EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Compliance and Inspection

Annual Report of the Good Clinical Practice Inspectors Working Group 2009

Adopted by the GCP IWG on 24 February 2010

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1. INTRODUCTION

This document is the second Annual Report of the GCP IWG[1]. This group was established in 1997 under the scope of Article 57(1)(i) of Regulation (EC) No. 726/2004.

The GCP IWG focuses on harmonisation and co-ordination of GCP related activities at Community level. The group's role and activities are described in more detail in its Mandate and Workplan and also in Volume 10, Chapter IV, of the Rules Governing Medicinal Products in the European Union. The group supports the co-ordination of the provision of GCP advice and maintains a dialogue with other groups such as CHMP[2], CVMP[3], EWP[4], PhV WP[5], CMD[6], GMDP[7] IWG and other groups, as needed, on areas of common interest.

This Annual Report is set out in line with the format and objectives of the 2009 Workplan.

2. MEETINGS

The plenary GCP IWG meetings and related subgroup meetings held during 2009 are summarised in the following table:

Plenary meetings dates	**Subgroup meetings dates** (involved in the discussion of specific topics and drafting documents)				
	GCP/GMDP	GCP/CMD(h)	GCP Computer Systems	GCP Quality Risk Management	GCP/ATP[8]
04 – 05/03/09	13/02/09	18/02/09	01/10/09	02/03/09	20/01/09
18 – 19/06/09		28/05/09	29/10/09	22/06/09	
15- 16/09/09		22/10/09		14/09/09	
09 – 11/12/09		16/12/09		08/12/09	

Joint meetings took place in the following dates:

- 04 March 2009: joint meeting with the CTFG
- 9 December 2009: joint meeting with interested parties.
- 10 December 2009: joint meeting with CHMP assessors

[1] Good Clinical Practice Inspectors Working Group
[2] Committee for Medicinal Products for Human Use
[3] Committee for Medicinal Products for Veterinary Use
[4] Efficacy Working Party
[5] Pharmacovigilance Working Party
[6] Co-ordination Group for Mutual Recognition and Decentralised Procedures
[7] Good Manufacturing Distribution Practice Inspectors Working Group
[8] Advanced Therapy Product

3. INSPECTIONS CONDUCTED IN SUPPORT OF THE CENTRALISED PROCEDURE

A. General overview

The CHMP requested 39 inspections in 2009 and 43 inspections were conducted by the inspectorates of the EU member states in the same year. The number of inspections requested and conducted is not consistent due to the fact that several inspections requested in the last 3 months of the year 2008 have been conducted in 2009 and some inspections requested in the last 3 months of 2009 will be carried out in 2010. The data in this report relates to inspections carried out.

In figure 1, the number of inspections conducted in 2009 is shown by region and type of inspection. The most inspections have been carried out in the Rest of the World region (42%) followed by inspections in North America (37%) and EU/EEA[10] (21%).

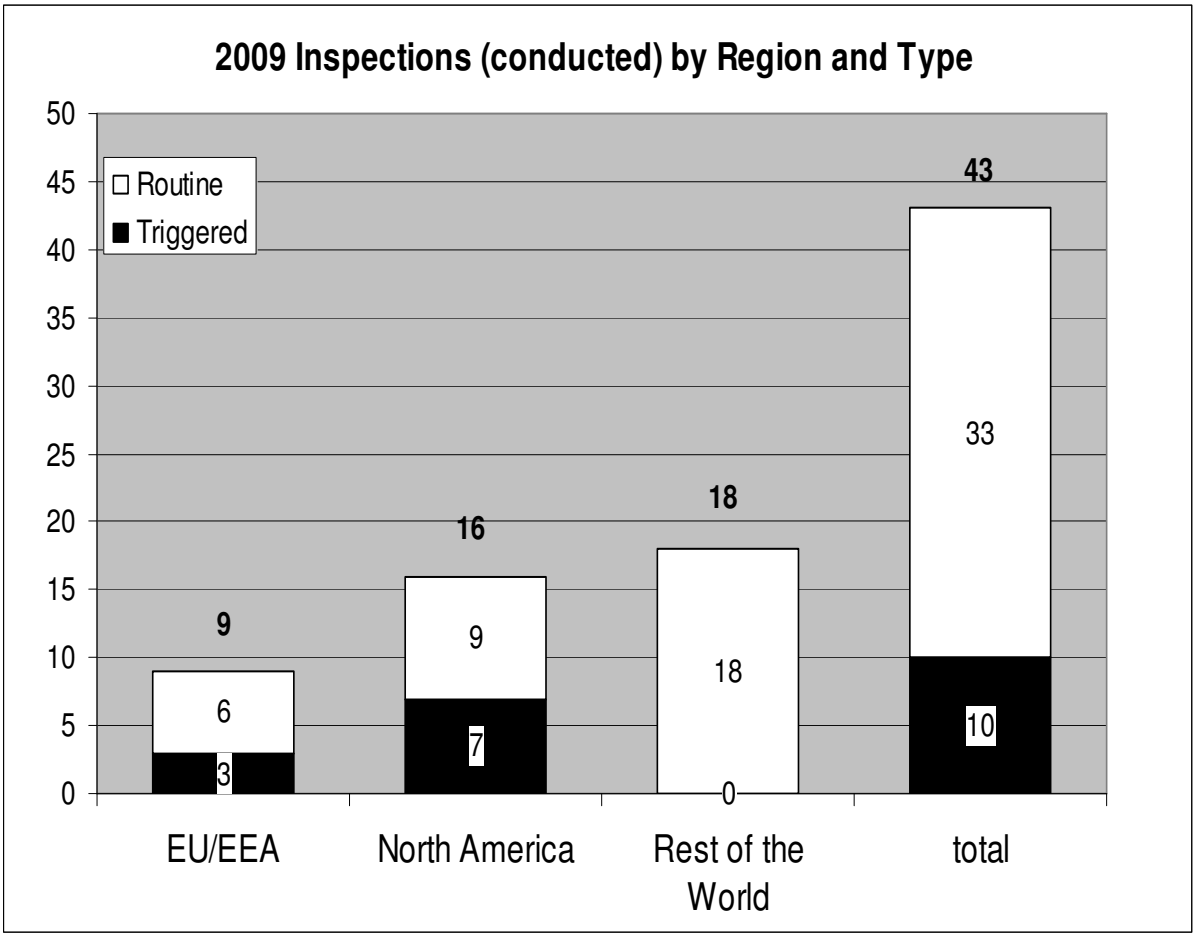

Figure 1: Inspections conducted per region and type of inspection.

Figure 2 represents the number of inspections conducted per type of site. Most inspections have been conducted at clinical investigators (65%).

[10] European Union/European Economic Area/European Free Trade Association

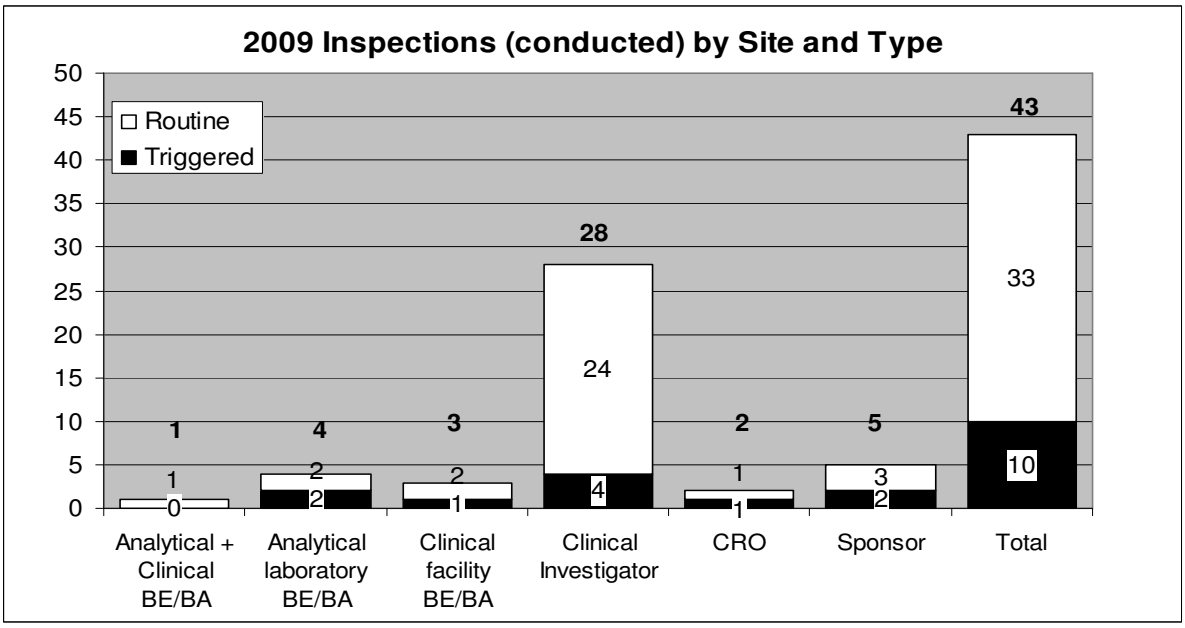

Figure 2: Inspections conducted per type of site and type of inspection.

B. Categorization of findings

A total of 621 deficiencies, comprising 35 critical (5.65%), 301 major (48.5%) and 285 minor (45.9%) were recorded for the 43 inspections conducted in 2009.

The main findings observed in the 2009 inspections are detailed below in accordance to the GCP categorization of findings agreed by the GCP IWG. It should be noted that the data presented here is preliminary data and a more detailed report will be published later in the year.

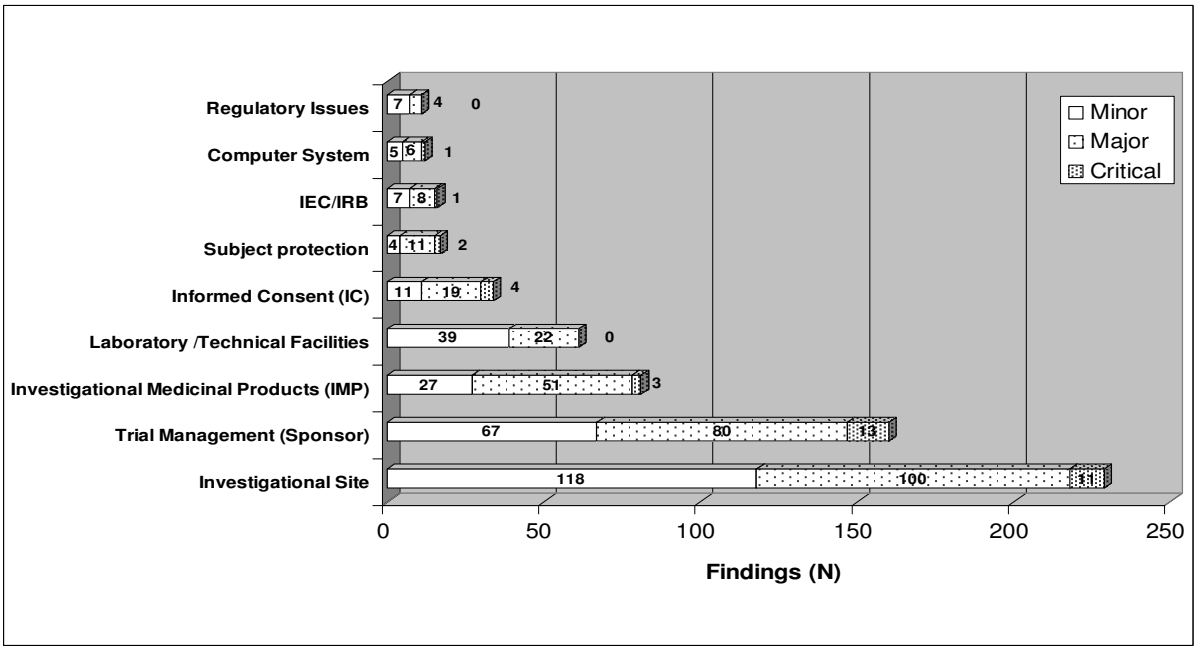

Figure 4. Number of findings with regard to the main categories graded by critical, major and minor.

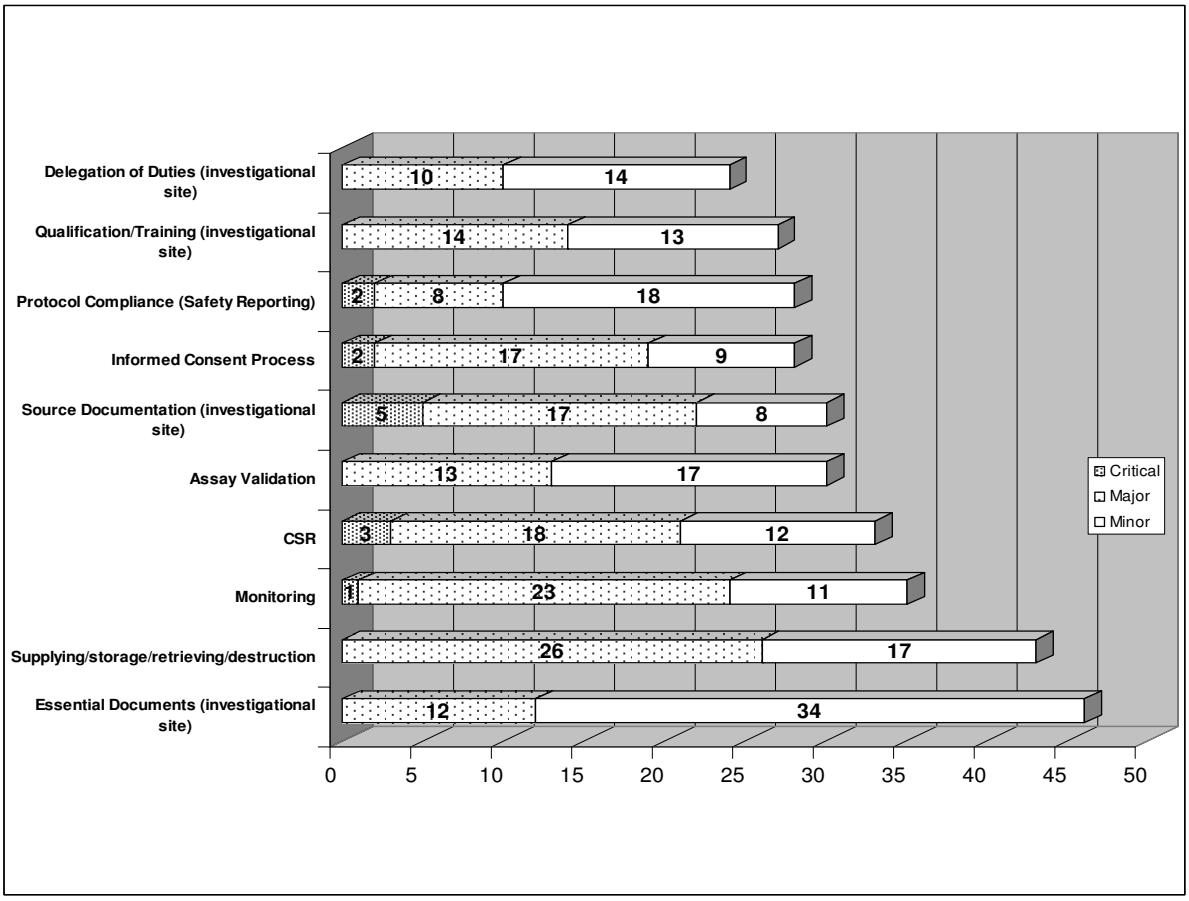

Figure 5. The 10 top findings classified by the grading.

4. HARMONISATION TOPICS

4.1 Procedures and Guidance documents

The GCP IWG has finalised the following guidance on GCP Inspection required in accordance with article 29 of Directive 2005/28/EC:

- Guidance for coordination of GCP inspections and co-operation between GCP inspectors, the Reference and Concerned Member States and CMD(h), in the context of the evaluation of the GCP compliance of marketing authorization applications for Mutual Recognition and Decentralized Procedures" now available in Chapter IV of Volume 10 of the Rules Governing Medicinal Products in the European Union.
- Record keeping and archiving of documents obtained or resulting from the Good Clinical Practice inspection. Pending publication by the Commission in Chapter IV of Volume 10 of the Rules Governing Medicinal Products in the European Union.

The following document is under preparation or still pending:

- Actions taken after completion of Good Clinical Practice inspection.

4.2 Inspection cooperation in the community

a) Cooperation between the MS

- In 2009 all the inspections requested have been joint inspection involving inspectors from at least two Member States
- A joint meeting GCP IWG and CHMP assessors took place on 10 December 2009 with practical presentations from the inspectors' and assessors' perspective on the experience with some GCP inspections carried out for the centralized procedure. The issues discussed included the interpretation/understanding of findings, communication between inspectors and assessors during the procedure, difference in views, expectations and suggestions for process improvement.

b) Cooperation with 3rd countries (see also section 7.6)

- Observers from third countries have always been invited to observe the EU GCP inspections performed on those countries in the context of the centralized procedure.

4.3 GCP Training and development

The following activities have taken place during this year:

- The 7th GCP IWG Training Course in Rome (Italy) on 11-14, October 2009. Participants included inspectors from EEA (Austria, Belgium, Bulgaria, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Spain, Sweden, UK) and from third countries (Argentina, Australia, Canada, Croatia, Ghana, India, Japan, The Former Yugoslav Republic of Macedonia, Mexico, South Africa, Switzerland, Taiwan, Turkey, USA). The course covered the following topics:
    - Update on pharmaceutical legislation (paediatric and advanced therapies)
    - Update on the EMEA-FDA GCP inspection initiative
    - General aspects of inspection and basic skills
    - GCP inspections and regulatory oversight of clinical trials in 3rd countries with presentation from Argentina, Australia, Canada, Ghana, Japan, India, Mexico, South Africa, USA and WHO
    - Practical aspects of third country inspections from the EU inspector's perspective
    - Computer system validation
    - Cases of serious breaches, GCP non compliance and of fraud/misconduct
    - Break-out sessions every day with discussion points on the different topics covered in the agenda

- During the GCP Inspector meetings held in 2009, the following topics have been addressed:

    - Develop peer review of case studies.
    - Sharing and discussion of inspection reports, including grading of anonymised findings.
    - Develop and monitor opportunities for joint inspections.

5. TOPICS OF INTEREST

The GCP IWG has finalized and published the following document focused on topics of interest:

- Questions and Answers on investigational medicinal products (IMPs) in bioavailability and bioequivalence trials.

The GCP IWG has also prepared a template form for a non-compliance alert for the attention of the GCP inspectors/clinical assessors in relation to Art. 12.2 of the Clinical trial Directive 2001/20/EC.

The GCP IWG has supported the preparation by the Efficacy Working Party of a guideline on validation of bio-analytical method released for public consultation until 31 May 2010.

The GCP IWG has under preparation (UP) or pending (P) to prepare the following documents focused on topics of interest which will be included in the 2010 Workplan:

- Reflection paper on expectations for electronic source documents used in clinical trials (UP).
- Reflection paper on quality risk management in clinical trials (UP).
- Reflection paper on the conduct of clinical laboratory analyses for clinical trials (UP).
- Document with specific triggers for assessors in the context of the ethical conduct of clinical trials in 3rd countries (P).

6. COLLABORATION WITH EUROPEAN COMMISSION

6.1 Implementation of Directive 2001/20/EC and of Directive 2005/28/EC and related guidance documents

See section 3.1.

6.2 EudraCT Database

Some inspectors from the GCP IWG have participated in the training for the pilot phase of the EudraCT data warehouse.

6.3 EU enlargement

- Croatia, Former Yugoslav Republic of Macedonia and Turkey have attended the GCP IWG meetings held in 2009 as observers, with the exception of the September one.
- Delegates from these countries have also attended the 8th GCP IWG training workshop in Rome (see section 4.3).

6.4 Regulation on Advanced Therapies

The GCP IWG, through the GCP/ATP subgroup and on behalf of the Commission has drafted a revision of the "Detailed Guideline on Good Clinical Practice specific to Advanced Therapy Medicinal Products" following the public consultation and therefore contributing to the implementation of Article 4(2) of the Advanced Therapies Regulation. They have also advised on the necessary modifications to Directive 2005/28/EC and related GCP guidelines in the context of this Regulation.

7. LIAISON WITH OTHER GROUPS

7.1 GMDP

The GMPD and GCP IWGs, through the GCP/GMDP, have contributed to the preparation and finalization of the following documents:

- Revised Annex 13 following comments from public consultation and pending to be publish by the Commission.
- Q&A on storage and transportation of IMPs

7.2 Ad Hoc PhV IWG

Safety issues raised during a GCP inspection of a centralized product have been considered in the scope of the PhV inspection of the MAH concerned by that product.

7.3 CTFG

A joint meeting GCP IWG-CTFG took place on 4 March 2009 discussing the following points:

- Proposal of principles and process for the coordination of EU GCP Inspection
- Risk based approach for the supervision of clinical trials
- IMP related issues (e.g. labelling, definition of IMP/NIMP/background therapy etc.)
- Definition of IMP/NIMP/background therapy
- Other issues

7.4 CMD(h)

The GCP IWG and the CMD(h), mainly through the GCP/CMD(h) subgroup has contributed to:

- The finalization and publication of the Guidance for coordination of GCP inspections in the context of the evaluation of the GCP compliance of marketing authorization applications for Mutual Recognition and Decentralized Procedures (see section 4.1).
- The agreement of a pilot process for the preparation of an annual risk based programme of routine GCP inspections of the contract research organisations most often used in the conduct of the bioequivalence trials included in marketing authorisation applications for generic products in the mutual recognition and decentralised procedure has been finalised. The pilot will be run for 12 months to gain experience.
- The finalization of a document for assessors on triggers for selection of applications and sites to be inspected in the context of generic applications.
- The discussion of processes for:
    - Exchange of information on inspections,
    - Communication of inspections findings,
    - Selection of trial/sites for inspection.
- The coordination of one inspection in the context of the MRP/DCP for generic applications.

7.5 Heads of Medicines Agencies

See section 7.3

7.6 Other Regulatory Agencies

The initiation of the pilot phase of the EMEA FDA GCP initiative which announcement and terms of engagement are published in the EMEA external website:

- EMEA-FDA GCP Initiative,
- EMEA/FDA GCP Initiative - Terms of engagement and procedures for participating authorities.

7.7 Joint meeting with interested parties:

A joint meeting GCP IWG and interested parties took place on 10 December 2009. Delegates from ACRO, AESGP, EGA, EuropaBio, EFPIA, EORTC, EUCROF and EFGCP attended this meeting. The agenda covered the following topics:

For the details of the activities of the GCP IWG for next year see the Workplan for 2010