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und Ernährungssicherheit GmbH

Health. Nutrition. Safety.
Our Concern.

Biological Products

Definitions

Requirements

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What is a biological medicine?

- A biological medicinal product (MP) is a product, the active substance of which is a biological substance, which is produced by or extracted from a biological source.

⟹ Different possibilities to get a Marketing Authorisation (MA) for a biological MP

Differences: biological - chemical

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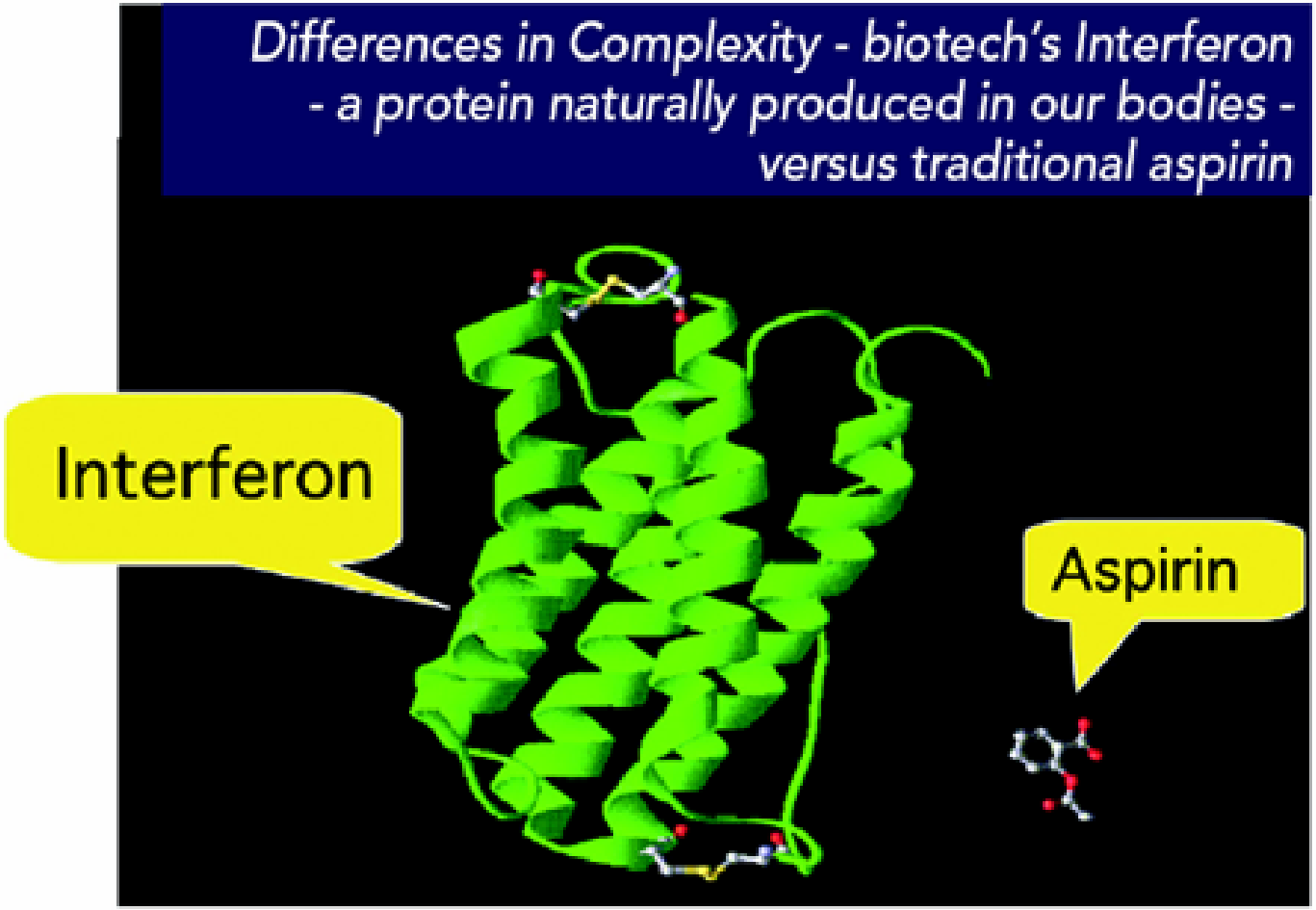
- Biological medicines are different from traditional chemical medicines
  - Size
  - Complex spatial structure
  - “heterogenous”

⇒ Difficult to characterise biological medicines in the traditional way by analysing their individual components

⇒ Mainly administered by injection – not orally

⇒ “immunogenic response” – human body´s reaction.



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Biological medicine

- Manufacturing process:
  - Highly complex procedure
  - Extreme care must be taken to ensure safety of the product
  - Much more tests needed during manufacturing process

Biological & Biosimilar MPs

- Today patients have access to:
  - >150 biotechnology drugs & vaccines
  - Patent of certain biological medicines are expiring
  - Follow on verisons are being developed

→ Biosimilar medicines

- Intended to have the same mechanism of action as the original biological MP
- Designed to treat the same diseases as the innovators product

Generics vs. Biosimilar

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Regulatory perspective – “Biogeneric” ??

- Can a biological MP be a generic ?
  - In THEORY – YES
  - In PRACTICE – UNLIKELY (may be possible where molecule is not complex and fully characterised).
  - RESULT: Biosimilar Medicinal Product

Biosimilar applications:

- Review of the Pharm. legislation
  - Enabled MA applications for biological products, based on abridged non-clinical and clinical data requirements compared to the originators dossier.

Biosimilar vs. generic MPs

- generics of chemistry-based medicines are identical copies
  - –Strict definition of „sameness“
- biosimilars
  - –„sameness“ – difficult due to their nature and the complexity of their manufacturing process.

Biosimilars

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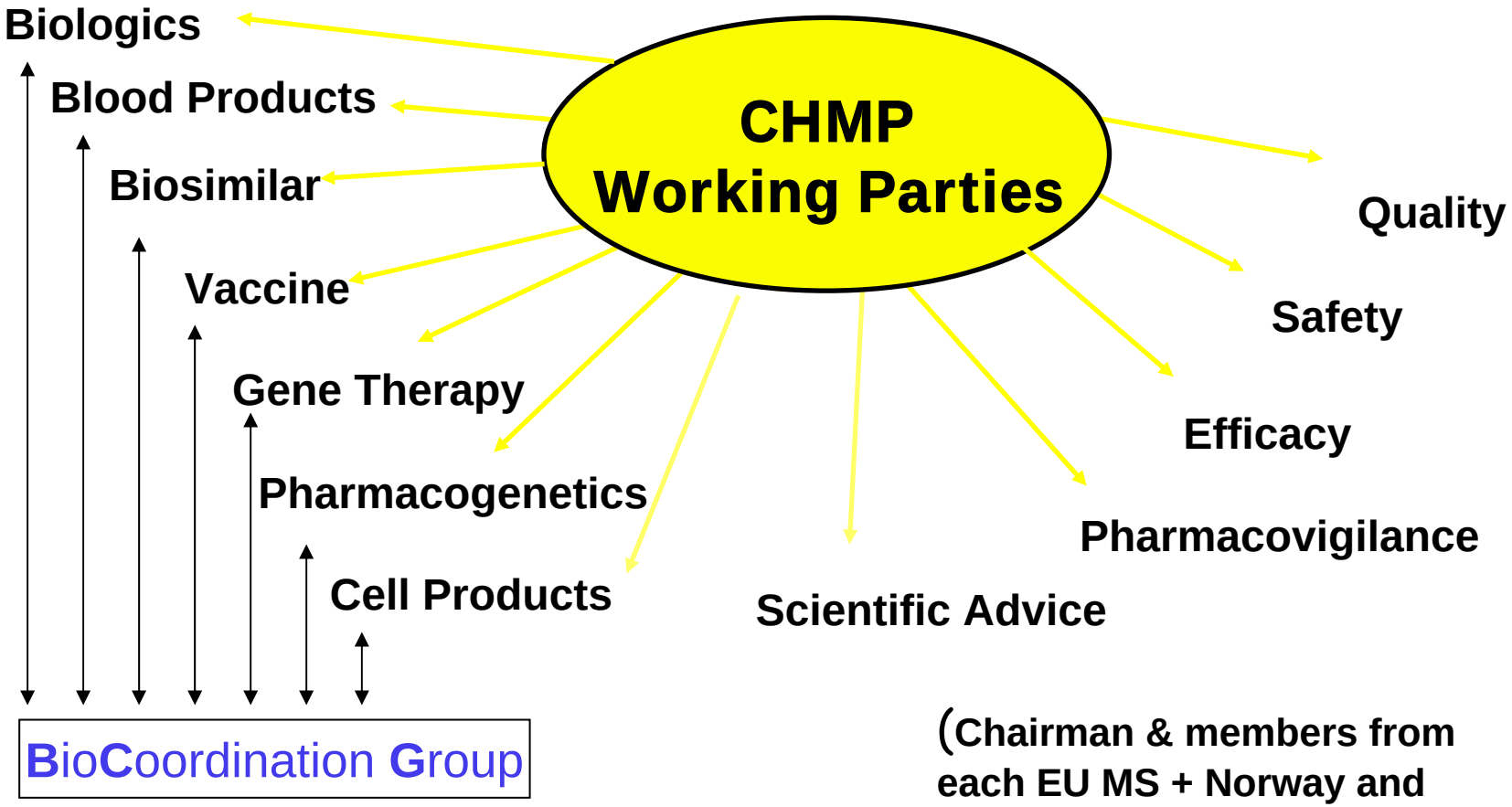
- Analytical tests are not sufficient to demonstrate the sameness of two biological products or that they are identical.
- Appropriately designed preclinical and clinical studies are required to prove that biosimilar products have the same clinical properties as the innovator product.

EMEA activities: Biologicals



(Chairman & members from each EU MS + Norway and Iceland)

+ Specific ad-hoc working groups or subgroup meetings when needed

Biosimilar – Guidelines

- Guideline on Similar Biological Medicinal Products (SBMP). CHMP/437/04
- Quality guideline on SBMP
- (non)-clinical guideline on SBMP
- Product-class specific guidelines on SBMP - (non)-clinical

Zurück Suchen Favoriten
Adresse http://www.emea.europa.eu/htms/human/humanguidelines/multidiscipline.htm Wechseln zu

Scientific Guidelines for Human Medicinal Products

Background
Quality & Biologicals
Quality (Chemical & Herbal)
Biologicals
Non-Clinical
Clinical Efficacy & Safety
Multidisciplinary

Multidisciplinary Guidelines

This section contains all Guidelines in relation to: Multidisciplinary areas consisting of guidelines which might be individually related to either Quality, Safety or Efficacy areas for which guidelines are prepared by collaboration of several working parties

C = Concept Paper D = Draft Guideline A = Adopted Guideline O = Overview of Comments

Title	C	D	A	O	Reference Number	Publication Date	Effective Date	Other Remarks
Paediatrics								
Investigation of medicinal products in the term and preterm neonate NEW		◆			EMEA/267484/07	Release for consultation Sep 2007		Deadline for comments 15 May 2008
Conduct of Pharmacovigilance for medicines used by the paediatric population	◆	◆	◆	◆	EMEA/CHMP/235910/05	June 2006		
Reflection Paper: Formulations of Choice for the Paediatric Population	◆			◆	EMEA/CHMP/PEG/194810/2005		Sep 2006	
Note of Explanation to accompany publication of Reflection Paper on Formulations of Choice for the Paediatric Population (EMEA/CHMP/PEG/194810/2005)	◆				EMEA/196218/05	Jun 2005		
Impact of Brain Immaturity when investigating medicinal products intended for Neonatal use	◆				EMEA/181377/06	Release for consultation Jun 2006		Deadline for comments 31 Dec 2006
Impact of Lung and heart Immaturity when investigating medicinal products intended for Neonatal use	◆				EMEA/CHMP/PEG/114218/06	Release for consultation Mar 2006		Deadline for comments 30 Sep 2006
Impact of Liver Immaturity when investigating medicinal products intended for Neonatal use	◆				EMEA/CHMP/PEG/194605/05	Release for consultation Jul 2005		Deadline for comments 31 January 2006
Discussion Paper on the Impact of Renal Immaturity when Investigating Medicinal Products Intended for Paediatric Use	◆				CPMP/PEG/35132/03	Dec 2004	Dec 2004	
Cell Therapy								
Revision of the Points to Consider on Xenogeneic Cell Therapy Medicinal Products	◆				CHMP/165085/07	Release for consultation May 2007		Deadline for comments 31 Aug 2007
Xenogeneic Cell Therapy Medicinal Products	◆				CPMP/1199/02	Dec 2003	Jun 2004	
Human cell-based medicinal products		◆			CHMP/410869/06	Release for		Deadline for

Internet
Start Posteingang - Micros... Biosimilar Scientific Guidelines f... 07-11-26 Biosimilar JP EGA May07 Programme Security DE

Suchen Favoriten

http://www.emea.europa.eu/htms/human/humanguidelines/multidiscipline.htm

Harmonisation of Requirements for Influenza Vaccines			◆		CPMP/BWP/214/96	Mar 1997	Apr 1997	
Biosimilar								
Similar medicinal products containing recombinant interferon alpha NEW		◆			CHMP/BMWP/102046/06	Release for consultation Oct 2007		Deadline for comments Apr 2008
Similar biological medicinal products containing low molecular weight heparins - Non-Clinical Issues	◆				CHMP/BMWP/496286/06	Release for consultation Jan 2007		Deadline for comments 30 Apr 2007
Comparability of Biotechnology-Derived Medicinal Products after a change in the Manufacturing Process - Non-Clinical and Clinical Issues	◆	◆	◆		CHMP/BMWP/101695/06	Jul 2007	Nov 2007	
Immunogenicity Assessment of Biotechnology-derived Therapeutic Proteins	◆	◆			CHMP/BMWP/14327/06	Release for consultation Jan 2007		Deadline for comments 31 July 2007
Similar Biological Medicinal Products containing Recombinant Alpha-Interferon annex to the guideline on Similar Biological Medicinal Products containing Biotechnology Derived Protiens as Active Substance – (Non) Clinical Issues	◆				CHMP/BMWP/7241/2006	Release for consultation Apr 2006		Deadline for comments 1 Aug 2006
Similar Biological Medicinal Products Containing Biotechnology-Derived Proteins as Active Substance: Quality Issues			◆		CHMP/49348/05	Feb 2006	Jun 2006	
Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues			◆		CHMP/42832/05	Feb 2006	Jun 2006	
Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues - Guidance on Similar Medicinal Products containing Recombinant Erythropoietins			◆	◆	CHMP/94526/05	Mar 2006	Jul 2006	
Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues - Guidance on Biosimilar Medicinal Products containing Recombinant Granulocyte-Colony Stimulating Factor			◆		CHMP/31329/05	Feb 2006	Jun 2006	
Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues - Guidance on Similar Medicinal Products containing Somatropin			◆		CHMP/94528/05	Feb 2006	Jun 2006	
Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-Derived Proteins as Active Substance: Non-Clinical and Clinical Issues - Guidance on Similar Medicinal Products containing Recombinant Human Insulin			◆		CHMP/32775/05	Feb 2006	Jun 2006	
Similar Biological Medicinal Product			◆		CHMP/437/04	Sep 2005	Oct 2005	
Comparability of Medicinal Products containing Biotechnology-derived Proteins as Active Substance -Quality Issues			◆		CPMP/BWP/3207/00 Rev. 1	Dec 2003	Dec 2003	
Comparability of Medicinal Products containing Biotechnology-derived Proteins as Drug Substance - Non Clinical and Clinical Issues (Replaced by CHMP/BMWP/101695/06)			◆		CPMP/3097/02	Dec 2003	Jun 2004	
Development of a CPMP Guideline on Comparability of Biotechnology-derived Products	◆				CPMP/BWP/1113/98	Jun 1998		
Gene Therapy								

Overarching Guideline

- Guideline on Similar Biological Medicinal Products. CHMP/437/04 (CHMP Adopted).
- Main points:

  Outline concepts and basic principle

  Biological, Biotech. (rDNA), Immunological & Blood plasma derived products

  Considerations: analytical methods, processes, clinical experience.
- Quality guideline
  - Main issues
    - state-of-art analytical methods to characterise both similar and reference products
    - Manufacturing process should be well developed

(Non)-Clinical Guideline

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- Guideline on general principles
  - Clinical equivalence
  - Safety studies
  - Immunogenicity
  - Pharmacovigilance
- Product Class specific Annexes
  - Insulin
  - Somatropin
  - Epoetin
  - Others ?
    - Annexes provide specific (non)clinical data requirements

Biological MPs

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→ Different possibilities to get a Marketing Authorisation (MA) for a biological MP

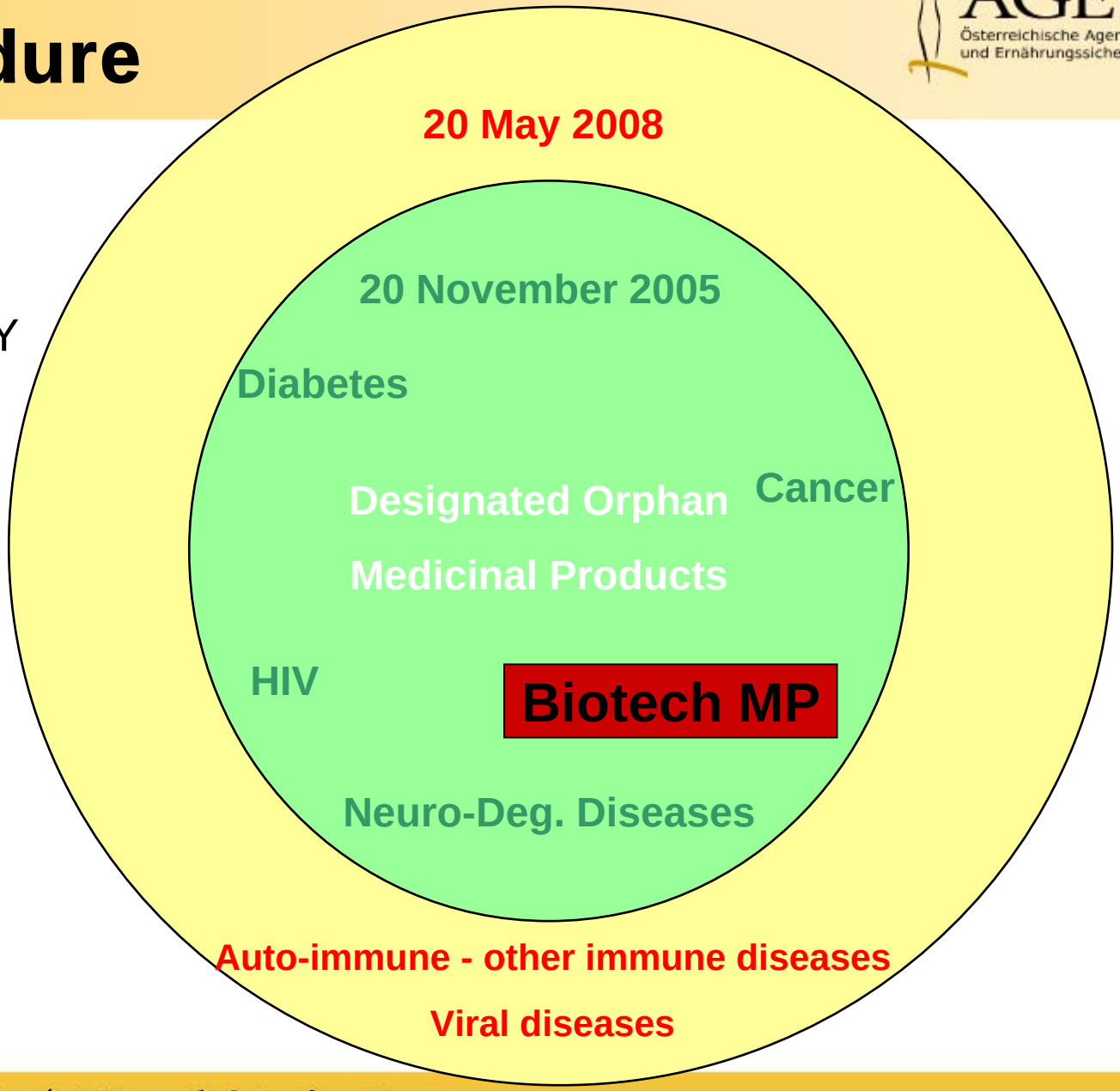
MPs – to be authorised via CP
Reg. 726/2004 - Annex

- Medicinal products developed by means of one of the following biotechnological processes:
  - — recombinant DNA technology,
  - — controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells,
  - — hybridoma and monoclonal antibody methods.

→ CP mandatory

Scope of Centralised Procedure

OBLIGATORY



Biosimilar Medicinal Products

- Dir 2001/83 as amended (Dir 2004/83), Art. 10 (4)
  - A biological MP – similar to a reference biological product
  - Where there are differences (particularly) in raw materials or manufacturing processes of biosimilar and reference product, then results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided.
  - If the MP is not manufactured by a biotechnological process – DCP can be used.

Biosimilar Medicinal Products

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- Information to be supplied shall not be limited to Modules 1, 2 and 3 (pharmaceutical, chemical and biological data), supplemented with bio-equivalence and bio-availability data.
  - The type and amount of additional data (i.e. toxicological and other non-clinical and appropriate clinical data) shall be determined on a case by case basis in accordance with relevant scientific guidelines.

Dossier requirements for Biosimilar MPs

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Module 1 - Normal Requirements

Module 2 - Normal Requirements

Integrated CE
(Comparability Exercise)

Quality, Module 3 - FULL	+ CE
Non-clinical, Module 4 - Reduced	+ CE
Clinical, Module 5 - Reduced	+ CE

Dossier requirements for Biosimilar MPs

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- A manufacturer will compare his biosimilar MP against the Reference MP in laboratory tests and clinical trials
  - Inorder to ensure that the Q/S/E profile is comparable.
  - Some non-clinical and clinical data are required for biosimilars (for generics „only“ pharmacokinetics)

How is a biosimilar medicine authorised?

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- Innovative medicines benefit from a period of market exclusivity under patent law and from a period of data protection following the pharmaceutical legislation. After expiry of these periods, companies can obtain a MA for a biosimilar medicine.
- As the biological reference medicine has been authorised for several years, there is available information, which does not need to be reproduced.

How is a biosimilar medicine evaluated?

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- Due to the complex method of production of biological medicines, the active substance may differ slightly between the biological reference and the biosimilar medicine.
  - Therefore, studies comparing the two medicines have to be carried out.
    - These studies involve a step-by-step process starting with a comparison of the quality and the consistency of the MP and of the manufacturing process.
    - Studies are also conducted to compare the S/E of the medicines. These studies should demonstrate that there are **no meaningful differences** between the biosimilar and the biological reference medicines in terms of S/E.

Monitoring the Safety of a biological MP

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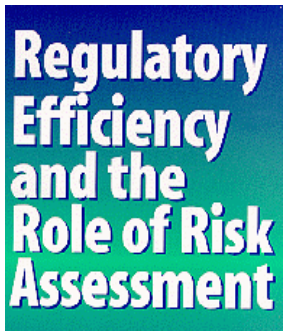
- The safety of all medicines, including biosimilar medicines, is also monitored after authorisation.
  - Each MAH marketing a new MP is required to set up a system to monitor the safety of the products that is marketed, including any immunological responses to the administration of biological products.
  - The regulatory authorities may also perform an inspection of this system. If there are specific precautions to be considered when taking the reference medicine, the biosimilar medicine will require in general the same safeguards.

Product/Company	Status
Omnitrope (somatropin)/Sandoz	Authorised – April 2006
Valtropin (somatropin)/Biopartners	Authorised – April 2006
Alpheon (interferon alfa)/Biopartners	Negative – June 2006
Binocrit (epoetin alfa)/Sandoz Epoetin alfa Hexal (epoetin alfa)/Hexal Abseamed (epoetin alfa)/Medice	Authorised – August 2007

- Regulators constantly need to adjust to new developments and adapt and facilitate these to the benefit of public health.



- ICH guidelines now incorporating more of a risk based approach – challenge for all : industry and regulators to develop strategies.
- Regulators recognise the global arena in which industry operates and the need for regulatory efficiency.

- Global harmonisation and Regulatory flexibility are often stated as goals, however, we must recognise some of the limitations of different region's regulatory structures and legislation
- Hope to gain a broad understanding of industry activities and how regulatory structures will be influenced and could be adapted in future.

Thank you !

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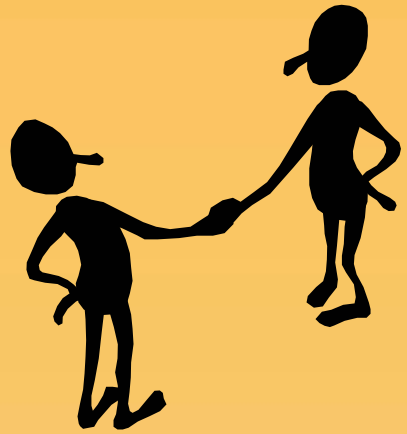

My remarks do not necessarily reflect
the official view of AGES PharmMed.

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