply with any Federal regulations governing the research, the policies or procedures of the IRB, or institutional policies governing human research. Examples of Non-compliance include:

- Conducting human research without IRB approval (e.g., before or after expiration of approval, during a suspension of IRB approval, or after termination of IRB approval)
- Disregarding or otherwise violating IRB-approved informed consent procedures (e.g., failing to obtain consent/assent, using unapproved or outdated consent, assent, or information sheets, missing signatures, failing to document consent process)
- Deviating from the protocol approved by the IRB
- Modifying an approved protocol without IRB consent
- Failing to report or delayed reporting of Unanticipated Problems (UPIRSOs) or Serious/Continuing Non-Compliance to the IRB
- Failing to report or delayed reporting of changes to the protocol or drug/device information in a timely manner
- Use of project-specific advertising materials not approved by the IRB
- Failing to maintain adequate records
- Failing to train research team members in the proper procedures
- Conducting research activities at a site that was not approved by the Board
- Failing to follow recommendations by the IRB to ensure the safety of research subjects

Serious Non-compliance is any incident of non-compliance that places a participant at increased risk of harm or compromises the scientific integrity of the data collected for the study.

Continuing Noncompliance: A repeated pattern of noncompliance by an individual investigator or research staff member either on a single protocol or multiple protocols.

PROCEDURE:

Non-compliance is the failure to comply with applicable federal regulations, the policies or procedures of the IRB, or institutional policies governing human research. In some cases, Non-compliance may constitute or may result in Unanticipated Problems Involving Risks or Others (UPIRSOs), which will be reviewed and processed in accordance with the Unanticipated Problems SOP.

Investigator Responsibilities

1. The Principal Investigator is responsible for reporting any issues of Non-compliance with the protocol currently approved by the IRB, regulations, or IRB requirements in writing **within 5 business days** of becoming aware of the event. The report should include the following details:
 - Subject initials and/or subject number, if applicable
 - Description of the event and any relevant circumstances
 - Date the event occurred
 - Date the Investigator or study staff became aware of the event
 - An explanation and corrective action plan for the delay in reporting of the event, if the event was reported after the reporting deadline
 - Confirmation of whether or not the event affects the risk/benefit ratio of the study. If so, an explanation should be included along with an explanation of action to be taken as a result of the event (e.g. revisions to the informed consent form or investigational plan)
 - Description of whether or not changes are warranted to the consent form or protocol as a result of the event
 - An indication of whether the deviation was planned
 - An indication of whether or not the event was initiated to eliminate an immediate, apparent hazard to a study subject. If this is the case, a rationale should be provided.

2. If a deviation to the IRB-approved protocol or other Non-compliance event occurs, the Investigator must make an assessment to determine whether or not the event is reportable. If a Protocol Deviation or deviation to IRB requirements, laws, or regulations meets any of the following criteria, it may be considered Serious Non-compliance and must be reported to the IRB:
 - The deviation affects the rights, safety, or welfare of subjects
 - The deviation compromises the scientific integrity of the data collected for the study
 - The deviation involves serious or continuing noncompliance with federal, state, local or institutional human subject protection regulations, policies, or procedures

3. Planned Protocol Deviations

The Investigator must obtain pre-approval from SDH IRB for planned protocol deviations and changes in research activity as follows:

- If the research is federally funded, conducted under an FWA, or is a clinical investigation of a drug or biologic, then all planned protocol deviations must be submitted to SDH IRB for review and approval prior to implementation, except when necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7)].
- If the research is a clinical investigation of a *device* and the research is not federally funded and not conducted under an FWA, then only planned protocol deviations that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data should be submitted to SDH IRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(a)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7)]. In this case, Protocol Deviations necessary to eliminate apparent immediate hazards to the human subjects should be reported within 5 business days.

The reason for these different requirements regarding planned protocol deviations is that the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) drug and biologic divisions have adopted the regulatory interpretation that every planned protocol deviation is a change in research that needs prior IRB review and approval before implementation; however, the FDA device division operates under a distinct regulation (See 21 CFR 812.150(a)(4)).

IRB Responsibilities

1. Investigators must be educated (i.e., through approval letters, manuals, and/or other training opportunities) by the IRB of their regulatory obligation to report Serious Non-compliance issues promptly after they become aware of them.
2. The IRB has the obligation to review and respond to reports of Serious or Continuing Non-compliance, which may be made to the IRB by the Principal Investigator, a member of the research staff, the Sponsor. Allegations of Non-compliance may be reported to the IRB by an IRB staff or Board member, a research subject, or any concerned party.
3. Upon receipt of a report of Non-compliance, the IRB Chair or designee will conduct a pre-review of the report to determine whether the event meets the definition of Serious or Continuing Non-compliance. If the pre-review determines that the event is neither Serious nor Continuing Non-compliance, the IRB Chair or designee will acknowledge the report from the Investigator. The IRB will provide written documentation acknowledging the reported event(s).

If the person conducting the pre-review determines that the event is Serious or Continuing Non-compliance, then the IRB Chair or designee will provide the report to the full board for review at the next available meeting. The IRB Chair or their designee may, at his/her discretion, convene an ad-hoc board meeting if the next scheduled IRB meeting is not proximal. Promptness of review will depend on the severity and circumstances of the event.

4. The Board may request additional information from the Investigator, research staff, Sponsor, or IRB staff related to local patient events, safety data, safety monitoring reports, or other relevant information in order to assist with their assessment of the Non-compliance issue. The IRB may also request that the Investigator or a sponsor representative attend a board meeting to provide additional information.

If an allegation of Non-compliance is made, the Board may request additional information from the Investigator, complainant, research staff, Sponsor, or other parties. The IRB reserves the right to conduct a site audit to confirm details or obtain more information related to the allegation, research study conduct, or to observe research activities or the consenting process.

5. Upon full board review, the Board will make a determination regarding whether or not the Non-Compliance is either Serious or Continuing. They will also consider and determine what type of action should be taken. Actions may include, but are not limited to:
 - Request for modification of the protocol
 - Modification of inclusion or exclusion criteria to mitigate the newly identified risks
 - Implementation of additional procedures for monitoring subjects
 - Corrective and preventative action plans to prevent future protocol/regulatory deviations
 - Suspension or Termination of all or part of the research
 - Modification of informed consent documents to include a description of newly recognized risks
 - Provision of additional information about newly recognized risks to previously enrolled subjects
 - Request consultation from an individual with additional expertise
 - Other actions determined appropriate by the Board
 - No action required

Board decisions or other actions related to Non-compliance that are reviewed at a convened board meeting will be documented in the meeting minutes.

6. After Board review, the IRB Chair or designee will inform the Investigator of the review and notify him/her of any changes to the IRB approval (e.g. changes to the consent form, additional conditions of approval, etc.) in writing along with a statement of the reasons for its decision. The Investigator will have the opportunity to respond to the Board's decision either in person or in writing.

If the Board has determined the Non-compliance to be Serious or Continuing, the IRB Chair or designee will be responsible for reporting the event in writing to the appropriate regulatory authority governing the research (e.g. FDA and/or OHRP) and to the IRB's Institutional Official within one month of review by the IRB. This may be done through direct correspondence, or by providing copies of correspondence or meeting minutes either in paper format or electronically. In addition, when an HCA facility is impacted by Non-

compliance, the CEO(s) of the impacted facilities will also be promptly informed of the event in compliance with company policies.

If the Board decides to suspend or terminate the research, the **Suspension and Termination SOP** will be followed.

REFERENCES:

1. 45 CFR 46.103(b)(5)(i), mandating compliance with “[w]ritten procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of...any serious or continuing noncompliance with [45 CFR 46(A)] or the requirements or determinations of the IRB... .”
2. 45 CFR 46.109; 21 CFR 56.109: IRB Review of Research, mandating IRB review and approval of human participant research.
3. 21 CFR 56.108(b)(2), mandating compliance with “[w]ritten procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of...any serious or continuing noncompliance with [21 CFR 56(C)] or the requirements or determinations of the IRB... .”
4. FDA Guidance for Clinical Investigators, Sponsors, and IRBs
<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>
5. DHHS Attachment C: Recommendation on Protocol Deviations
<https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2012-march-30-letter-attachment-c/index.html>
6. HCA Policy: CSG.FED.002, Research Misconduct in PHS Grants, available in Atlas

TITLE: Suspension or Termination of IRB Approval	SOP 16
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PURPOSE:

The purpose of this policy is to set forth the policies and procedures governing Suspension and Termination of IRB approval of a research activity. This policy fulfills the regulatory requirements of 21 CFR 56.108(b)(3) and 45 CFR 46.103(b)(5), which require IRBs to establish and follow written procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any Suspension or Termination of IRB approval of a research activity

DEFINITIONS:

Suspension of IRB Approval is the temporary withdrawal of IRB approval for all or part of a research activity, but is short of permanently stopping all research procedures.

Termination of IRB Approval is the permanent withdrawal of IRB approval for all research activity.

PROCEDURES:

The IRB has the authority to suspend or terminate any research activity that is not being conducted in accordance with the IRB’s requirements, or that has been associated with unexpected serious harm to subjects.

IRB Responsibilities

The IRB may decide to suspend or terminate a study for the following reasons:

- Unanticipated problems involving risks to human subjects or others
- The Board determines that the risk/benefit ratio is no longer appropriate
- Serious Non-compliance with the regulations or with IRB requirements
- Continuing Non-compliance with the regulations or with IRB requirements
- Failure to adhere to regulations, laws, or the requirements or determinations of the IRB
- Other reasons determined appropriate by the board

It is not considered a suspension or termination when a PI, prior to or after discussion with the IRB, voluntarily agrees to change the research activity, add additional restrictions or close the research. Suspension and terminations are generally used for when the PI is not willing to adhere to the parameters put forth by the IRB.

Suspension

The Board may decide to suspend a specific research activity or suspension may include additional related projects. The Board will consider the particular issue(s) at hand and make a determination regarding which activities will be suspended. This may include suspension of enrollment only (while allowing study procedures to continue for previously enrolled subjects), or suspension of

some or all research-related activities, or suspension of a specific Sub-Investigator or research staff member from performing certain procedures.

Should Suspension occur, the IRB Chair or designee will document the Board's determination in a writing to the Investigator. The letter shall also include the Board's rationale for the Suspension and should clearly explain what is required for the Investigator to obtain reinstatement of IRB approval. The IRB Chair or designee will ensure that the Principal Investigator is notified of the Suspension promptly after the Board's decision.

Any Suspension shall be promptly reported to the following:

- The Principal Investigator
- SDH IRB's Institutional Official (IO)
- If Federally funded, the granting department or agency head, as well as OHRP. Instructions for reporting to OHRP are on their website.
- If the research is an FDA-governed study, the FDA. Instructions for reporting to the FDA are on their website.

The Investigator shall be informed of Suspension promptly. This may be done through direct correspondence, or by providing copies of correspondence or meeting minutes either in paper format or electronically. In addition, when an HCA facility is impacted by Suspension, the CEO(s) of the impacted facilities will also be promptly informed of the event in compliance with company policies.

Under Suspension, the research activity remains "active" and thus still requires Continuing Review reports to be submitted in order to avoid expiration of IRB approval.

Termination

If the Investigator has failed to provide the required completed documents per the conditions of Suspension, and/or the Board finds that Termination of the research is appropriate, the Board may elect to terminate IRB approval. The Board should consider the issue at hand and make a determination regarding whether any activities will need to continue after termination, such as those required to safeguard the rights or welfare of research subjects. The Board may require the Investigator to notify current participants in writing that the study has been terminated and stipulate withdrawal procedures. Termination typically includes the termination of IRB approval for all research activities. However, the board may elect to allow certain project activities, such as safety follow-up visits, to continue. These details should be clearly communicated to the Investigator in the Termination Letter.

Should Termination occur, the IRB Chair, IRB members, or IRB staff will document the Board's determination in writing to the Investigator. This correspondence should also explain the board's rationale for the Termination and may include a request for a Final/Close-Out Report, if applicable. The IRB Chair, IRB members, or IRB staff will ensure that the Principal Investigator is notified of the Termination as soon as possible, promptly after the Board's decision.

Any Termination shall be promptly reported to the following:

- The Principal Investigator
- SDH IRB's Institutional Official (IO)
- If federally funded, the granting department head or agency head as well as the OHRP. Instructions for reporting to OHRP are on their website.
- If FDA governed study, to the FDA. Instructions for reporting to the FDA are on their website.

The Investigator shall be informed of Termination promptly. This may be done through direct correspondence, or by providing copies of correspondence or meeting minutes either in paper format or electronically. In addition, when an HCA facility is impacted by Termination, the CEO(s) of the impacted facilities will also be promptly informed of the event in compliance with company policies.

Investigator's Responsibilities

Once the Investigator or his/her designated staff member receives a notification to cease research activities, he/she must adhere to the conditions outlined in the Board's letter.

Appeals

Should the Investigator wish to appeal the Board's decision, he/she will have an opportunity to do so in writing or in person. This can be done by emailing the IRB Chair or IRB Coordinator to submit the written appeal or to submit a request for an appeal in person so that the proper arrangements can be made with the Board. The appeal will be considered at the next convened IRB meeting. The Board will consider the request and review any supporting documentation submitted. Once a final decision has been made, the IRB Chair or designee will promptly provide written correspondence documenting the Board's final decision to the Investigator.

Final Close-Out

Even if a Suspension or Termination of the research has occurred, the Investigator should still provide a Final/Close-Out Site Report to SDH IRB for review at the conclusion of the project in order to comply with regulations.

REFERENCES:

1. 45 CFR 46.103(b)(5)
2. 45 CFR 46.113 Suspension or termination of IRB approval
3. 21 CFR 56.108(b)(3)
4. 21 CFR 56.109 "An IRB shall review and have the authority to require modifications in... or disapprove all research activities" and "shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of

the reasons for its decision and give the investigator an opportunity to respond in person or in writing.”

5. 21 CFR 56.113- “An IRB shall have authority to suspend or terminate approval of research that is not begin conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration”.
6. Reporting of Suspension/Termination to FDA:
<https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/reportproblemsto-fda/ucm136102.htm>

TITLE: Closure, Expiration, and Reinstatement	SOP 17
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PURPOSE:

The purpose of this policy is to set forth the procedures for Closure and Expiration of IRB Approval. This policy fulfills the regulatory requirements of 21 CFR 56.108(a)(3) to ensure prompt reporting of changes in research activity and 45 CFR 46.103(b)(5), which require IRBs to establish and follow written procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any Suspension or Termination.

DEFINITIONS:

Research (according to OHRP) “means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Closure occurs when the Principal Investigator submits a Final/Close-Out Report to the IRB to indicate that all study activities have ceased. “Closure” for the purposes of this section is considered to be the closure of IRB oversight of the non-exempt human subject research activities engaged in by the Principal Investigator. After IRB closure, it is likely that additional study activities will take place at the local Institution (albeit unless transferred to another IRB, non-exempt research with human subjects may not continue to be engaged in by the Investigator) or elsewhere (as in a study involving multiple centers where the Institution has completed their engagement in non-exempt research activities but other centers or a third party sponsor may continue non-exempt activities under their own independent IRB oversight).

Expiration is defined as the reaching of an IRB expiration date without the investigator requesting (or IRB approving) a continuing review extending that date.

PROCEDURES:

Closures

Ongoing approval of a research project at least annually is required so long as the project continues to involve human subjects. A research project no longer involves human subjects once the investigators have finished obtaining data through interaction or intervention with subjects or obtaining identifiable private information about the subjects, which includes the using, studying, or analyzing identifiable private information. Once all such activities described in the IRB-approved protocol are finished, the research project no longer needs to undergo continuing review.

Natural Closures: Given the higher risk nature of FDA governed research, research that otherwise may no longer need continuing review by an IRB has more strict criteria than all other research.

For FDA governed research: Generally, an FDA governed study no longer needs IRB oversight when the following criteria is reached¹²:

- the research is permanently closed to the enrollment of new subjects by the Principal Investigator;
- all subjects enrolled by the Principal Investigator have completed all research-related interventions;
- there are no planned long-term follow-up data gathering activities on subjects enrolled by the Principal Investigator; AND
- the Principal Investigator has completed all his/her data analysis (or, as may be the case in a sponsored multicenter study, the Principal Investigator is not conducting the data analysis).

For all other research: Unless an IRB determines otherwise (i.e. why Continuing Review is necessary for the protection of human subjects), Continuing Review of research is not required by the IRB (i.e. neither by convened board nor Expedited Review) in the following circumstances:

- Research eligible for Expedited Review (as initial review or continuing review) in accordance with the criteria from Expedited Review;
- Research reviewed by the IRB in accordance with the Limited IRB Review option as required for IRB Exempt Status;
- Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
 - Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
 - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

Administrative Closures: The IRB or Institution administration may also administratively close IRB oversight of the research at any time and for any purpose. This type of closure is not considered a “termination” that triggers regulatory reporting requirements but simply an administrative closing (noting that the Institution itself may also initiate this administrative closure). In these instances, should it be the desire of the Institution to allow the Investigator to continue with non-exempt research activity, the IRB should cooperate with the transition to another qualified IRB in a manner that assures uninterrupted IRB oversight. Examples of situations when administrative closure of a study generally occur are as follows:

- The investigator/staff are no longer affiliated with institution.
- the Institution itself is no longer engaged in the research (although research activity may continue elsewhere).
- The Institution Official or IRB chooses to transition oversight to an external IRB.
- It is determined by the Institution or IRB that the IRB is currently (or expected to be) no longer able to give adequate oversight (i.e. due to change of membership, change of IRB resources etc.).

¹² Noting, however, that the continuing review of a protocol may reach the point of Expedited Review; for example when a protocol reaches the point where 1) the research remains active only for long-term follow-up of subjects (the research is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions) or 2) where the remaining research activities are limited to data analysis.

Non-IRB Administrative Monitoring: After closure of local IRB oversight, should additional research activity continue (e.g. activities that do not need continuing review such as long term follow-up or data analysis in a non-FDA governed study, activities deferred to the oversight of external IRBs, etc.), the Institution may desire to maintain an accounting of such continuations to which this responsibility may be assigned to the IRB Coordinator at the Institution's convenience. When this occurs, such periodic queries from the IRB Coordinator regarding study continuance are not to be construed as or considered requests for Continuing Reviews by the IRB but merely an operational request on behalf of the Institution. The IRB Coordinator may also request an affirmation that the remaining activities have not changed in a manner that would require IRB oversight.¹³

Investigator Responsibilities:

Once all research activities are complete, the Principal Investigator must submit a Final/Close-Out Site Report to the IRB. This form should provide the IRB with final enrollment numbers and a summary of Unanticipated Problems (UPIRSOs) and Serious/Continuing Non-compliance (e.g. significant protocol deviations) that have occurred since the last Continuing Review.

For research being conducted under an IDE, regulations require that the Investigator submit a final report to the sponsor and to the reviewing IRB within 3 months after termination or completion of the investigation, per 21 CFR 812.150(a)(6).

The Investigator should submit a Final/Close-Out Site Report to the IRB when the following conditions have been met:

- The research is permanently closed to enrollment at the site(s) approved by SDH IRB
- All subjects enrolled at the site(s) have completed all research-related interventions and interactions, including those related to collection of long-term follow-up data
- No additional identifiable private information about the subjects is being collected, used, studied, or analyzed at the site.

The Investigator must maintain study records for a minimum of 3 years after the end of the study.

IRB Responsibilities:

Once the IRB receives a Final/Close-Out Site Report, a member of the IRB or designated person will acknowledge the report. If additional information is required of the Principal Investigator, this may be requested or verified. In addition, IRB member or designee may use their discretion to defer the review of the report at an upcoming convened board meeting.

Expiration of IRB Approval

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, the IRB approval expires automatically and the research must stop except for where the IRB finds that it is in the best interest of the individual subjects to continue

¹³ This type of non-IRB administrative monitoring can also be done for studies determined to be exempt as well as research deferred to external IRBs.

to participate in the research interventions or interactions until their orderly termination. When this happens, no new enrollment can occur.

Investigator Responsibilities:

The Investigator is responsible for ensuring that the research has current IRB approval by confirming this via formal correspondence before conducting any research activities. The Principal Investigator is ultimately responsible for assuring that the IRB receives the Continuing Review Site Report and supporting documentation in a timely manner for IRB review. Failure to do so may result in expiration of IRB approval.

IRB Responsibilities:

Upon initial or continuing review of research, the IRB should indicate the date on which IRB approval expires on the initial or continuing review approval letter. Although the IRB may send a courtesy expiration reminder to the Principal Investigator or their designated contact person, this is not a requirement.

When an IRB approval has expired, the cessation of activity requiring IRB oversight on that date is not considered an IRB suspension or termination and thus does not require reporting to the federal agencies as a Suspensions or Terminations. However, should the Investigator continue to conduct non-exempt human subjects research activities without the required IRB oversight, this may be reportable to OHRP, FDA, and to the Institutional Official as Serious or Continuing Non-compliance.

If IRB approval for a research study expires, the IRB will provide the Principal Investigator with a letter to notify them that IRB approval has expired and stating that research activities must cease.

Expiration of IRB approval does not need to be reported to the OHRP or FDA as it is not a suspension or termination of IRB approval, however serious or continuing noncompliance with regulations still must be reported (*e.g.*, an investigator continuing to perform the research after repeatedly being notified of IRB approval expiration).

Please refer to the Non-compliance SOP for more information.

Reinstatement

Reinstatement for Closed Studies

If a research study is closed by the submission of a Final/Close-Out Site Report to the IRB, the investigator may request reinstatement of the study at any time before the last IRB approval expiration date by submitting a request in writing to the IRB. This request may be reviewed via Expedited Review and approved by the Chair or another Expedited Reviewer who is a member of the IRB. Any reinstatement requests received after the last IRB approval expiration date may be considered by the Chair or IRB on a case-by-case basis. The Chair or the IRB will use their discretion to determine whether or not the request will be considered and what supplemental

documents or information may be required. At a minimum, a Continuing Review Submission must be submitted for review.

Reinstatement for Expired Studies

If a research study has been administratively closed by the IRB due to the expiration of IRB approval, the investigator may request reinstatement of the study at any time before one year after the last IRB approval expiration date. In these cases, the investigator must submit a request in writing to the IRB. This request may be reviewed via Expedited Review by the Chair or another Expedited Reviewer, or by the Full Board, depending upon what level of review the project is eligible for. Any reinstatement requests received after the last IRB approval expiration date may be considered by the Chair or IRB on a case-by-case basis. The Chair or the IRB will use their discretion to determine whether or not the request will be considered and what supplemental documents or information may be required. At a minimum, a Continuing Review Submission must be submitted for review.

ATTACHMENTS/REFERENCES:

1. 812.150(a)(6) Final reports to IRB for studies conducted under an IDE.
2. 45 CFR 46.103(b)(5)
3. 21 CFR 56.108(b)(3)
4. Guidance on Continuing Review:
<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-continuing-review-2010/index.html>

TITLE: Maintenance of Federal Registrations	SOP 18
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PURPOSE:

The purpose of this policy is to set forth the process for maintenance of registration with DHHS for St. David’s HealthCare Institutional Review Board (SDH IRB).

PROCEDURE:

Initial Registration

1. The IRB will register with the Department of Health and Human Services (DHHS) IRB database according to regulation. Specifically, the IRB will be registered with the following agencies/departments under their respective conditions *prior* to review of research falling under their jurisdiction:
 - a. The Food and Drug Administration (FDA) if:
 - i. The IRB is located in the United States and reviews clinical investigations regulated by FDA under sections 505(i) or 520(g) of the Food, Drug and Cosmetic Act; or
 - ii. The IRB is located in the United States and reviews clinical investigations that are intended to support applications for research or marketing permits for FDA-regulated products.
 - b. The Office for Human Research Protections (OHRP) if the IRB reviews research involving human subjects conducted or supported by the Department of Health and Human Services (DHHS).
2. The IRB must provide all information required by the respective registrations, usually through the online registration system located at <http://ohrp.cit.nih.gov/efile>.

Renewal of Registration

1. The IRB must renew its registration prior to its expiration (usually every three years), taking whatever means are necessary to remind itself of such expiration date. All information will be updated at this renewal cycle.

Updating Registration Information Prior To Renewal

1. The IRB must update its information upon the following events and within the regulated timeframes:
 - a. **For Both FDA and OHRP Registrations:**
 - i. **Change of IRB Contact:** Within 90 days of the change.
 - ii. **Change of IRB Chair:** Within 90 days of the change.
 - iii. **Change in IRB Board composition:** Within 30 days of the change.
 - iv. **Decision to disband the IRB:** Within 30 days of permanent cessation of the IRB's review of research.

- b. **For FDA Registrations:**
 - i. **Decision to review new types of FDA-regulated products** (such as a decision to review studies pertaining to devices or food additives where the IRB was only registered to review drug products): Within 30 days of the decision.
 - ii. **Decision to discontinue reviewing clinical investigations regulated by FDA:** Within 30 days of the change.
- c. **For OHRP Registrations:**
 - i. **Decision to discontinue reviewing DHHS conducted or supported research:** Within 30 days of the cessation of review of all DHHS conducted or supported research.

REFERENCES:

N/A

TITLE: Humanitarian Use Device (HUD) and Expanded Access Use	SOP 19
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Treatment Uses of Humanitarian Use Devices (HUD) Under Humanitarian Device Exemptions (HDE)

DEFINITIONS:

Humanitarian Use Device (HUD): a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year ([Section 3052 of the 21st Century Cures Act \(Pub. L. No. 114-255\)](#)).

Humanitarian Device Exemption (HDE): a marketing application for an HUD (Section 520(m) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)). An HDE is exempt from the **effectiveness** requirements of Sections 514 and 515 of the FD&C Act and is subject to certain profit and use restrictions.

Limitation of Policy:

This policy only applies to the **treatment use** of a HUD in a non-investigational setting. This means that no data will be collected or be submitted as part of a pre-market approval application to the FDA. If HUD use falls under an investigational study in which data is being collected for research or in support of an application for premarket approval to the FDA, standard rules of review of investigational devices apply. (See Initial and Continuing Review SOP).

In the case of **emergency use** of a HUD, the standard policies related to emergency use of an investigational device/product will apply (See Emergency Use SOP).

PROCEDURE:

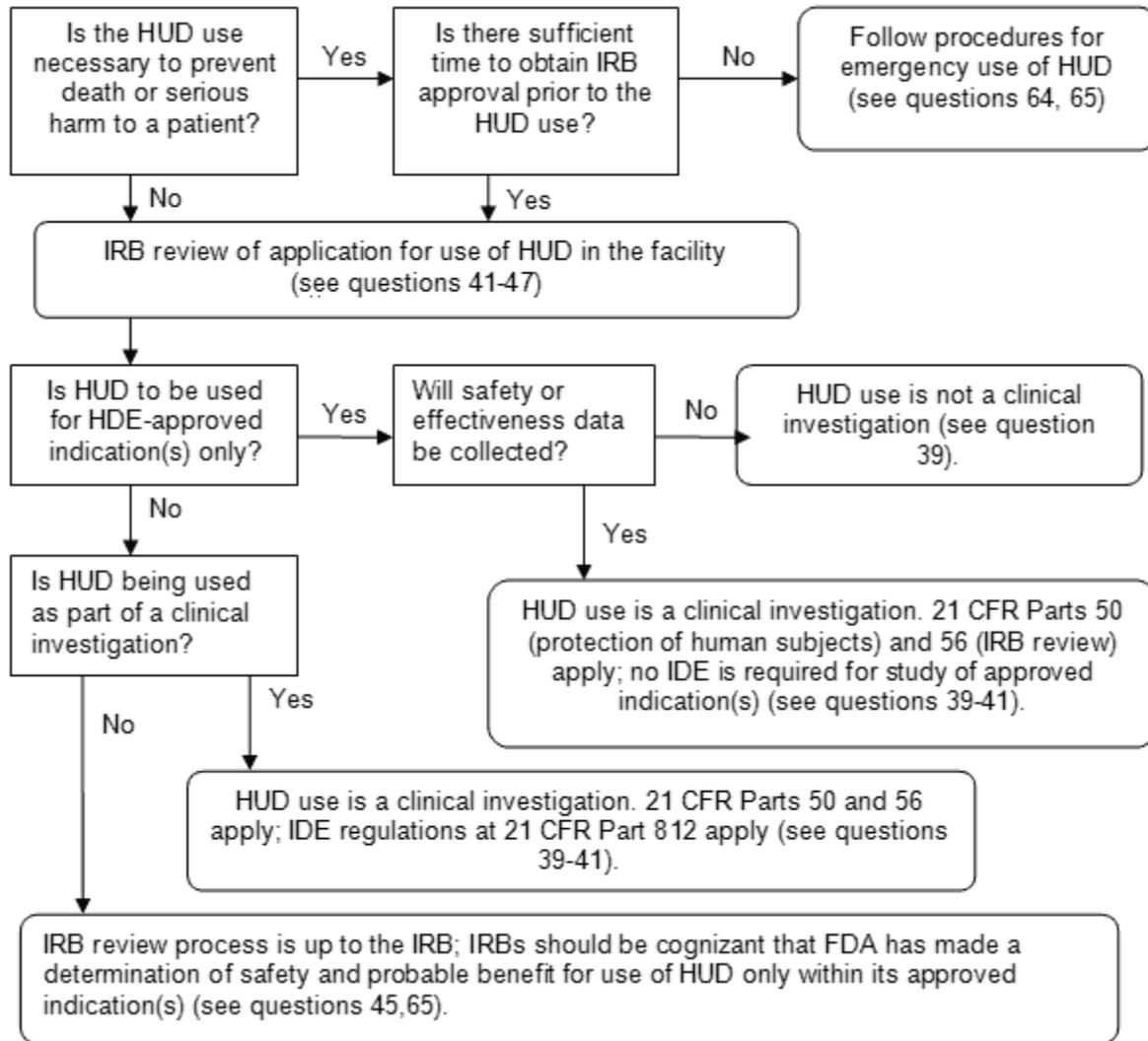
Note: The federal Humanitarian Use Device (HUD) regulations permit the marketing of a limited group of devices (HUDs) if the FDA has approved the sponsor’s Humanitarian Device Exemption (HDE) application **and** an IRB has approved the use of the device.

1. The IRB must first verify that the HDE is to be used primarily for non-research medical care (i.e. diagnosis or treatment only) and not under a clinical investigation. Assuming treatment use only, this makes this a non-research review function for the IRB. This includes assuring that there are no additional activities surrounding the use of the HUD/HDE that do constitute human subjects research and if there is, then a separate review of the research is required by the IRB independent of the HDE approval.
2. Unless an emergency exists, the full committee must do the initial review of an HDE¹⁴ (see Emergency Use- Non-Research SOP).

¹⁴ Regulations specifically state that the initial review must be done via convened board and not by expedited review. All continuing reviews, however, can be done via expedited review. If a physician wishes to use an HDE

3. The IRB generally approves use of the HDE by default without any further restrictions (subject to continuing review and the reporting of UPIRSOs) OR may impose additional restrictions including but not limited to:
 - a. Use only under an approved clinical protocol;
 - b. Use only on a case-by-case basis; OR
 - c. Use under other restrictions imposed by the IRB
4. As use of an HDE for treatment purposes does not constitute research the IRB shall be able to use the Expedited Review procedures for continuing review, unless otherwise determined by the Chair or the Committee.
5. If the HDE will be used in research (i.e. such as in a clinical investigation to gather data to convert the FDA classification from HDE to PMA status) or there is additional affiliated research on the HDE treated population (i.e. surveys, quality of life evaluations), the IRB shall follow its usual policies and procedures for reviewing such a research protocol including but not limited to the Significant Risk / Non-Significant Risk determination if the research is a clinical investigation.
6. The IRB does not oversee treatment consent forms; the Institution is responsible for these when the HDE is used for treatment purposes. Research consent forms are not appropriate for HDEs approved for treatment only.

not under current IRB approval, absent an emergency use as defined elsewhere in this policy, they must wait until a convened board meeting occurs.



15

Review and Approval for Expanded Access Use (a.k.a. Compassionate Use)

Under their Expanded Access Program, the FDA may authorize the use of an investigational drug, device or biologic product to treat patients with serious or life-threatening diseases or conditions that have no satisfactory or comparable alternative therapy to diagnose, monitor, or treat the disease or condition. While the expanded access use may not be under a clinical investigation protocol, its use is still investigational thus the FDA requires IRB approval and all required elements of informed consent.

1. The IRB must first verify that the FDA has granted Expanded Access for the therapeutic product (i.e. an Expanded Access IND or IDE). Alternatively, the IRB can grant conditional approval pending verification that the FDA has granted expanded access but this communication must be clear that the use of the product cannot begin until the IRB obtains such verification.

¹⁵ HUD Decision Chart obtained from:

<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm110194.htm>

2. In general, initial review for Expanded Access can only be approved by a convened board of the IRB¹⁶.
3. In cases of single patient expanded access, initial review may be provided by the Chair (or designee) outside of a convened meeting of the IRB. In this case, the physician submitting the IND must include a “Request for Authorization to Use Alternative IRB Review Procedures” by selecting the appropriate box on the Form 3926 to request a waiver of full IRB review under § 56.108(c). FDA Guidance indicates that such a waiver is appropriate for individual patient expanded access INDs when the physician obtains concurrence by the IRB Chair or another designated IRB member before treatment use begins, in lieu of obtaining IRB review and approval at a convened IRB meeting at which a majority of the members are present. A physician submitting an individual patient expanded access IND using Form FDA 1571 may include a separate waiver request with their application to the FDA.
4. The IRB will provide documentation of their review in writing to the investigator.
5. All other IRB policies apply (i.e. continuing review, reporting of UPIRSOs, etc).

REFERENCES:

1. FDA Guidance: Expanded Access to Investigational Drugs for Treatment Use- Questions and Answers, Guidance for Industry, Updated October 2017, <https://www.fda.gov/media/85675/download>.
2. FDA Webpage: For Physicians: A Guide to Non-emergency Single Patient Expanded Access Submissions, <https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-guide-non-emergency-single-patient-expanded-access-submissions>

¹⁶ There is no category in the list of eligible Expedited Reviews for Expanded Access. Subsequent minor changes or continuing reviews may be done via expedited review if the criteria is met.

TITLE: Emergency Use (Non-Research)	SOP 20
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PURPOSE:

The purpose of this SOP is to define use of investigational agents in emergent situations for non-research purposes.

DEFINITIONS:

Emergency Use is defined as the use of an investigational drug, device or biological product or a humanitarian use device with a human subject in a life-threatening situation in which all three regulated criteria are met:

1. **The person is in a life-threatening situation.** **Life-threatening**, as defined by the FDA [21CFR56.102(d)], includes the scope of both life-threatening and severely debilitating, as defined below:
 - i) **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted, and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
 - ii) **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
2. **There is no standard acceptable treatment available**, and
3. **There is not sufficient time to obtain IRB approval.**

BACKGROUND:

Emergency Exemption from Prospective IRB Approval

This exemption allows for one emergency use of a test article (or Humanitarian Use Device, or HUD) without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The Principal Investigator should notify the IRB prior to such use whenever possible. However, this notification should not be construed as an IRB approval. The IRB does not have a role in giving “permission” prior to the use of a non-FDA approved investigational drug or device in an emergent situation. This is entirely at the discretion of the treating physician and, where indicated,

the hospital pharmacy. The Investigator is still required to obtain patient informed consent even under these emergent circumstances unless it is not feasible. Notification should be used by the IRB to initiate tracking to ensure that the investigator files a report to the IRB within the five working day time-frame. The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. An IRB must either convene and give "full board" approval of the emergency use or, if the three conditions above are met and it is not possible to convene a quorum within the time available, the use may proceed without any IRB approval.

Some manufacturers will agree to allow the use of the test article (or Humanitarian Use Device), but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, the IRBs may send to the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements. Although, this is not an "IRB approval," the acknowledgment letter has been acceptable to some manufacturers and has allowed the shipment to proceed.

Exception From Informed Consent Requirement

Even for an Emergency Use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from, the subject.
3. Time is not sufficient to obtain consent from the subject's legal representative.
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life and, if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the Principal Investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article.

POLICY:

For emergency use of an investigational drug or device without FDA market approval for non-research purposes, the IRB requires the following three steps:

- In an emergent situation, a physician may use the drug or device to save the patient's life. He/she must notify the IRB in writing within five days after use. This must include documentation of the emergency use in the specific patient, documentation supporting how this event meets the criteria for being considered a life-threatening/severely debilitating situation (as described in the definition above) and the signed patient informed consent. If

written consent was not obtained, then the physician must submit written documentation that the four criteria under the “Exception From Informed Consent Requirement” section above in this policy were met.

The exemption allows for only one (1) emergency use of a test article without prospective IRB review. Any subsequent use of the investigational product at the institution must have prospective IRB review and approval; however, it would be inappropriate to deny emergency treatment to subsequent individuals if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

REFERENCES:

1. 21 CFR 50.24
2. FDA Information Sheet: Emergency Use of an Investigational Drug or Biologic, dated January 1998, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-investigational-drug-or-biologic>.

TITLE: Waiver of Consent for Planned Research in Emergency Settings	SOP 21
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POLICY:

- A. The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:
1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
 2. Obtaining informed consent is not feasible because:
 - i) The subjects will not be able to give their informed consent as a result of their medical condition;
 - ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
 - iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
 3. Participation in the research holds out the prospect of direct benefit to the subjects because:
 - i) Subjects are facing a life-threatening situation that necessitates intervention;
 - ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
 - iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
 4. The clinical investigation could not practicably be carried out without the waiver.
 5. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
 6. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (1)(g)(v) below.

7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 - i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
 - ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
 - iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
 - iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
 - v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
- B. The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
- C. The IRB determinations required by paragraph (1) of this section and the documentation required by paragraph (5) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 21 CFR 56.115(b).
- D. Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or

investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 21 CFR 312.30 or 21 CFR812.35.

- E. If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (1) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

REFERENCES:

1. 21 CFR 50.24
2. 21 CFR 56.115(b).
3. 21 CFR 312.30
4. 21 CFR 812.35