DETAILED GUIDELINE FOR HANDLING INCIDENTAL FINDINGS IN NTU

Background

Under HBRA, an **"Incidental finding" (IF)** is defined as a finding about a research subject that has potential health or reproductive importance to the research subject and is discovered in the course of conducting research but is unrelated to the purposes, objectives or variables of the study. These findings might be expected or unexpected, and could potentially have serious implications for a subject's well-being. During the informed consent taking process, a research subject should be allowed to consent if he/she wishes to be re-identified in the case of an IF, if the proposed biomedical research expressly provides for such re-identification.

Ethical management of IF is thus necessary and researchers have an obligation to anticipate these findings and make a plan in advance of starting the research, that addresses what, when and how findings will be communicated to the research subjects.

General Considerations

From the researcher perspective there are three potential approaches to incidental findings:

1. Routine reporting of all incidental findings
2. Reporting of incidental findings in predefined domains or under specific circumstances
3. No reporting of incidental findings.

Although there may be benefits arising to participants when an IF is discovered, there are also some risks that need to be considered when choosing an approach to handling such discoveries. IFs may have direct negative impact on participants (anxiety, cost, employment, insurance), and these may extend to the wider family (especially genomic abnormalities). Researchers also need to recognize that not every incidental finding is clear-cut and such reporting may result in anxiety and out-of-pocket expense resulting from further investigations that ultimately may be found to have been unnecessary. Incidental findings may not be evident until time has elapsed (even years) after the research assessment, by which time their significance may have changed.

The researcher should also reflect on the participant's views in relation to IFs. For example, some participants might want to hear them, while others might not. When proposing to report incidental findings, researchers broadly have two further decisions to make:

1. Asking whether participants wish to receive IFs, and then only reporting back to the subset of individuals who has requested this.
2. Choosing to report back IFs to all individuals (i.e. no choice given to participants).

Although the first option might seem intuitively correct, there are risks with this strategy. Did the individual really appreciate the basis or implications for their decision when they agreed to take part? Can you really *not* tell someone they are having a heart attack, when they are sitting in the research centre, on the basis that they said "no" to receive IFs? Conversely, reporting back IFs to all participants may also potentially problematic: they really might *not* want to hear them, and have to deal with the potential negative implications.

General Framework

There is no perfect strategy that fits all research studies. If IFs are common and generally beneficial, it may be suitable to have routine, perhaps even as a routinely delivered research report. Alternately, if the incidental findings are of uncertain significance, or might have a deep negative impact that goes beyond the participant (e.g. genetics), it might be preferable to have no reporting.

The key is thus to reflect and anticipate on what IFs might come up in your research, and formulate an approach that is defensible, ethically correct and acceptable. The approach should take into account participant perspectives. The researcher should then describe the **IF Management Plan** for the **IRB to review**, as part of the study protocol, and with suitable justification.

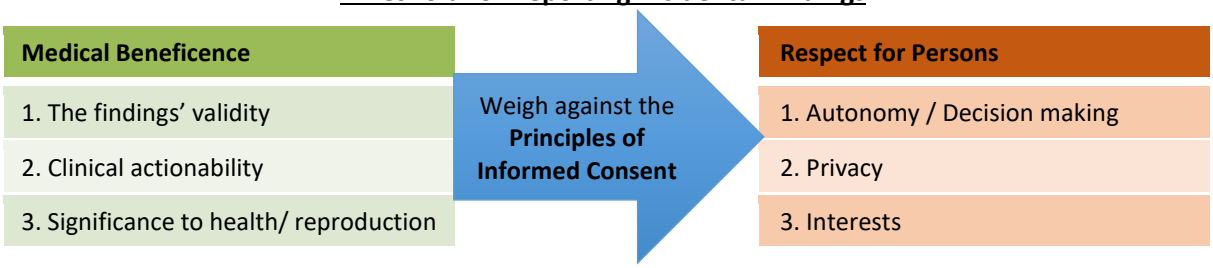
In general the **Informed Consent Form (ICF)** should then include an explanation for potential participants of what IFs are, and how these will be handled by the research team. If the potential participant finds the approach acceptable, then they will likely consent and proceed with the study. If the potential participant does not agree with the IF Management Plan, then they may choose to not take part in the research.

Incidental Findings Policy at NTU

Following on from the general points above, the following procedures are to be followed in NTU.

1. PIs are to determine the potential of IF occurring in a research study at the outset of planning for the study, and not after the study has started. If the potential for a significant IF exists, the PI should decide whether these IFs will be notified to the research subjects.
2. If the PI chooses to notify the findings to the research subject, then the **threshold for reporting IFs** (from a spectrum of IFs; as it might range along a spectrum from those requiring immediate disclosure and medical follow-up, to those whose disclosure is likely to impose anxiety and harm rather than benefits) should be determined. If PI chooses not to notify IFs to research subjects, PIs should just provide justifications in your IRB applications.
3. In determining the threshold for reporting IFs, PIs should be guided by the principles of medical beneficence, including (a) the findings' validity, (b) clinical actionability, and (c) significance to health/ reproduction. This should be weighed against the principles of informed consent i.e. to respect a subjects' (a) autonomy /decision making, (b) privacy, and (c) interests.

Threshold for Reporting Incidental Findings



4. The PI should then establish a process to report and disclose this discovery in an ethical and sensitive manner. The burden on researchers (and the costs) related to the return of results and the inclusion of a competent professional (e.g. clinician) to verify/evaluate the IF should be considered carefully when developing a management plan.
5. This plan for the possible return of results (scope, form and time frame) to the research subjects should then be included in the Informed Consent Form, the study protocol and in the ethics application submitted to the NTU-IRB with proper justifications. NTU-IRB shall review the ethics application and approval is subjected to the determination of NTU-IRB.
6. During recruitment, the benefits and burdens of IFs should be discussed explicitly with the research subjects during the informed consent process, including the plan for contacting the research subject about the IF should it later occur.
7. In some settings you might wish to offer subjects the option of opting out of learning about IFs. However, be aware of the possibility that IFs of serious clinical significance (life-threatening) might need to be notified to the research subjects regardless of the initial choice made by the research subjects. This should be explicitly disclosed during the informed consent taking process.
8. Where appropriate, PIs are advised to provide a disclaimer that the IFs were obtained from experimental scans/tests which are NOT of clinical grade. If applicable, it should also be stated that these IFs were not read by registered clinicians/radiologists, and further consultations from a relevant registered practitioner should be obtained. PIs may wish to assist in providing referrals for appropriate follow-ups elsewhere.

Flowchart for Handling Incidental Findings