EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

<2014-05-07>

Submission of comments on Eudralex; Volume 4; EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use; Annex 15: Qualification and Validation draft dated 6 February 2014

Comments from:

Name of organisation or individual
Recipharm Stockholm AB (corporate 556666-8249)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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1. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
Chapter 9.5 page 12		With reference to our comments on the 'EMA Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities' (enclosed), applying the PDE approach to all medicinal substances would be extremely cost and resources-demanding for most companies (particularly contract manufacturers since the scientific knowledge from clinical pharmacological data is limited within this organizations). Additionally the PDE approach generates no value at all regarding non-hazardous substances. The PDE-approach should only apply to highly hazardous substances, particularly cytotoxics. The really highly hazardous medicinal compounds are today manufactured in dedicated equipment/plant according to the principles in PIC/ S PI006-03. In section 7.6.2 states "Dedicated equipment should be used … for products with a high safety risk…." Furthermore, in Section 7.11.3(d) is the paragraph "For certain allergenic ingredients, penicillins, cephalosporins or potent steroids and cytotoxics, the limit should be below the limit of detection by best available analytical methods. In practice this may mean that dedicated plants are used for these products. Highly hazardous medicinal compounds that previously were manufactured in dedicated equipment from now on, with reference to 'EMA Guideline on setting health based exposure limits for use in risk identification in	

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		the manufacture of different medicinal products in shared facilities', can be introduced in shared facilities. If focus and resource waste is on PDE calculation for ALL products instead of performing critical cleaning validation activities on a properly manner, the patient protection from highly hazardous contaminants in medicinal products will decrease. We suggest that the scientific "1/1000 of the lowest therapeutic dose in next batch"-approach shall apply for non-hazardous substances. However, this traditional scientific approach is not applicable for certain highly hazardous substances (substances that before were dedicated) and therefore the PDE approach shall apply for such substances.	
Glossary (Cleaning Validation) page 14		You can not be sure that "all traces" are removed. It depends on the analytical method. With highly sensitive analytical methods acceptable traces will be detected!! We recommend a redefinition from "cleaning validation is documented evidence that an approved cleaning procedure will remove all traces of the previous product used in the equipment" to "cleaning validation is documented evidence that an approved cleaning procedure results in equipment with predetermined cleanliness level.	