兒童受試者之保護

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CITI Topics

- Research Involving Minors (45 CFR 46 Subpart D)
- Research with Children (以兒童作爲研究對象)
- Research in Public Elementary and Secondary Schools (在公立中小學校中進行研究)


LAKES ELEMENTARY
LEOPARDS
LAKES
ELEMENTA
SCHOOL
Est. 1964


How Did You Figure It Out?
Does Anyone Have a Different Answer?
Can You Convince Us?
What Might Come Next?
What Do You Notice?
What Do You Think?
Do You See Any Patterns Here?
Early Work
Writing prompt
DLR
AR
Team Goals
respect
transitions
quiet down quickly
AM Goals
Finish up Turtle Bay activities
PM Goals
Rocket Math
ADD
Sea Turtle Paragraph from 2-Column notes
1:00 Special Guests
Explain homework
Give Me
Pictures
Words
Numbers
Labels
Happy Birthday
Jan.
Feb.
Mar.
Apr.
May
June
July
Aug.
Sept.
Oct.

Children are vulnerable subjects!

IRB's responsibility

- An IRB/IEC should safeguard the rights, safety, and well-being of all trial subjects. **Special attention should be paid to trials that may include vulnerable subjects**. (ICH E6 GCP)

人體試驗委員會應確保受試者之權利, 安全以及福祉受到保護, 且對於易受傷害受試者之臨床試驗, 應特別留意

藥品優良臨床試驗準則　　第四條

Regulations (相關法規)

- DHHS 45 CFR 46 Protection of Human Subjects
  - Subpart A (the "**Common Rule**"): Basic HHS Policy for Protection of Human Research Subjects
  - **Subpart D: Additional Protection for Children Involved as Subjects in Research**
- FERPA (Family Education Rights and Privacy Act)
- PPRA (Protection of Pupil Rights Amendment)

Subpart D

- 適用於所有由DHHS執行或贊助的研究
- 免除適用之研究(exemptions)

Exemptions (免除適用之研究)

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices
2. Research about educational tests
3. Observations of children in public settings when the **researchers do not interact with the subjects**, such as observations of internet behavior in public forums on non-sensitive issues

Exemptions (免除適用之研究)

4. Studies using **existing data** about children, (a) **if it is publicly available**, or (b) if it is recorded in such a way by the investigator that the **identity of the children cannot be determined** either directly or indirectly
5. Taste and food quality evaluations and consumer acceptance studies, under some circumstances
6. Studies conducted by federal departments or agencies about government programs, such as welfare programs

不符合免除條件

1. Research involving interviews 訪問
2. Research involving surveys 調查
3. Observation in which the researcher participates in the activities observed
   觀察研究者本身亦參與其中之行爲觀察研究

案例一：教導學生小說與非小說的寫作體裁是否可增進學生的閱讀理解能力

- 對象:將升上小三的學生
- 方法:甲校使用新教學法,乙校使用原教學法,三年級結束時比較兩校學生之閱讀理解能力
- 問題:此研究是否符合減免條件?

案例二：處理悲傷情緒

- 研究者想知道引導式寫作及繪畫如何幫助小學生面對父母離婚的狀況。他希望可以對兒童進行訪問
- 問題:此研究是否符合減免條件?


activities
graph from
notes
Special
Guests
• Explain homework
Classroom Job
Team One
Lunch Trays
Paper

Definitions

- **Children**
- **Assent**
- Permission
- Parent
- Guardian

"Children"

- Children are persons who have not attained the **legal age** for consent to treatments or procedures involved in the research.
- 尚未到達行使同意權的**法定年齡**的人爲兒童

“Emancipated Minors”

- 脫離父母監護的兒童
- 構成條件:結婚,服役,法庭裁令

民法

- 第 12 條
  - 滿二十歲爲成年。
- 第 13 條
  - 未滿七歲之未成年人，無行爲能力。
  - 滿七歲以上之未成年人，有限制行爲能力。
  - 未成年人已結婚者，有行爲能力。

Assent

- Assent means a child's **affirmative agreement** to participate in research.

  兒童肯定的同意
- Failure to object should not be construed as assent.

  無法拒絕不代表同意


Notice?
Think?
Here?
Words
Numbers
Labels
Give Me Five
Early Work
Writing prompt
DLR
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respect
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quiet down quickly
AM Goals
Finish up Turtle Bay activities
PM Goals
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ADD
Sea Turtle
graph from
Column notes
Special Guests
Explain homework
PHYSICAL/POLITICAL WORLD
PHYSICAL/POLITICAL UNITED STATES
PHYSICAL/POLITICAL ALASKA

The Belmont Report

- Respect for persons
  - …second, persons with diminished autonomy are entitled to protection.
  - …The extent of protection afforded should depend upon the **risk** of harm and the likelihood of **benefit**.

Minimal Risk 最低風險

- The probability and magnitude of harm or discomfort anticipated in research are not greater in and of themselves than
  - those ordinarily encountered in daily life or
  - during the performance of routine physical or psychological examinations or tests.
- 最低風險意指傷害或不適的可能性及強度不大於其平日的生活遭遇或進行例行生理或心理檢測時的程度

4 Research Categories

I. Research **not involving greater than minimal risk** (46.404)	III. Research involving **greater than minimal risk** and **no prospect of direct benefit** to individual subjects, but likely to yield **generalizable knowledge** about the subject's disorder or condition (46.406)
II. Research involving **greater than minimal risk** but presenting the **prospect of direct benefit** to the individual subjects (46.405)	IV. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (46.407)

Category I

- 風險不大於最低風險(minimal risk)

Category II

- 風險大於minimal risk,但受試者可望獲得直接效益 (prospect of direct benefit)
  - 預期效益下有合理的風險
  - 效益/風險比至少與替代方法一樣

Category III

- 風險大於minimal risk且對受試者**無預期效益**,但對於所研究的疾病或狀態,可能產生**可概推性的知識**(generalizable knowledge)
  - 風險**些微超過**最低風險(**minor increase** over minimal risk)
  - 與受試者之日常經驗相當(醫療,心理,社會,教育)
  - 所產生的知識對瞭解或治癒該疾病有其重要性

Category IV

- IRB審查後,認爲該研究不適用第I,II或III類研究,而無法逕行通過
  - 該研究對影響兒童健康及福祉之重大問題能提供進一步的資訊
  - 由Secretary of DHHS任用各領域專家組成審查委員會並作成決定

執行上的困難

- 每個人對"風險"的感覺不同
- 問題出在"minimal risk"
  - 標準爲何? (人事時地物)
  - 如何量化? (minor increase?)

Street Calculus

By Garry Trudeau

188位IRB主席對風險的看法

JAMA 2004; 291:476-482

對11歲健康兒童進行下列步驟	Minimal risk	Minor increase	>Minor increase
靜脈抽血(10mL)	152 (81%)	32 (17%)	2 (1%)
MRI (no sedation)	90 (48%)	66 (35%)	17 (9%)
性行爲之保密性調查	83 (44%)	55 (29%)	36 (19%)
皮膚過敏源試驗	43 (23%)	81 (43%)	51 (27%)
藥物動力學研究(死亡率: 1/10000)	13 (7%)	56 (30%)	111 (59%)
腰椎穿刺(清醒之健康兒童)	4 (2%)	30 (16%)	147 (78%)

定量minimal risk?

- 所謂
  - "日常生活中遭遇的風險"
  - "進行例行生理或心理檢測時的風險"
- 其標準爲何?

Quantifying the Federal Minimal Risk Standard

Implications for Pediatric Research Without a Prospect of Direct Benefit

David Wendler, PhD
Leah Belsky, AB
Kimberly M. Thompson, ScD
Ezekiel J. Emanuel, MD, PhD

United States federal regulations
approve pediatric research that
direct" benefit only when the ris
minimal. The federal regulations

JAMA 2005; 294:826-832

研究結論

- 健康兒童日常生活中遭遇最大的死亡風險來自於乘車
- 健康兒童日常生活中遭遇最大的傷害風險來自於運動
- 相較於生活中遭遇的風險,例行性檢查的風險很低
- Minimal risk的參考標準
  - 傷害風險: 1 in 250 (相當於打美式足球受傷的機率)
  - 死亡風險: 1 in 100,000 (相當於15-19歲青少年在較危險的情況下乘車的死亡率)

IRB之審查重點

- Risk/benefit分類(I, II, II, or IV)
- 取得父母親或監護人允許(permission)及兒童同意(assent)的必要性及合理性

IRB審查要項

Risk \ Benefit	**Prospect of Direct Benefit**	**No Prospect of Direct Benefit**
Minimal risk	• Parental permission • Child's assent	• Parental permission • Child's assent
Minor increase over minimal risk	• Risk/benefit ratio • Parental permission • Child's assent	• Knowledge • Subject's experience • Parental permission • Child's assent
More than a minor increase over minimal risk	• Risk/benefit ratio • Parental permission • Child's assent	無法由IRB通過

Child's assent (46.408(a)(e))

- IRB須考量兒童是否有能力行使同意權,考量因素包括年齡,成熟度於心理狀態
- 某些情況下可免除assent,如
  - 年紀太小 (<7 years old)
  - 兒童可望自研究中得到直接益處,且參與研究是唯一管道
  - 其他符合Subpart A中免除知情同意(waiver of informed consent)之相關規定
- When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

Rule of thumb

- <7: too young to assent
- 7 – 12: capable of assenting, but no written documentation needed.
- >12: capable of full participation in the consent process (i.e. giving assent and documenting that decision in writing)

McGuire C and Chadwick GL. Protecting Study Volunteers in Research: A Manual for Investigative Sites, 3rd ed. University of Rochester

Parental permission (46.408(b)(c)(d))

- 依據Subpart A中有關知情同意(46.116)與知情同意文件(46.117)之規定
- Category I & II–one parent is sufficient
- Category III & IV–both parents must give their permission unless one parent is deceased, unknown, incompetent, etc
- Waiver of permission (e.g. for neglected or abused children)

案例三

預防青少年之間藉由性行爲傳染的疾病 (STDs)

- 研究目的: 了解青少年在得到STDs之前所知道的相關訊息爲何,以及這些資訊是否會影響他們的性行爲
- 受試者:已接受治療之青少年,這些青少年在決定接受治療時不須取得父母同意
- 研究方法:訪談,無任何治療及個人資料收集
- 問題:可否免除父母許可?

可否免除父母同意?

- 風險是否超過最低程度？
- 免除父母同意是否會影響受試者的權利與福利？
- 研究是否可在無免除同意之情況下實行？
- 是否於研究結束後提供父母有關訊息？
- 免除父母同意是否違反當地法律?

Child Advocate 兒童代言人

- 研究對象爲由政府或其他機構監護的兒童
- 除了兒童的監護人外,IRB有權要求研究中增聘兒童代言人
- 一位兒童代言人可代言多位兒童
- 兒童代言人應具備相關工作背景與經驗,如社福人員
- 兒童代言人不能與研究,計畫主持人或兒童之監護機構有關聯

總結

- Children are vulnerable subjects.
- 45 CFR 46 Subpart D
- Parental permission vs. child's assent
- Risk/benefit classification of research

Thank you for your attention!