European Medicines Agency
Inspections

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ANNUAL REPORT OF THE GOOD CLINICAL PRACTICE INSPECTORS WORKING GROUP 2008

Adopted by the GCP IWG on 3 March 2009

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1. INTRODUCTION

The GCP IWG[1] (formerly Ad Hoc meeting of Good Clinical Practice Inspectors) 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], GMP[7] Inspectors and other groups, as needed, on areas of common interest.

The GCP IWG has decided to publish Annual Reports as part of the process of improving transparency. This document is the first report from this group and is set out in line with the format and objectives of the 2008 Workplan.

2. MEETINGS

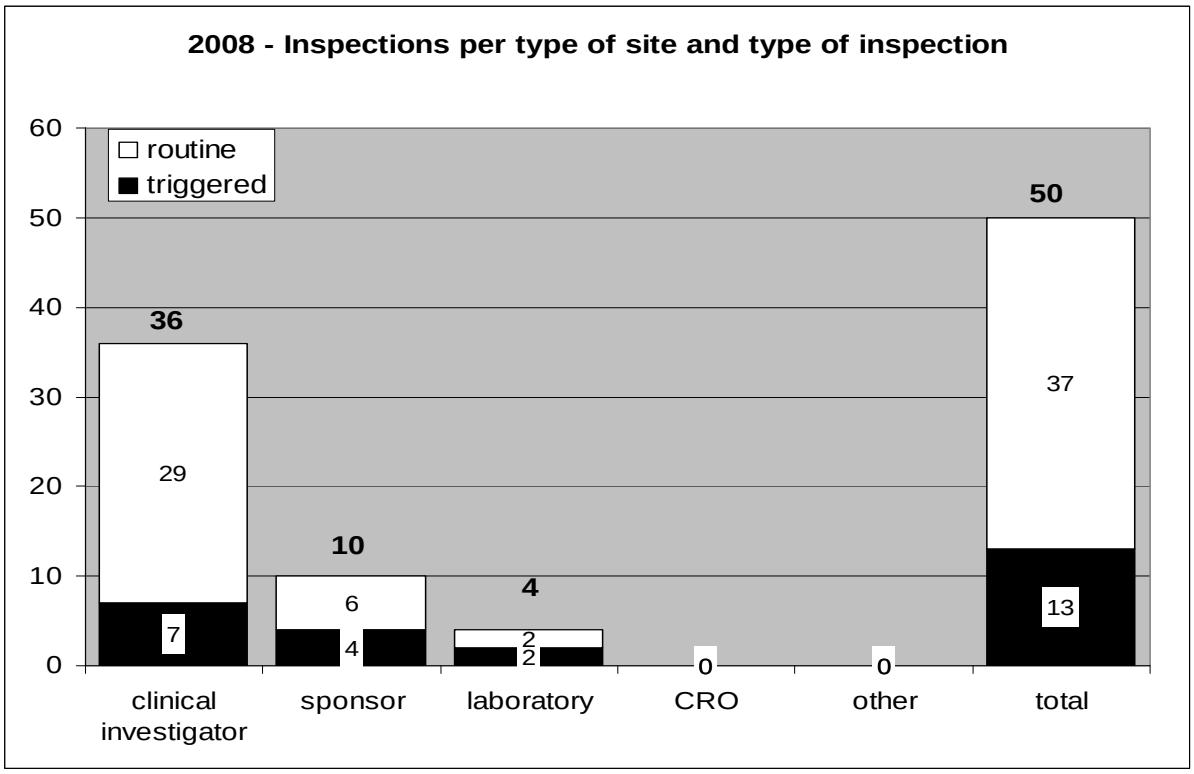
The GCP IWG meetings held during 2008 are summarised in the following table:

Plenary meetings dates	**Subgroup meetings dates** (involved in the discussion of specific topics and drafting documents)		
	GCP/GMP	GCP/CMD(h)	GCP/ATP[8]
• 12-13 March 2008 • 18-19 June 2008 • 10-11 September 2008 • 03-04 December 2008	• 22 January 2008	• 19 March 2008 • 17 June 2008 • 22 October 2008 • 19 November 2008	• 14 March 2008 • 30 April 2008 • 15 May 2008

3. INSPECTIONS CONDUCTED IN SUPPORT OF THE CENTRALISED PROCEDURE

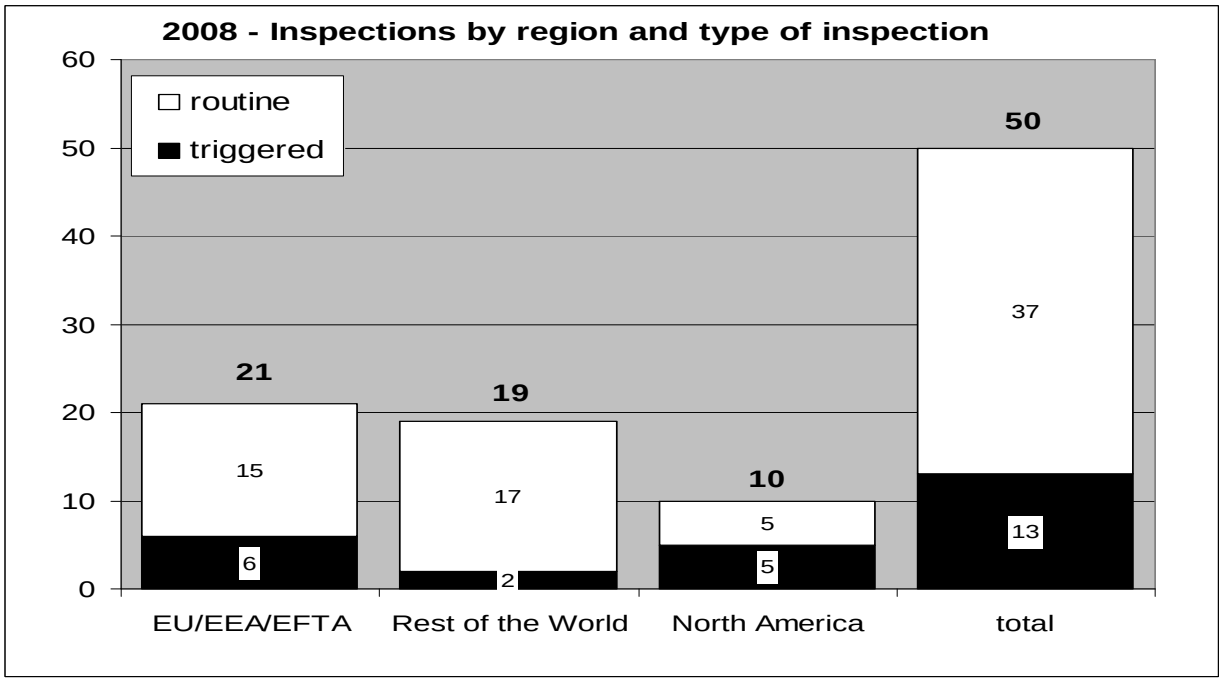
The following graphs provide some statistics on inspections. In graph 1 it can be shown that the CHMP requested in 2008 to inspect 50 sites of which 37 were routine inspection requests and 13 triggered inspection requests. When the information is analyzed per type of site, the higher number of inspections fall under the clinical investigators (72%) followed by the sponsor (20%). No inspections were requested this year for CROs[9].

[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 Practice Inspectors Working Group
[8] Advanced Therapy Product
[9] Contract Research Organisation



Graph 1: Inspections requested by the CHMP per type of site and type of inspection.

In graph 2, the number of inspections requested in 2008 is shown per region and type of inspection. In 2008 the number of third country inspections (excluding Switzerland as it is part of EFTA) requested are slightly superior (58%) to those in EU/EEA/EFTA[10].



Graph 2: Inspections requested by the CHMP per region and type of inspection.

EMEA is undertaking a project to analyze the findings of all GCP inspections requested by the CHMP and anonymised information of the outcome of this categorization of findings may be available by the time of the 2009 annual report.

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

4. HARMONISATION TOPICS

4.1 Procedures and Guidance documents

The GCP IWG has finalized the following guidance on GCP Inspection requested in accordance with Article 29 of Directive 2005/28/EC which are now publicly available in Chapter IV of Eudralex Volume 10 of the Rules Governing Medicinal Products in the European Union:

- Guidance for exchange of GCP Inspection Reports according to Directive 2001/20/EC Art 15.2 (June 2008),
- Guidance for the conduct of GCP inspections (June 2008):
  - Annex I to Guidance for the conduct of GCP inspections - investigator site (June 2008),
  - Annex II to Guidance for the conduct of GCP inspection - clinical laboratories (June 2008),
  - Annex III to Guidance for the conduct of GCP inspections - computer systems (June 2008),
  - Annex IV to Guidance for the conduct of GCP inspections - Sponsor and CRO (June 2008),
  - Annex V to Guidance for the conduct of GCP inspections - Phase I Units (November 2008),
  - Annex VII to Guidance for the conduct of GCP inspections - Bioanalytical part, Pharmacokinetic and Statistical Analyses of Bioequivalence Trials (November 2008).
- Guidance for the preparation of GCP inspections (June 2008).
- Guidance for the communication on GCP inspections and findings (June 2008).
- Guidance for the preparation of Good Clinical Practice inspection reports (June 2008).

The following document, although not required in Eudralex Volume 10 -Chapter IV, it has also been included here at the request of this GCP IWG:

- Procedure for standardisation of GCP inspection entries in EudraCT (November 2008).

The following documents are in preparation in collaboration with the CMD(h) group and expected to be published by the Commission in 2009 in Chapter IV of Eudralex Volume 10 of the Rules Governing Medicinal Products in the European Union:

- 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,
- Selection of the trials/sites to be inspected:
  - context of assessment of applications for marketing authorisation,
  - surveillance of clinical trials in Member States.
- Actions taken after completion of Good Clinical Practice inspection.
- Annex VI to Guidance for conducting GCP Inspections – Record keeping and archiving of documents obtained or resulting from the Good Clinical Practice inspection.

4.2 Joint Inspections

In 2008, 42 out of 50 inspections requested have been joint inspection involving inspectors from at least two Member States.

4.3 GCP Training and development

Regarding training and development, the following activities have taken place during this year:

- The 6th GCP IWG Training Course in Granada (Spain) on 5-8, October 2008. Participants included inspectors from EEA (Austria, Bulgaria, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Spain, Sweden, UK) and from third countries (Argentina, Brazil, Croatia, Ghana, The Former Yugoslav Republic of Macedonia, South Africa, Switzerland, Turkey, USA and WHO[11]) as well as one assessor from Spain and Germany, respectively. The course covered the following topics:

    - General aspects of inspection and basic skills of inspectors,
    - Updates on pharmaceutical legislation (paediatric and advanced therapies),
    - The investigator related aspects of the inspections from the perspective of the assessors and EU/FDA[12] inspectors,
    - Inspections of the data management, statistical analysis and electronic source documents from the perspective of the assessors and EU/FDA inspectors,
    - Third country inspections with focus on regulatory and ethical requirements,
    - Presentations from Argentina, Brazil, Ghana, South Africa, USA and WHO on the conduct of GCP inspections and regulatory oversight of clinical trials in these countries,
    - Practical aspects for the conduct of third country inspections,
    - Study cases of fraud/misconduct,
    - Accreditation of Phase I units in UK,
    - Requirements for GCP training of investigators.

- During the GCP Inspector meetings held in 2008, discussions on the following topics has taken place:

    - 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 documents focused on topics of interest:

- Reflection paper on advice to applicants/sponsors/CROs of bioequivalence studies, which is already publicly available in the EMEA external website.

The GCP IWG has in preparation the following documents focused on topics of interest:

- Reflection paper on expectations for electronic source documents used in clinical trials. The GCP IWG has to review the outcome of the consultation, which finalized by the end of April 2008, for its further finalization in 2009.
- Draft Q&A on the documentation and traceability of the IMPs used in bioequivalence studies. This document has to be revised and then it will be published for public consultation in 2009.

[11] World Health Organisation
[12] Food and Drug Administration

The following documents are still pending and they are included in the 2009 Workplan of the group:

- Reflection paper on quality risk management in clinical trials.
- Guidance on the use of computer systems for clinical trials either as a reflection paper or through preparation of a concept paper.
- Reflection paper on the conduct of laboratory analyses for clinical trials.
- Document with specific triggers for assessors in the context of the ethical conduct of clinical trials in 3rd countries.
- Inspection processes in the context of:
    - large-scale clinical trials,
    - statistical analysis and reporting,
    - inspections of clinical trials conducted in developing countries (ethical and quality considerations) and to support the conduct of inspections in those countries.

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

The GCP IWG has provided some recommendations in relation to the modification of the inspection record template in order to improve the inspection entries in relation to the inspections of BE trials.

6.3 EU enlargement

Croatia, Former Yugoslav Republic of Macedonia and Turkey have attended the GCP IWG meetings held in 2008 as observers.

6.4 Regulation on Advanced Therapies

The GCP IWG, through the GCP/ATP subgroup, has contributed to the implementation of Article 4(2) of the Advanced Therapies Regulation by providing recommendations to the European Commission on the content of the "Detailed Guideline on Good Clinical Practice specific to Advanced Therapy Medicinal Products", which was released by the Commission for consultation in June 2008.

7. LIAISON WITH OTHER GROUPS

7.1 GMP/GDP IWG[13]

The GCP IWG and the GMP/GDP IWG, mainly through the GCP/GMP subgroup, has finalized this year the following documents, which current status is also detailed:

[13] Good Manufacturing Practice/Good Distribution Practice Inspectors Working Group

- Annex 13 Reference and Retention samples. A proposal has been included as part of the revised Annex 13, which has been released for public consultation by the Commission until end of February 2009.
- Definition of Reconstitution. A proposal has been included as part of the revised Annex 13, which has been released for public consultation by the Commission until end of February 2009.
- Content of IMP[14] Batch Certificate. This document has been finished and will be published by the European Commission in 2009.

7.2 CTFG[15]

A GCP IWG delegation attended a CTFG meeting in December 2008 to prepare for a joint meeting in 2009.

7.3 CMD(h)

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

- The preparation of the "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" expected to be published by the Commission in the first quarter of next year.

- The discussion of processes for:

  - Exchange of information on inspections,
  - Communication of inspections findings,
  - Selection of trial/sites for inspection.

- The coordination of some inspections in the context of the MRP/DCP[16] for generic applications.

7.4 Other Regulatory Agencies

Development of contacts between EU and 3rd country agencies, on GCP matters (inspection processes and contacts, joint inspections, exchange of inspections information), has taken place in 2008 through:

- The involvement of inspectors from the US FDA, Argentina, Ghana, Brazil, South Africa and WHO in the GCP Inspectors training course held in Granada, Spain. (see section 3.3).
- The participation of FDA CDER[17] inspectors from the DSI[18] in the GCP IWG meeting held in December 2008.

[14] Investigational Medicinal Product
[15] Clinical Trials Facilitation Group
[16] Mutual Recognition Procedure/Decentralised Procedure
[17] Food and Drug Administration Center for Drug Evaluation and Research
[18] Division of Scientific Investigations

8. LIAISON WITH THE PUBLIC

- Delegates from the GCP IWG have participated and given presentations on behalf of the group in different European Conferences, covering different topics of public interest.
- The GCP IWG plan agreed to have an information day in 2009 with interesting parties.

For the details of the activities of the GCP IWG for next year see the Workplan for 2009.