



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

<25<sup>th</sup> June 2014>

Submission of comments on <Concept paper on the revision of the guideline on immunogenicity assessment of biotechnology-derived therapeutic proteins> (EMA/CHMP/BMWP/42832/2005)

## Comments from:

Name of organisation or individual

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*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).*



## 1. General comments

Stakeholder number <i>(To be completed by the Agency)</i>	General comment (if any)	Outcome (if applicable) <i>(To be completed by the Agency)</i>
	<p>The fractals is a mathematical formalism which can be used to describe the surface morphology and the degree of surface irregularity of natural occurring biological systems like virus, cells, and proteins. Fractal analysis would be considered as a method for the elucidation of the morphology overcoming the limits of the Euclidean shape and facilitating the evaluation of the physicochemical stability of nano- and bio- technological products in aqueous and biological media, facilitating the <i>in vivo</i> experiments and the development process.</p> <p>The fractal analysis accompanying by the conventional analytical methods could be a complementary approach to evaluate and precisely clarify the real dimensionality of nano- and bio- technological products. In addition this analytical method can be considered as part of the dossier to be submitted to the regulatory body of experts. It can be mentioned, that this approach can also be used in the future to specify the similarity of biotechnological off-patent products with those of the original. By using the fractal approach, the Biotechnological / Pharmaceutical Industry can disclose the effectiveness of biotechnological and biosimilar products and to claim their usefulness to the patient by reducing their side effects, mainly the immunogenicity which is correlated with their stability.</p>	

## 2. Specific comments on text

Line number(s) of the relevant text <i>(e.g. Lines 20-23)</i>	Stakeholder number <i>(To be completed by the Agency)</i>	Comment and rationale; proposed changes <i>(If changes to the wording are suggested, they should be highlighted using 'track changes')</i>	Outcome <i>(To be completed by the Agency)</i>
51-52		<p>Comment: <i>The fractal morphology and the fractal dimension of aggregates, impurities, xenogeneic structures and leachables of therapeutic proteins and biotechnological products are of great importance in order to quantify the changes in their morphology that influences their side effects and particularly immunogenicity.</i></p> <p>Proposed change (if any): Quality issues, such as impurities, aggregates, xenogeneic structures and leachables, need to be assessed, <b>by adapting the quantification of their morphology using fractal analysis.</b></p>	
		<p>Comment:</p> <p>Proposed change (if any):</p>	
		<p>Comment:</p> <p>Proposed change (if any):</p>	

Please add more rows if needed.