GCPs의 International Harmonization 방향

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연세의대

Good Clinical Practice(GCP)는 1970년 후반에 미국에서 FDA기 신의약품의 제조 및 판매허가와 관련된 사항 즉 임상시험 의뢰사와 모니터의 역할과 책임, 임상시험심사위원회의 역활, 임상시험연구자의 의무, 피험자들의 보호와 동의 등에 관한 규정안을 제안하면서, 이들 관련 규정안을 총칭하여 GCP라 칭하며 현재에는 의약품의 임상시험시 관련기관들의 제규정들에 적절하게 규정한 지침을 뜻한다.

임상시험은 인간을 대상으로 하는 연구이기 때문에 임상시험에 앞서 이러한 임상시험이 윤리적이고 과학적인 방법으로 실시되어야 한다. 그러므로 GCP규정을 시행하는 목적은 임상시험에 참여하는 피험자들의 권리와 안전을 도모하고, 임상시험과정 및 임상시험 결과의 과학적 검증 및 시험결과의 정확성및 신뢰성을 얻기 위함이라 하겠다.

처음으로 미국에서 시작된 GCP규정은 각국에 영향을 주었는데, 이로인해 미국에 수입되는 의약품의 적용과 다국적기업 성격의 제약회사, 우루과이 라운드의 영향으로 세계 각국들이 GCP규정을 설정하게 되었다. GCP 규정은 독일(1986년), 프랑스(1987년), 영국(1989년)에 실시되었고, 유럽공동체의 형성으로 EC의 GCP규정안이 1990년 고시되어 1992년부터 실시되고 있으며, 일본도 1985년 의약품 임상시험 시행기준안을 공포하고 임상시험 기준시행법이 1990년부터 시행되고 있다. 우리나라에서도 80년대에 들어오면서 GCP법제화를 준비하여, 1987년 "의약품임상시험관리기준"을 제정공포하였으나, 임상시험실시기관과 관련자들의 인식미비로 그간 시행을 미루어 오다 1995년 10월부터 GCP의 전면 시행이 이루어지게 되었다.

이러한 각국의 GCP는 각 나라마다의 상황에 따라 근소한 차이는 있으나 비교적 원칙적인 사항에서는 일치한다고 할 수 있겠다. 우선 차이를 보이는 몇 가지를 살펴보면, IRB 구성원 및 내용을 볼때 차이는 아래 표 1, 2와 같다. 이러한 단편적인 차이가 보여주듯이 각국의 GCP는 근소한 차이가 있는바, 향후 전반적인 정보 교환 및 임상공동연구를 위해 약간의 교정 및 수정이 필요하다고 사료된다.

THE PRINCIPLES OF ICH GCP

1. Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistont with GCP and the applicable regulatory requirements(s).
2. Before a trial is initiated, foreseeable risks and incnveniences should be weighed against the antieipated benefit for the indiividual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
4. The available noneclinical and clinical information on an investigatinal product should be adequate to support the proposed clinical trial.
5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol.
6. A trial should be conducted in compliance with the protocol and amendment(s) that have received prior institutional review board(IRB)/indcpendent ethics committed(IEC) approval/favourable opinion.
7. The medical care given to, and medical decisions made for, subjects must always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial should be qualified by cducation, training, and experience to perform his or her respective task(s).
9. Freely given informed consent should be obtained from every subject prior to clinical trial participation.
10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting interpretation and verification.
11. The confidentiality of records that could identity subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements(s).
12. Investigational products should be manufactured, handled, and stored in accordance with applicable Good Manufacturing Practice(GMP). They should be used in accordance with the aproved protocol and amendments(s).
13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

SECTION II : During the Clinical Conduct of the Trial

In addition to having on filc the above documents, the following should be added to the files during trial and evidence that all new relevant information is documented as it becomes available.

	Tilte of Doucument	Located in Files of	
		Investigator	Sponsor
2.1	INVESTIGATOR'S BROCHURE UPDATES	X	X
2.2	ANY REVISION TO :	X	X
2.3	INDEPENDENT ETHICS	X	X
	COMMITTEE/INSTITUTIONAL REVIEW	X	X
	BOARD RESPONSIBILITIES		
2.4	REGULATORY AUTHORISATIONS	X	X
	NOTIFICATIONS WHERE REQUIRED	(where required)	
	FOR		
2.5	CURRICULUM VITAE FOR NEW	X	X
	INVESTIGATOR(S) AND/OR		
	SUBINVESTIGATOR(S)		
2.6	UPDATES TO NORMAL VALUES FOR ANY	X	X
	MEDICAL/LABORATORY/TECIINICAL		
	PROCEDURES/TESTS		
2.7	UPDATES OF MEDICAL/LABORATORY/	X	X
	TECHNICAL PROCEDURES/TESTS	(where required)	
2.8	DOCUMENTATION OF	X	X
	INVESTIGATIONAL PRODUCT(S) AND		
	TRIAL-RELATED MATERIALS SHIPMENT		
2.9	CERTIFICATE(S) OF ANALYSIS FOR NEW		X
	BATCHES OF INVESTIGATINAL		
	PRODUCTS		
2.10	MONITORING REPOR FOR VISITS		X
2.11	RELEVANT COMMUNICATIONS OTHER	X	X
	THAN SITE VISITS		
2.12	SIGNED INFORMED CONSENT FORMS	X	

2.13	SOURCE DOCUMENTS	X	
2.14	SIGNED, DATED AND COMPLETED CASE REPORT FORMS(CRF)	X (copy)	X (original)
2.15	DOCUMENTATION OF CRF CORRECTIONS	X (copy)	X (original)
2.16	NOTIFICATION BY ORIGINATING INVESTIGATOR TO SPONSOR OF SERIOUS ADVERSE EVENTS INCLUDING CAUSALITY ASSESSMENTS	X	X
2.17	NOTIFICATION BY SPONSOR AND/OR INVESTIGATOR TO REGULATORY AUTHORITY(IES) OF SERIOUS DVERSE ASSESSMENTS	X (where required)	X
2.18	NOTIFICATION BY SPONSOR TO ALL INVESTIGATORS OF SERIOUS ADVERSE EVENTS INCLUDING CAUSALITY ASSESSMENTS		X
2.19	NOTIFICATION BY EACH INVESTIGATOR TO THE RESPONSIBLE IEC/IRB OF SERIOUS ADVERSE EVENTS INCLUDING CAUSALITY ASSESSMENTS	X	
2.20	INTERIM OR ANNUAL REPORTS TO IEC/IRB	X	
21	SUBJECT SCREENING LOG	X	X (where required)
2.22	SUBJECT IDENTIFICATION LIST	X	
2.23	SUBJECT ENROLMENT LOG	X	
2.24	INVESTIGATIONAL PRODUCTS ACCOUNTABILITY AT THE SITE	X	X
2.25	SIGNATURE SIIEET	X	X
2.26	RECORD OF RETAINED BODY FLUIDS/ TISSUE SAMPLES(IF ANY)	X	X

SECTION III : After Completion of Termination of the Trial

After completion or termination of the trial, all of the documents identified in sections I and II should be in the file together with the following

	Tilte of Doucument	Located in Files of	
		Investigator	Sponsor
3.1	INVESTIGATIONAL PRODUCT(S) ACCOUNTABILITY AT SITE	X	X
3.2	DOCUMENTATION OF INVESTIGATIONAL PRODUCT DESTRUCTION	X (if destroyed at site)	X
3.3	COMPLETED SUBJECT IDENTIFICATION LIST	X	
3.4	FINAL CLINICAL STUDY REPORT (when completed)	X (if applicable)	X
3.5	COMPLIANCE STATEMENT AUDIT CERTIFICATE(if available)		X
3.6	FINAL TRIAL CLOSE-OUT MONITORING FEPORT		X
3.7	TREATMENT ALLOCATION AND DECODING DOCUMENTATION		X

Table 1. Composition of IRB Members

	U.S.A	KGCP	Japan	E.C.
Total No.				
	At least 5 : both sex	More than 4 ; (medical, dental, herbal phamacology, nursing)	At least 5	Mcdical+ Non-medical member
Background				
	At least 1 ; Non-scientific member	At least 1 ; doctor	At least 1 ; Non-scientific member	
	At least 1 ; Non-affiliated member	At least 1 ; Non-medical, phamaceutical science		
Designation				
		by the head of the center	by the head of medical institutin	
Participation in one's own proposal		No	No	
Function	Consultant	Advisary committee		

Table 2. Contents of IRB Regulations in GCPs

	U.S.A	KGCP	Japan	E.C.
Scope	+	+	+	+
Composition of member	+	+	+	−
Function	+	+	+	+
Review process	+	+	+	−
Approval criteria	+	−	−	−
Expedited review	+	−	−	+
Coopperative research	+	+	+	+
Suspention, termination	+	+	−	−
Record maintenance	+	+	+	+
Non compliance	+	−	−	−
Inspection & audit	+	−	−	−

GUIDELINE FOR TIIE INVESTIGATOR'S BROCIIURE

ICH Harmoniscd Tripartite GCP Guidcline

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APPENDIX 1 :
TITLE PAGE(Example)

SPONSOR'S NAME

Product :
Research Number :
Name(s) : Chemical, Generic (if approved)
Trade Name(s) (if legally permissible and desired by the sponsor)

INVESTIGATOR'S BROCHURE

Edition Number :
Release Date :
Replaces Previous Edition Number : **Date :**

ICH Harmonised Tripartite GCP Guideline

GUIDELINE FOR ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

SECTION 1 : Before the Clinical Phase of the Trial Commences

During this planning stage the following documents should be generated and should be file before the trial formally starts

	Tilte of Doucument	Located in Files of	
		Investigator	Sponsor
1.1	INVESTIGATOR'S BROCHURE	X	X
1.2	SIGNED PROTOCOL AND AMENDMENTS, IF ANY SAMPLE CASE REPORT FORM(CRF)	X	X
1.3	INFORMATION GIVEN TO STUDY SUBJECT -INFORMATION SHEET	X	X
	-INFORMED CONSENT FORM	X	X
	-ADVERTISENENT FOR SUBJECT RECRUITMENT(if aplicable)	X	
1.4	CLINICAL TRIAL BUDGET	X	X
1.5	INSURANCE STATEMENT	X	X
1.6	SIGNED AGREEMENT BETWEEN INVOLVED PARTIES	X	X
1.7	DATED, DOCUMENTED APPROVAL OR OPINION OF INDEPENDENT ETHICS COMMITTEE (IEC)/INSTITUTIONAL REVIEW BOARD (IRB) ON ORIGINAL :	X	X
1.8	INDEPENDENT ETHICS	X	

	COMMITTEE/INSTITUTIONAL REVIEW BOARD COMPOSITION		
1.9	REGULATORY AUTIIORITY ARTHORISATION/APPROVAL/ NOTIFICAION OF PROTOCOL	X (where required)	X
1.10	CURRICULUM VITAE OF INVESTIGATOR(S) AND SUBINVESTIGATOR(S)	X	X
1.11	NORMAL VALUES FOR ANY MEDICAL/ LABORATORY/TECHNICAL PROCEDURE OR TEST INCLUDED IN THE PROTOCOL USED TO EVALUATE TREATMENT EFFECTS OR SAFETY	X	X
1.12	MEDICAL/LABORATORY/TECHNICAL PROCEDURES/TESTS	X (where required)	X
1.13	SAMPLE OF LABEL(S) ATTACIIED TO TREATMENT CONTAINER(S)		X
1.14	INSTRUCTIONS FOR HANDLING OF TRIAL INVESTAGATIONAL PRODUCTS AND TRIAL-RELATED MATERIALS	X	X
1.15	DETAILS OF SHIPMENT OF INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS	X	X
1.16	CERTIFICATE(S) OF ANALYSIS OF INVESTIGATIONAL PRODUCT(S) SHIPPED		X
1.17	TREATMENT ALLOCATION AND DECODING DOCUMENTATION FOR BLINDED AND NON-BLINDED COMPARATOR STUDIES WHERE TREATMENT ALLOCATED BY TIIRD PARTY	X (or third paity)	X

1.18 MASTER RANDOMISATION LIST	X (or third party)
1.19 PRE-TRIAL MONITORING REPORT	X
1.20 TRIAL ININATION MONITORING REPORT	X