MINISTERIO
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agencia española de
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DIRECCIÓN DE LA
AGENCIA ESPAÑOLA
DE MEDICAMENTOS Y
PRODUCTOS SANITARIOS

COMMENTS TO THE GUIDELINES ON THE FORMALISED RISK ASSESSMENT FOR ASCERTAINING THE APPROPRIATE GOOD MANUFACTURING PRACTICE FOR EXCIPIENTS OF MEDICINAL PRODUCTS FOR HUMAN USE.

SUBMITTED BY THE AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS (AEMPS), SPAIN

Madrid, 26 April 2013.

This document contains the comments from the *Agencia Española de Medicamentos y Productos Sanitarios* to the Draft "Guidelines on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use" (SANCO/D/6/SF/mg/ddg1.d.6(2013)17926) submitted for public consultation.

Excipients exert a considerable impact on the quality of the medicinal products, and these guidelines will contribute to a more rational and risk-based approach of the supervision and controls performed by the manufacturers of medicinal products.

Section 8 lists some risks for their consideration by the manufacturer. One of the elements refers to the use of dedicated equipment and/or facilities, where, in our opinion, the risks would arise from the opposite situation, i.e. the use of multi-product or non-dedicated equipment and/or facilities, and we suggest rephrasing this item. In this section we would like to include a reference to the stability of the excipient, as some excipients may be prone to degradation or alteration (oxidization, hygroscopy...). In the last bullet point of this section, we would like to replace "storage conditions" for "storage/transportation conditions".

Under the 5th bullet point of section 9, the risks of falsification or fraudulent adulteration of an excipient should be explicitly mentioned, as their occurrence and probability may differ from those of simple quality defects.

Also under section 9 a reference to composite excipients is included. It is a general opinion that mixtures of excipients without active ingredients are generally not considered as intermediates. However, mixing and processing individual excipients to render composite excipients may have a significant impact in the overall quality and performance of the medicinal product, and this feature must have a great weight in the final decision.

Concerning the high level GMP principles listed in section 11, we would like to ask for the inclusion of a clarification on how to proceed in section g) when a retest date (and not the expiry date) is given for the excipients.

The guidelines avoid making references to quality guidelines and quality standards applied by some excipients manufacturers, such as proper GMP for medicinal products, HACCP certifications, IPEC GMP for excipients, ISO 9000 norms... It could be useful, for illustrative

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purposes, to name some of the existing standards in the document, although only as an example and advising that this list is not exhaustive.

As a general remark, this approach involves a considerable amount of information and documentation to be assessed by competent authorities. It is still to be determined if this assessment will be part of the evaluation of the marketing authorizations and/or if it will be performed on a selected excipient(s) in the course of GMP inspections.

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