European Medicines Agency

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EMEA WORKSHOP ON BIOSIMILAR MONOCLONAL ANTIBODIES

Chairperson: Christian Schneider

Date: Thu 2 July 2009 (Room 2A)

Time: 9am- 6pm (GMT)

PROGRAMME

EMEA, 2nd floor (Room 2A), 7 Westferry Circus, Canary Wharf, London, E14 4HB

Background:

This EMEA Workshop on Biosimilar Monoclonal Antibodies is intended to discuss the feasibility of the scientific development and authorisation of monoclonal antibodies via the Biosimilar regulatory pathway. The Workshop is **by invitation only**.

Participants:

CHMP, Working parties, Regulators, Academia, Innovator and Biosimilars industry

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09.00-09.10	**WELCOME AND KEYNOTE PRESENTATION**	**Speakers:** Xavier Luria (EMEA)
09.10-09.30	**Towards biosimilar monoclonal antibodies - pros and cons**	Christian Schneider (PEI)
09.30-11.30	**SESSION 1 CMC (Chair: J.H. Trouvin)**	
09.30-10.00	**Presentations (Session 1) (30 mins)**	
	Presentation by Innovator Industry (10 mins)	Georg Kresse, Roche (EBE/Europabio)
	Presentation by Biosimilars Industry (10 mins)	Martin Schiestl, Sandoz (EGA)
	Presentation by an EU regulator (10 mins)	Kowid Ho (AFSSAPS)
	Panel discussion	Chaired by J.H. Trouvin (AFSSAPS)
10.00-11.30	**QUESTIONS (Session 1)**	

"Existing regulatory framework"		
1.1	Are mAbs considered to be "well-characterized" biologicals?	
1.2	Is available guidance for quality characterisation guideline (EMEA/CHMP/BWP/157653/2007) sufficient for biosimilar mAbs, or should there be additional aspects?	
"Differences in structure that might be acceptable"		
1.3	To what extent are current methods for physicochemical characterization sensitive enough to detect differences between two more complex molecules like mAbs?	
1.4	To what extent could biological and/or functional assays including potency assays substitute for a gap in sensitivity?	
1.5	What should be the relative role of the biological assays including potency assay in biosimilar comparison?	
1.6	To what extent could quality data substitute for gaps in knowledge (or non-availability for whatever reason) in functional assays?	
1.7	To what extent should glycosylation be "similar", given the functional (modulatory) activity of some sugar moieties?	
1.8	Assuming that the reference medicinal product is a mixture of different "variants" of the antibody: Does a biosimilar antibody also have to contain the same variants in comparable amounts or is one variant acceptable?	

1.9	To what extent could certain differences be acceptable, given the broad experience that exists with mAbs?	
1.10	What role could ICH Q8 and Q9 (including quality risk analysis and risk management) play?	

11.30-13.00	**SESSION 2 Non-Clinical Issues (Chair: Beatriz Silva-Lima)**	
11.30-12.00	**Presentations (Session 2) (30 mins)**	
	Presentation by Innovator Industry (10 mins)	Danuta Herzyk (EBE/Europabio) Merck
	Presentation by Biosimilars Industry (10 mins)	Alexander Berghout, Sandoz (EGA)
	Presentation by an EU regulator (10 mins)	Beatriz Silva-Lima, (INFARMED)
	Panel discussion	Chaired by Beatriz Silva-Lima, (INFARMED)
12.00-13.00	**QUESTIONS (Session 2)**	
2.1	To what extent do we ask for non-clinical studies in relevant species, given that the relevant species is often monkey and thus the number of animals per group is limited?	
2.2	How could pharmacodynamic measures ("fingerprinting") be supplementary to quality development?	
2.3	For antitumoural mAbs, to what level would a comparison on the functional level beside ADCC/CDC (if relevant) be required? What level is feasible (e.g. signalling events)?	
2.4	What is the impact of formulation on in vivo behaviour (injection site and infusion rate comparability)? How could it best be studied?	
13.00-14.00	**Lunch**	
14.00-16.00	**SESSION 3 Clinical Issues RMP / PhV (Christian Schneider)**	
14.00-14.30	**Presentations (Session 3) (30 mins)**	
	Presentation by Innovator Industry (10 mins)	Jay Siegel, J&J (EBE/Europabio)
	Presentation by Biosimilars Industry (10 mins)	Islah Ahmed, Hospira (EGA)
	Presentation by an EU regulator (10 mins)	Christian Schneider, (PEI)
	Panel discussion	Chaired by Christian

		Schneider (PEI)
14.30-16.00	**QUESTIONS (Session 3)**	
"Pharmacokinetics/Pharmacodynamics		
3.1	What role could new methodologies play (e.g. simulation, modelling, biomarkers)	
3.2	In which population(s) should PK/PD be measured?	
"Extrapolation of efficacy and safety"		
3.3	To what extent can efficacy be extrapolated from one indication to another in different scenarios (taking into account the intended mechanism of action as well as other potential mechanisms of action), given that other information (physicochemical and biological characterization) will be comparable? a) for immunomodulators, e.g. from psoriasis to rheumatoid arthritis, or other conditions b) for antitumoural antibodies c) for antitumoural antibodies that are also indicated in inflammatory conditions	
3.4	To what extent can safety be extrapolated, given that patient populations can be quite different? What can be done post-marketing?	
3.5	For antitumoural mAbs, what would be acceptable patient sub-population in different indications?	
"Outcome measures"		
3.6	Which endpoints should be used as a general strategy: a) endpoints that measure patient benefit, but which might be less sensitive to detect differences (might especially be important for antitumoural mAbs and their acceptance) b) endpoints that measure similarity more sensitively, like activity endpoints c) If similarity endpoints are used, should these be rather conforming to guidelines, or could these be newly developed endpoints?	
3.7	What role could new methodologies play, e.g. simulation or modelling?	
3.8	To what extend would a risk-based approach to immunogenicity be applicable, given that mAbs do, unlike recent biosimilars, not have endogenous counterparts?	

16.30-18.00	**CONCLUSIONS OF THE WORKSHOP**	**Christian Schneider**
	Should the biosimilar framework be opened for differences in the amino acid sequence?	
	Could some concepts be applicable to 2nd generation products?	