1. PURPOSE

1.1. The purpose of this document is to provide guidance to researchers on incidental findings.

2. BACKGROUND

2.1. The HHS and FDA regulations (45 CFR 46 and 21 CFR 50 and 56, respectively) are silent regarding the return of incidental findings to research subjects, and neither directly require nor disallow this activity. It is important to note there is ongoing debate within the research community about best practices for returning incidental findings, as well as variations in guidelines and regulations across institutions and countries. The provision of returning incidental findings to research subjects is primarily supported by the principle of beneficence. Ethical considerations, participant preferences, and the nature of the research all play a role in shaping the decision to return incidental findings.

3. What are incidental findings?

3.1. Incidental findings are discoveries of individual-level findings or observations of potential clinical significance that are unrelated to the goals of the research. Incidental findings are discovered unintentionally. These findings could have important implications for the individual's health or well-being.

3.1.1. Examples:

- Discovery of a tumor or a vascular malformation found from imaging;
- Discovery of a laboratory test abnormality found on a "healthy" control subject;
- Discovery of a genetic abnormality or risk factor;
- Discovery of non-paternity determined by genetic testing of both parents;
- Discovery that a subject may be suicidal from the results of a quality-of-life survey.

4. Who should decide if incidental findings should be returned or provided to subjects?

4.1. The return of findings refers to the ethical and practical consideration of whether and how researchers should communicate incidental findings to subjects who have participated in a research study. The decision whether to return incidental findings could include the subject's treating physician, the investigator and research staff, the IRB, or a genetic counselor or other relevant specialist who can provide appropriate context and guidance. The decision to return incidental findings to subjects involves balancing ethical considerations such as the subject's right to know versus the potential harm that could arise from the knowledge.

4.1.1. Example: During a genetic study aimed at identifying markers for a specific disease, researchers discover an incidental finding indicating a high risk for another serious genetic disorder in a participant or their child. Choosing to inform the participant about the incidental finding might result in opportunities for early intervention and medical management of the disorder, leading to increased quality of life. However, disclosure of the finding may also impact the participant's emotional and/or psychological well-being by triggering anxiety or excessive worrying.

4.1.2. Example: A study involving cognitive assessments reveals an unexpected decline in memory and cognitive function for one participant, indicating potential early signs of dementia. Choosing to share the incidental finding might lead to profound emotional distress for the participant and their family members. A formal diagnosis of dementia could negatively impact the participant's sense of self and cause anxiety about their future cognitive decline. However, not sharing the incidental

finding may lead to missed opportunities of medical management of the disorder, leading to potential health risks and decreased quality of life.

The benefits and risks related to disclosure of findings to participants (or family members) must be carefully considered.

5. Who should receive incidental findings?

5.1. Subjects directly, the Legally Authorized Representative (LAR) of adult subjects who lack competence, or to the parents or guardians of pediatric subjects. The incidental findings might also be provided to the subject's health care provider at the subject's request or other governing agencies as required.

6. Who should return the incidental findings?

6.1. It is preferred that an individual with a clinical relationship with the subject deliver or be involved with the delivery of information about the incidental finding. When the researcher is not a clinician or does not have a clinical relationship with the subject, other choices may be more appropriate, such as a genetic counsellor. The person returning the incidental finding should be prepared to provide appropriate support and resources to help the participant navigate and cope with the new the information and prevent undue stress.

7. What should researchers do about incidental findings?

7.1. Researchers should be proactive and plan ahead when conducting research that has potential for incidental findings. This means establishing clear protocols for returning findings to subjects, ensuring that the information is accurate, comprehensible, and delivered in a supportive manner. For example, include a plan regarding the possible discovery and reporting of such findings in the protocol and communicating this plan during the informed consent process. The plan should detail how results will be interpreted for both approved, clinical interventions, and research/experimental interventions. The plan should also include the process for reporting the finding, such as the parameters for disclosure, the information that will be disclosed, how and when this communication may occur, implications and risks of disclosure of the findings, and recommendations for follow up or confirmation. Finally, it is important to maintain thorough documentation of the entire process, including assessments, expert consultations, and communications with the subject to ensure accountability and transparency.

8. What if the Protocol and/or Consent Form do not mention incidental findings?

8.1. This may be possible if incidental findings were not contemplated during initial study design, or the intervention or test was unlikely to bring about incidental findings. If this occurs, it may still be appropriate to return findings to participants. Again, the benefits and risks of disclosure should be carefully considered.

Other Resources:

Attachment F - Recommendations on Reporting Incidental Findings | HHS.gov