# Best Practices for Health Research Involving Children and Adolescents

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# The TCPS and Children

- Same general guidelines apply to children as well as adults
- Specific sections deal with children and other vulnerable populations—Those who lack capacity for consent
- Leaves some questions unanswered

# Why a Best Practices for Health Research Involving Children and Adolescents?

- Detailed guidance for paediatric research
- Update NCEHR's *Report on Research Involving Children* (1993)
- Provide more detailed guidance and discussion than *Tri-Council Policy Statement*
- Paediatric research increasingly becoming a global endeavor

# Development of the *Best Practices*


Summer-Fall 2011: Final *Best Practices*

# Structure: The 10 Guidelines

I. Inclusion of Children in Research

II. Consent To Research

III. Assent of the Child

IV. Dissent of the Child

V. Departures From Consent

VI. Evaluation of Risks and Benefits

VII. Privacy and Confidentiality

VIII. Return of Research Results

IX. Payment in Research

X. Composition of Research Ethics Boards

# Guideline I: Inclusion of Children in Research

| TCPS 2 | Best Practices |
| --- | --- |
| Children **shall not** be inappropriately excluded from research solely on the basis of their age or developmental stage (4.4) | *The inclusion of children in research promotes their safety and well-being.* |

The *Best Practices* also contemplates the limited inclusion of **institutionalized** children and those with **life-threatening disease**

# Inclusion in Clinical Trials and Novel Therapies

"the inclusion of children ***might not be appropriate*** at all stages of clinical trials. There is a significant difference in the risks undertaken in a ***Phase I trial***, when little is known about the effects of a drug on humans, versus ***Phase III or IV***...."

"This **does not mean**, though, that children **should never participate** in Phase I or II clinical trials.

there are circumstances when it would be appropriate to include children, e.g.

trials for diseases that affect only paediatric populations; and

the use of adults would yield little or no useful information.

Yet, even in these circumstances it is desirable to obtain initial safety and tolerability data from adult studies."

# Guideline II: Consent to Research

| TCPS 2 | Best Practices |
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| …(b) the researcher seeks and maintains consent from authorized third parties in accordance with the **best interests** of the persons concerned… (3.9) | *Researchers should obtain the free and informed consent of the competent child or, if incompetent, of his/her parents.*<br><br>…When providing consent on behalf of their child, the parents should base their decision on the child's **best interests**…. |

# Parental Consent For Phase I and II Clinical Trials

"Pharmaceutical research also raises the question of whether parents can consent to the participation of their child in a ***Phase I*** clinical trial....

Children may benefit from the research even if the probability of success is low. Children may also get an indirect benefit through altruism for others. In any case, the best interest of the child should prevail."

# Guideline III: Assent of the Child

| TCPS 2 | Best Practices |
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| …the researcher shall ascertain the wishes of that individual with respect to participation. (3.10)<br><br>Many individuals who lack legal capacity to make decisions may still be able to express their wishes in a meaningful way, even if such expression may not fulfil all of the requirements for consent. (3.10) | *To the extent possible, researchers should obtain the assent of the child according to his/her level of development and capacities.*<br>Best Practices also contemplates:<br>*Assent Process*:<br>• After parental consent<br>• Provided freely (without parental pressure)<br>*Age Divisions*:<br>• Newborns/infants<br>• School age (7-13 years)<br>• Adolescents (14-18 years) |

# Guideline IV: Dissent of the Child

| TCPS 2 | Best Practices |
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| Prospective participants' dissent **will preclude** their participation. (3.10) | *The dissent of the child, **who is capable of understanding**, must be respected.* |

# Guideline VI: Evaluation of Risks and Benefits

| TCPS 2 | Best Practices |
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| …(b) the research **does not expose the participants to more than minimal risk without the prospect of direct benefit**; or (c) where the research entails only minimal risk, it should at least have the prospect of providing benefits to participants or to a group that is the focus of the research and to which the participants belong." (4.6) | *The participation of a child in research should offer the possibility of a **direct benefit** to the his/her health.*<br><br>*Where **no direct benefit** is likely, the results should benefit other children of the same age or with the same disease, condition or disability, and the child **should not be exposed to more than minimal risk**.* |

# Evaluation of Risks and Benefits in Clinical Trials

"Participation of children in late phase trials (III or IV) is perhaps the most justifiable from a risk perspective. Generally, by these phases the toxicity and efficacy of the drug will be known, at least in adults….

However, addressing the challenge of risk in early phase trials (I or II) is more difficult. These trials will generally, by their nature, have higher than minimal risks. Under TCPS2, these risks ***preclude*** the participation of ***healthy*** children, although other guidance such as CIOMS suggests that there might be circumstances when their inclusion is possible."

# GUIDELINE VIII: RETURN OF RESULTS – GENERAL/INDIVIDUAL

| TCPS 2 | Best Practices |
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| In general, researchers **should ensure** that participating individuals, groups and communities are informed of how to access the results of the research. (Ch. 4)<br><br>Researchers **shall explain** to participants the **types of findings** that may be revealed, and the potential implications of these findings, to permit participants to make informed choices about whether or not to receive information. (13.3) | *Researchers should broadly disseminate general research results.*<br><br>*Individual results should be communicated if they have **significant implications** for the health of the child.* |

# GUIDELINE VIII: RETURN OF RESULTS – **INCIDENTAL FINDINGS**

| TCPS 2 | Best Practices |
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| Researchers have an **obligation to disclose** to the participant any material incidental findings discovered in the course of research. (3.4) | *Incidental findings should also be communicated to the competent child or, if incompetent, to the parents if the findings have* ***significant implications for the child.***<br><br>*If feasible, the incompetent child should be informed.* |

# Guideline IX: Payment in Research

| TCPS 2 | Best Practices |
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| (j) information about any payments, including incentives for participants, reimbursement for participation-related expenses and compensation for injury....(3.2)<br><br>REBs and researchers should be cognizant of situations where undue influence, coercion or the offer of incentives may undermine the voluntariness of a participant's consent to participate in research. (3.1) | *Payment should be discussed during the consent process and, if appropriate, during the assent process. An REB should review the payment plan proposed.*<br>*Best Practices* also contemplates:<br>***reimbursement*** payments to parents and/or children for their direct expenses related to participation (e.g. transportation, meals);<br>***compensation*** payments to compensate parents and/or children for their time and inconvenience caused by participation;<br>***appreciation*** payments, which are bonuses given to children after their participation to thank them;<br>***incentive*** payments to encourage the participation of children in research. |

# Final Thoughts and Questions

Many nuances between TCPS2 and *Best Practices*

- *Assent/Dissent*: what complications do you anticipate in obtaining assent, or addressing dissent?
- Do you think the participation limitations regarding very vulnerable children are appropriate?
- Should healthy children be permitted to participate in clinical trials?

# Send Your Comments and Suggestions

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**Websites for download of *Best Practices*:**

http://www.pediagen.org/

http://www.humgen.org/int/