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The Rules Governing Medicinal Products in the European Union

EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use

Introduction

Document History	
The *first edition* of the Guide was published, including an annex on the manufacture of sterile medicinal products.	1989
The *second edition* was published; implementing Commission Directives 91/356 of 13 June 1991 and 91/412 of 23 July 1991 laying down the principles and guidelines on good manufacturing practice for medicinal products for human use as well as for veterinary medicinal products. The second edition also included 12 additional annexes.	January 1992
An update of legal references was made. In the meantime, the guide is updated as needed on the website of the European Commission, several additional annexes added.	August 2004
Re-structuring of GMP guide, consisting of Part I for medicinal products for human and veterinary use and Part II for active substances used as starting materials, implementing Directives 2004/27/EC and 2004/28/EC. The current guide includes 17 Annexes, the former Annex 18 being replaced.	October 2005
Update of the text and introduction of a new Part III	December 2010

Introduction

The pharmaceutical industry of the European Union maintains high standards of Quality Management in the development, manufacture and control of medicinal products. A system of marketing authorisations ensures that all medicinal products are assessed by a competent authority to ensure compliance with contemporary requirements of safety, quality and efficacy. A system of manufacturing authorisations ensures that all products authorised on the European market are manufactured/ imported only by authorised manufacturers, whose activities are regularly inspected by the competent authorities, using Quality Risk Management principles. Manufacturing authorisations are required by all pharmaceutical manufacturers in the European Union whether the products are sold within or outside of the Union.

Two directives laying down principles and guidelines of good manufacturing practice (GMP) for medicinal products were adopted by the Commission. Directive 2003/94/EC applies to medicinal products for human use and Directive 91/412/EEC for veterinary use. Detailed guidelines in accordance with those principles are published in the Guide to Good Manufacturing Practice which will be used in assessing applications for manufacturing authorisations and as a basis for inspection of manufacturers of medicinal products.

The principles of GMP and the detailed guidelines are applicable to all operations which require the authorisations referred to in Article 40 of Directive 2001/83/EC, in Article 44 of Directive 2001/82/EC and Article 13 of Directive 2001/20/EC, as amended. They are also relevant for pharmaceutical manufacturing processes, such as that undertaken in hospitals.

All Member States and the industry agreed that the GMP requirements applicable to the manufacture of veterinary medicinal products are the same as those applicable to the manufacture of medicinal products for human use. Certain detailed adjustments to the GMP guidelines are set out in two annexes specific to veterinary medicinal products and to immunological veterinary medicinal products.

The Guide is presented in three parts and supplemented by a series of annexes. Part I covers GMP principles for the manufacture of medicinal products. Part II covers GMP for active substances used as starting materials. Part III contains GMP related documents, which clarify regulatory expectations.

Chapters of Part I on “basic requirements” are headed by principles as defined in Directives 2003/94/EC and 91/412/EEC. Chapter 1 on Quality Management outlines the fundamental concept of quality management as applied to the manufacture of medicinal products. Thereafter, each chapter has a principle outlining the quality management objectives of that chapter and a text which provides sufficient detail for manufacturers to be made aware of the essential matters to be considered when implementing the principle.

According to the revised Article 47 and Article 51, respectively, of the Directive 2001/83/EC and Directive 2001/82/EC, as amended, detailed guidelines on the principles of GMP for active substances used as starting materials shall be adopted and published by the Commission. Part II was established on the basis of a guideline developed on the level of ICH and published as ICH Q7A on “active pharmaceutical ingredients”. It has an extended application both for the human and the veterinary sector.

In addition to the general matters of Good Manufacturing Practice outlined in Part I and II, a series of annexes providing detail about specific areas of activity is included. For some manufacturing processes, different annexes will apply simultaneously (e.g. annex on sterile preparations and on radiopharmaceuticals and/or on biological medicinal products).

A glossary of some terms used in the Guide has been incorporated after the annexes. Part III is intended to host a collection of GMP related documents, which are not detailed guidelines on the principles of GMP laid down in Directives 2003/94/EC and 91/412/EC. The aim of Part III is to clarify regulatory expectations and it should be viewed as a source of information on current best practices. Details on the applicability will be described separately in each document.

The Guide is not intended to cover safety aspects for the personnel engaged in manufacture. This may be particularly important in the manufacture of certain medicinal products such as highly active, biological and radioactive medicinal products. However, those aspects are governed by other provisions of Union or national law.

Throughout the Guide, it is assumed that the requirements of the Marketing Authorisation relating to the safety, quality and efficacy of the products, are systematically incorporated into all the manufacturing, control and release for sale arrangements of the holder of the Manufacturing Authorisation.

For many years, the manufacture of medicinal products has taken place in accordance with guidelines for Good Manufacturing Practice and the manufacture of medicinal products is not governed by CEN/ISO standards. The CEN/ISO standards have been considered but the terminology of these standards has not been implemented in this edition. It is recognised that there are acceptable methods, other than those described in the Guide, which are capable of achieving the principles of Quality Management. The Guide is not intended to place any restraint upon the development of any new concepts or new technologies which have been validated and which provide a level of Quality Management at least equivalent to those set out in this Guide.

The GMP guide will be regularly revised in order to reflect continual improvement of best practices in the field of Quality. Revisions will be made publicly available on the website of the European Commission:
http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm