Laws and Regulations applied to clinical researches in Taiwan

台灣人體研究之相關法規

人體試驗相關法規
Laws and Regulations applied to clinical researches in Taiwan

- 一般法律 **General Law**
- 行政命令 **Regulations**
- 基準 **Guideline**

人體試驗相關一般法律
General Law

- 民法 **Civil Law**：損害賠償 compensation
- 刑法 **Criminal Law**：傷害、過失
- 電腦處理個人資料保護法 **Computer-Processed Personal Data Protection Law (Aug 1, 1995)**
- 醫療法 **Medical Care Act Articles 8, 78, 79, and 80 (Feb 5, 2005)**
- 醫師法 **Physician Act**

Laws: The Medical Care Act

- **Art. 8-Definition of "Human trial": Any experimental research conducted by medical institutions on humans**
  - **New medical techniques,**
  - **New drugs,**
  - **New medical devices**
- **Art. 78 – "Teaching hospitals" must propose "research protocols" to the Review Board of DOH for the approval of human trials.**
- **Art. 79 -Informed Consent**
- **Art.80- Requirement to submit Report to authorities. Authorities has right to cease trial for safety reason.**

醫療法第八條

本法所稱人體試驗，係指醫療機構依醫學理論於人體施行新醫療技術、藥品或醫療器材之試驗研究。

醫療法第七十八條

為提高國內醫療技術水準及醫療，或預防疾病上之需要，教學醫院經擬定計畫，報請中央衛生主管機關核准，或經中央衛生主管機關委託者，得施行人體試驗。非教學醫院不得施行人體試驗。

醫療法第七十九條

- 醫療機構施行人體試驗時，應善盡醫療上必要之注意，並應先取得接受試驗者之書面同意；受試驗者為無行為能力或限制行為能力人，應得其法定代理人之同意。
- 前項書面，醫療機構應記載下列事項，並於接受試驗者同意前先行告知：

  一、試驗目的及方法。

  二、可能產生之副作用及危險。

  三、預期試驗效果。

  四、其他可能之治療方式及說明。

  五、接受試驗者得隨時撤回同意。

醫療法第八十條

- 醫療機構施行人體試驗期間，應依中央主管機關之通知提出試驗情形報告；中央主管機關認有安全之虞者，醫療機構應即停止試驗。
- 醫療機構於人體試驗施行完成時，應作成試驗報告，報請中央主管機關備查。

Physician Act

A physician guilty of any of the following conditions shall be disciplined by the Medical Association or the competent authority.

1. major or repeated professional mistakes
2. taking advantage of professional opportunity to commit a criminal act, confirmed by a conviction
3. excessive use of medication or treatment not due to treatment needs
4. violating medical ethics in his or her professional practice
5. any inappropriate professional behavior apart from the previous four clauses and each clause in Article 28-4

醫師法

第二十五條（移付懲戒之情形）

醫師有下列情事之一者，由醫師公會或主管機關移付懲戒：

一、業務上重大或重複發生過失行為。

二、利用業務機會之犯罪行為，經判刑確定。

三、非屬醫療必要之過度用藥或治療行為。

四、執行業務違背醫學倫理。

五、前四款及第二十八條之四各款以外之業務上不正當行為。

行政命令 Regulations

- 醫療法施行細則 --95年6月20日公告The Enforcement rules of the Medical Care Act Jun 20,2006
- 藥品優良臨床試驗準則--94年1月7日公告 Guideline for Good Clinical Practice (1996,2001, Jan 7, 2005)

Regulations: The Enforcement Rules of Medical Care Act

- **Art. 2 - Definition of new medical techniques, new drugs, and new medical devices of human trials.**
- **Art. 54 – Required elements of a research protocols.**
- **Art. 55 – Approval process of human trial maybe authorized.**
- **Art. 56 – Consent process**
- **Art. 57 – Medical care after withdrawal from trial.**

醫療法施行細則第二條

本法第八條所稱新醫療技術，指下列各款情形之一：

一、以藥品或醫療器材以外之物質，植入或移植人體施行治療，其安全或療效未經證實者。

二、以新程序或新方法施行者。

三、其他在國外已施行於人體，中央主管機關認在國內有施行人體試驗之必要，並經公告者。

本法第八條所稱新藥品，指下列各款情形之一：

一、新成分、新療效複方或新使用途徑之藥品。

二、其他在生產國已核准使用於人體之藥品，中央主管機關認在國內有施行人體試驗之必要，並經公告者。

本法第八條所稱新醫療器材，指下列各款情形之一：

一、新原理、新結構、新效能或新材料之醫療器材。

二、其他在生產國已核准使用於人體，中央主管機關認在國內有施行人體試驗之必要，並經公告者。

醫療法施行細則第五十四條

醫療機構依本法第七十八條第一項規定擬定之人體試驗計畫，應載明下列事項：

一、試驗主題。

二、試驗目的。

三、試驗方法：

（一）接受試驗者標準、招募方法及數目。（二）試驗設計及進行方法。（三）試驗期限及進度。（四）追蹤或復健計畫。（五）評估及統計方法。

四、接受試驗者同意書內容。

醫療法施行細則第五十四條

五、試驗主持人及主要協同人員之學、經歷及其所受訓練之背景資料。

六、國內或國外之實驗室、動物實驗或其他研究，已發表之文獻報告。

七、在國外主要國家已核准進行人體試驗者，其證明文件。

八、所需藥品或儀器設備，包括必須進口之藥品或儀器名稱、數量。

九、預期試驗效果。

十、可能傷害及處理。

醫療法施行細則第五十五條

- 中央主管機關得將本法第七十八條第一項規定核准教學醫院所擬定人體試驗計畫之權限，委託相關團體為之。

醫療法施行細則第五十六條

醫療機構依本法第七十九條第一項所定書面同意之取得及第二項所定告知，應符合下列規定：

一、書面同意及告知之內容，應以接受試驗者或其法定代理人可理解之方式為之。

二、應給予充分時間考慮。

三、不得以脅迫或其他不正當方法為之。

醫療機構於人體試驗期間，應依接受試驗者或其法定代理人之需要，隨時說明人體試驗相關問題。

醫療法施行細則第五十七條

醫療機構依第七十九條第一項規定施行人體試驗時，對不同意或撤回同意施行人體試驗者，仍應施行常規治療，不得減損其正當醫療權益。

GCP in Taiwan

- 1996 Taiwan announced GCP as a guideline
- 1998, GCP Inspection Workshop in Taiwan (by FDA)
- 2000, GCP inspection for all trials for registration purpose.
- 2005, Adopt ICH-GCP to replace GCP – Taiwan and set as Regulations.

國內GCP公佈時間

- 藥品優良臨床試驗規範 Guideline
  - 八十五年11月20日公布 1996
  - 九十年9月20日修正公布公布 2001
- 藥品優良臨床試驗準則regulation
  - 九十四年1月6日頒佈 2005

Results of GCP Inspection in 2000-03

Deficiencies Found in GCP Inspection

	Item inspected	No. of deficiency 2000/01/02/03
1.	Authorization and Management	4/ 0/ 3/ 0
2.	Clinical Trial Protocol	5/ 8/ 4/ 6
3.	Informed Consent	8/ 7/ 24/ 24
4.	IRB	22/16/16/7
5.	Verify source data with case report form	77/62/103/88
6.	Drug Accountability and Management	30/30/68/71
7.	Record Archiving	27/29/20/20
8.	Computer System and Data Management	24/23/16/19
	Total	181/182/254/244

No. of Trials inspected 31/31/37/47

Results of GCP Inspection in 2000-03

Outcome of GCP Inspection	No. of Cases 2000-03
Accepted	19 (12%)
Accepted after clarification	117 (76%)
Re-inspection on another site	6 (4%)
Rejected	12 (8%)
Total	155

For Cause Inspection

- Severe adverse event : possible drug related and possible protocol violation during a phase II trial
- Stop new patients enrolment
- Immediate on site inspection and review all cases with the sponsor
- No protocol violation except some missing documentation, sponsor stop the trial for safety reason later.

Taiwan Site Inspected by FDA

- Pivatol trial of Adefovir in treating Chronic Hepatitis B with major site in Taiwan
- A 1-week FDA inspection in July, 2002
- Satisfactory result with drug approved by FDA later

基準Guideline (31)

Major guidelines

- 醫療機構人體試驗委員會組織及作業基準 - 92年11月12日公告 **Operational Guidelines for clinical trial Committees of medical institute. Date: Nov 12, 2003 (revised from WHO：Operational Guidelines for Ethics Committees That Review Biomedical Research)**
- 人體研究倫理政策指引 - 96年7月17日公告 **Human Research Ethics Policy Guidelines. July 17, 2007 - 8** Points

Point 1：Purpose of Human research

Human Research Ethics Policy Guidelines

- Human research shall be conducted for the purpose of improving the welfare of human beings, and shall be conducted under the principles of respecting the voluntary wishes of the subjects under study, and protecting their privacy and right to health.

人體研究倫理政策指引

1. 人體研究應以增進人群之福祉為目的，本尊重受研究者之自主意願，保障其隱私與健康權之原則為之。

Point 2 Definition of Human research

- Unless otherwise prescribed in laws and regulations, human research shall include all processes seeking to acquire, analyze, and investigate human tissue or information concerning individual behavior, thinking, physiology, psychology, sociology, genetics, and medicine for the purpose of research.

2. 人體研究除法令規定外，凡以研究為目的，取得、分析、調查人體之組識或個人之行為、理念、生理、心理、社會、遺傳，以及醫學有關資訊之過程均屬之。

Point 3 consent

- Human research shall, as much as possible, be performed only after notifying the subjects using clear and understandable methods concerning relevant aspects, and obtaining their written consent.
- The content of notification in the preceding paragraph shall include at least the research goal and timetable, name of the investigator, name of the research institution, source of research funding, a summary of the research content, subjects' rights and the duties of research personnel, mechanisms for safeguarding subjects' personal privacy, foreseeable risks within a reasonable score, remedial measures that can be applied for in the event of damages, and name of and method of contacting liaison person in the event of relevant problems.

3. 人體研究應就最大之可能，以明確度可理解之方式，告知受研究者有關事項，並取得其書面之同意後為之。

- 前項告知內容至少必須包括研究之目的與期程、研究主持人之姓名、研究機構之名稱、研究經費之來源、研究內容之大要、受研究者之權益與研究人員之義務、保障受試者個人隱私之機制、合理範圍內可預見之風險及造成損害時得申請之補救措施、相關問題之聯絡人姓名及其聯絡之方式等。

Point 4 Scientific sound

- Human research shall be planned on the basis of the best scientific evidence and assumptions. With regard to the acquisition and analysis of data and use of results, subjects' private personal information shall not be disclosed without their consent under any circumstances. Risks shall be controlled as much as possible. There shall be a proper response plan including remedial measures addressing any damages possibly caused during the research process.

4. 人體研究應本最佳之科學實證與假設規劃，在資料取得、分析處理與成果運用之過程中，非經受研究者同意，均不得揭露其個人隱私資料；並應盡最大之可能管控風險發生；對於研究過程中可能導致之損害，應有包括損害補救措施在內之妥善因應計劃。

Point 5 Consent research only

- Materials acquired during research shall not be used for purposes other than original notices and written consent. When it is necessary to use such materials for other research purposes, the subjects' consent must be obtained again in accordance with the regulations of Point 3.

5. 研究取得之材料，不得作為原始告知及書面同意以外之用途，其有作為其他研究用途之必要者，應另行依第三點之規定，取得受研究者同意。

Point 6 vulnerable persons

- Human research shall not be conducted on minors or on underprivileged persons. However, this restriction shall not apply when such research is clearly beneficial to the subjects' collective or individual interests, and when the subjects' legal guardians or most appropriate relations have been notified, and their written consent obtained.

6. 人體研究不得以未成年人或弱勢者作為對象。但顯有助益於其集體或個別權益，經告知其法定代理人或最適關係人，並取得同意者，不在此限。

Point 7 Ethics committees

- Research organization shall establish ethics committees or commission the ethics committees of other organizations to perform review of human research ethics matters.
- At least one-third of the members of the ethics committee shall be legal specialists or other impartial public figures; each ethics committee shall contain at least two persons from outside the organization in question.
- Ethics committee shall review and approve human research, and shall bear responsibility for the supervision of project implementation and handling of research results.

7. 研究機構應設倫理委員會或委託其他機構之倫理委員會，負責人體研究倫理事項審查。委員會之成員，至少應有三分之一以上為法律專家及其他社會公正人士，並應有二人以上為機構外人士。委員會對審查通過之人體研究，計畫執行過程與研究成果備查負有監督責任。

Point 8 Commercial benefit

- Subjects shall be informed of any commercial benefit possibly derived from human research; any necessary agreements shall be made in writing.

8. 人體研究所可能衍生之商業利益，應告知受研究者，並以書面為必要之約定。

- 研究用人體檢體採集與使用注意事項 - 95年8月18日公告Guidelines for Collection and Use of Human Specimens for Research Date: Aug 18, 2006

Trial behavior

- 臨床試驗受試者招募原則 - 96年6月6日公告
  Guidelines for recruitment of clinical trial subject
  Date: June 6, 2007
- 「醫療機構及醫事人員發布醫學新知或研究報告倫理守則」90.11.12 Ethical guideline for announcement of research result. Nov 12. 2001
- 「醫師與廠商間關係」守則- 95年9月8日公告
  Guidelines for relationship between medical doctor and industry. Sep 8, 1996

Specific trial guideline

- 薬品臨床試験一般基準General guidelines for pharmaceutical clinical trial
- 醫療器材優良臨床試驗基準 – 96年5月30日公告 Guideline for Good Clinical Practice of medical device. May 30, 2007
- 薬品生體可用率及生體相等性試驗基準. 95年5月17日公告.Guidance for Bioequivalence and Bioavailability studies of pharmaceuticals. May 17, 2006
- 銜接性試驗基準91年5月公告. Ethnic factors in the acceptability of foreign clinical data. May 2002

Special population

- 腎功能不全病患之藥動學試驗基準 91年7月公告 Guidance for pharmacokinetics inpatients with renal impairment function. July 2002
- 小兒族群的藥動學試驗基準Guidance for studies of drugs in support of special populations :Pediatrics
- 年老病患的藥品臨床試驗基準 Guidance for studies of drugs in support of special populations :Geriatrics
- 肝功能不全病患的藥動學試驗基準Guidance for pharmacokinetics in patients with hepatic impairment function.

Operation of special procedures

- 體細胞治療人體試驗申請與操作規範 92年11月4日公告 Operation Guideline for Somatic Cell therapy Nov 4,2003
- 基因治療人體試驗申請與操作規範 86, 91.9.13 Operation Guideline for Genetic therapy clinical trial. Sep.13, 2002
- 臍帶血收集及處理作業規範91年1月18日公告Guideline for umbilical blood collection and operation. Jan. 18,2002
- 胚胎幹細胞研究的倫理規範-91年2月8日公告Ethical Guideline for embryonic stem cell 2002/2/19
- 人體細胞組織優良操作規範91年12月13日公告Regulation of Human cell and Tissue-Based Products. Dec. 13, 2002

Review process

- 藥品臨床試驗計畫書主要審查事項 Major Review items in Clinical trials of pharmaceuticals
- 醫療機構人體試驗委員會得快速審查之案件範圍 95年2月3日公告Types of clinical trials that could be expedited reviewed by IRB. Feb 3 2006.
- 臨床試驗報告之格式及內容基準 - 92年4月14日 Structure and contents of Clinical Trial Report. Apr.14, 2003

Informed consent

- 藥品臨床試驗受試者同意書範本96年5月30日公告 Examples of informed consent for pharmaceutical clinical trial. May 30, 2007
- 藥物基因體學研究之受檢者同意書內容參考指引 Guidance for informed consent form of pharmacogenetic research (2005)

Qualification for investigator

- 執行國內藥品臨床試驗主持人資格條件 - 96年5月18日公告Qualification for investigator of Drug Clinical Trial.

96年5月18日公告

執行國內藥品臨床試驗主持人至少須符合以下資格條件：

- 須為專科醫師。
- 三年內未受醫師法第25條醫師懲戒之確定處分。
- 三年內未曾於擔任試驗主持人時，因重大或持續違反GCP者。
- 每3年參加醫學倫理相關課程不得少於9小時。

Guidelines of Specific drug trials

- 癌症治療薬品臨床試験基準Guidelines of drug clinical trials of malignant disease.
- 感染症治療薬品臨床試験基準Guidelines for drug clinical trials of infectious disease
- 内分泌及新陳代謝治療薬品臨床試験基準Guidelines for drug clinical trials of drugs in endocrine and metabolic disease
- 植物抽取新薬臨床試験基準 Guidelines for clinical trials of extract.
- 核醫放射性薬品臨床試験基準Guidelines for radioactive drug clinical trial
- 心血管治療薬品臨床試験基準 Guidelines for drug clinical trials in cardiovascular disease.