Innovative Therapy and Diagnosis

Background/Rationale: Delivering care in an environment that challenges the limits of knowledge, technology and skill means the need to innovate is ever present. Often innovative thinking fosters the development of promising new approaches to therapy and diagnosis. Innovation in medicine is valued and should be encouraged within our academic environment, understanding that innovation entails risk. A clinical situation that requires an innovative solution should be carefully evaluated to examine the risks and benefits to the patient. Outside assistance and evaluation from the IRB may be helpful (though not required by regulation) since the IRB has expertise and experience weighing the risks and benefits of novel treatment protocols.

The near and longer-term consequences of the innovative approach should be considered, particularly when special follow-up may be indicated. The patient should be fully aware that an innovative approach is being proposed, so that consent can be given. In some situations, it may not be possible to obtain consent from either a patient or a responsible family member, particularly in cases requiring emergency intervention. Nevertheless, a reasonable effort must be made. There may be situations where physicians elect not to pursue approval of innovative approaches to the practice of medicine through the PHRC. This mechanism is offered as a service to the clinical and research community for applications at the interface of medicine and research and is not intended to review the practice of medicine by a licensed physician.

Distinction between clinical care and research: Many innovative therapies and diagnostic techniques are developed at the interface between well-established clinical practice and research. These activities do not, however, become research until they are carried out in a systematic fashion to develop or contribute to generalizable knowledge. The category of "**innovative therapy**" is proposed as an intermediary step between clinical care and formal research. This review mechanism is intended to cover **a very limited number of patients** in whom unusual, innovative approaches are used for the primary goal of clinical diagnosis or therapy. The mechanism is intended to provide limited peer review for innovative approaches to unusual clinical situations, especially when the dissemination of knowledge of the treatment through case reports, presentations or other means may contribute significantly to medical knowledge. **This mechanism is not intended to replace formal human studies research protocols involving small numbers of patients. Also, these guidelines do not apply to**

- the planned or emergency use of an investigational drug or device;
- the common, accepted "off label" uses of FDA-approved medications; or
- **"pilot"** studies of approaches where additional larger studies are needed and/or planned.

Examples of innovative therapy appropriate for this mechanism:

1. Cryotherapy probe (FDA-approved) for osseous tumor ablation used elsewhere in the body in a patient unable to tolerate any other surgical approaches or standard ablative therapies like radiation.
2. Modification of standard surgical or diagnostic techniques for unusual or unique situations (e.g., new application of intrauterine therapeutic device to a new, remediable fetal anomaly which might allow pregnancy to proceed).
3. Diagnostic use of a research laboratory test for a very rare familial disorder when no commercial or other research laboratory routinely performing the test clinically is available.

Recognizing that the distinction between innovation and research is clearer on paper than in practice, the following guidelines and procedures for review and approval of innovative therapies have been adopted by the Human Research Committee.

Submission requirements (forward to the HRC offices at relevant institution):

1. Letter from treating physician co-signed by division chair or other knowledgeable physician peer. The letter submitted should include the following:

    - Description of the clinical situation and the planned innovative diagnostic or therapeutic approach to treating or diagnosing the disease or condition
    - Why other standard therapies are not appropriate
    - Rationale for determining that the approach is "innovative therapy or diagnosis" rather than a "pilot study" or widely accepted "off-label" use of a drug or device
    - Supporting documentation (attachments), if relevant or helpful, e.g., case report from another institution, abstract, or other data supporting your proposal

2. **Consent form requirements:** A formal MGH/BWH research consent form should not be submitted as these submissions are describing clinical diagnosis or treatment and not research. You may use a standard clinical procedure consent form or a customized PHRC consent form that includes the standard sections of a research consent form (purpose, procedures, contacts, costs, risks, benefits and alternatives) without any reference to "research." The PHRC administrative staff are available to assist in generating customized PHRC consent forms for innovative therapy or innovative diagnosis.

3. **Adverse event reporting**: Adverse events related to innovative therapeutic or diagnostic approaches must be reported in accordance with the PHRC Adverse Event Reporting Policy. Serious adverse events must be reported (within 24 hrs of event) by telephone, fax or e-mail followed by a full written report submitted within the Humans module of Insight within 10 working days/14 calendar days.

4. **Follow-up reporting on the outcome:** A report on the outcome of the innovative therapeutic or diagnostic approach must be submitted to the HRC offices **within one year** of PHRC approval. The follow-up report may be submitted as soon as the patient returns to routine clinical follow-up. Once the follow-up report is reviewed and accepted by the PHRC, the file will be closed.

PHRC processes: Submissions will be reviewed and approval given administratively by one of the chairpersons of the Human Research Committees. Approval will be given initially for one patient; thereafter the HRC will consider written requests to treat up to two additional patients using the same innovative approach. Situations may rarely arise in which it is not possible to obtain prospective approval; approval may occasionally be granted retrospectively, if appropriate. After treatment of a third patient has been completed, a final report on the experience with the innovative approach and further plans should be submitted to the Human Research Committee. Since the primary goal is clinical diagnosis or therapy, **up to 10 total patients may then be allowed at the discretion of the PHRC.** If the investigator wishes to evaluate the innovative approach systematically to develop or contribute to generalizable knowledge, a formal research protocol must be submitted for PHRC review.

If the physician wishes to continue to treat patients using this innovative therapeutic or diagnostic approach, he/she must file a request through the Chief Medical Officer, the Innovative Diagnostics and Therapeutics Committee (MGH) or another relevant departmental practice oversight committee to have the innovative approach adopted as a standard or acceptable therapy.

Use of Data: Data obtained as a result of these approved uses may be considered approved by the PHRC and used in grants, publications, or future PHRC protocol submissions with the following notation: **"This procedure/test/diagnostic evaluation/treatment was reviewed by the Human Research Committee (IRB) at MGH/BWH, and in accordance with institutional policy approved as an acceptable innovative approach to clinical diagnosis or therapy."** Investigators are reminded that they must comply with the Partners Confidentiality Policies and Guidelines when using patient data in these settings.