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Submission of comments on Consultation Document 'Definition of Investigational Medicinal Products (IMPs) and use of Auxiliary Medicinal Products (AMPs)'

Comments from:

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1. General comments

EUCROF	General comment (if any)	Outcome (if applicable)
	We welcome the opportunity to provide comments on the Consultation Document 'Definition of Investigational Medicinal Products (IMPs) and use of Auxiliary Medicinal Products (AMPs).	

2. Specific Comments Consultation Document Text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder No.	Comment and rationale; proposed changes	Outcome
54 - 56		Comment 'It follows that medicinal products with a marketing authorisation are IMPs too when they are to be used as the test product, reference product or placebo in a clinical trial.' It would be easier to read and understand to supplement this sentence as follows: Proposed Change: 'It follows that medicinal products with a marketing authorisation are IMPs ~~too~~ when they are to be used as the test product, reference product or placebo in a clinical trial. Consequently, IMPs fall within Article 3(3) of Directive 2001/83/EC.'	
87 - 100		Comment 'Only authorised AMPs may be used in a clinical trial unless an authorised AMP is not available in the Union or where the sponsor cannot reasonably be expected to use an authorised AMP. A justification to this effect shall be included in the protocol. Where there are problems with respect to the availability of authorised AMPs, unauthorised AMPs may be used in a clinical trial in justified cases. The price of the authorised AMP should not be considered as having an effect on the availability of such medicinal products. Subjects should not have to pay for IMPs, AMPs, medical devices used for their administration and procedures specifically	

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		required by the protocol, unless the law of the Member State concerned provides otherwise. Member States shall ensure that unauthorised AMPs may enter their territories for the purpose of their use in a clinical trial.' It is suggested to move the above two paragraphs in Section 3.2 "Requirements for AMPs" as they stipulate requirements for AMPs and do not describe what AMPs are (Section 3.1 "What is an AMP?") In addition, we suggest some restructuring of the paragraphs. Proposed Changes: 'Only authorised AMPs may be used in a clinical trial unless an authorised AMP is not available in the Union or where the sponsor cannot reasonably be expected to use an authorised AMP. ~~A justification to this effect shall be included in the protocol.~~ Where there are problems with respect to the availability of authorised AMPs, unauthorised AMPs may be used in a clinical trial in justified cases. A justification to this effect shall be included in the protocol. Member States shall ensure that unauthorised AMPs may enter their territories for the purpose of their use in a clinical trial.'	
102 - 109		Comment 'Medicinal products that do not have a marketing authorisation, but prepared in accordance with a magistral formula, i.e. prepared in a pharmacy in accordance with a medical prescription for an individual patient, and medicinal products prepared in a pharmacy in accordance with the prescriptions of a pharmacopoeia and intended to be supplied directly to the patients served by the	

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		pharmacy in question, i.e. officinal formula, as referred to in Article 61 (5) of the regulation (EU) No 109 536/2014.' It is not clear what the above paragraph wants to say in relation to IMPs / AMPs. It is not a full sentence. Probably, the intention is to say that these medicinal products can also be AMPs when required by the trial protocol but not falling in the category of IMP. However, this does not become clear.	
142		Comment 'authorisation Regulation (EU) No 536/2014 Annexes I and II set out the' There is a period missing between "authorization" and "Regulation".	
159 - 161		Comment 'Regulation (EU) No 536/2014 Article 46 states, "Safety reporting with regard to AMPs shall be made in accordance with Chapter 3 of Title IX of Directive 2001/83/EC", which cover authorized AMPs.' This of course is fact, however it is a bit confusing after demonstrating in lines 62 and 63 that AMPs fall within Article 3(3) of Directive 2001/83/EC, meaning that Directive 2001/83 does not apply for AMPs. It would be good to explain that Regulation (EU) No 536/2014 stipulates an exemption from Article 3(3) of Directive 2001/83/EC and therefore safety reporting with regard to AMPs shall be made in accordance with Chapter 3 of Title IX of Directive 2001/83/EC (although the rest of this Directive does not apply to	

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		AMPs).	
163 - 164		Comment 'Regarding unauthorised AMPs, sponsors are not legally required to report serious adverse reactions.' The new Pharmacovigilance Legislation (2010) also requires the reporting of non-serious adverse reactions (within 90 days). Proposed Change: 'Regarding unauthorised AMPs, sponsors are not legally required to report ~~serious~~ adverse reactions (serious or non-serious).'	
172 - 175		Comment 'While all SAEs and SARs should be included in the annual safety report of the relevant IMP, and non serious adverse events and non serious suspected adverse reactions should be reported in the Clinical Study Report.' The sentence reads a bit strange (semantically). In addition, it should be "non-serious" (with hyphen).	
176 - 177		Comment '… please see safety section of the Questions and Answers Paper Version XX.' The Question and Answer Paper should be further specified (Title) not only Version No.	
182 - 183		Comment '… reactions (as referred to in Article 42). Annex 1 – Types of AMPs	

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		with examples' Page Break is incorrect.	
192 - 195		Comment 'Rescue medications are medicines identified in the protocol as those that may be administered to the patients when the efficacy of the IMP is not satisfactory, or the effect of the IMP is too great and is likely to cause a hazard to the patient, or to manage an emergency situation.' Bridging wash-out periods of pre-medication is a common use of rescue medication. Proposed Change: 'Rescue medications are medicines identified in the protocol as those that may be administered to the patients when the efficacy of the IMP is not satisfactory, or the effect of the IMP is too great and is likely to cause a hazard to the patient, or to manage an emergency situation, for example when washing out pre-medication.'	
298 - 303		Comment 'For example the development of a new indication for a medicine used in women with breast cancer recently compared that medicine versus observation in patients who had received, regardless of trial, at least four cycles of neoadjuvant or adjuvant chemotherapy and were allowed concurrent hormonal adjuvant therapy. In this case that medicine would be considered an IMP and the	

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		neoadjuvant or adjuvant chemotherapy and hormonal therapy products would be AMPs.' The example given is not very clear. Is it meant that historical controls are used for comparison? "regardless of trial" could mean that the controls could be either trial participants or not. If historical controls are meant this should be said.	