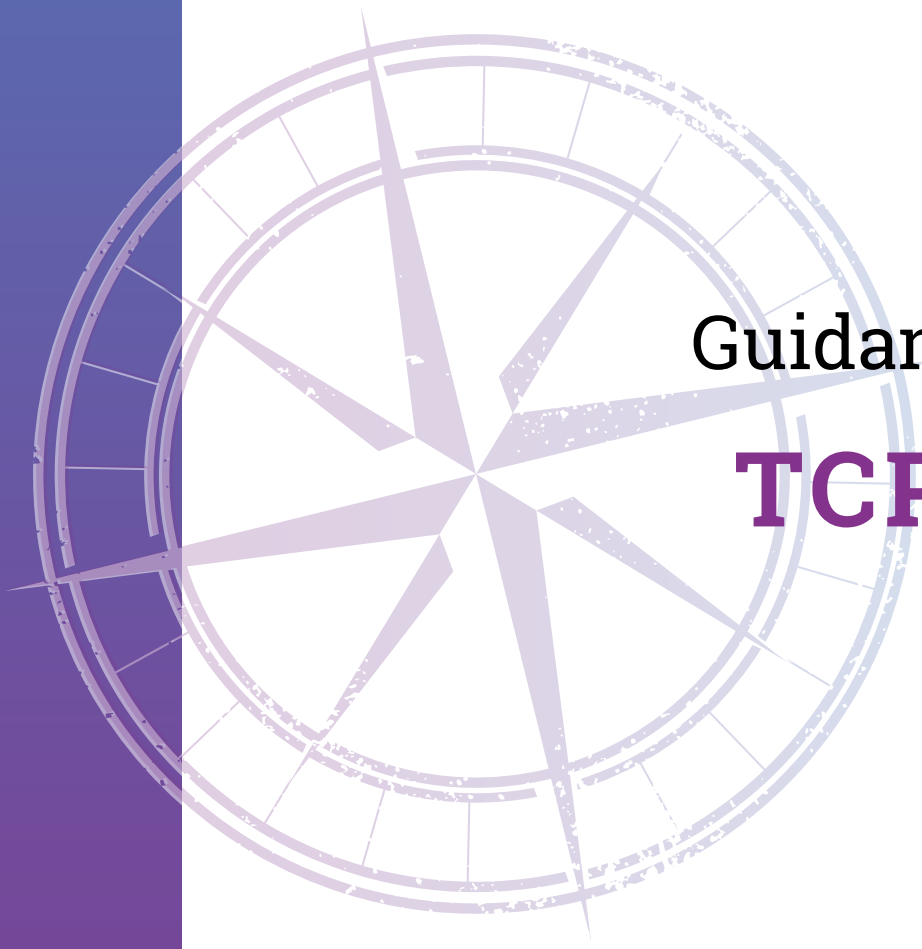
How to Address Material Incidental Findings



Guidance in Applying

TCPS2 (2018)

Article 3.4

Panel on Research Ethics

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PRE established the Material Incidental Findings (MIF) Subcommittee to provide expert policy advice on how to address material incidental findings. The committee was composed of ethicists and researchers with scholarly background in material incidental findings, as well as members of the Panel on Research Ethics. PRE would like to thank the members of the MIF Subcommittee who have generously shared their knowledge, experience and expertise in the development of this guidance:

- Carolyn Ells (McGill University), Chair of MIF Subcommittee and Chair of PRE
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PART I

CONTEXT

1. Introduction

Addressing material incidental findings in practice is a complex and challenging issue for researchers and research ethics boards (REBs). Article 3.4 of the TCPS 2 requires researchers to disclose material incidental findings to the participants, within the limits of consent provided by the participants or their authorized third party. This document complements and elaborates on Article 3.4, and is guided by the TCPS 2 core principles: Respect for Persons, Concern for Welfare, and Justice.

The document is intended to assist researchers and REBs in addressing material incidental findings that arise in the course of research involving humans. It offers guidance on issues such as determining the materiality of the finding, managing the disclosure of the finding, and researchers' communication of the finding to the participant, to the REB and to others. Criteria, options and examples are provided to support consistency in the management and evaluation of material incidental findings. As in other areas of research, consistency in application is important, but is of particular importance for research that involves multiple researchers and/or REBs.

> "Within the limits of consent provided by the participant, researchers shall disclose to the participant any material incidental findings discovered in the course of research." (TCPS 2, Article 3.4)

The Panel on Research Ethics encourages researchers, research ethics boards, and institutions to use this guidance to complement their educational initiatives and discussions of the topic, and to continue to share their practical experience and feedback for the further development of the document.

This guidance goes into effect on its release date.

2. Incidental Findings and Material Incidental Findings

An "incidental finding" is a discovery about research participants or prospective participants that is made in the course of research, but is outside the objectives of the research study. The introduction of Article 3.4 describes incidental findings to be "material" if they are reasonably determined to have significant welfare implications for the participant or prospective participant. Material incidental findings may appear at any stage, and in any type of research (TCPS 2, introduction to Article 3.4). Material incidental findings can also occur in retrospective research studies such as chart reviews.

Rapid technological advances, the evolution of research capabilities, large volumes of data, and the push for innovation contribute to increasing the probability of incidental findings in research involving humans. Examples of incidental findings that may be considered material include: an unexpected mass or vascular abnormality on a computed tomography (CT) scan or a magnetic resonance imaging (MRI); a genome sequence that reveals additional genetic variation for a participant, such as high risk for cancer; and a discovery of physical abuse or suicidality in studies unrelated to those phenomena.

PART II
GUIDANCE

3. The Determination of Materiality

3a. What Makes Incidental Findings Material?

Incidental findings would be considered material if they have all three of the following key determinants:

i. Analytical validity

The researchers have verified the accuracy and precision of the finding. Researchers should verify that the finding is not an artefact of the research methodology. If necessary, the researchers may seek the advice of experts for this purpose (see Section 3b of this document).

ii. Potential significance

The researchers have determined that the findings are potentially important to disclose to the participant, given that they may significantly affect the participant's welfare (health or otherwise). The TCPS 2 principles of Concern for Welfare and Respect for Persons place an obligation on researchers to disclose relevant findings to individual participants within the limits of consent provided by the participant; i.e. as part of the initial or ongoing consent process. The welfare implications could be relatively immediate, or may be in the future, for example in the case of children where the findings may only have an impact on the participants' adult lives. While researchers assess the potential significance of the findings to the participant, the findings may also have implications for people other than the participant, such as the participant's children or other family members (See Section 5a.iii of this document. See also Chapter 13 of TCPS 2 for guidance on how to address the return of findings in human genetic research).

Researchers and REBs should recognize that it is not always clear how to assess the significance of the finding for participants. Participants and researchers may have different perspectives on what is significant, and these may change over time. Where possible, researchers' knowledge of the participants' circumstances may help them in their assessment of the significance of the finding.

iii. Actionability

The researchers have determined that, in sharing such findings in a timely manner, the participant can initiate an action to remove or help manage the risk to his/her welfare, and/or can use this information to take steps that may result in the research participant's benefit, or where applicable, a relative's benefit. For example, this may be the case for children who are found to have an adult-onset condition, and the finding would have great relevance for an adult relative.

In consenting to receive material incidental findings, an authorized third party is expected to exercise authority in the best interest of the participant who lacks capacity to make his/her own decision. For example, an authorized third party must receive material incidental findings for a child that are actionable immediately or during childhood, but this is optional for findings that are actionable only in adulthood (See Section 5a.iv of this document regarding future contact with participants who acquire capacity).

3b. Who Makes the Determination of Materiality?

The TCPS 2 principle of Concern for Welfare places a responsibility on researchers to anticipate the impact of material incidental findings on participants, and exercise "care and sensitivity in determining who discloses material incidental findings that may have a negative impact on the welfare of participants, and how that disclosure is made" (TCPS 2, Application of Article 3.4). Researchers have the primary responsibility of selecting the appropriate person to make a determination of materiality. In making that selection, they should consider the following factors:

> "To determine whether an incidental finding is material, expertise relevant to the finding is required. If researchers do not have such expertise, and are unsure of how to interpret the findings or are uncertain whether findings are material, they should seek expertise relevant to the finding and/or refer to professional practices and standards." (TCPS 2, Application of Article 3.4)

i. Relevant Expertise

Researchers should identify the type of expertise required to determine the significance of the finding, and whether or not a finding is material. If the research team does not have expertise relevant to the finding, the researcher should seek the advice of an external expert in that field. Generally, an expert is a specialist in the discipline of the finding, who is recognized to have the experience and authoritative knowledge, technique or skill to make a reliable judgement on the materiality of the finding.

ii. Professional Standards

Researchers should also be guided by practices and standards developed by their professional associations or disciplines on the management of incidental findings. This provision is more likely to exist in areas of research where incidental findings are prevalent such as research that includes imaging and genetics.

4. The Management Plan

4a. Challenges in Managing Material Incidental Findings

Several factors make it challenging to manage material incidental findings. These include variables and unknown factors pertaining to the predictability, planning, discovery, validation, management, communication, review of, and consent to receipt of material incidental findings. These challenges have an impact on the researcher's obligation towards participants. The variables will affect the need for a plan to manage material incidental findings, and what the REB should be looking for in the review of the management plan.

4b. Does the Research Require a Management Plan?

The TCPS 2 principle of Justice places an obligation on researchers to treat people fairly and equitably. A consistent approach in the disclosure of material incidental findings should be followed – and therefore, researchers may need to develop a management plan, or at least a process to follow, in the event that they discover material incidental findings. Such a plan or process should recognize individual differences, and any developments or changes to context or circumstances.

Chapter 13 of TCPS 2 requires that researchers conducting genetic research develop a plan for managing information that may be revealed through their research (Article 13.2). Management plans are strongly encouraged for other areas of research where material incidental findings are likely.

Researchers should consider the following three scenarios:

i. Material incidental findings are reasonably foreseeable

The researcher anticipates that material incidental findings may be found in the course of the research. In a case like this, the researcher should develop a plan from the outset: (i) for review by the REB, and (ii) to inform participants about their disclosure strategy as part of the consent process. In cases where participants lack capacity to make their own decisions, the researcher's disclosure strategy must include informing an authorized third party.

> "Where material incidental findings are foreseeable… researchers should develop a management plan for review by the REB. For genetic research, researchers are required to develop a plan for managing information that may be revealed through their research, and submit the plan for REB review."
> (TCPS 2, Application of Article 3.4)

Genetics is an area of research where material incidental findings are reasonably foreseeable, and the ramifications of these findings (both positive and negative) may go beyond the individual participant to involve others with whom the individual shares genetic ancestry. Researchers and REBs should be guided by the provisions relevant to this area of research. This includes the requirement to:

- develop a plan for managing information that may be revealed through their genetic research;
- submit the plan to the REB; and
- advise prospective participants of the plan for managing new information revealed through the research (see TCPS 2, Article 13.2 and other guidance in Chapter 13: Human Genetic Research).

ii. Material incidental findings are not reasonably foreseeable

The researcher does not anticipate that material incidental findings will arise during the research. In a case like this, the researcher is encouraged to think about a process to follow in case material incidental findings occur, but does not necessarily require a detailed plan at the outset of the research. In the event of an unexpected discovery of incidental findings that are likely to be material, the researcher shall report the finding to the REB, and should develop a management plan for the REB's approval before implementing it. Where the welfare of the participants may be negatively impacted and time is of the essence to mitigate a risk, the researcher may implement required actions prior to reporting to the REB (see TCPS 2, Article 6.15, and Application of Article 3.4).

> "In other areas of research, material incidental findings may not be reasonably foreseeable, but can be discovered unexpectedly in the course of the research… The researcher should describe the process used to determine the materiality of the finding(s), and present a plan for disclosing such findings to the participants."
> (TCPS 2, Application of Article 3.4)

iii. The circumstances justify an exception to the obligation to disclose material incidental findings

Whether or not the researcher anticipates that material incidental findings may arise during the research, in some circumstances the disclosure of such findings would be impossible or impracticable. Such circumstances can justify an exception to the obligation to disclose material incidental findings. This is consistent with guidance in TCPS 2 that allows for such exceptions. Instead of a management plan, the researcher provides to the REB a justification for seeking such an exception. The Application of Article 3.4 sets out criteria for such exceptions.

> "Researchers may also request an exception to their obligation to disclose material incidental findings, based on the impracticability or impossibility of disclosing such findings to the participant. "Impracticable" refers to undue hardship or onerousness that jeopardizes the conduct of the research; it does not mean mere inconvenience. Disclosure may be impossible or impracticable when participants or their authorized third party may be deceased, or difficult to track due to insufficient identifiers, cost, or time elapsed. The onus is on the researcher to justify to the REB the need for the exception."
> (TCPS 2, Application of Article 3.4)

This may be the case, for example: for some population studies; or research that relies on biobanks where the policy is not to return individual results of findings, and participants would have consented to the no-return policy when initially recruited. In such cases, biobanks are encouraged to revisit their policy on the return of material incidental findings to participants. Biobanks may also consider revisiting the consent process that they previously followed when they next re-contact participants.

4c. Basic Elements of a Management Plan

The management of material incidental findings will differ depending on the research discipline and the context of the particular research study. The onus is on researchers to develop plans based on their best predictions. The onus is also on researchers, as part of the continuing ethics review process, to communicate to the REB and further develop their management plans as material incidental findings become evident in the research, and as details become available. Researchers and REBs should be guided by existing TCPS 2 provisions relevant to continuing ethics review, reports of unanticipated issues, and requests for changes to approved research (See TCPS 2, Articles 6.14, 6.15 and 6.16).

The management plan may include the following information as part of the initial ethics review. Where the management plan is provided only after material incidental findings become evident, as part of continuing ethics review, only the second and third elements are necessary. In either scenario, the REB may request that the researcher provide additional information if needed.

i. The likelihood of discovery of material incidental findings

- Is the discovery of material incidental findings reasonably foreseeable?
- If yes, when does the researcher anticipate that the research will yield such findings?

> "Material incidental findings may appear at any stage of the research. For example, material incidental findings can be discovered while screening for eligibility to participate in a study, while collecting baseline information, during study procedures, or during follow-up evaluations."
> (TCPS 2, introduction to Article 3.4)

ii. The management of the findings

- How does the researcher plan to determine the materiality of the findings? This may include the following:
    - □ Seeking additional expertise.
    - □ Obtaining appropriate resources (for example, to cover the cost of confirming the materiality of the finding where possible).
    - □ Assessing the analytical validity, potential significance, and actionability of the finding(s).
- What finding(s) does the researcher plan to disclose?
- What is the justification for not disclosing some finding(s)? Possible reasons may include, but are not limited to, impossible or impracticable to reach participants or authorized third party because they may be deceased (unless the findings have relevance beyond the participant such as for a parent or a child), or difficult to track due to insufficient identifiers, cost or time elapsed.
- Who on the research team will be responsible for communicating the finding(s) to participant(s)?

iii. Consent

- Will participants be able to choose the types of material incidental findings they wish to receive, or not receive, and at which stages of the research will they be able to do so? Will this information be sought from the participants at the beginning of the study or as part of the ongoing consent process?
- How will the researcher manage the consent process for those who do not have the decision-making capacity to consent on their own behalf? See TCPS 2 Chapter 3, Introduction to Section C, of for the definition of decision-making capacity. This may include the following:
    - □ Establishing a process for contacting participants if they acquire or regain capacity to make their own decisions.
    - □ Listing any limitations for participants to receive, or decline to receive, the material incidental finding(s). For example in the case of children, out of concern for the child's welfare, researchers have a duty to disclose findings that are actionable immediately or during childhood, even if the authorized third party expresses the desire not to know. This should be clearly communicated in the consent process.

4d. When Does the Researcher's Obligation to Disclose Material Incidental Findings End?

TCPS 2 does not specify when the obligation of the researcher ends with regard to the disclosure of material incidental findings. The reason for not making this determination is that the nature of each research project is different, and the types of research designs vary.

Normally, the researcher's obligation to disclose material incidental findings can be linked to the duration of the research study, and would cease with the closure of the research study with the REB. (See Application of Article 6.14 of TCPS 2 for guidance on when REB review is no longer required.) The duration of the researcher's obligation to disclose material incidental findings should be considered as part of the management plan submitted to the REB. Researchers should honor any commitments to, or agreements they made with, participants. In some cases, the availability of resources, such as funding, may restrict how disclosure of material incidental findings is handled.

> "Institutional ethics policies should include provisions that assist REBs, researchers and institutions to determine when continuing research ethics review is no longer required. Such provisions should consider different types of research designs (e.g., short-term project, longitudinal research, research with reporting back requirements). They should also consider issues, such as: the extent of any remaining risk to participants; the nature of plans (if any) for future interaction with participants; the status of any commitments to or agreements with participants (e.g., with respect to reporting findings); and/or the relative likelihood of future unanticipated events, material incidental findings, or new information."
> (TCPS 2, Application of Article 6.14)

5. Researchers' Communication about Material Incidental Findings

According to the TCPS 2, "Within the limits of consent provided by the participants, researchers have an obligation to disclose to the participant any material incidental findings discovered in the course of research" (TCPS 2, Article 3.4). The communication of the findings determined to be material is therefore dependent on the consent of the relevant participant(s) as part of the initial and/or ongoing consent process.

There are several aspects to consider, including:

- what information should be shared;
- when information should be shared;
- with whom information should be shared; and
- how information should be shared.

Researchers should anticipate communicating information relevant to material incidental findings to various players. The timing of this communication is equally important. The significance of the information will determine how and by whom a material incidental finding is conveyed. The actionability and urgency of sharing the material incidental findings will determine when it is conveyed.

5a. Communication to Participants – Challenges and Considerations

Researchers must provide all the available information for the participant to make an informed decision about whether to receive the material incidental finding. Researchers should consider the challenges, risks, and impacts when seeking their consent to receive material incidental findings as part of the initial or ongoing consent process, and/or when communicating with participants about material incidental findings.

i. Participant's consent

There are several challenges related to participants' consent to receiving material incidental findings. These include but are not limited to:

- The fact that participants can only be informed about the exact details of the findings after they are discovered.
- While the discovery of material incidental findings and knowledge of specific conditions in a timely manner can, in some instances, be lifesaving, it is often difficult to predict the significance of a given finding for the participant.
- In some situations, the possibility of material incidental findings may not have been previously raised in the consent process.
- It may be difficult for participants to understand the significance of the material incidental findings for them.
- The participant's circumstances may change over time, which can have an effect on the participant's decision to (continue to) agree, or refuse to receive the material incidental finding. See also TCPS 2 Article 13.3 for consent in genetic research.

Where the discovery of material incidental findings is foreseeable, researchers must alert participants during the initial consent process. If a material incidental finding appears unexpectedly in the course of research, researchers must, as part of the ongoing consent process, seek the participants' consent to receive the finding. If participants agree to receive the material incidental finding(s), researchers should assist them in understanding the finding.

> "Researchers should exercise care and sensitivity in determining who discloses material incidental findings that may have a negative impact on the welfare of participants, and how that disclosure is made. Researchers should assist participants in understanding the material incidental finding(s). Researchers' assistance may include suggesting that participants consider seeking additional advice from people they trust, such as family members, friends, experts or professionals. When necessary, researchers should direct participants to a qualified professional to discuss the possible implications of material incidental findings for their welfare."
> (TCPS 2, Application of Article 3.4)

ii. Impact on participants

In general, researchers should be aware of the possible risks of sharing the material incidental finding with participants. For example, participants may be anxious or distressed by receiving disclosure of the mere fact that there is a material incidental finding. Informing participants of the possibility that there has been a material incidental finding may raise their expectations. See also TCPS 2 Article 13.4 that encourages making genetic counselling available, where possible, when sharing results of genetic research with participants.

iii. Impact beyond participants

A layer of complexity is added when the decision to consent to receive the material incidental finding involves others, such as family members in the case of genetics. It is also the case when the decision has implications for an authorized third party who may, for example, be the parent of a child (TCPS 2, Articles 3.9 and 3.10). This may occur when a genetic finding is not immediately relevant for a child because the condition is adult-onset, but would have great relevance for a parent who carries the variant. Researchers do not normally have an obligation to share material incidental findings beyond the participant, but may do so based on the participants' expressed preferences (TCPS 2, Article 3.11), and in exceptional circumstances, e.g. in the case of discovering a serious or life-threatening condition that can be prevented or alleviated through intervention (TCPS 2, Article 13.3).

iv. Contacting participants

Researchers should make reasonable efforts to contact participants or, if applicable, a relative whose welfare may be impacted by the material incidental findings. There may be limitations to contacting participants or their authorized third party who may be deceased or difficult to track because of insufficient identifiers, cost or elapsed time. Such complexities may make it impossible or impracticable to contact participants (see Section 4b.iii of this document).

There is added complexity when participants initially lack capacity to consent on their own behalf. Researchers should consider, as part of the consent process, whether to disclose the material incidental finding or indicate their intent for future contact with participants once they acquire or re-gain the capacity to consent to receive the finding on their own behalf. Researchers should invite participants to maintain and update their contact information.

In some cases, where material incidental findings are discovered in the course of research, but were not addressed in the initial consent process, the REB may request that the researcher contact the participant(s) to seek their consent. In doing so, researchers should be careful not to inadvertently reveal unnecessary details about the material incidental finding before the participant has consented to receive it.

In research involving secondary use of information, researchers should discuss with their REB their obligation to disclose material incidental findings to participant(s), and their strategy to contact relevant participant(s) where appropriate. For example, in the case of genome sequencing where identifiers are retained and where material incidental findings have been identified, the researchers should discuss with the REB their plan to communicate with participants. In this example, contacting participants may impact participants' privacy and confidentiality where the possibility of material incidental findings was not raised as part of the consent process.

5b. Communication with Other Players

i. Researchers must communicate with their REB

For a number of reasons, researchers may need to communicate with their REB at various stages of the research. For example, when researchers can reasonably foresee material incidental findings, they must inform their REB and should develop a management plan for review by the REB. When researchers later discover a material incidental finding, whether foreseeable or unexpected, they must report it to the REB. When researchers are contemplating changes to their management plan, they can consult their REB. When researchers make changes to their management plan, they must seek their REB's approval (see TCPS 2, Articles 6.15 and 6.16).

If researchers wish to depart from the terms of consent, either not to disclose or to disclose a material incidental finding to the participant, they must seek their REB's approval.

In general, REBs should recognize the tension between the researcher's obligation to disclose, and the requirement to follow the appropriate consent process. REBs must strike a balance between two of the core principles of the TCPS 2: Respect for Persons and Concern for Welfare. They should weigh the risks and potential benefits of respecting the participants' initial consent and their confidentiality, against the impact of receiving the material incidental findings on the participants' welfare.

> "Where the researchers have undertaken, in the course of the consent process, not to disclose material incidental findings, and researchers discover an unforeseeable material incidental finding that can be addressed with a potentially significantly beneficial intervention, researchers should consult their REBs to determine whether there is a sufficient ethical basis to disclose the finding to the participant, and if so, how to disclose it."
> (TCPS 2, Application of Article 3.4)

Under certain circumstances, it may be impracticable or impossible for researchers to disclose the material incidental findings to participants. Researchers must justify the need for such an exception and seek their REB's approval (see Section 4b.iii of this document).

In the absence of specialized expertise among its membership, the REB should seek the additional expertise required for the review of the management plan (see TCPS 2, Article 6.5).

ii. Researchers may have other reporting obligations in certain circumstances

Researchers are expected to be aware of other reporting obligations, such as those set out in professional codes of conduct or in legislation (e.g. child welfare or communicable disease legislation), that may require disclosure of information. Researchers should inform participants of the limits to confidentiality as part of the consent process