PINTAD recommendation to the reporting of incidental findings in clinical trials involving imaging

Part I:

Background

Anyone involved in managing data in clinical trials has an implied obligation to the well-being of study subjects. Part of this care involves the careful review, reporting and action when incidental findings are noted. Those best positioned to fulfill that obligation are the treatment teams directly involved in the patient's care and associated healthcare professionals. This expectation is rooted in the direct relationship the treatment team has with the individual patient, their access to patient history, and current symptoms.

Purpose of this Recommendation

There has been a recurring debate on the societal/ ethical obligations and the question whether incidental findings reporting should be required in the context of independent reviewers reading images in the setting of imaging core laboratories (i.e. secondary reviewers).

This document aims to raise awareness on the complexity of the incidental findings reporting in the context of independently read clinical imaging trials. Independent reviewers are by design removed from the treatment management team, typically in space and often in time. Their reading purpose typically pertains to a narrowly defined research question that is assessed after the patient has been seen and evaluated by the treatment team for the management of the patient's treatment. There is no direct contact between the patients and the independent reviewers, in fact the independent reviewers are carefully blinded to patient identity, location and much of the medical history and clinical data.

The Challenge

We acknowledge that finding consensus on this important issue is difficult as at times the ethical imperative to do good may appear to be in conflict with a recommendation that consider legal or procedural obligations and their downstream effects.

The underlying ethical challenge for the independent image reviewers arises when a consent form is signed by a subject where it states that the medical images are sent to a third party (e.g. an imaging core laboratory) for further reading. There may be an implicit understanding by the patient that **any** findings will be transmitted to the treating physician. In general, patients do not understand the subtlety of Incidental Findings and the limitations of the constrained third party read, but believe they are having a "second opinion" by inference. The incidental finding ethical concerns are largely resolved, if, in the informed consent, the subject is notified that these second reads will not be reported back to the Principle Investigators (Wolff et al).There is an implicit ethical dilemma for readers in the situation where the subject is NOT informed that Incidental Findings will not be evaluated by a third party.

There may also be individual readers that chose to escalate a finding based on their concern for the safety and health of a particular patient.

PINTAD Recommendation

Within the framework of patient management and patient care, treatment teams and sites acquiring images for clinical trials should be responsible for having a process in place that ensures the reporting of incidental findings. The process should be anchored in the study protocol and consent forms. We as members of PINTAD believe this approach ensures the most timely, responsible and robust process concerning patient safety.

It also allows for the potential involvement of other expert readers when appropriate, but does not confound responsibility or suggest a precedence that may lead to unintended consequences. The ability to potentially include other expert readers, outside of the immediate treatment team, may be important in the context of research reads of imaging modalities or imaging methods that staff acquiring the imaging may not be familiar with.

It is PINTAD's recommendation that informed consent forms should clearly state that for therapeutic and diagnostic trials no Incidental Findings from blinded independent central readings will be provided to the subject.

Part II:

Many of the PINTAD members were also aligned on the following:

Readers at imaging core laboratories are ill-positioned to be engaged in the reporting of incidental findings as the data available to them is typically limited to minimize any potential bias and allow focus on a particular research question. Patient care should be provided by licensed health care professionals who have a more complete understanding of the patient's health status. Furthermore, in most cases those involved in the independent review of the images are not licensed in the jurisdictions of the full geographic range of study subjects. While the technology has advanced over the recent years, imaging core laboratories are handicapped by the fact that the images are still typically reviewed with some time lag. Commonly the reading occurs weeks or months after it has been acquired, affecting the timeliness of any potential observations. Thus, we recommend against the involvement of imaging core laboratories in the reporting of incidental findings.
Safety reads by their very nature have a broader defined scope that typically requires the reporting of anticipated and unanticipated findings. This recommendation does not cover the specific needs of such reads.

In alignment with the Presidential Commission for the Study of Bioethics communication on the Ethical Management of Incidental and Secondary Findings (2013) we propose that for clinical trials:

- To the extent possible, the particular likelihood and type of anticipated and unanticipated incidental findings should be described in the trial protocol by the sponsor.
- It is understood that in all imaging tests there is a potential for incidental findings that may or may not have clinical importance. Local or locally facilitated review should be performed for the purpose of the subject's local care, treatment decision making and reporting of such incidental findings. Stakeholders should be aware that such incidental findings might incur additional cost and risk should further diagnostic testing be performed.

- Whether and how such anticipated and potential unanticipated incidental findings may be communicated to the trial subject should be explained as part of the consent process. It should be clarified that imaging submitted to a third party, such as imaging core laboratories, will not be evaluated for incidental findings and incidental findings will not be reported by these third parties.
- It should be evaluated whether in the context of the local policies and procedures clinical trial subjects may be given the opportunity to decline the receipt of any or certain incidental findings dependent on the nature of the finding.
- The responsibility for the reporting and management of incidental findings within clinical trials lies with the subject's treatment team.
    - The subject's treatment team comprises the licensed medical professionals at the investigator site who have direct interaction with the subject and make patient care decisions.
    - Independent researchers and reviewers performing clinical trial assessments on subject data are not considered part of the treatment team.
    - If sufficient expertise to formally interpret the imaging is not available at the site
        - the clinical trial should not be conducted at that site, or
        - the study sponsor should identify expertise that is provided locally (or via teleradiology, telemedicine or telepresence), licensed locally, legally able to provide care in the local jurisdiction, and able to provide such expertise in a timely manner completely independent from third party independent reviewer process.

References:

Wolf SM et al., (2008) Managing incidental findings in human subject research: analysis and recommendations. J Law Med Ethics 36(2):219-248.

Commission for the Study of Bioethics communication on the Ethical Management of Incidental and Secondary Findings (2013) Anticipate and Communicate https://bioethics.gov