



Reunión de Autoridades Nacionales Reguladoras de Productos Biológicos en Latino América y El Caribe

**Documentos de Referencia Disponibles en la Regulación de
Productos Biológicos/Biotecnológicos**

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María L. Pombo
*Consultor temporal OPS
Vacunas y Biológicos*



CONTENIDO

- Objetivo de la presentación
- Antecedentes
- Documentos de referencia disponibles en la regulación de productos biológicos/biotecnológicos:
 - OMS
 - EMEA
 - ICH



OBJETIVO DE ESTA PRESENTACIÓN

Es una necesidad expresada por parte de los países de la Región el actualizarse en relación a los documentos existentes para evaluar este tipo de productos.

Así mismo, es muy importante para la Región el subsanar las deficiencias existentes en cuanto a la armonización de la regulación de estos productos, de allí que se espera que surjan iniciativas por parte de los participantes en la identificación de aspectos relevantes a considerar para contar con un documento de registro sanitario armonizado en los países de América Latina y El Caribe.



ANTECEDENTES

La OMS define a los productos biológicos como medicamentos obtenidos a partir de microorganismos, sangre u otros tejidos vivos, cuyos procedimientos de fabricación pueden incluir uno o más de los siguientes elementos: crecimiento de cepas de microorganismos en distintos tipos de sustratos, empleo de células eucariotas, extracción de sustancias de tejidos biológicos, incluidos los humanos, animales y vegetales, productos obtenidos por ADN recombinante ó hibridomas, y la propagación de microorganismos en embriones o animales, entre otras.



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ANTECEDENTES

Según la OMS, los productos biológicos abarcan:

- Vacunas
- Alergenos
- Antígenos
- Hormonas
- Citocinas
- Enzimas
- Derivados de sangre entera y de plasma humanos
- Sueros inmunes
- Inmunoglobulinas
- Anticuerpos monoclonales
- Productos de fermentación (incluidos productos elaborados por ADN recombinante) y
- Agentes empleados para diagnóstico *in vitro*.



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DOCUMENTOS DE REFERENCIA EMPLEADOS EN LA REGULACIÓN DE PRODUCTOS BIOLÓGICOS / BIOTECNOLÓGICOS



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REFERENCIAS ACTUALES SOBRE REGULACIÓN DE BIOTECNOLÓGICOS

- ✓ Actualmente, **no hay una definición clara o uniforme** de productos biotecnológicos, bioterapéuticos, biosimilares, por parte de diversos entes a nivel internacional considerados “de referencia” para los países de la Región, como son: OMS, ICH, EMEA, FDA, Health Canada, etc.

A manera de ejemplo:

- **WHO** emplea el nombre de medicamentos biológicos terapéuticos y a la fecha no existe definición para estos productos en sus documentos de referencia.

La única definición escrita es la que aparece en el borrador del documento discutido en Corea del 28 – 29 de mayo en donde se señala que son productos bioterapéuticos, algunos de los cuales son producidos por tecnología de AND recombinante.



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REFERENCIAS ACTUALES SOBRE REGULACIÓN DE BIOTECNOLÓGICOS

- ✓ En el caso de los “ biosimilares” sucede lo siguiente:
 - ✓ **WHO** no ha definido aún como denominará a estos productos, puesto que se proponen 2 mecanismos distintos para su registro sanitario:
 - Biosimilar approach
 - Stand-alone approach
 - **EMA** los denomina biosimilares y los define como medicamentos biológicos los cuales son similares a biológicos previamente registrados.
 - **FDA** los llama “follow-on protein products”, y los define como productos a base de proteínas y péptidos que intentan ser suficientemente similares a productos biológicos previamente registrados.



REFERENCIAS ACTUALES SOBRE REGULACIÓN DE BIOTECNOLÓGICOS

Si bien no existen definiciones claras y armonizadas acerca de estos productos, existen múltiples documentos de referencia para la regulación y control de productos biológicos/biotecnológicos, las cuales se nombran a continuación.



REFERENCIAS OMS SOBRE REGULACIÓN DE BIOTECNOLÓGICOS

WHO Technical Report Series, No. 822, 1992:

Annex 1 Good manufacturing practices for biological products

Annex 3 Guidelines for assuring the quality of monoclonal antibodies for use in humans

© World Health Organization
World Health Organization Technical Report Series, No. 771, 1988

Annex 7

REQUIREMENTS FOR HUMAN INTERFERONS MADE BY RECOMBINANT DNA TECHNIQUES

(Requirements for Biological Substances No. 41)

© World Health Organization
World Health Organization, Technical Report Series, No. 786, 1989

Annex 3

REQUIREMENTS FOR HUMAN INTERFERONS PREPARED FROM LYMPHOBLASTOID CELLS

(Requirements for Biological Substances No. 42)

© World Health Organization
WHO Technical Report Series, No. 814, 1991

Annex 3

Guidelines for assuring the quality of pharmaceutical and biological products prepared by recombinant DNA technology

© World Health Organization
WHO Technical Report Series, No. 878, 1998

Annex 1

Requirements for the use of animal cells as *in vitro* substrates for the production of biologicals

(Requirements for Biological Substances No. 50)



REFERENCIAS EMEA / ICH SOBRE REGULACIÓN DE BIOTECNOLÓGICOS

EMA e ICH también poseen múltiples documentos relacionados con la evaluación de calidad, seguridad y eficacia de productos biotecnológicos, las mismas están disponibles en las correspondientes páginas Web:

www.emea.europa.eu/humans/human/humanguidelines/biologicals.htm
www.ich.org



Scientific Guidelines for Human Medicinal Products - Biologicals Guidelines - Microsoft Internet Explorer provided by Pan Amnet

Address: <http://www.emea.europa.eu/humans/human/humanguidelines/biologicals.htm>

European Medicines Agency

Scientific Guidelines for Human Medicinal Products

Background

Quality & Biologicals

Quality (Chemical & Medical)

Biologicals

Non-Clinical

Clinical Efficacy & Safety

Multi-disciplinary

Biologicals Guidelines

● = Concept Paper ● = Draft Guideline ● = Adopted Guideline ● = Overview of Comments

Title	Reference Number	Publication Date	Effective Date	Other Remarks
Drug Substance				
Manufacture, Characterisation and Control of the Drug Substance				
Allergen products: Production and quality issues	CHMP/BWP/204831/07	Release for consultation Sept 2007		Deadline for comments 31 March 2008
Production and Quality Control of Monoclonal Antibodies and Related Substances	CHMP/BWP/157653/07	Release for consultation May 2007		Deadline for comments 30 Nov 2007
Potency testing of cell based immunotherapy medicinal products for the treatment of cancer	CHMP/BWP/273475/06	Dec 2007	May 2008	
Quality of biological active substances produced by stable transgene expression in higher plants	CPMP/BWP/48316/06	Release for consultation Sept 2006		Deadline for comments Mar 2007
Revision of the Note for Guidance on Allergen Products	CHMP/BWP/229472/05 Rev. 1	Release for consultation Sep 2005		Deadline for Comments Dec 2005

Microsoft Internet Explorer provided by Pan American Health Organization

Address: <http://www.ich.org/ich/comp/276-254-1.html>

ICH

Q/S/E/M

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Welcome to the official web site for ICH

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.

The purpose is to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines.

The objective of such harmonisation is a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines whilst maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health. This Mission is embodied in the [Terms of Reference of ICH](#).

The ICH Secretariat can be contacted on admin@ich.org

ICH Secretariat, c/o IFPMA, 15 ch. Louis-Dunant, P.O. Box 195, 1211 Geneva 20, Switzerland
 Tel: +41 (22) 338 32 06, Telefax: +41 (22) 338 32 30



DOCUMENTOS DE REFERENCIA DISPONIBLES EN EL CD DE LA REUNIÓN



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WHO

D1	Challenge in Bitherapeutics WHO Drug Information Vol 22, No. 1, 2008
D2	Meeting report. WHO informal consultation on regulatory evaluation of therapeutic biological medicinal products. 19 – 20 April 2007
D3	Good Governance for Medicines Promoting Transparency in Medicines Regulation and Procurement. December, 2006
D4	WHO Informal consultation on international nonproprietary names (INN) policy for biosimilar products. 4 – 5 September 2006 INN working document 07.211
D5	Annex 1. Requirements for the use of animal cells as in vitro substrates for the production of biologicals. (Requirements for biological substances No. 50) WHO technical report series No. 878, 1998
D6	Annex 3: Guidelines for assuring the quality of monoclonal antibodies for use in humans. WHO technical report series No. 822, 1992



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WHO

D7	Annex 3. Guidelines for assuring the quality of pharmaceutical and biological products prepared by recombinant DNA technology. WHO technical report series No. 814, 1991
D8	Annex 3. Requirements for human interferons prepared from lymphoblastoid cells. (Requirements for biological substances No. 42) WHO technical report series No. 786, 1989
D9	Annex 7. Requirements for human interferons made by recombinant DNA techniques. (Requirements for biological substances No. 41) WHO technical report series No. 771, 1988
D10	WHO International biological reference preparations Held and distributed by the WHO International laboratories for biological standards Cytokines/Growth factors http://www.who.int/bloodproducts/catalogue/en/index.html
D11	WHO Regulatory Guidance for Biosimilar Products Power point presentation. May 2007



ICH Harmonised Tripartite Guidelines

A1	Quality of biotechnological products: stability testing of biotechnological/biological products Q5C. 1995
A2	Specifications: Test procedures and acceptance criteria for biotechnological/biological products Q6B. 1999
A3	Comparability of biotechnological/biological products subject to changes in their manufacturing process Q5E. 2004 Final concept paper Q5E. 2002
A4	Stability testing of new drug substances and products Q1A (R2). 2003
A5	Good manufacturing practice guide for active pharmaceutical ingredients Q7. 2000
A6	Preclinical safety evaluation of biotechnology-derived pharmaceuticals S6. 1997



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EMEA

B1	Committee for medicinal products for human use (CHMP) Guideline on similar biological medicinal products. CHMP/437/04. 2005
B2	Committee for medicinal products for human use (CHMP) guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues. EMA/CHMP/BWP/49348/2005
B3	Committee for medicinal products for human use (CHMP) Concept paper on similar biological medicinal products containing low molecular weight heparins-non-clinical issues. EMA/CHMP/BMWP/496286/2006
B4	Committee for medicinal products for human use (CHMP) 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 granulocyte-colony stimulating factor. EMA/CHMP/BMWP/31329/2005
B5	Committee for medicinal products for human use (CHMP) 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 soluble insulin. EMA/CHMP/BMWP/32775/2005



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EMEA

B6	Committee for medicinal products for human use (CHMP) 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 erythropoietin. EMEA/CHMP/BMWP/94526/2005
B7	Committee for medicinal products for human use (CHMP) 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. EMEA/CHMP/BMWP/94528/2005
B8	Committee for medicinal products for human use (CHMP) Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues. EMEA/CHMP/BMWP/42832/2005
B9	Committee for human medicinal products (CHMP) Guideline on comparability of biotechnology-derived medicinal products after a change in the manufacturing process. Non-clinical and clinical issues. EMEA/CHMP/BMWP/101695/2006
B10	Committee for medicinal products for human use (CHMP) Guideline on immunogenicity assessment of biotechnology-derived therapeutic proteins. EMEA/CHMP/BMWP/14327/2006



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EMEA

B11	Committee for proprietary medicinal products (CPMP) Guideline on comparability of medicinal products containing biotechnology-derived proteins as active substance. Non-clinical and clinical issues. EMEA/CPMP/3097/02/2003
B12	Committee for proprietary medicinal products (CPMP) Guideline on comparability of medicinal products containing biotechnology-derived proteins as active substance: quality issues. EMEA/CPMP/BWP/3207/00/2003
B13	ICH Topic Q 5 E Comparability of biotechnological/biological products Note for guidance on biotechnological/biological products subject to changes in their manufacturing process. CPMP/ICH/5721/03
B14	Committee for medicinal products for human use (CHMP) Concept paper on similar biological medicinal products containing recombinant alpha-interferon. Annex to the guideline on similar biological medicinal products containing biotechnology derived proteins as active substance-(non) clinical issues. CHMP/BMWP/7241/2006 End of consultation 1 August 2006
B15	Press release European Medicines Agency adopts first positive opinion for a similar biological medicinal product. 2006 EUROPABIO. Biological and Biosimilar Medicines. Healthcare Biotech Fact Sheet. 2005



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Health Canada

C1

Draft guidance for sponsors: Information and submission requirements for subsequent entry biologics (SEBs)
2008/01/30 Distributed for comment purposes only

icdra

C2

12th International conference of drug regulatory authorities. Recommendations
http://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/ecc_final



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Gracias por su atención

Todos los documentos mostrados en esta presentación y entregados en el CD de la reunión están disponibles en la página Web de Vacunas y Biológicos desarrollada por la OPS

www.paho-vb.org