相關背景與 IRB 組成

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IRB 的相關背景

Reference Material

- U.S. Government Regulations
  - Code of Federal Regulations : Title 45, Part 46
  - Code of Federal Regulations : Title 21, Part 50
  - Code of Federal Regulations : Title 21, Part 56
- Ethical Codes
  - The Nuremberg Code
  - The Declaration of Helsinki
  - The Belmont Report

Ethics and Regulations

- **Ethics : The Belmont Report**
  - 目標為 protection of human subjects
  - 有 3 個principles 但無明確的 guidance
- **Regulations : 45 CFR 46**
  - 目標同 The Belmont Report
  - 內含 IRB 必須遵從的 bureaucratic rules
  - Silent about the ethical value

The Nuremberg Code

- 得到參與試驗者的自願同意是絕對必要的
- 試驗的目的必須能為社會帶來福祉
- 人體試驗必需有動物實驗的結果為依據
- 試驗過程應避免不必要的身體或心智痛苦和傷害
- 任何預知可能造成死亡或傷害的試驗絕不可進行

The Nuremberg Code

- 受試者的風險必須低於試驗可能帶來的益處
- 必須有合格的人員執行試驗
- 不可造成不必要的身心傷害
- 必須有妥善的準備與安全措施
- 受試者可隨時要求退出試驗

The Declaration of Helsinki

- 在 1964 年，國際醫學協會針對人體試驗又提出了赫爾辛基宣言
- 倫理相關規定類似紐倫堡公約
  - 研究計畫的設計與執行需經獨立的委員會審查
  - 著名雜誌的編輯開始要求研究需依赫爾辛基宣言，結果的發表需有審查委員會的同意函

The Belmont Report

- 貝爾蒙特報告於 1976 年被提出
- 二主要部分
  - Basic Principles
  - Applications：實用性較佳
- 三項倫理原則
  - 尊重個人（respect for person）：知情同意
  - 有益（beneficence）：風險/利益評估
  - 公平（justice）：受試者的選擇

Respect for person

- 當受試者有能力瞭解試驗過程時, 對是否參與試驗應有絕對的自主權, 對於是否要參與試驗或退出試驗有絕對的自由
- 衍生出的規範包括:
  - 需獲得受試者書面的同意書(informed consent)
  - 應尊重受試者的隱私
  - 當受試者的自主權有障礙時(弱勢族群), 應給予更多的保護

Beneficence

- 對受試者的風險應該最小
- 研究者應盡量降低受試者可能的風險, 並增加預期的益處
- 和參與試驗所得益處相比, 風險應為合理相關
- 要求研究者和 IRB 需就風險/利益做詳細的評估
- 受試者的隱私應受保護

Justice

- 受試者的選擇應該公平
- 受試者族群 vs 試驗結果有益的族群

Overview Topics

- **Primary Responsibility of IRB**

  Protect the rights and welfare of human research participants

- **The Belmont Circle**
  - Public / Subject
  - Federal Government
  - Investigator
  - Institution / Sponsor
  - IRB

Related Organizations

- DHHS
  - OHRP
    - The Office for Human Research Protections
    - 45 CFR 46 （The Common Rule）
    - 管理使用 federal funds 的研究
    - 是 DHHS 中管理人體試驗的單位
  - FDA
    - The Food and Drug Administration
    - 21 CFR 50, 56
    - 管理涉及 drug, biologic, or medical device 的研究

Related Organizations

- **PRIM & R**
  - Public Responsibility In Medicine and Research
  - Was founded in 1974 : Promote the ethic conduct through education
- **ARENA**
  - Applied Research Ethics National Association
  - PRIM&R 的 membership
  - IRB community 的 leadership

主管機關之相關規範

- 75年:醫療法(94年修正)
- 76年:醫療法施行細則(95年修正)
- 82年:新藥安全監視制度
- 85年:藥品優良臨床試驗規範
- 92年:醫療機構人體試驗委員會組織及作業基準
- 94年:藥品優良臨床試驗準則

醫療法與醫療法施行細則

- 醫療法:主要法律規範
  - 第八條:對人體試驗的範圍作出定義
  - 第七十條:人體試驗之病歷應永久保存
  - 第七十八條至八十二條:一般性的規範
  - 第一百零二、一百零五、一百零七與一百零八條 ： 訂定了違反者與其醫療機構的罰則
- 醫療法施行細則:第二、五十、五十一與五十二條 與新醫療法部份重複

Organizing the Office

Organizing the Office

- IRB 的運作應考慮：
  - Quality
  - Efficiency
  - Consistency

Written Procedures

- 目的
  - 建立 consistency
  - 降低 errors
  - 明確描述成員各自的 responsibility
  - 對新的成員能快速有效的給予 training
  - 對complaints, lawsuits 可提供partial defense
- 方式
  - Followed
  - 定期重新 revisited
  - 必要時隨時 revised

Staff 的功能

- 準備 the meeting agenda
- 對需審查的 proposals 先進行screening
- 在 IRB meeting 時做紀錄
- 管理 data base 和 information
- 分派 SAE 和 amendments 的處理
- 適當處理 protocol 的 violation
- 對 subjects 的抱怨能適當處理
- 負責 education 和 training
- 負責機構內和機構外的合作關係

我們的相關規範 - 總則 2-1

- 醫療機構人體試驗委員會組織及作業基準
  - 為保障受試者權益，施行人體試驗之醫療機構（以下簡稱試驗機構）應依本基準之規定組成人體試驗委員會（以下簡稱委員會）為必要之審查。

    前項委員會，試驗機構得以倫理委員會或其他適當名稱定之。
  - 委員會審查人體試驗計畫，應考量尊重自主之倫理原則，確保受試者接受充足之資訊、並經理性思考、於未受脅迫或操控之情形下，自願參與試驗。

    受試者為無自主性或自主性較低者，應予以加強保護。

我們的相關規範 - 總則　2-2

- 委員會審查人體試驗計畫，應考量善益之倫理原則，以試驗潛藏之危險性不超出其可能之益處為準，保護受試者不受不必要之傷害，並促成其福祉。
- 委員會審查人體試驗計畫，應考量正義之倫理原則，確保受試者具公平參加試驗及受平等對待之機會，不得以未來不可能分享試驗成果之羣體為施行試驗之對象。

辦理委員會相關事務之人員

- 委員會應獨立於試驗機構執行職務。試驗機構應編制足夠之專任或兼任人員，依下列規定辦理委員會之相關事務：
  - 人員之職務及其義務、責任應明定之。
  - 人員應簽署保密協定。
  - 應有供人員處理事務及儲存檔案之處所。

Organizing the IRB Committee

The IRB Committee 2-1

- **Committee Size**
  - At least 5 members
  - Majority : more than half
  - Adequate expertise and diversity
  - At least one have no meaningful association
- **Consultants**
  - No standard procedure or guideline
- **Alternate IRB members**
  - More than one member for an IRB roster position

The IRB Committee 2-2

- **Subcommittee**
  - Expedited process
  - Primary review
  - Continuing review
  - Compliance audits
  - IRB policy and procedures
  - SAEs
- **SAEs**
  - Reviewed first by the investigator
  - IRB Chair
  - Forwards for full-committee review

The IRB Meeting

- Length, frequency and time of meeting
  - No DHHS or FDA's regulations
  - Length : ≤ 4hours
  - Frequency : 依 workload 和 review 的 efficiency
  - Time : 應遷就委員的時間
- 合理的 meeting 取決於 ：
  - 須 full-committee 審查的計畫數量
  - 大多數委員可參加的時間
  - 審查的效率

人體試驗委員會之組成及召開 3-1

- 委員會置委員七人至二十一人，其中一人為主任委員，一人為副主任委員，均由試驗機構選任之，並報請中央衛生主管機關備查。
- 前項委員除有關醫事專業人員外，應有三分之一以上為法律專家、社會工作人員及其他社會公正人士。委員中應有二人以上為非試驗機構內之人員，並不得全部為單一性別。

人體試驗委員會之組成及召開 3-2

- 委員會得分設若干組，每組置委員五人至九人，其中一人為召集人，均由試驗機構就委員會委員聘兼之。其中非醫事專業委員應有一人以上，並有至少一人為非試驗機構內人員。
- 委員任期為二年，連聘得連任。但每次改聘人數以不超過委員總人數二分之一為原則。

人體試驗委員會之組成及召開 3-3

- 委員會及其各組召開審查會議，應有半數以上之委員出席。但委員會及其各組應出席委員，均不得少於五人。委員出缺未達前項應出席人數時，試驗機構應即補聘之。補聘之任期至該期委員會委員任期屆滿時為止。
- 會議主席由主任委員或其指定之委員擔任。非醫療專業委員若全部未出席，不得進行會議；非試驗機構內委員若全部未出席時，亦同。

委員資格

- 試驗機構應明定委員之遴聘資格及專業資歷等必要條件，並公開之。委員應經講習。
- 委員有下列情形之一者，當然解聘：
  - 任期內累計無故缺席三次以上或超過應出席次數三分之一以上。
  - 負責審查案件，因可歸責事由致會議延期，累計三次以上。
  - 嚴重違反利益迴避原則。
- 中央衛生主管機關對委員之姓名、職業及與試驗機構之關係，得以公開。
- 利害關係人或主管機關得調閱委員自委員會支領費用之記錄、憑據。

會議之利益迴避原則 3-1

- 於下列情形應離席，不得參與討論、表決：
  - 受審試驗計畫之主持人、共同或協同主持人或委託人為委員之本人、配偶或三親等以內之親屬。
  - 受審試驗計畫之主持人、共同或協同主持人與委員為另一申請或執行中之專題研究計畫之共同或協同主持人。
  - 受審之試驗計畫為整合計畫或其子計畫，而委員為該整合計畫或其子計畫之主持人、共同或協同主持人。
  - 其他經委員會決議應離席者。

會議之利益迴避原則 3-2

- 於下列情形得不離席，但不得參與表決：
  - 受審試驗計畫之主持人、共同或協同主持人為委員最近五年內，曾指導博碩士論文之學生或博士後研究員。
  - 受審試驗計畫之主持人、共同或協同主持人或委託人曾為委員之博碩士論文或研究計畫指導者。
  - 受審試驗計畫之主持人、共同或協同主持人為委員之同系、所、科同仁。
  - 其他經委員會決議不得參與表決者。

會議之利益迴避原則 3-3

- 委員與試驗機構或試驗計畫委託人之下列關係，應揭露之：
  - 聘僱關係。但試驗機構內人員，毋須揭露。
  - 支薪之顧問。
  - 財務往來狀況。
  - 本人、配偶與三親等以內之親屬對試驗機構或試驗計畫委託人之投資。
- 依委員之特殊專業知識及經驗，若其迴避將致委員會難以為適當之決定時，得經委員會決議毋須為第一款及第二款之迴避，但應於會議記錄載明之。

CERTIFICATION EXAMINATION FOR IRB PROFESSIONALS

經驗分享

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96.08.27

Council for Certification of IRB Professionals
affiliate of PRIM&R

CCIP

- Foundations and Concepts of IRB Practice : 25%
- Organizational and Personnel Knowledge : 15%
- IRB Functions and Operations : 45%
- Records and Reports : 15%

考試方式

- 250 題單一答案的複選題
- 考試時間 4 小時
- 考題可簡單區分為:
  - 簡單的觀念題：直接的答案
  - 複雜一點的考題：比較性質
  - 難度較高的考題：情境題

簡單的觀念題

- Assuring privacy of the subjects and the research data and the requirement to obtain informed consent from subjects best reflects which ethical principle:

A. Beneficence;
B. Respect for Persons;
C. Justice;
D. Do no harm.

直接的答案

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D. Do no harm.

簡單的觀念題

- According to the Belmont Report, respect for persons typically demands that subjects :

A. Share in the benefits of the research;
B. Gain maximum benefit from research;
C. Waive any rights or benefits from research;
D. Enter into research voluntarily with adequate information.

直接的答案

According to the Belmont Report, respect for persons typically demands that subjects :

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- Gain maximum benefit from research
- Waive any rights or benefits from research
- Enter into research voluntarily with adequate information

簡單的觀念題

The regulations define a quorum as :

- **One more than half of those present at the meeting**
- **One more than half of those present at the meeting and on the roster**
- **One more than half of those on the roster**
- **The regulations do not define quorum**

直接的答案

The regulations define a quorum as :

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- **One more than half of those on the roster**
- **The regulations do not define quorum**

簡單的觀念題

A protocol revision approved by the IRB is effective for what period of time :

- 365 days beyond date of approval
- 11 months beyond the date of approval
- The length of time specified by the investigator in the initial request for IRB review of the protocol revision
- Until the expiration date of the most recent continuation review for the protocol

直接的答案

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比較性質的考題

- An example of evidence that the Declaration of Helsinki, in contrast to the Nuremberg Code, was taken seriously by American scientists is:

A. The Tuskegee trial was immediately stopped;
B. Scientists began, for the first time, to obtain informed consent from research subjects;
C. Many scientific journal editors began to request that if a human research study were to be published it must have been performed within ethical standards;
D. All of the above.

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C. Many scientific journal editors began to request that if a human research study were to be published it must have been performed within ethical standards;
D. All of the above.

難度較高的考題 – 情境題

- Which of the following scenarios is in compliance with federal regulations regarding the consenting procedure for enrollment of subjects in research?

A. The Investigator identifies a hospitalized patient who is eligible for enrollment in a research study. The patient, because of his illness, is not competent to give informed consent and there is no legal guardian, or next of kin/family to approach. Because the research has the potential for direct benefit to the patient, and standard care of the patient will be continued during the study, the Investigator approaches two physicians who are not affiliated with the study who concur with the medical opinion of the Investigator about enrollment of the patient and who sign the research consent from for the enrollment of the patient into the study;

B. The Principal Investigator is away at a conference. A Co-Investigator identifies a potential research subject and is unable to find the approved and validated consent form. The Co-Investigator documents the subject's consent with an available expired consent form once the up-to-date consent from is located. The Co-Investigator documents in the research record this variance in consent procedure;

C. At the conclusion of the research study, at the time of final data audit by the sponsor, the Investigator discovers that a number of the signed consent forms are missing. The Investigator, with agreement of the sponsor, contacts those specific research subjects and has them sign and date a new consent form;

D. The Investigator identifies a research subject who is eligible for a research study and approaches him/her regarding participation. The Investigator begins the presentation of the study and gives the consent form to the potential subject. The Investigator notes that the validation stamp on the consent form is out of date. The Investigator completes a brief discussion of the study and reschedules a meeting with the research subject to execute the full consent procedure after contacting the IRB to determine the requirements to obtain an updated consent form.

情境題－題目

- Which of the following scenarios is in compliance with federal regulations regarding the consenting procedure for enrollment of subjects in research?

情境題－選項 A

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情境題－選項 B

B. The Principal Investigator is away at a conference. A Co-Investigator identifies a potential research subject and is unable to find the approved and validated consent form. The Co-Investigator documents the subject's consent with an available expired consent form once the up-to-date consent from is located. The Co-Investigator documents in the research record this variance in consent procedure;

情境題－選項 C

C. At the conclusion of the research study, at the time of final data audit by the sponsor, the Investigator discovers that a number of the signed consent forms are missing. The Investigator, with agreement of the sponsor, contacts those specific research subjects and has them sign and date a new consent form;

情境題－選項 D

D. The Investigator identifies a research subject who is eligible for a research study and approaches him/her regarding participation. The Investigator begins the presentation of the study and gives the consent form to the potential subject. The Investigator notes that the validation stamp on the consent form is out of date. The Investigator completes a brief discussion of the study and reschedules a meeting with the research subject to execute the full consent procedure after contacting the IRB to determine the requirements to obtain an updated consent form.

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The Exam

- Get plenty of rest the night before exam
- Eat a good breakfast
- Arrive early
- Make sure to answer ALL the questions

Questions ???