

Monitorización del ensayo clínico

Dr. Salvador Ribas Ribas

E-mail: salvador.ribas@gmail.com

**III CURSO PARA INVESTIGADORES SOBRE NORMAS
DE BUENA PRÁCTICA CLÍNICA (BPC)**

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*ICH HARMONISED TRIPARTITE GUIDELINE
GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R1) dated 10 June 1996, p.26-28*

Definition

- ▣ ICH is a unique project that brings together the regulatory authorities of:
 - European Union;
 - Japan;
 - United States; and
 - Experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration

Monitoring

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Purpose

The purposes of trial monitoring are to verify that:

- (a) The rights and well-being of human subjects are protected.
- (b) The reported trial data are accurate, complete, and verifiable from source documents.
- (c) The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).

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Extent and Nature of Monitoring

- ▣ The sponsor should ensure that the trials are adequately monitored. The sponsor should determine the appropriate extent and nature of monitoring.

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Monitor's responsibilities

The **monitor(s)** in accordance with the sponsor's requirements should ensure that the trial is conducted and documented properly by carrying out the following activities when relevant and necessary to the trial and the trial site:

(a) Acting as the main line of communication between the sponsor and the investigator.

(b) Verifying that the investigator has adequate qualifications and resources (see 4.1, 4.2, 5.6) and remain adequate throughout the trial period, that facilities, including laboratories, equipment, and staff, are adequate to safely and properly conduct the trial and remain adequate throughout the trial period.

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Monitor's responsibilities (cont.)

(c) Verifying, for the investigational product(s):

- (i) That storage times and conditions are acceptable, and that supplies are sufficient throughout the trial.
- (ii) That the investigational product(s) are supplied only to subjects who are eligible to receive it and at the protocol specified dose(s).
- (iii) That subjects are provided with necessary instruction on properly using, handling, storing, and returning the investigational product(s).
- (iv) That the receipt, use, and return of the investigational product(s) at the trial sites are controlled and documented adequately.
- (v) That the disposition of unused investigational product(s) at the trial sites complies with applicable regulatory requirement(s) and is in accordance with the sponsor.

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Monitor's responsibilities (cont.)

- (d) Verifying that the investigator follows the approved protocol and all approved amendment(s), if any.
- (e) Verifying that written informed consent was obtained before each subject's participation in the trial.
- (f) Ensuring that the investigator receives the current Investigator's Brochure, all documents, and all trial supplies needed to conduct the trial properly and to comply with the applicable regulatory requirement(s).
- (g) Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial.
- (h) Verifying that the investigator and the investigator's trial staff are performing the specified trial functions, in accordance with the protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals.

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Monitor's responsibilities (cont.)

- (i) Verifying that the investigator is enrolling only eligible subjects.
- (j) Reporting the subject recruitment rate.
- (k) Verifying that source documents and other trial records are accurate, complete, kept up-to-date and maintained.
- (l) Verifying that the investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial.

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Monitor's responsibilities (cont.)

- (m) Checking the accuracy and completeness of the CRF entries, source documents and other trial-related records against each other. The monitor specifically should verify that:
 - (i) The data required by the protocol are reported accurately on the CRFs and are consistent with the source documents.
 - (ii) Any dose and/or therapy modifications are well documented for each of the trial subjects.
 - (iii) Adverse events, concomitant medications and intercurrent illnesses are reported in accordance with the protocol on the CRFs.
 - (iv) Visits that the subjects fail to make, tests that are not conducted, and examinations that are not performed are clearly reported as such on the CRFs.
 - (v) All withdrawals and dropouts of enrolled subjects from the trial are reported and explained on the CRFs.

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Monitor's responsibilities (cont.)

- (n) Informing the investigator of any CRF entry error, omission, or illegibility. The monitor should ensure that appropriate corrections, additions, or deletions are made, dated, explained (if necessary), and initialled by the investigator or by a member of the investigator's trial staff who is authorized to initial CRF changes for the investigator. This authorization should be documented.
- (o) Determining whether all adverse events (AEs) are appropriately reported within the time periods required by GCP, the protocol, the IRB/IEC, the sponsor, and the applicable regulatory requirement(s).
- (p) Determining whether the investigator is maintaining the essential documents.
- (q) Communicating deviations from the protocol, SOPs, GCP, and the applicable regulatory requirements to the investigator and taking appropriate action designed to prevent recurrence of the detected deviations.

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Monitoring Procedures

The monitor(s) should follow the sponsor's established written SOPs as well as those procedures that are specified by the sponsor for monitoring a specific trial.

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Monitoring report

- (a) The monitor should submit a written report to the sponsor after each trial-site visit or trial-related communication.
- (b) Reports should include the date, site, name of the monitor, and name of the investigator or other individual(s) contacted.
- (c) Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken and/or actions recommended to secure compliance.
- (d) The review and follow-up of the monitoring report with the sponsor should be documented by the sponsor's designated representative.

Monitoring - THE TRIAL MASTER FILE

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ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL.

Essential Documents are those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements.

Trial master files should be established at the beginning of the trial, both at the investigator/institution's site and at the sponsor's office. A final close-out of a trial can only be done when the monitor has reviewed both investigator/institution and sponsor files and confirmed that all necessary documents are in the appropriate files.

Monitoring tools

- ▣ El manual de operaciones
- ▣ El manual del CRD
- ▣ El manual de laboratorio
- ▣ Etc.

Monitoring tools

Doses abbreviations

Abbreviation	Meaning	Latin Term
ac	before meals	ante cibum
bid	twice a day	bis in die
cap	capsule	capsula
gt	drop	gutta
hs	at bedtime	hora somni
od	right eye	oculus dexter
os	left eye	oculus sinister
po	by mouth	per os
pc	after meals	post cibum
pil	pill	pilula
prn	as needed	pro re nata
q2h	every 2 hours	quaque 2 hora
qd	every day	quaque die
qh	every hour	quaque hora
qid	4 times a day	quater in die
tab	tablet	tabella
tid	3 times a day	ter in die

Monitoring tools

Drugs abbreviations

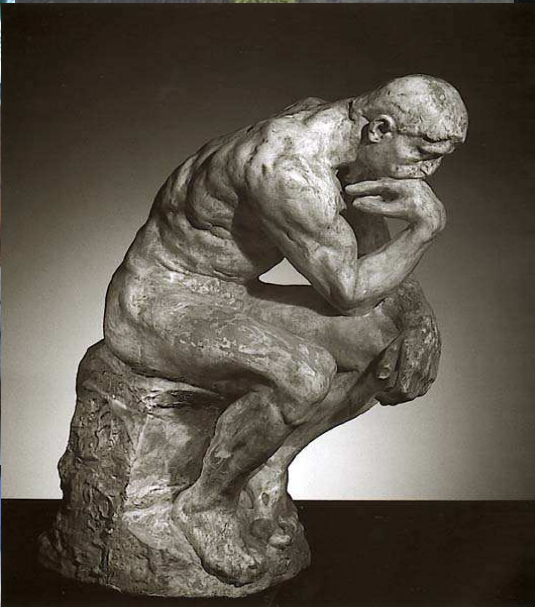
Common Drug Abbreviations

Abbreviation	Meaning	Abbreviation	Meaning
APAP	acetaminophen	PTU	propylthiouracil
ASA	aspirin	SR	slow release or
BC	birth control	TAC	triamcinolone
Ca, Ca ⁺⁺	calcium	TCN	tetracycline
Cl	chloride, chlorine	TMP/SMX	sulfamethoxazole and
Cod	codeine	TMP/SMZ	sulfamethoxazole and
CR	controlled release	TR	time release
DM	dextromethorphan	XL	extended release
DCN, DN100	Darvocet N-100	XR	extended release
doxy	doxycycline	Zn, Zn ⁺⁺	zinc
DXM	dextromethorphan	ZnSO ₄	zinc sulfate
EC	enteric coated		
EC ASA	enteric coated aspirin		
ER	extended release		
Fe, Fe ⁺⁺	iron		
FeSO ₄	ferrous sulfate (iron)		
HC	hydrocortisone		
HCO ₃	bicarbonate		
HCTZ	hydrochlorothiazide		
HCT	hydrocortisone		
HS	half strength		
INH	isoniazid		
K, K ⁺	potassium		
KOH	potassium hydroxide		

Antimicrobial Abbreviations:

AMC	Amoxicillin/Clavulanic Acid
AMI	Amikacin
AMP	Ampicillin
AXO	Ceftriaxone
BAC	Bacitracin
CEP	Cephalothin
CHL	Chloramphenicol
CIP	Ciprofloxacin
COT	Trimethoprim/Sulfamethoxazole

El clinical research associate entre ...



GRACIAS

por vuestra atención