



European Medicines Agency  
Inspections

London, 5 October 2009  
Doc. Ref. EMEA/INS/GMP/648678/2009

**GMP/GDP INSPECTORS WORKING GROUP  
GMP/GDP IWG**

**CONCEPT PAPER ON THE REVISION OF CHAPTER 7 OF THE GMP GUIDE**

<b>AGREED BY GMP/GDP IWG</b>	September 2009
<b>DEADLINE FOR COMMENTS</b>	31 January 2010

Comments should be provided to [gmp@emea.europa.eu](mailto:gmp@emea.europa.eu)

<b>KEYWORDS</b>	<i>GMP, Contract Manufacture and Analysis, Chapter 7</i>
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This Concept Paper outlines a proposal to review Chapter 7 of the GMP guide in order to provide further guidance on outsourced GMP activities

## **INTRODUCTION AND PROBLEM STATEMENT**

Chapter 7 of the EU GMP guide provides specific guidance on the requirements when full or partial manufacture and analysis activities are outsourced and stresses how these activities must be correctly defined, agreed and controlled in order to avoid misunderstandings which could result in a product or work of unsatisfactory quality. In doing so the guide calls for written contracts between the Contract Giver and the Contract Acceptors which clearly establishes the duties of each party. Today many, if not most, companies routinely outsource some of their GMP regulated activities other than operations traditionally considered as manufacture and analysis.

The guidance in Chapter 7 is high level and generally still applicable to these other outsourced GMP activities but was drafted at a time when the outsourcing of GMP activities was principally restricted to only manufacture and analysis. Whilst the existing guiding principles outlined in Chapter 7 are clearly extendable to these out sourced activities, there is no explicit and unambiguous guidance as to whether such outsourced activities are inside or outside the scope of GMP guidance.

## **2. DISCUSSION**

During inspections, GMP inspectors commonly see that a company has outsourced an activity which if it were performed would normally be subject to inspection. Examples typically include amongst many:

- Qualification and validation work for new premises
- Maintenance and calibration of equipment and premises
- Storage and distribution
- Artwork generation and print ready material
- Assessment and sourcing of starting and packaging materials
- QP and other professional services such as GMP audits of suppliers
- Washing and depyrogenation and or sterilisation of packaging materials used in manufacture.
- Hosting of IT functions
- Document archiving and storage

Whilst some of these activities may arguably be interpreted as either contract manufacture and/or analysis, this is not always clear, and in some cases inspectors report that they sometimes experience difficulty in deciding what would constitute a satisfactory documented arrangement. Similarly on occasions a company may argue that an outsourced activity is outside the scope of GMP inspection.

Furthermore during the review of the GMP guide in the light of the implementation of ICH Q10, Pharmaceutical Quality System a number of amendments to Chapter 1, Quality Management, and Chapter 2, Personnel have been proposed including additions to reference key principles applicable to outsourced activities. It was however noted by the ICH Q10 implementation ad-hoc review group during this review that Chapter 7 of the GMP Guide appeared to merit a more substantial review than simply amendments to align with the Guide with Q10.

## **3. RECOMMENDATION**

It is therefore recommended that the scope and detailed content of Chapter 7 should therefore be reviewed and a gap analysis prepared between the existing guidance and modern pharmaceutical supply chain management, with a view of making proposals for a revision of guidance.

The above relates primarily to the GMP for formulated product but similar arguments and criticism of Part 2 of the GMP Guide. Consideration of to what extent Part 2 may also require amendment should be considered as part of the review, however it is recognised that the change process for Part 2 (being based on ICH Q7A) may limit the scope for revision.

#### **4. PROPOSED TIMETABLE**

Experience from the revision of chapters 1 and 2 of the guide suggests that following agreement of this concept paper, a draft proposal for review by the GMDP IWG could be prepared by the May 2010 meeting of that group.

It is anticipated that the start of consultation on a new guideline could be achieved by September 2010 with a finalised guideline been complete by September 2011 for adoption by the Commission.

#### **5. RESOURCE REQUIREMENTS FOR PREPARATION**

A drafting group of Inspectors (5 – 6) will need to be formed, which will meet via teleconference as well as in the margins of the GMDP IWG meetings and at dedicated drafting group meetings of which at least four will be required. A rapporteur has not yet been nominated. A number of MSs have already shown an interest in contributing to the drafting group.

#### **6. IMPACT ASSESSMENT (ANTICIPATED)**

As the majority of companies will, for internal Quality System and business reasons already have contractual agreements in place for many of the activities expected to be covered by the revised guidance it is expected that the additional regulatory burden will be light.

The relatively small resource implications for preparation of a Guideline are fully justified and are compensated by the fact that application of a revised Guideline will make technical arrangements more transparent for a number of out sourced GMP activities out side of the current scope of the existing Guide.

The review of this chapter of the EU GMP Guide is part of the ongoing general development of suitable quality standards leading to better control over the supply chain and is also inline with the implementation of ICH Q10 in the European Region. It will result in a clearer and more consistent assessment of out sourced GMP activities, set clearer standards and expectations for industry, and therefore be helpful for a harmonised regulatory policy.

#### **6. INTERESTED PARTIES**

In the preparation of the revised guideline, the drafting group will liaise and exchange experiences with experts from national authorities supervising of GMP in Member States as well as those in other regions such as PICs and MRA partners. The draft guideline will be made publicly available to interested parties for a 6-month consultation period before finalisation.

#### **7. REFERENCES TO LITERATURE, GUIDELINES ETC**

1. Chapter 7 of the EU Guide to GMP
2. ICH Q10 Pharmaceutical Quality System