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**Boston
Children's
Hospital**

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Manager
Department Research
Applicability Boston Children's
Hospital- Policies
& Procedures

IRB Autonomy Policy/Procedure

Internal Approval

SVP, Research

EVP & Chief Scientific Officer, Research

Scope

This policy describes the areas considered during the Institutional Review Board (IRB) review process, which allow the IRB to ensure the protection of human subjects and its ability to remain autonomous.

Policy Statements

Boston Children's Hospital has established two Institutional Review Boards (IRB):

1. IRB #1 (IRB Registration #IRB00000352)
2. IRB #2 – Rapid Response (IRB Registration #IRB00010042).
 - a. IRB #2 has been designated as a rapid response IRB and is constituted to be able to meet quickly when an urgent need arises.
 - b. The need to meet rapidly could be based on timing and the need to begin research quickly (i.e. disaster research, research involving time sensitive outbreaks of disease, etc.).

Both IRB's are responsible for reviewing "research with human subjects," as defined by the Department of Health and Human Services (HHS), and "clinical investigation," as defined by the Food and Drug Administration (FDA).

1. To accomplish this goal, the IRBs review research protocols to consider those issues in design and conduct that could potentially affect the safety, rights, and welfare of human subjects.

2. The IRBs' primary responsibility is the protection of research subjects.
3. There is no individual, group of individuals, or entity within or outside Boston Children's Hospital that can override a decision of the IRBs, except to add restrictions or to disapprove an already approved activity.
4. The IRBs function independently of other entities in the organization.

Authority of the IRB

Boston Children's Hospital grants the IRB the following authority:

1. to approve, require modifications to secure approval, or disapprove all research activities overseen and conducted by the organization.
2. to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements or that is associated with unexpected serious harm to participants.
3. to observe, or have a third party observe, the consent process; and
4. to observe or have a third party observe, the conduct of the research.

Officials of Boston Children's Hospital may not approve any research that has not been approved by the Institutional Review Board.

Other IRB items of authority:

1. The IRB may consider any issue or concern it deems necessary in order to adequately protect the rights and welfare of research subjects.
2. The IRB may request references, as appropriate, and may consult with any individual it deems necessary in order to assure adequate review.
3. As part of its review, the IRB must determine the period of time until the next continuing review. Additional reviews may occur more frequently than once per year, if necessary.

Independence of the IRB

No individual or group of individuals may inappropriately try to influence the deliberations and decisions of the IRB.

Any IRB member may report any attempt to influence the decision of the IRB to the Vice President of Research Administration and the Chief Executive Officer of Boston Children's Hospital.

The Vice President Research Administration and the Chief Executive Officer of Boston Children's Hospital will investigate and resolve the incident so there is no undue influence placed on the IRB's activities and determinations.

Procedures

The list of functions described below are by no means complete and serves only as guidance. For further criteria, see the *IRB Reviewer Worksheets*.

Scientific Review and Merit

The IRB has the authority to examine the scientific study design to determine its impact on the rights and welfare of human subjects. Although each department is required to establish a scientific review process, the IRB also reserves the right to review the science as it impacts the risk/benefit assessment and human subject protections.

1. Are the specific aims clearly defined and specified?
2. Are there adequate preliminary data to support the conduct of the protocol?
3. Is there appropriate justification for the research?
4. Is the proposed design adequate to answer the questions being asked?
5. Are the objectives likely to be achievable within the conduct of the protocol?
6. Are any plans for randomization and/or placebo and control arms described and justified?

Principal Investigator (PI) and Research Staff Qualifications

The IRB considers the qualifications of the PI when reviewing protocols. It is also the responsibility of the Department Chair or Division Chief to confirm, as part of their sign off on the protocol, appropriate PI and research staff credentials. This type of information is most accessible to the Department Chair or Division Chief.

The IRB may ask for any type of information it requires in order to verify that individuals have the appropriate qualifications and expertise to conduct the research safely on individuals listed as investigators or research support staff.

Resources

The IRB takes into consideration the resources available to ensure that all aspects of the project and follow-up are conducted rigorously and with due regard for the safety and well-being of the research subjects.

1. Are there appropriate resources (e.g., equipment, lab capacity, space, etc.) to ensure the optimal safety of the research subjects?
2. Does the investigator have the resources to assure the appropriate monitoring of subjects during and after the research?
3. Is there a possible need for counseling or support services during and/or as a result of the study; and, if so, are these resources available?
4. Are there provisions for research related injuries?

Equitable Selection of Subjects and Inclusion/Exclusion Criteria

The IRB determines whether the selection of subjects is equitable. In making this determination, the IRB must be certain there is a fair sharing of the burdens and benefits of the research.

1. Is the subject population selected so that the burdens fall on those most likely to benefit?
2. Does the nature of the research justify the proposed subject population?
3. Are the criteria for the source of subjects clear and defined?
4. Have the inclusion and exclusion criteria taken into consideration subject safety and welfare concerns?
5. If women, children, or minorities are excluded, has this been adequately justified?
6. What provisions are made to include non-English speaking individuals? If they are excluded, is there adequate justification?
7. Are there adequate data to permit the inclusion of children/adolescents?

Recruitment

The IRB reviews the procedures utilized to recruit research subjects. Such procedures include any type of posting, flyer, notice, letter, and approaching of research subjects for the purpose of recruiting for the research.

1. Are the methods for recruitment clearly defined?
2. Are the timing and location for recruitment acceptable?
3. Are the recruitment materials clear, comprehensive, and not overstate the benefits of the research?
4. Are there acceptable procedures for screening subjects prior to recruitment?
5. If recruitment must occur during a critical or stressful period, what precautions have been taken to eliminate potential coercion?
6. Have the recruitment materials and practices been developed to avoid undue influence in deciding whether or not to participate?

Research Protocol Procedures

The IRB reviews in detail the procedures required for the conduct of the research protocol to ensure that the risks are minimized, and the benefits are maximized. The IRB reviews the procedures to ensure they may be conducted safely, and with appropriate oversight and expertise. The IRB also reviews what will happen with the information collected during the study, and whether there are adequate provisions for follow-up if necessary.

1. Is there an adequate rationale for the proposed procedures?
2. Has the investigator provided a complete description of the procedures to be performed,

- including the associated risks and benefits?
3. Is there a clear differentiation between those procedures that may be required for standard care and those required for research purposes?
 4. What will occur with the information the procedures provide?
 5. Are there plans to inform research subjects about their specific data, and data from the study results in general?
 6. When appropriate, are the procedures and assessment combined with those that are already performed for diagnostic or treatment purposes?

Drug and Device Considerations

If a research protocol involves the use of drugs, devices, or biologics, the IRB must ensure that the protocol complies with all relevant FDA regulations. Additional detailed IRB policies have been developed for investigational drugs and devices. The following are some of the general issues that are considered by the IRB:

1. Is the status of the drug or device adequately described?
2. If necessary, is the supporting documentation from the sponsor included with the submission (investigational brochure, package inserts/labeling, FDA letters of determination regarding status of the drug device)?
3. What have the preclinical or initial clinical trials shown?
4. Is the phase of the study (Phase 1, 2, or 3) appropriate for investigational drugs?
5. If the study involves a marketed drug/device for an unapproved indication is an Investigational New Drug (IND) or Investigational Device Exemption (IDE) necessary?

Data Analysis and Data Safety Monitoring Plan (DSMP)

Although data analysis and the establishment of a data and safety monitoring plan (DSMP) are often reviewed as part of the departmental scientific review process, in order to maximize benefits and minimize potential harm to subjects, the IRB has the responsibility for ensuring that the data obtained from the study will be useful. In addition, it is the IRB's responsibility to be certain that an appropriate data and safety monitoring plan exists for all protocols as appropriate for the nature of the study. The following are some considerations:

1. Is the rationale for the number of subjects reasonable?
2. Are there defined and justified plans for data and statistical monitoring?
3. Have endpoints and stopping rules been defined, if necessary?
4. Are there provisions for a data and safety monitoring plan, and are they appropriate for the conduct of the specific research?

Risks and Benefits

The IRB must determine that the risk to the subject is minimized by implemented procedures that are

consistent with sound research design and that do not expose the subject to risk unnecessarily. In evaluating the risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from the risks and benefits of therapies the subject would receive even if not participating in the research). The risk will be reviewed in relation to the benefit the subject will receive. In general, the higher the risk the greater the benefit one would expect. The IRB will also consider potential risks to a community that may result from the research for examples stigmatization. The IRB will not consider the long-range effects of applying the knowledge gained in the research as among those risks or benefits that fall within the purview of its responsibility.

1. Are the risks and benefits well described?
2. What is the probability and magnitude of the risks?
3. Have the risks been minimized and potential benefits maximized as much as possible?
4. Has the possibility of unknown risks been addressed?
5. Are there appropriate monitoring procedures to identify risks?
6. Are there appropriate mechanisms to address risks if they occur?
7. Should the period of initial approval be less than one year in order to monitor for potential risks?

Pediatric Considerations

As the majority of research at Boston Children's Hospital involves pediatric and adolescent subjects, the IRB is required to make the appropriate risk benefit assessments for compliance with HHS and FDA regulations Subpart D. In addition, the IRB must be assured that there are adequate additional protections for children.

1. Has the investigator provided a suggested risk/benefit assessment with appropriate supporting information?
2. Does the IRB agree with the risk/benefit determination?
3. If the risk is greater than minimal is there a potential for direct benefit, or are the following four conditions met:
 - a. the risk represents a minor increase over minimal risk;
 - b. the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
 - c. the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
 - d. adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

Vulnerable Populations

The federal regulations have special protections for three defined vulnerable populations:

1. Children
2. Prisoners
3. Pregnant women, fetuses, and neonates

The IRB is required to follow the required subparts of the federal regulations to address all of the required findings. However, it is important to recognize that many other forms of vulnerability exist. These categories may include socially or economically disenfranchised, decisionally impaired, terminally ill, illiterate subjects, and migrant workers. The IRB should consider the following issues when conducting review involving other vulnerable populations:

1. Are the participants likely to be vulnerable to coercion or undue influence?
2. Does the IRB require additional special expertise or consultation to become knowledgeable about the vulnerable population?
3. What additional safeguards can the IRB require in the research to protect their rights and welfare?

Payments and Costs

The IRB reviews any payments made to research subjects and any costs the subjects may incur as a result of participating in the research. The IRB must be certain that any payments do not unduly influence a parent, child, or adolescent to participate, and are paid fairly. The IRB must also determine whether any payments are reasonable based upon the complexities and inconveniences of the research.

1. Has the investigator appropriately broken-down payments to the categories of reimbursement, compensation, tokens of appreciation, and incentives?
2. Are the amounts and forms of payments (e.g., gift certificates, toys) reasonable in relation to the research?
3. Who receives the payment the parent and/or child? Is this appropriate?
4. Is there a need to prorate any payment if a subject does not complete the trial?
5. Are there adequate plans to avoid out of pocket expenses?
6. Are there provisions for care and payments in the event of a research related injury?

Privacy and Confidentiality

When appropriate, the IRB must determine that there are adequate provisions for assuring the privacy of research subjects and for maintaining the confidentiality of the research data. The IRB reviews the plans for how privacy is protected and the collection, storage, and analysis of data.

1. How will the investigator take into consideration privacy concerns when approaching and involving a research subject?

2. Does the investigator take steps to assure privacy?
3. How will the research data be collected, recorded, and maintained?
4. Are there adequate provisions to protect privacy and confidentiality?
5. Are there adequate plans for storing and coding data?
6. Has the use of identifiers been eliminated or minimized?
7. Has the investigator adequately addressed in the protocol and consent whether research data will be included in a medical record?
8. Has the investigator described who will have access to data and under what conditions?
9. As necessary, have the HIPAA provisions and requirements been met?

Consent, Parental Permission, and Assent

The IRB must determine that consent will be sought from each prospective subject or legally authorized representative, and that

it will be adequately documented. When children are involved, parental permission will be documented, and assent obtained as required by the regulations.

The IRB must also determine whether the permission of one or both parents is required.

Assent is to be obtained from those children capable of understanding the research and its ramifications, unless the child:

1. is not capable or
2. the intervention involved in holds out the prospect for direct benefit that is important to the health and wellbeing of the child and is available only within the context of the research.

The IRB may waive or alter the procedure for informed consent only when consistent with federal and state regulations.

The IRB will review consent, parental permission, and assent documents to be sure that all required regulatory elements are addressed.

Related Content

- IRB Policies
 - Informed Consent/Assent (For more information on the regulatory requirements of consent)
 - Research and Human Subject Definition (For more information on HHS and FDA definitions)
- IRB Form: Reviewer Worksheets (For complete criteria of categories of function)

Approval Signatures

Step Description

Approver

Date

Applicability

Boston Children's Hospital- Policies & Procedures

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