Pharmacists' involvement in clinical trials and ethical committees

Seminar H3 – 26 March 2014

Marisa Dell'Aera - Rachele Giuliani
AOU CONSORZIALE Policlinico – Bari - Italy

Conflict of interest:

Nothing to disclose

….a longstanding issue…

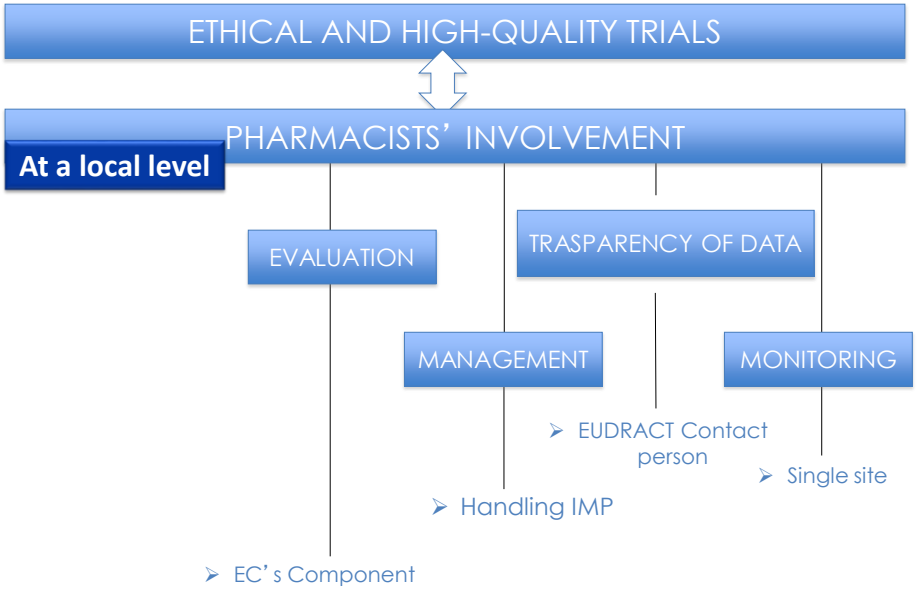
1994
vol.8, n° 3-4

NEED

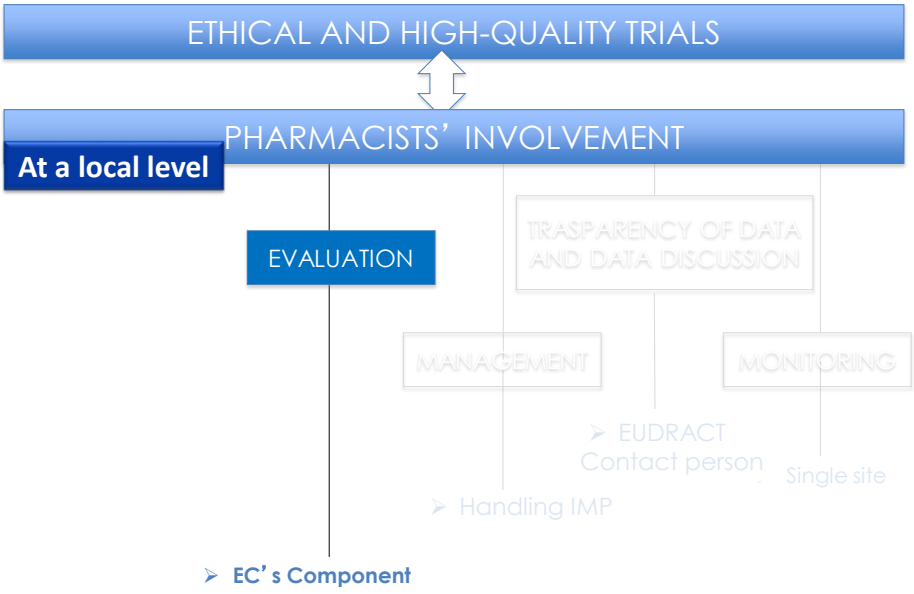
Develop specific competences to critically assess scientific information

(Evidence Based Medicine Vs Real Clincal Practice)

- ***EC 's members***
- ***Responsibility within Scientific Secretaries***
- ***Trial Management***



Pharmacists' involvement in clinical trials and ethical committees



Pharmacists' involvement in clinical trials and ethical committees

EVALUATION

EC's Component

What has the EC to consider evaluating clinical trials ?

- ✓ *Adequacy of the Study Team*
- ✓ *Structural Adequacy/Quality*
- ✓ *Insurance*
- ✓ *Clarity of information in booklets and leaflets used for patient enrollment*
- ✓ *Informed Consent*
- ✓ *Protocol* **PHARMACIST**
- ✓ *Investigator's Brochure/IMPD* **PHARMACIST**

EU Durective2001/20/CE

EVALUATION

EC' s Component

What has the EC to consider evaluating clinical trials ?

- ✓ *Adequacy of both the PI and the co-Investigators*
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EU Durective2001/20/CE

Pharmacists' involvement in clinical trials and ethical committees

Investigator's Brochure/IMPD **PHARMACIST**

Physical, chemical, and pharmaceutical properties and formulation

Non-clinical studies

Effects in humans

Summary of data and guidance for the investigator

Contraindications
Special Warnings and Special Precautions for use
Interactions

SAFETY

Pharmacists' involvement in clinical trials and ethical committees

EVALUATION

EC' s Component

What has the EC to consider evaluating clinical trials ?

- ✓ Adequacy of both the PI and the co-Investigators
- ✓ Structural Adequacy/Quality
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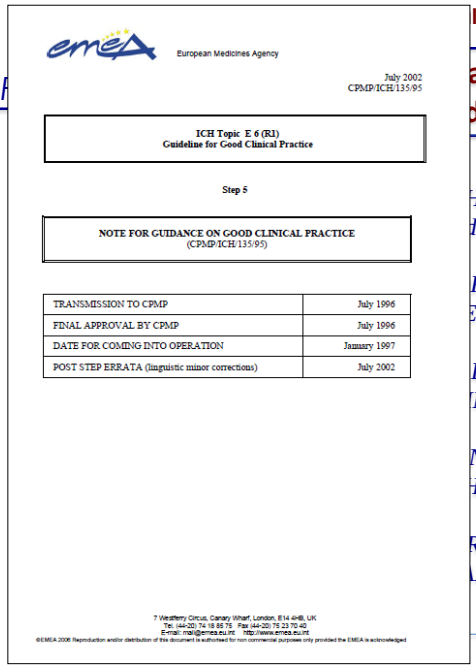
EU Durective2001/20/CE



European Medicines Agency

July 2002
CPMP/ICH/135/95

ICH Topic E 6 (R1)
Guideline for Good Clinical Practice

Step 5

NOTE FOR GUIDANCE ON GOOD CLINICAL PRACTICE
(CPMP/ICH/135/95)

TRANSMISSION TO CPMP	July 1996
FINAL APPROVAL BY CPMP	July 1996
DATE FOR COMING INTO OPERATION	January 1997
POST STEP ERRATA (linguistic minor corrections)	July 2002

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 85 75 Fax (44-20) 75 23 70 40
E-mail: mail@emea.eu.int http://www.emea.eu.int

l trials and ethical committees

acist with a particular expertise in
dology of health research and GCP

ICH E6
JULY 1991-2002

HESIS PLAUSIBILITY
H ENDPOINT

R ADEQUACY
ELINE ADEQUACY

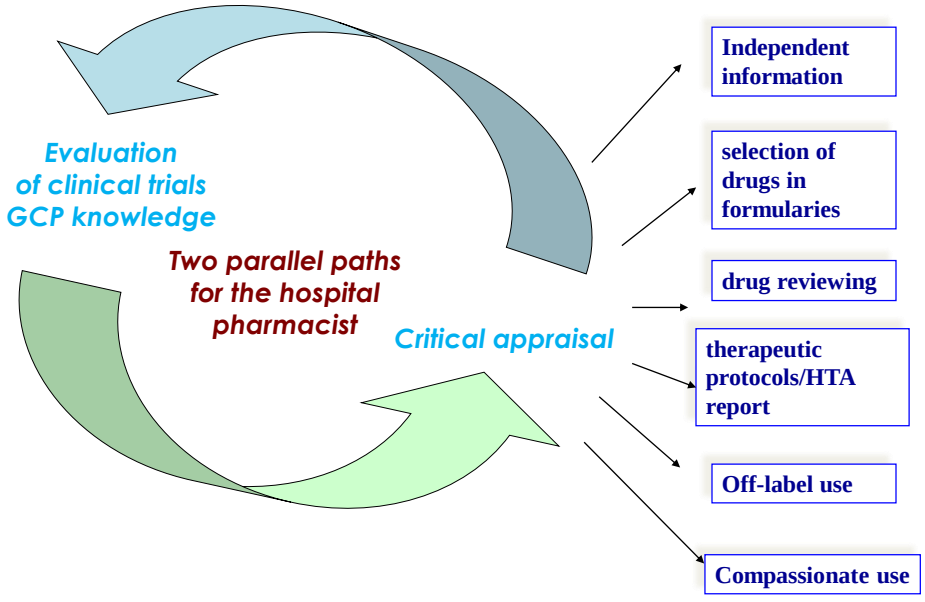
DESIGN
MIZATION

ND SAFETY ASSESSMENT
H IB INFORMATION

RIORITY ASSESSMENT MARGIN
L ANALYSIS

EU Durective2001/20/CE

Pharmacists' involvement in clinical trials and ethical committees



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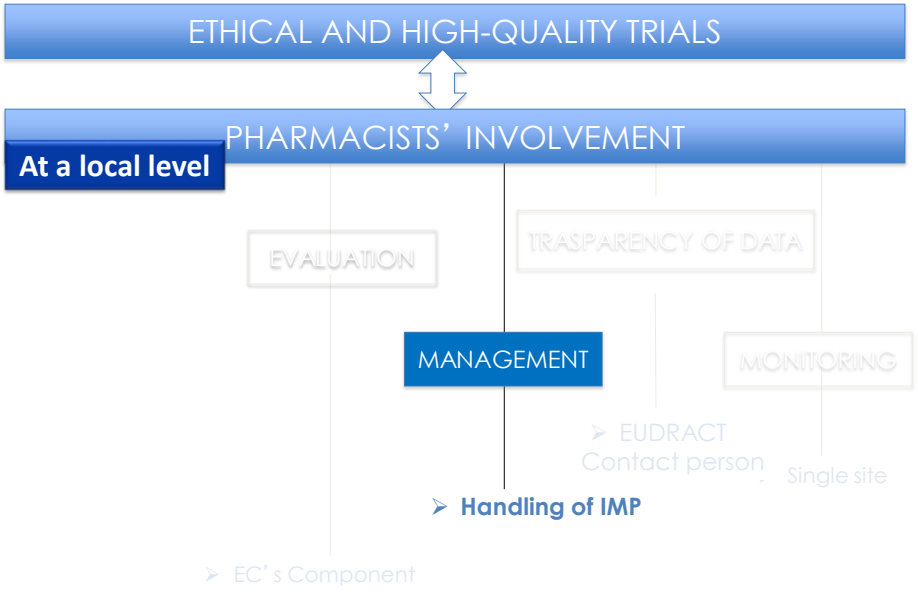

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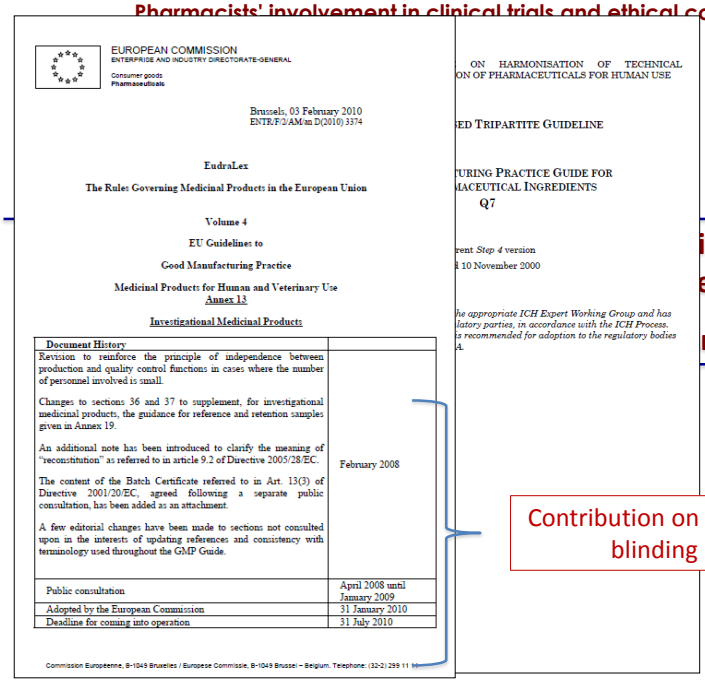


EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL
Consumer goods
Pharmaceuticals

Brussels, 03 February 2010
ENTR/F/2/AM/nn D(2010) 3374

EudraLex

The Rules Governing Medicinal Products in the European Union

Volume 4

EU Guidelines to

Good Manufacturing Practice

Medicinal Products for Human and Veterinary Use
Annex 13

Investigational Medicinal Products

Document History	
Revision to reinforce the principle of independence between production and quality control functions in cases where the number of personnel involved is small. Changes to sections 36 and 37 to supplement, for investigational medicinal products, the guidance for reference and retention samples given in Annex 19. An additional note has been introduced to clarify the meaning of "reconstitution" as referred to in article 9.2 of Directive 2005/28/EC. The content of the Batch Certificate referred to in Art. 13(3) of Directive 2001/20/EC, agreed following a separate public consultation, has been added as an attachment. A few editorial changes have been made to sections not consulted upon in the interests of updating references and consistency with terminology used throughout the GMP Guide.	February 2008
Public consultation	April 2008 until January 2009
Adopted by the European Commission	31 January 2010
Deadline for coming into operation	31 July 2010

Commission Européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel – Belgium. Telephone: (32-2) 299 11 11

ON HARMONISATION OF TECHNICAL
ON OF PHARMACEUTICALS FOR HUMAN USE

ED TRIPARTITE GUIDELINE

TURING PRACTICE GUIDE FOR
IACEUTICAL INGREDIENTS
Q7

rent *Step 4* version
10 November 2000

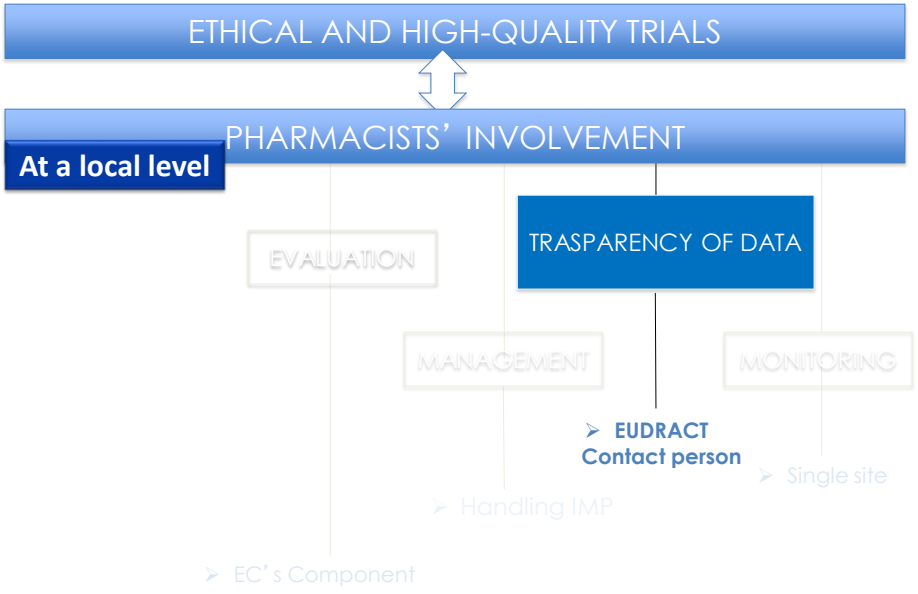
he appropriate ICH Expert Working Group and has
latory parties, in accordance with the ICH Process.
is recommended for adoption to the regulatory bodies
A.

icular expertise in
es and GMP

nnex 13)

Contribution on randomization and blinding procedures

Pharmacists' involvement in clinical trials and ethical committees



Pharmacists' involvement in clinical trials and ethical committees

MANAGEMENT

Handling IMP

TRASPARENCY OF DATA: EUDRACT REGISTRY

Pharmacist with a particular expertise in health research methodology and GCP

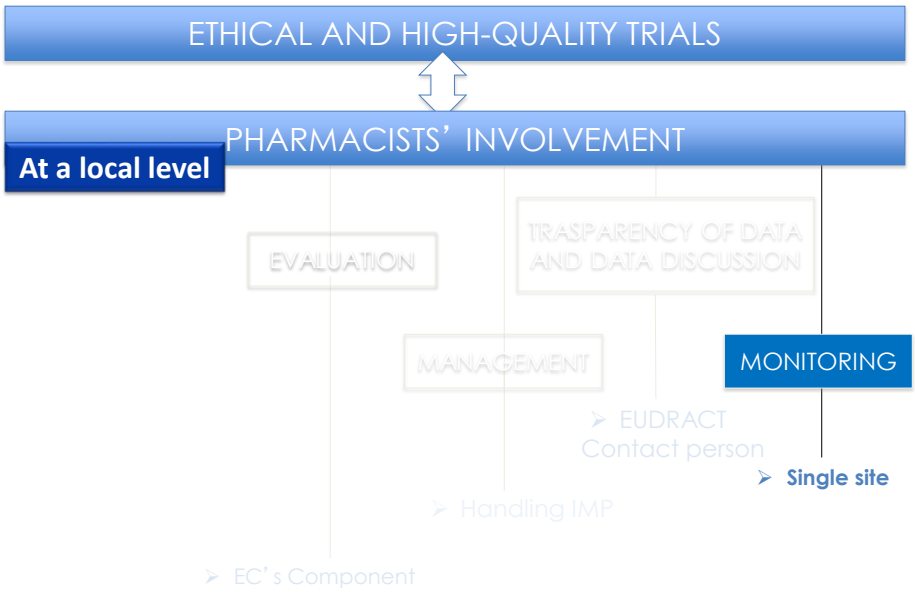
May 2004 *September 2004* *October 2004*

✓*EU DATABASE REGISTRATION*

Improve Transparency *Promote Cooperation*

Avoid Redondancy

Pharmacists' involvement in clinical trials and ethical committees



Pharmacists' involvement in clinical trials and ethical committees

MONITORING

single Experimental Centre

- Networks of Monitors
- Clinical trial Quality Teams
- Research cores

Non-profit Research

Networks of Monitors

2003

110 *Giornale italiano di Farmacia clinica, 17, 4, 2003*

In questa logica si deve defin
macista-monitor: un elemento
quanto già esiste e ciò che viene
novativo. Al controllo della mod
e dell'esattezza delle informazi
scheda raccolta dati (funzione n
dalla CRO), si aggiunge una veri
propositiva con la valutazione di
tazione si inserisce nella pratica
raggio formale secondo le GCP è
grato di aspetti sostanziali e va
senso, il farmacista clinico occ
privilegiata, perché è parte integr
cui la sperimentazione si svolge
stire in modo totalmente autonon
nitoraggio.

È attraverso la figura del
Comitato Etico, quindi, può dive
attivo e intelligente» (6).

Applicazione pratica

Il concetto fin qui sviluppato
farmacia ospedaliera e territoriale
di competenza e di ottimizzare
funzioni dei Comitati Etici locali
bilità specifiche per quanto riguarda il monitoraggio

GISSI HF	R & P
• Studio controllato, randomizzato, in doppio cieco	• Studio controllato, randomizzato, in doppio cieco
• Centri coinvolti: circa 400	• Medici coinvolti: circa 600 MMG
• Pazienti previsti: circa 7000	• Pazienti previsti 12000
• pazienti con scompenso randomizzati a n-3 PUFA o a placebo (1° randomizzazione) e rosuvastatina o placebo (2° randomizzazione)	• Pazienti con rischi cardiovascolari multipli, randomizzati a n-3 o placebo
• Monitoraggio (farmacisti ospedalieri): 1° visita dopo 3-5 pazienti randomizzati; visita annuale; visita fine studio	• Monitoraggio di routine da parte della Commissione ASL: - su un campione di medici partecipanti; - con visite mirate su indicazione

Clinical Trial Quality Teams

AIFA Notification 23 April 2008

AIFA Project aim at improving the Quality within non-profit clinical trials

- **Partecipants Network**
- **Clinical Trial Quality Team (CTQT)**

Hospital Pharmacists, Scientific Director, Quality Control

Clinical Trial Quality Teams

MONITORAGGIO DELLE SPERIMENTAZIONI CLINICHE NO PROFIT: PROGETTAZIONE E SVILUPPO DI UN PERCORSO PRESSO L'AZIENDA OSPEDALIERA DI VERONA

C. Al Sataan, E. Malo, F. Venturini, G. Scroccaro

Servizio di Farmacia, Azienda Ospedaliera di Verona - Verona

MONITORAGGIO DEGLI STUDI INDIPENDENTI: ESPERIENZA DI UN'A.O.U.

S. Intini, M. Dell'Aera, M. Cetrone, M. Lattarulo

R.U.O. di Farmacia, A.O.U. Policlinico «Consorziale» - Bari

IL C.T.Q.T. (CLINICAL TRIAL QUALITY TEAM) E IL M.I.A. (MONITOR INTERNO AZIENDALE) ATTORI INDISPENSABILI NEL MONITORAGGIO DELLA SPERIMENTAZIONE CLINICA NO PROFIT

I. Lorenzi, C. F. Intra, E. Zaninoni, P. Barabino, E. Panetta, G.Buffa, R. Rossi

U.O. Farmacia, IRCCS, Gaslini - Genova

Research Cores

I FARMACISTI ALL'INTERNO DEI NUCLEI DI RICERCA CLINICA A SUPPORTO DELLA RICERCA, DALLA PRESENTAZIONE ALL'AVVIO DEGLI STUDI CLINCI

F. M. Bacchetto (1), E. Ghiotto (1), A. Ciaglia (2), G. Scannapieco (2)

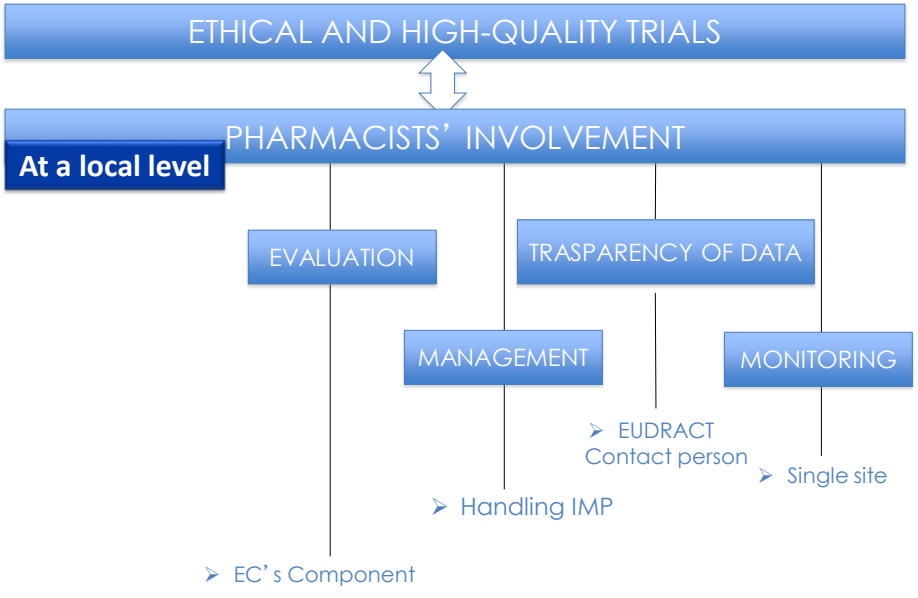
1. Dipartimento dei Servizi Sanitari-Farmacia Ospedaliera, Azienda ULSS 9 - Treviso (TV); 2. Dipartimento Funzionale Uffici di Staff, Azienda ULSS 9 - Treviso

NUCLEI PER LA RICERCA CLINICA E COMMISSIONI PER LA RICERCA IN MEDICINA TERRITORIALE: UN'INFRASTRUTTURA A SOSTEGNO DELLA RICERCA

M. Franceschi (1), L. Agnoletto (1), D. Bastarolo (2), S. Brasola (3), L. Castellani (4), A. Fratucello (5), R. Joppi (1), L. Mezzalira (1), L. Perantoni (6), C. Poggiani (1), C. Roni (1)

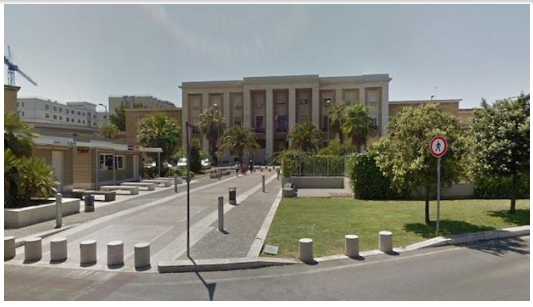
1. Servizio Farmaceutico; 2. Farmacia Ospedaliera - Azienda ULSS 20,Verona; 3. Servizio Farmaceutico, Azienda ULSS 21 - Legnago (VR); 4. Servizio Farmaceutico; 5. Farmacia Ospedaliera - Azienda ULSS 22 - Bussolengo (VR); 6. Farmacia Ospedaliera, Ospedale di Negrar (VR)

Pharmacists' involvement in clinical trials and ethical committees



The experience at the Policlinico of Bari

Pharmacists' involvement in clinical trials
at a MULTICENTER and INTERNATIONAL level



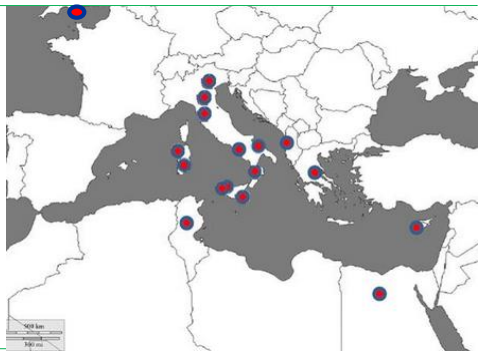
Integrated research network

not for profit investigator-driven Consortium

AOU Policlinico of Bari is involved as one of the Beneficiaries of a Project funded by the EU Commission (FP7 Programme)

A research network including:

- 16 partners
- 6 European countries
- 4 non- European countries
- 18 recruiting sites
- 2 clinical trials
- 1 observational study



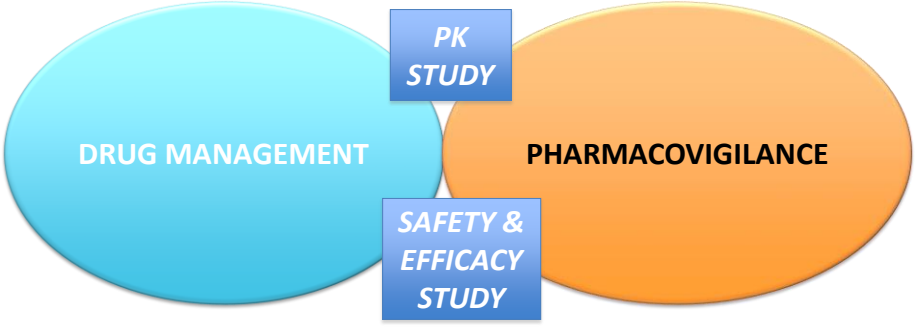
Research Network

international scientific institutions **for** a **multi-cultural** network

COUNTRY	INSTITUTION
Albania	QENDER SPITALORE UNIVERSITARE NENEA TIRANE
Cyprus	MINISTRY OF HEALTH OF THE REPUBLIC OF CYPRUS
Egypt	CAIRO UNIVERSITY, FACULTY OF MEDICINE, PEDIATRIC HOSPITAL, HEMATOLOGY DEPARTMENT
Germany	UNIVERSITAETSKLINIKUM ERLANGEN
Greece	NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS
Italy	**AZIENDA OSPEDALIERO UNIVERSITARIA CONSORZIALE POLICLINICO DI BARI** - AZIENDA OSPEDALIERA ANTONIO CARDARELLI - AZIENDA OSPEDALIERA OSPEDALI RIUNITI VILLA SOFIA-CERVELLO - AZIENDA OSPEDALIERA DI PADOVA - FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS - FONDAZIONE ITALIANA L. GIAMBRONE PER LA GUARIGIONE DELLA THALASSEMIA CONSORTIUM FOR BIOLOGICAL AND PHARMACOLOGICAL EVALUATIONS (COORDINATOR)
The Netherlands	UNIVERSITEIT LEIDEN
Tunisia	CENTRE NATIONAL DE GREFFE DE MOELLE OSSEUSE
UK	THE ROYAL LONDON HOSPITAL (EC's submission in progress)

Pharmacists' involvement in clinical trials and ethical committees

Hospital Pharmacy of AOU Policlinico of Bari Coordinating Role for:



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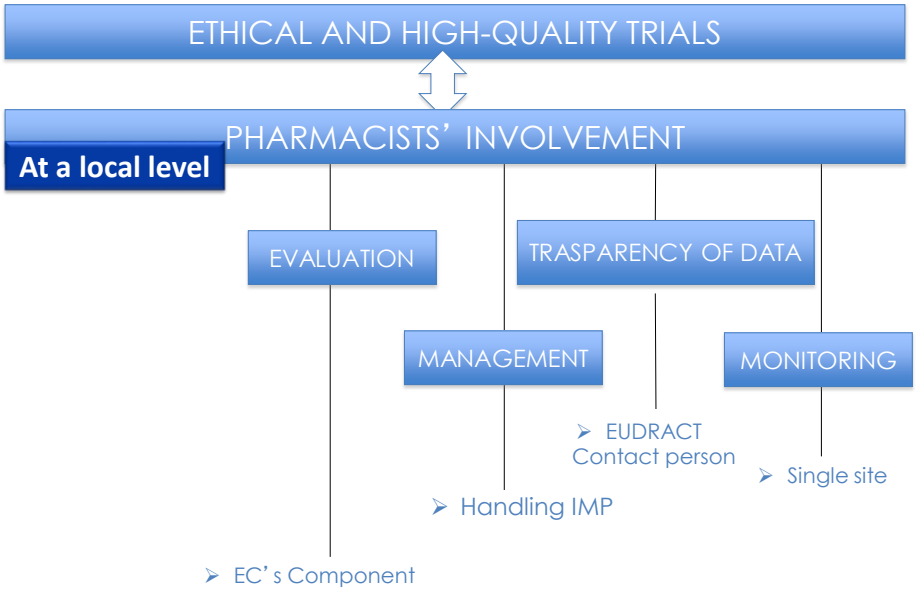

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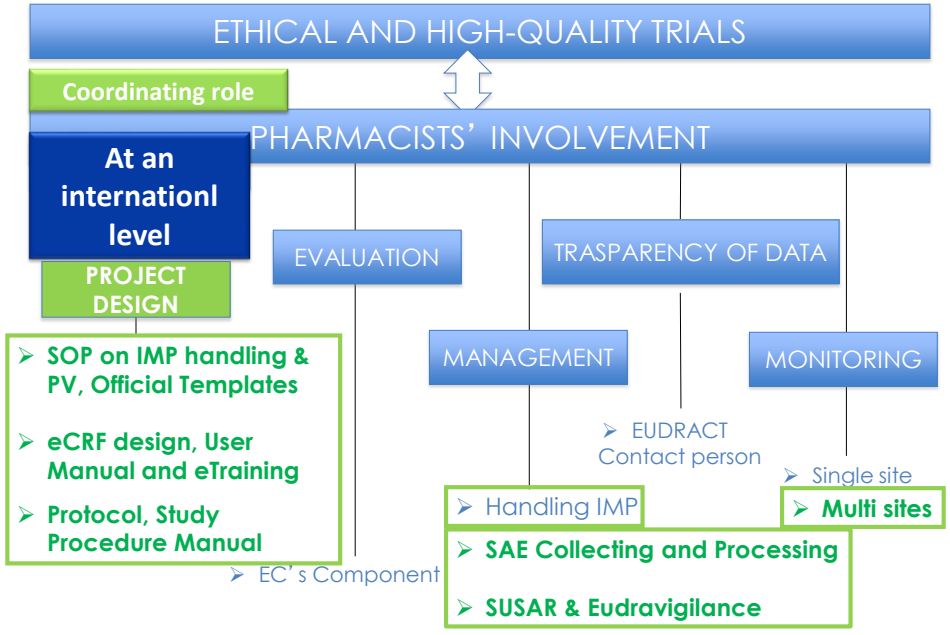

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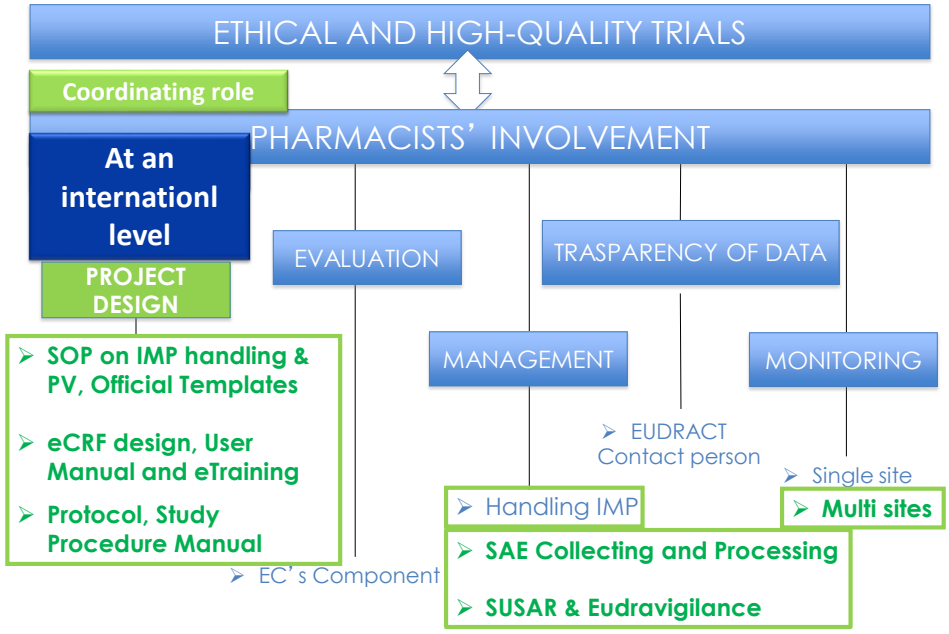

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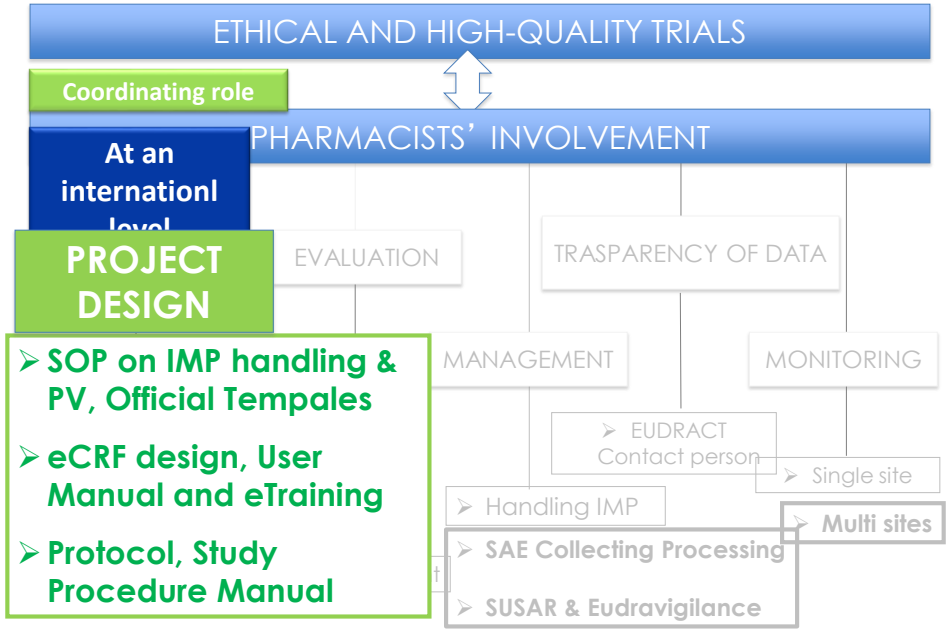


SOP on IMP handling & PV, Official Tempales

PROJECT DESIGN

DRUG MANAGEMENT

SOP on IMP handling & PV, Official Tempales

PROJECT DESIGN

DRUG MANAGEMENT

Scientific Document SD.044
"Standard Operating Procedure o
PK Study IMP's safe reception and storage"

Scientific Document SD.045
"Standard Operating Procedure on
safe reception and storage of IMPs"

Scientific Document SD.046
"Standard Operating Procedure on Disposal
of IMPs "

SOP on IMP handling & PV, Official Tempales

PROJECT DESIGN

DRUG MANAGEMENT

PHARMACOVIGILANCE

Scientific Document SD.001 "Standard Operating Procedure on Safety Reporting"

Scientific Document SD.002 "Standard Operating Procedure on Processing Safety Case Reports"

Scientific Document SD.003 "Standard Operating Procedure on Archiving Safety Case Reports"

SOP on IMP handling & PV, Official Tempales

PROJECT DESIGN

DRUG MANAGEMENT

PHARMACOVIGILANCE

OFFICIAL DOCUMENT TEMPLATES

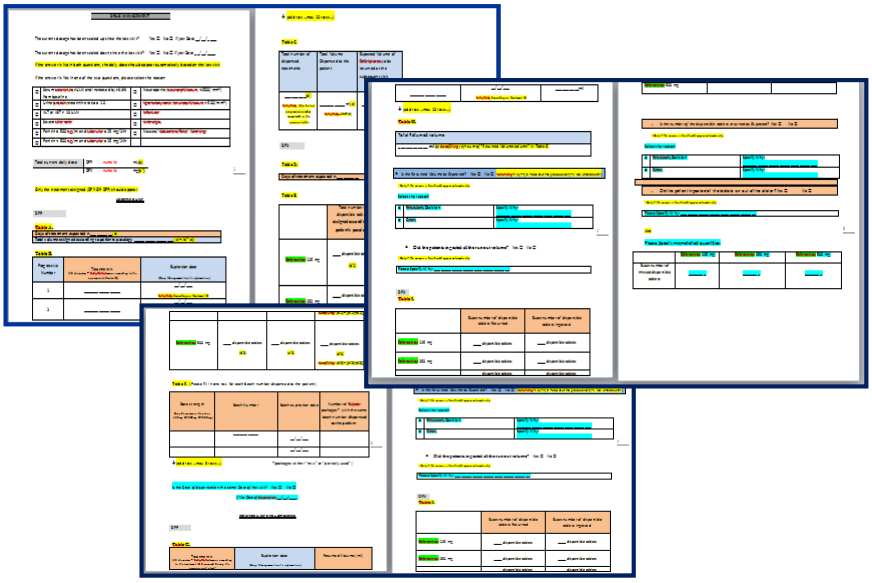
Product Receipt Form, Label Log, Accountability Log, Disposal Authorization Request Etc..

IMPs' LABELS DRAFT

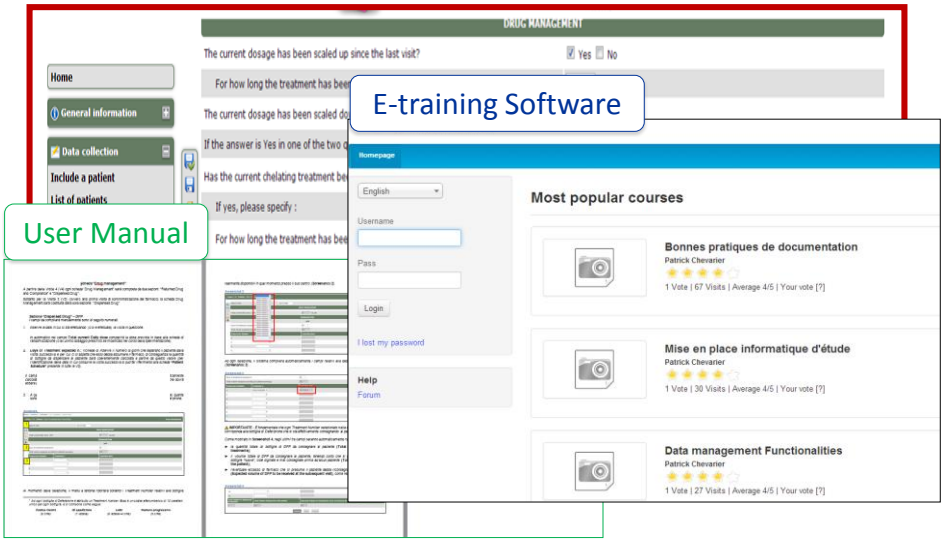
English, Arabic, Italian, Greek, Albanian, French

Directive 2003/94/EC Art.15

eCRF: Drug Management Section Design, User Manual, eTraining



eCRF: Drug Management Section Design, User Manual, eTraining



Protocol, Study Procedure Manual

PROJECT DESIGN

Amendements

PROTOCOL

6. INVESTIGATIONAL MEDICINAL PRODUCTS

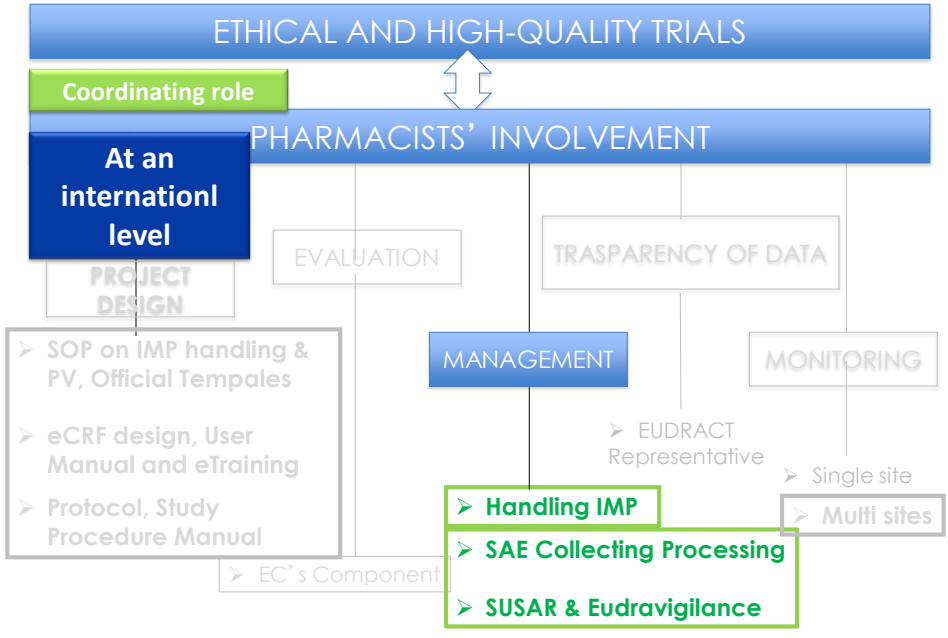
6.4 Handling of investigational medicinal products

STUDY PROCEDURE MANUAL

2. INVESTIGATIONAL MEDICINAL PRODUCTS (IMPs)
2.1. 2.1 IMPs DETAILS
2.1.1. IMPs dose adjustments
2.2. IMPs SUPPLY AND RECEIPT
2.3. IMPs STORAGE CONDITIONS
2.4. ADMINISTRATION
2.4.2. When should the IMP be administered?
2.4.3. How the IMPs dispensed to patients should be identified?
2.4.4. How the IMP should be administered?
2.4.5. How do I assess subjects' treatment compliance?
2.4.6. Which treatment the patient should receive at the end of the study?
2.5. IMPs DISPOSAL
....

9. SERIOUS ADVERSE EVENTS REPORTING

Pharmacists' involvement in clinical trials and ethical committees

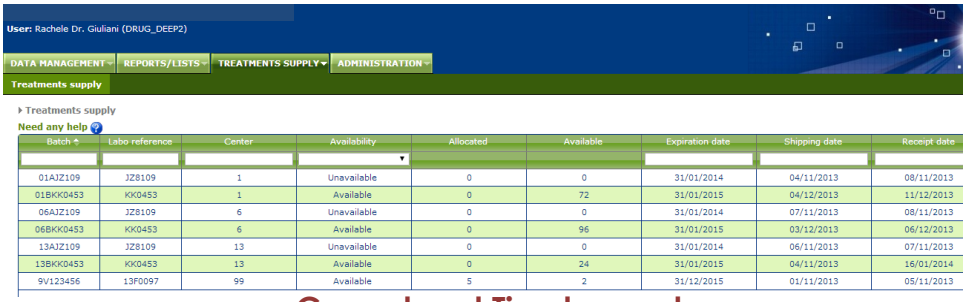


Handling IMP: coordinating role among sites

MANAGEMENT

D.M. 200
06/11/2007 Art. 15

Intermediate warehouse for the direct supply of all the 12 Italian Sites involved (IMP importation)



Batch	Labo reference	Center	Availability	Allocated	Available	Expiration date	Shipping date	Receipt date
01AJZ109	JZ8109	1	Unavailable	0	0	31/01/2014	04/11/2013	08/11/2013
01BKK0453	KK0453	1	Available	0	72	31/01/2015	04/12/2013	11/12/2013
06AJZ109	JZ8109	6	Unavailable	0	0	31/01/2014	07/11/2013	08/11/2013
06BKK0453	KK0453	6	Available	0	96	31/01/2015	03/12/2013	06/12/2013
13AJZ109	JZ8109	13	Unavailable	0	0	31/01/2014	06/11/2013	07/11/2013
13BKK0453	KK0453	13	Available	0	24	31/01/2015	04/11/2013	16/01/2014
9V123456	13F0097	99	Available	5	2	31/12/2015	01/11/2013	05/11/2013

Correct and Timely supply

Handling IMP: coordinating role among sites

MANAGEMENT

D.M. 200
06/11/2007 Art. 15

Intermediate warehouse for the direct supply of all the 12 Italian Sites involved (IMP importation)

Coordination of the drug management activities and Documentation for all the Sites (Italian and Non-Italian) – Mediator among Sites and IMP Producer

Disposal Procedures Support

SAE Collecting and Processing - SUSAR & Eudravigilance

SAE Collecting and Processing - SUSAR & Eudravigilance

- Receiving and reviewing all the SAE form
- Preparing a draft case narrative based on the provided information;
- identifying, organizing and sending queries for the site;
- forwarding by e-mail/fax to the **QPPV** and **MM**, to the **IMP Producer** and to the **DSMC**
- Requesting and processing follow-up info

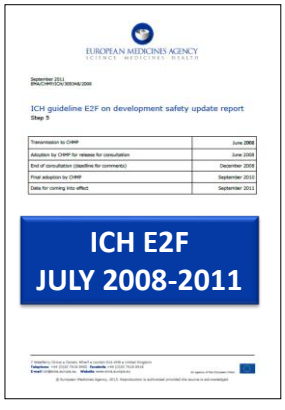
Assessment of Expectedn

EUDRAVIGILANCE

AIFA notification September 2012 to adopt and implement CT-3 EU guidelines of 2011 and ICH E2F.

AIFA training course September 2013: Hospital Pharmacist→ QPPV

SAE Collecting and Processing - SUSAR & Eudravigilance



ICH E2F JULY 2008-2011

SAFETY AGREEMENT

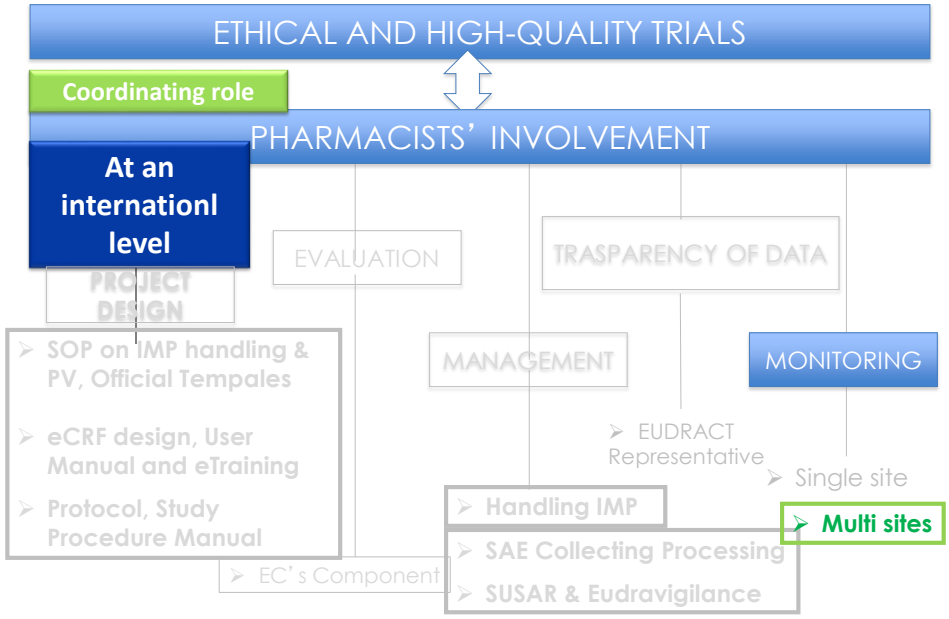
DEVELOPMENT SAFETY REPORT (DSUR)

Every 12 month starting from DIBD

PERIODIC SAFETY REPORT

Every 6 month starting from DIBD

Pharmacists' involvement in clinical trials and ethical committees



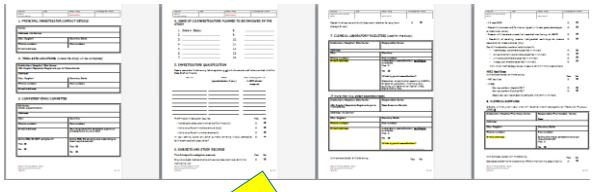
Monitoring Activities at a Multeicenter Level

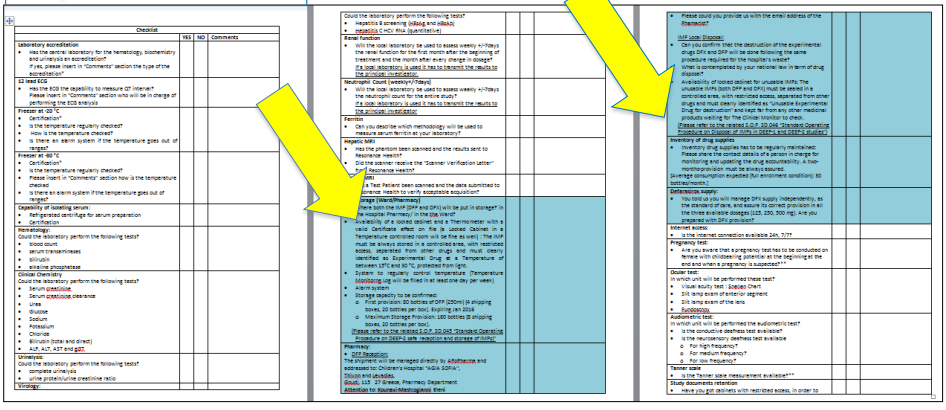
MONITORING

Site Assessment Check List

PSQV: Pre Study Qualification Visit

Prequalification Check list





Monitoring Activities at a Multeicenter Level

MONITORING

Visit at Sites as Sponsor representative together with the delegated CRA

SIV: Site Initiation Visit

MOV: On Trial Monitoring Visit

COV: Close Out Visit

Pharmacists' involvement in clinical trials and ethical committees

1994
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….a longstanding issue…

- ***EC's members***
- ***Responsibility***

Strengthen of our contribution in the field of clinical research and of independent research mainly

Thank you