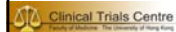


Fraud and Misconduct In Clinical Trials

Slides and script were developed
by
Professor J Karlberg
and
read by Mr. J Thorburn

Clinical Trials Centre
The University of Hong Kong

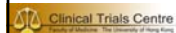


Fraud

Deception carried out for the purpose of achieving personal gain while causing injury to another party.

Misconduct

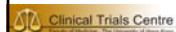
Dishonest or bad management, especially by persons entrusted or engaged to act on another's behalf.



The effect of Fraud and Misconduct

The same

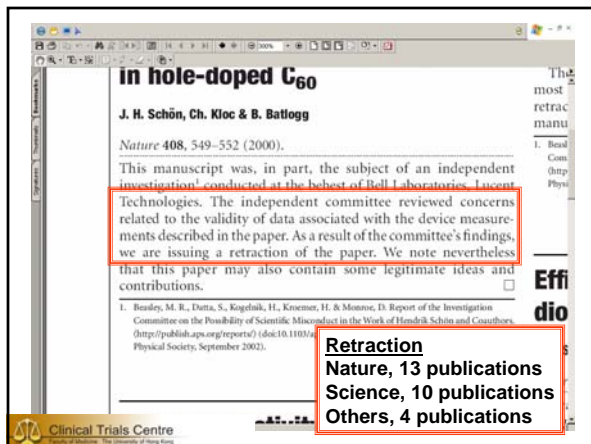
- questionable clinical trial data
- the data may not be used for drug regulatory purposes

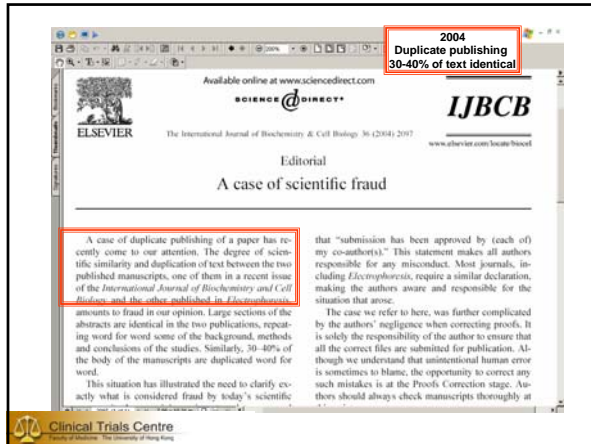


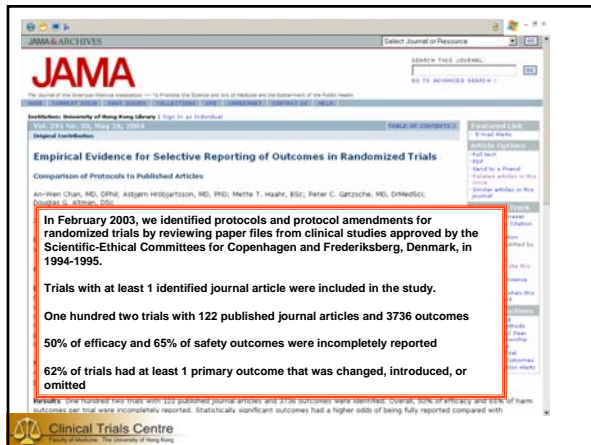
Fraud or Misconduct?

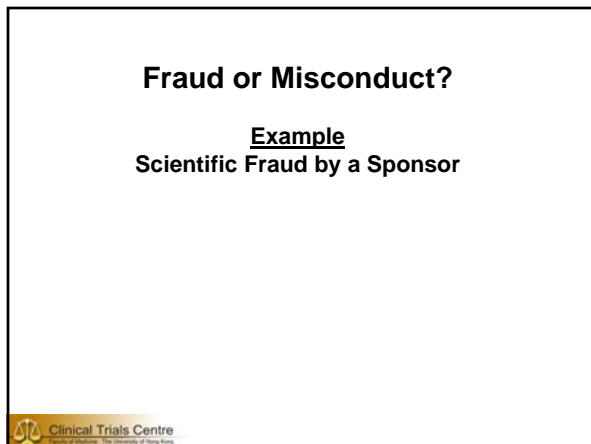
Examples Scientific Fraud by Researchers In Publications











Fraud or Misconduct?

Scientific Fraud
In Clinical Trials

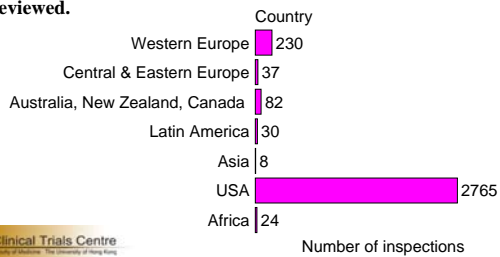
Sponsor Audits
During the conduct of a trial

Regulatory Authority Inspections
After completion of a trial

Sep 1, 2004
Pyotr G. Platonov, Sergei Varshavsky
Applied Clinical Trials

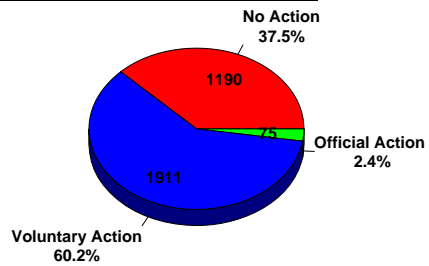
Review of 10 years US FDA Inspections

In total, data from **3178 inspections** whose files have been closed with a final classification as of 4 May, 2004 were reviewed.



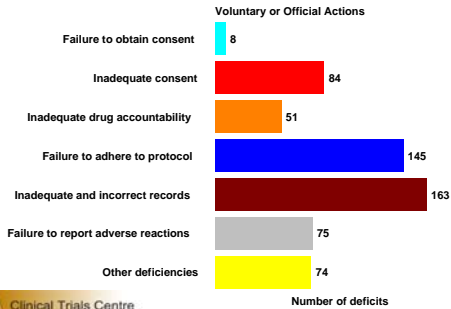
Sep 1, 2004
Pyotr G. Platonov, Sergei Varshavsky
Applied Clinical Trials

Review of 10 years US FDA Inspections



Sep 1, 2004
 Pyotr G. Platonov, Sergei Varshavsky
 Applied Clinical Trials

Review of 10 years US FDA Inspections



FDA's Electronic Freedom of Information Reading Room - Warning Letters and Responses

This page is designed to simplify the search for Warning Letters and Responses. Choose any of the seven search categories and view or download the Warning Letter or Response. Use the Warning Letters and Responses Search Form for advanced searching. All Warning Letters and Responses are available in PDF format. The ADOBE ADOBE Reader is required to view PDF files. Click on the ADOBE icon and download the free reader. Warning Letters posted after June 25, 2001 and Responses posted after September 22, 2002 are also available in HTML format.

Letters described in FDA Warning Letters may have been subject to subsequent interaction between FDA and the recipient of the letter that may have changed the regulatory status of the issues discussed in the letter. If you wish to obtain immediate additional information on the current status of an issue in a particular Warning Letter on this website, please contact the Agency or the recipient of the letter directly. Inquiries to FDA should be sent to: Food and Drug Administration Division of Freedom of Information (HFD-20), 5000 Fisher Lane, Rockville, MD 20857. Instructions for how to submit an FOI request appear below at: <http://www.fda.gov/oc/foi/submitfoirequest.html>

The Food and Drug Administration cannot assure the accuracy of information submitted to the Agency without a complete review of the submitted materials and resolution of the issues discussed therein. To make certain information available to the public, the Agency has undertaken a pilot program to post Responses to Warning Letters before evaluating the documents and resolving the issues. The Responses are restricted to the extent permitted by the Freedom of Information Act.

- Search Most Recent Warning Letters
- Search Most Recently Posted Responses
- Search Warning Letters by Category
- Search Warning Letters by Subject
- Search Warning Letters by Issuing Office
- Search Warning Letters by Date
- Search Warning Letters and Responses with Search Form



Company Name	Address	Issuing Office	Description	Status	Date
Ancher Centers Midwest Company	111 4005	Kansas City District Office	COMP/Manufactured Facility/Unauthorized	FCGI	10/17/04
Arizona Institute of Medicine & Surgery	40062	Los Angeles District Office	Mammography Quality Standards	FCGI	10/17/04
Asip Med AB LLC	111305	Center for Devices and Radiological Health	Current Good Manufacturing Practice/Unauthorized	FCGI	10/17/04
Ativo Sealcoat, Inc.	82302	New York District Office	Sealcoat NACCP/Unauthorized	FCGI	10/17/04
Arconomid, Peter M., M.D.	121404	Center for Devices and Radiological Health	Clinical Investigator	FCGI	10/17/04
Asahi Medical Company, Ltd.	900304	Center for Devices and Radiological Health	Good Manufacturing Practice for Medical Devices	FCGI	10/17/04
Ashtford Farms LLC	80980	New York District Office	Regulatory/Quality System/Unauthorized	FCGI	10/17/04
Asit Sport Science Home Headquarters	20803	Center for Food Safety and Applied Nutrition	Emergency Use/Drug Device or Other/Unauthorized	FCGI	10/17/04
AstraZeneca Pharmaceuticals LP	22280	Philadelphia District Office	COMP/Inspected Pharmacist/Unauthorized	FCGI	10/17/04
Astra Instrumentation LLC	92140	Cincinnati District Office	Quality System/Regulation/Unauthorized	FCGI	10/17/04
Atchafalaya Cerebral Processors, Inc.	51663	Atlanta District Office	COMP in Manufacturing, Packing, or Holding Food for Human Consumption/Sealcoat NACCP/Unauthorized	FCGI	10/17/04
ATF Fitness Products, Inc.	111304	Philadelphia District Office	Dietary Supplement/Labeling/Unauthorized	FCGI	10/17/04
Athers Lunenburg Hospital	50180	New Orleans District Office	Mammography Quality Standards	FCGI	10/17/04
Ativo Sealcoat, Inc.	102204	Atlanta District Office	Sealcoat NACCP/Unauthorized	FCGI	10/17/04
Ativa Veterinary Associates, P.C.	130201	New York District Office	Regulatory/Quality System/Unauthorized Drug Use/Unauthorized	FCGI	10/17/04

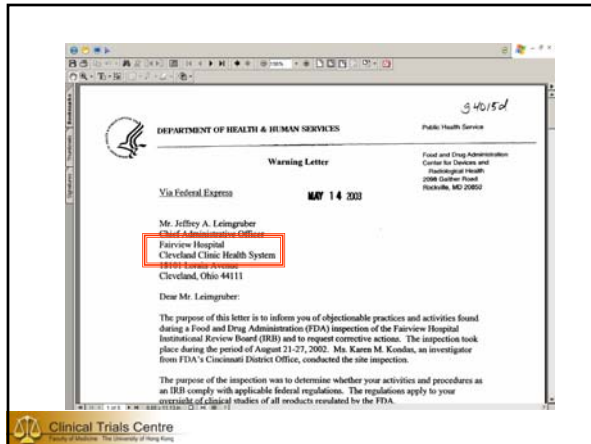


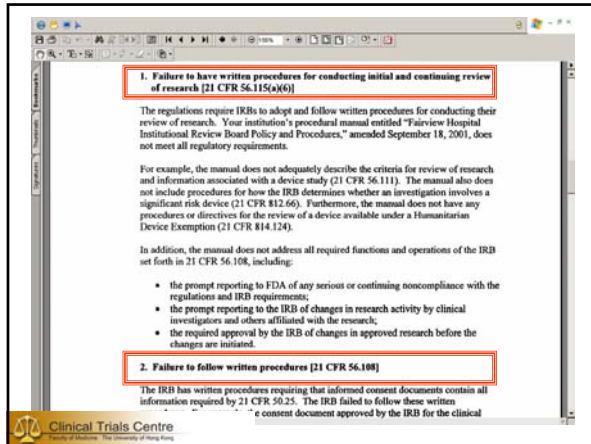
FDA Warning Letters

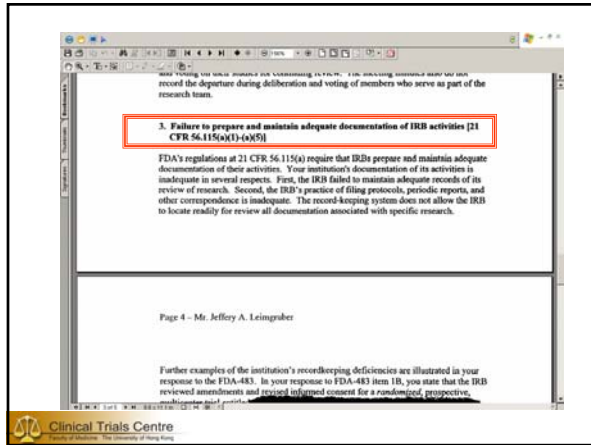
IRB
Institutional Review Board

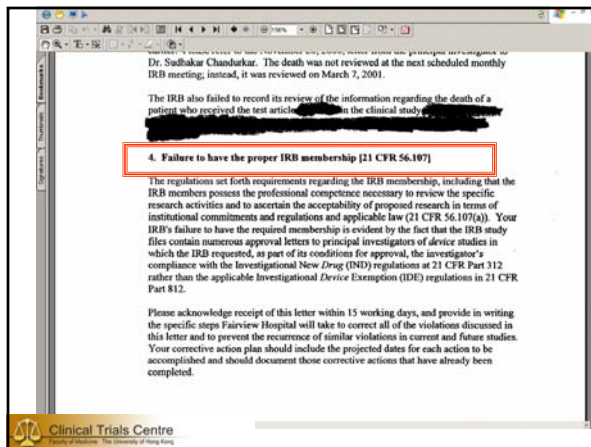
EC
Ethics Committee

Name	ID	Address	Center Name	IRB Name	Compliance Status
Wagreen Company	891584	Chicago District Office	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Fairview Hospital	51403	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Central Florida Eye Institute	31204	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Cleveland Hospital Medical Center	119305	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Downey Regional Center (RC)		Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Hennepin County's IRB		Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Iowa Regional Medical Center		Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Kaweah Delta Health Care District (KDC)	55554	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Lake Charles Memorial Hospital	92763	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Lehigh Institutional Review Board	32763	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Midwest Heart Foundation	83154	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
New York Eye & Ear Infirmary	121103	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
North Texas IRB	81403	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Oak Lawn Institutional Review Board	81763	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 Yes 2008
Barns Adams and Lash Center	45554	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Shaggs, Carol, MD	25403	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
Shenandoah Surgical Hospital (SH)	92704	Center for Devices and Radiological Health	Center for Devices and Radiological Health	Institutional Review Board	PSG1 No
CSO Transportation	41854	Chromalloy District Office	Center for Devices and Radiological Health	Identifiable Competence Evaluation	PSG1 No



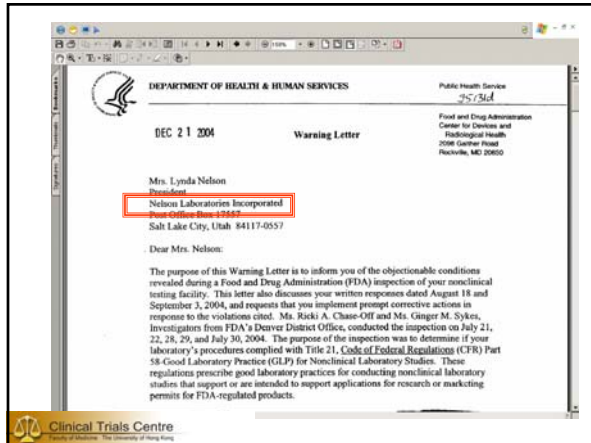


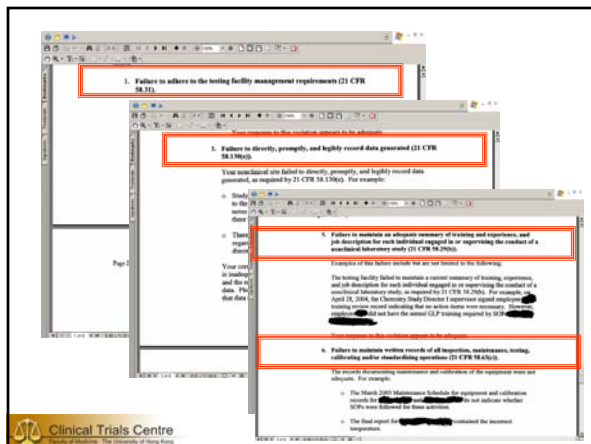




FDA Warning Letters

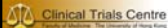
Pre-clinical Laboratory

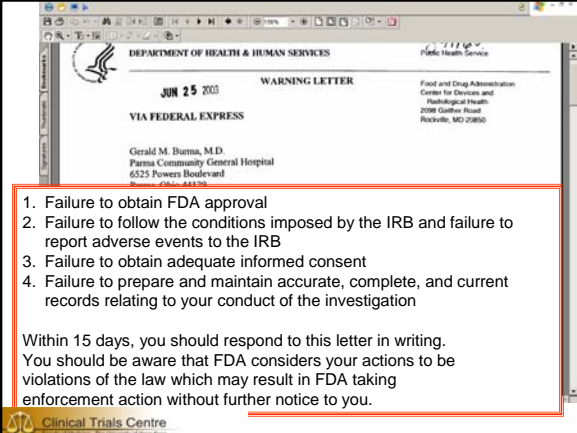




FDA Warning Letters


Investigators

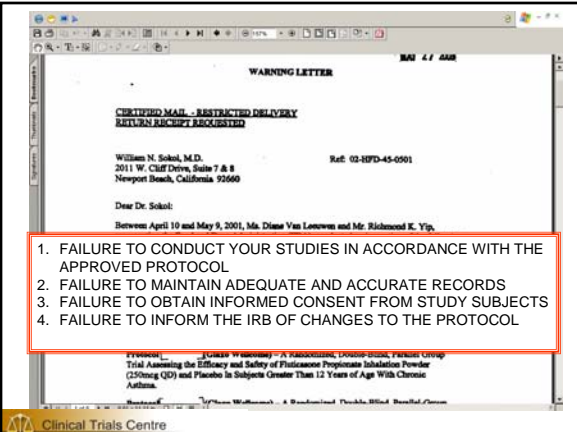




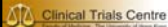
1. Failure to obtain FDA approval
2. Failure to follow the conditions imposed by the IRB and failure to report adverse events to the IRB
3. Failure to obtain adequate informed consent
4. Failure to prepare and maintain accurate, complete, and current records relating to your conduct of the investigation

Within 15 days, you should respond to this letter in writing. You should be aware that FDA considers your actions to be violations of the law which may result in FDA taking enforcement action without further notice to you.





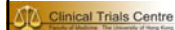
1. FAILURE TO CONDUCT YOUR STUDIES IN ACCORDANCE WITH THE APPROVED PROTOCOL
2. FAILURE TO MAINTAIN ADEQUATE AND ACCURATE RECORDS
3. FAILURE TO OBTAIN INFORMED CONSENT FROM STUDY SUBJECTS
4. FAILURE TO INFORM THE IRB OF CHANGES TO THE PROTOCOL



FDA Actions

Investigators

- Disqualification
- Fully restricted
- Restricted

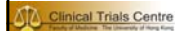


Number of Investigators

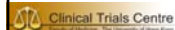
Year	Number of Investigators
1964-1969	8
1980-1989	19
2000-2005	47
2006-2011	24
2012-2017	11

Disqualified or totally restricted clinical Investigators who are not eligible to receive investigational products. N=95

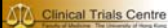
Restricted N=14

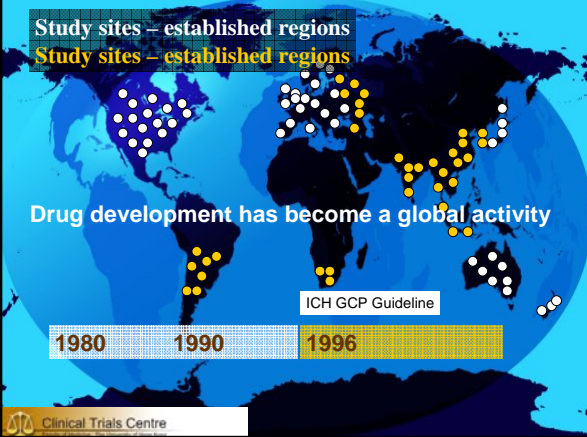


Name Address	Action Date
BENNETT ROBIN, MD SILVER SPRING, MD	1964
KATHLEEN E ROBERTS, MD SAN FRANCISCO, CA	1964
LEO CASS, MD CAMBRIDGE, MA	1965
WILLIAM A ABRUZZI JR, MD WAPPINGERS FALLS, NY	1966
LEO LOWE, MD NEW YORK, NY	1966
SAMUEL SPLITTER, MD HAMPSTEAD, NY	1968
SHELDON R BENDER, MD PHILADELPHIA, PA	1969
JAMES A. HALIKAS MINNEAPOLIS, MN	2001
HUIBERT M VRIESEENDORP, MD MARSHFIELD, WI	2001
CAREY L. QUARLES, PHD WELLINGTON, CO	2002
EDUARDO CARO ACEVEDO, MD DAYAMON, PR	2002
LEON C. LAHAYE, MD LAFAYETTE, LA	2002
ALLYN M. NORMAN, DO, GETZVILLE, NY	2002
CHAVARÁMPLAKYL P. MATHEW, MD, NEW ORLEANS, LA	2003
ROY C. PACE, MD MEMPHIS, TN	2003
CARL ANDREW DeABATE, MD WASHINGTON, DC	2004
EUGENIA A MARCUS, MD, NEWTON, MA	2004
ROGER D. ANDERSON, MD PITTSBURGH, PA	2005



GCP Training One Way to Prevent Fraud and Misconduct



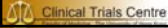


Study sites – established regions
Study sites – established regions

Drug development has become a global activity

ICH GCP Guideline

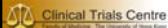
1980 1990 1996



Year official GCP Guideline established



Fenn (2001) International Journal of Pharmaceutical Medicine;15(4):169-173

US	1980
Germany	1987
UK	1988
Nordic Countries	1989
France	1990
EC	1990
Australia	1991
WHO	1993
ICH GCP	1996
Japan	1985
Korea	1995
Taiwan	1996
Singapore	1998
China	1999
Thailand	2001
Indonesia	2001
Hong Kong	
Philippines	





On the 1st of May 2004, the Directive 2001/20/EC on clinical research became law across the 25 member states of the European Union.

The European Union Directive 2001/20/EC, dated 4 April 2001, is concerned with 'the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of Good Clinical Practice in the conduct of clinical trials on medicinal products for human use'.

2004, the Directive 2001/20/EC
Training of Investigators and Clinical Research Teams
 Principal Investigators will be legally required to send their qualifications and any GCP training or experience obtained from work with clinical trials to the local ethics committees for opinion on their suitability to conduct clinical trials.

Details of training sessions **must be recorded** by the Investigator and the members of the research team.

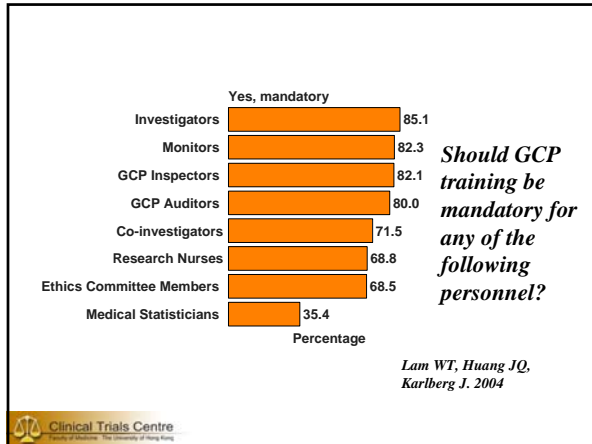



State FDA, Beijing

SFDA provides GCP accreditation of study sites in China and Hong Kong.

The site must submit an application to SFDA. After inspection GCP accreditation may be granted.

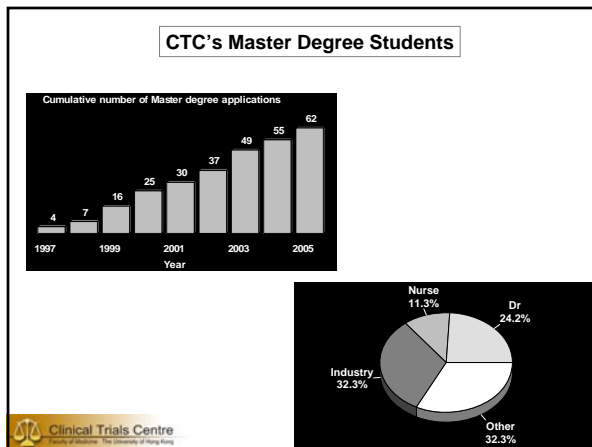




GCP Training
Clinical Trials Centre
The University of Hong Kong

Master Degree (400 hours)
Diploma Degree (200 hours)
Certificate Degree (100 hours)

Clinical Trials Centre
The University of Hong Kong

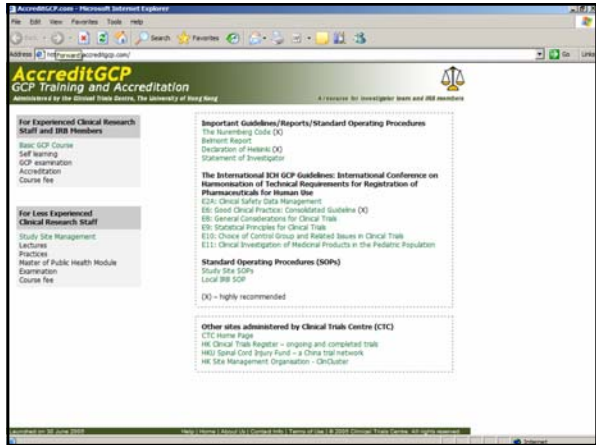


GCP Training
Clinical Trials Centre
The University of Hong Kong

GCP Accreditation

www.AccreditGCP.com





AccreditGCP
GCP Training and Accreditation
Administered by the Clinical Trials Centre, The University of Hong Kong

For Experienced Clinical Research Staff and IRB Members
 Basic GCP Course
 Self learning
 GCP examination
 Accreditation
 Course fee

For Less Experienced Clinical Research Staff
 Study Site Management
 Lectures
 Practice
 Master of Public Health Module
 Examination
 Course fee

Important Guidelines/Reports/Standard Operating Procedures
 The Nuremberg Code (DC)
 Belmont Report
 Declaration of Helsinki (DC)
 Statement of Investigation

The International ICH GCP Guidelines: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
 E2A: Clinical Safety Data Management
 E6: Good Clinical Practice - Consolidated Guideline (DC)
 E8: General Considerations for Clinical Trials
 E9: Statistical Principles for Clinical Trials
 E10: Choice of Control Group and Related Issues in Clinical Trials
 E11: Clinical Investigation of Medical Products in the Pediatric Population

Standard Operating Procedures (SOPs)
 Study Site SOP
 Local IRB SOP
 DC - highly recommended

Other sites administered by Clinical Trials Centre (CTC)
 CTC Home Page
 HK Clinical Trials Register - ongoing and completed trials
 HKI Shared Core Inquiry Fund - a Data Trial-network
 HK Site Management Organization - QICOuter



AccreditGCP
GCP Training and Accreditation
Administered by the Clinical Trials Centre, The University of Hong Kong

Basic GCP Course
For IRB staff This is a self learning GCP training programme that has been developed for clinical study site staff and for Ethics Committee members.
Notes: The programme can be taken individually or jointly, for instance, by all study site team members or Ethics Committee members as a continuous educational activity.
Accreditation: The accreditation will be awarded after candidates has a GCP examination.
Fee: There is no fee for HKU/QRH staff for the basic GCP training programme. For other participants there will be a fee of HK\$ 2,000 for taking the GCP examination.
 For any enquires about the course, you are welcome to contact Dr James Thurham, CTC by phone at 2555 4567, or by email to thturham@ctc.hk

Course Contents	Total 10 hrs
The clinical trial lifecycle A web based powerpoint presentation	3 hrs 15 min
Research ethics Video: Evolving concern: protection of human subjects	25 min
CD Rom video lecture	3 hrs 10 min
Ethics Committee operation Video: Criteria for protocol review	40 min
Fraud and misconduct in clinical trials Video: 90 minutes of mix and match	15 min
Video: Testing Questions Glass/Adobe A web based powerpoint presentation	25 min
Reading The Nuremberg Code Declaration of Helsinki E6: Good Clinical Practice - Consolidated Guideline	1 hr 30 min
GCP examination	
