July 13, 2012

Submission of comments on 'Public Consultation Paper Review or the Variations Guidelines' by European Commission (Sanco.ddg1.d.5(2012)817838

Comments from:

Name of organisation or individual
ECHAMP (European Coalition on Homeopathic and Anthroposophic Medicinal Products, E.E.I.G.) registered in the transparency register of the Commission and the Parliament with the user number 85825114058-57

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. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	In homeopathy and anthroposophic medicine, the range of essential remedies is considerably larger compared to other fields of the pharmaceutical industry. Due to the strongly individualised character of the therapeutic approaches homeopathy and anthroposophic medicine need a large range of starting materials (in the range of thousands) and of specific medicinal products. The order of magnitude of dossiers to be maintained per authorisation holder easily can meet the figure of 500 or 1.000 or more, while the turnover gained per product is low to very low (for example less than 50 packages per year). Besides having many different starting materials the large number of products naturally brings a large number of variations with it at all stages of production. In addition, there are numerous characteristics of identical specifications for wide ranges of products: Homeopathic medicinal products of identical dosage form, especially if beyond a certain degree of dilution, share a number of characteristics like composition of excipients, final product specification, primary packaging etc. Hence, a single modification of one of those common characteristics may soon refer to more than 1.000 files	

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	per applicant in one MS. Other frequently identical characteristics of the dossier might be specific for a certain type of starting material, as e. g. the methods for testing impurities in plant materials (one method for testing pesticides could be cited in up to 500 dossiers of one applicant in one MS). **So, it is extremely important for this industry, that the regulatory and administrative burden linked to variations should be restricted to a minimum while guaranteeing the quality and the safety of the products.** These specific characteristiscs were already acknowledged in the considerations of Commission Regulation (EC) No 1234/2008 (consideration 2): ….”For reasons of proportionality, homeopathic and traditional herbal medicinal products which have not been granted a marketing authorisation but are subject to a simplified registration procedures should remain excluded from the scope of the Regulation.” In view of the considerations given above, it is just consequent that registrations are excluded from the scope of the Variation Regulation (EC) No. 1234/2008. **However, marketing authorisations of homeopathic medicinal products are purely national**	

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	authorisations for legal reasons; they now will be introduced under the scope of the European variation system. As a matter of principle, the dossier characteristics mentioned above, especially with respect to the content of the quality dossier as well as with respect to safety issues, apply to dossiers of homeopathic marketing authorisations as well as to those of registrations. **In addition, in most Member States of the EU no separate rules exist for registrations and this leads to the fact, that, in practice, the rules of the Variation Regulation and subsequent rules like the classification guideline also are applied to registrations.** Therefore, appropriate rules for handling the variations of these purely national marketing authorisations as well as registrations in countries where the Variation Rules of the EU are applied to registrations are necessary for reasons of proportionality. **A pragmatic system of variations is needed for our industry in Europe in order to maintain the amount of products required for the therapeutic approaches over the life cycle.**	

2. 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)*
Page 7, Item A.3 **Change in the name of the actives substance or of an excipient**		Comment: For homeopathic medicinal products changes of name of active substances, already in accordance with pharmacopoeia, in general happen as adaptation to change of name of monograph of the Ph.Eur. or the relevant national (homeopathic) pharmacopoeia. Rationale: The scientific names of the many starting materials used for homeopathic medicinal products are mainly of herbal origin, scientific names use to change rather frequently. With respect to the information of consumers this is of less important relevance. In order to keep the proportionality principle, it should be possible to consider the adaptation of the names in the frame of the periodic reporting. Comment/rationale: The excipients used in production of homeopathic medicinal products generally are well introduced conventional classical pharmaceutical substances like lactose, ethanol, purified water etc where the names are since very longtime in accordance with a pharmacopoeia. In addition, IA_{IN} classification would undermine the transition period acknowledged for implementation of pharmacopoeial changes. Proposed change (if any): A.3 Change in name of the active substance or excipient	

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		a) <u>All substances except b)</u> Conditions to be fulfilled: 1,2 Documentation to be supplied: 1, 2 Procedure type: IA_{IN} **b) Homeopathic medicinal products with the active substance/excipient in line with official pharmacopoeia monograph** Conditions to be fulfilled: 1,2, 3 Documentation to be supplied: 1, 2 Procedure type: IA New condition: 3. Name and change in line with official monograph (Ph. Eur. or recognised national pharmacopoeia).	
P 50 B.II.d.1. h) **Change in the specification parameters and/or limits of the finished product** **Update of the dossier to**		Comment/Rationale: Update of a specification parameter for the finished product solely in order to comply with the <u>updated</u> Ph.Eur. monograph should be classified as a Type IA, as it is classified so far within the proposed classification for changes in the “CMDh Recommendation for classification of unforeseen variations acc. to Art. 5 of ... (EC) No 1234/2008”. Furthermore following the classification of **B.III.2.b “**Change of a monograph – Change to comply with an update of the relevant monograph of the Ph.Eur. or national pharmacopeia of a Member State”, which is also classified as a IA.	

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comply with the provisions of an updated general monograph [...]		Moreover: - Condition 7 (“the change does not concern any impurities”) should be deleted. As it is the decision of the European Pharmacopoeia to change the specification also in regards of impurities for a certain Ph.Eur. monograph, it should NOT lead to a Type IB by default for updating the relevant monograph in the dossier. - Documentation to be supplied point 2 “Comparative table of current and proposed specifications”: this requirement should be eliminated, at least if the variation submitted includes the sole update of a general monograph and no other change to the specification is introduced by the manufacturer. The workload for compiling and providing a comparative table for a sole update of pharmacopoeial specifications(s) seems unproportional as it is of no additional use for the assessor of the variation, as there is no scope of action both for manufacturers as well as assessors. Proposed change (if any): B.II.d.1 h) Update of the dossier to comply with the provisions of an updated genereal monograph of the Ph.Eur. for the finished product Conditions to be fulfilled: 1,2,3,4, ,8 Documentation to be supplied: 1, Procedure type: IA~~IN~~	

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B.V.d.1		Comment: Update of the quality dossier of a homeopathic medicinal product Rationale: Because of the national competence, renewal and dossier update procedures frequently still are to be done. Often, these procedures include a complete revision of the quality dossier including transfer to the CTD formate for the following reasons (1) The CTD formate for homeopathic medicinal product was introduced later than for conventional medicinal products, and this revision still remains to be done. (2) Since some years, since the harmonisation efforts of HMPWG become visible in the EU, the dossier requirements are increasing. This frequently may imply a need to completely revise the quality dossier. On the other hand, the quality dossiers are less dense, comparatively simple, using generic well-known active substances and excipients as well as classical dosage forms, all of them described in official pharmacopoeias. The big amount of medicinal products with low to very low turnover is particular for this niche of the pharmaceutical business while the quality variations use to be simple. Therefore a revision of the quality dossier would be far from complex and comparable to the extent of a revision of the quality dossier in the frame of a referral procedure (case B.V.b.1.b).	

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		Proposed change (if any): New: B. V.d) Homeopathic medicinal products **B. V.d.1 Update of the quality dossier of a purely national homeopathic medicinal product: The update of the quality dossier** **Conditions to be fulfilled:** **Documentation to be supplied:** **Procedure Type: II**	
		Comment: Proposed change (if any):	
		Comment: Proposed change (if any):	

Please add more rows if needed.