

WHO regulatory guidance for biosimilar products

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World Health
Organization

Outline

- Context
- Regulatory support offered by WHO
- Advice from WHO oversight bodies or consultative groups
- WHO Initiation of regulatory activity for biosimilar products



Context



WHO normative activities for biological medicines

- implemented for more than 50 years
 - mandated by Member States

WHO is expected to be both a driving force and a key reference point on normative issues for biological medicines

Constitutional responsibility

- WHO is mandated by its Member States to "...develop, establish and promote **international standards for biological products**"
- Biological products are defined as substances of biological origin, that are assayed by biological tests, and are used in prophylaxis, therapy or diagnosis of human diseases
- In practice this covers vaccines, blood products, biological therapeutics and selected in vitro diagnostics

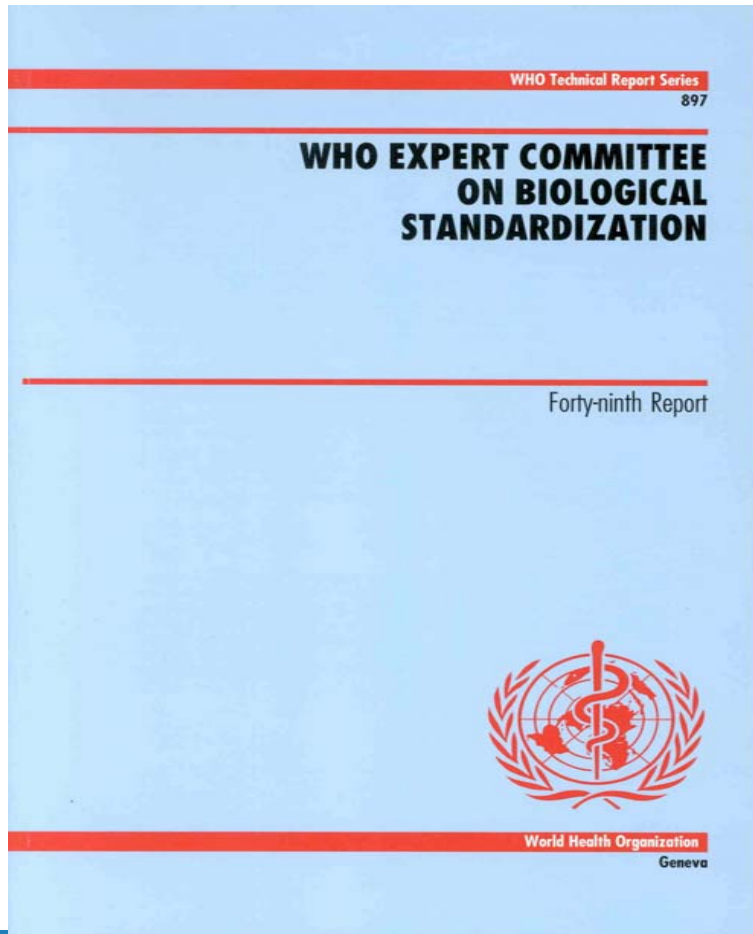
Setting norms and standards and promoting their implementation is affirmed as a core activity of WHO for the period 2008-2013

Regulatory support offered by WHO



Norms and standards – WHO products

Global written standards Global nomenclature



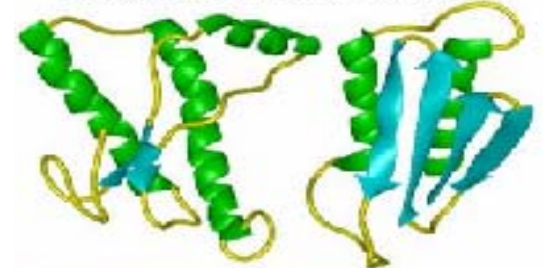
Global measurement standards



Standards evidence base

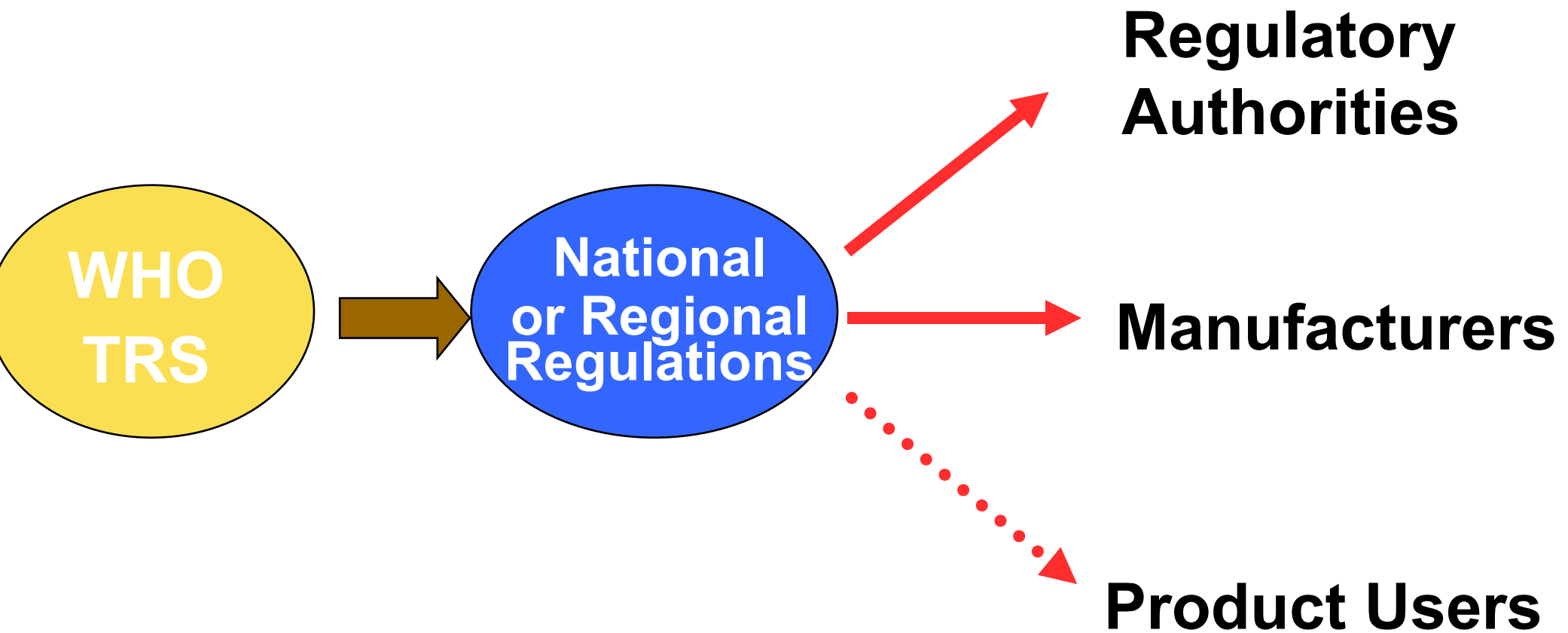


Pathogenesis: Change in Prion protein



WHO Written Standards

A tool for harmonization of specification worldwide



WHO written standards - for biotech products

- **Biological products derived from rDNA, TRS 814, 1991**
- **Human interferons made by rDNA, TRS 771, 1988**
- **Monoclonal antibodies, TRS 822, 1992**



WHO reference materials - biotherapeutic products

- **cytokines/growth factors**
- **endocrinological substances**
- **recombinant coagulation factors**



Advice from WHO oversight bodies or consultative groups



ECBS recommendations

- 1. WHO should organize a meeting of interested parties to review the issues in depth and help WHO develop consensus on the global needs, priorities and potential role for global standardization in the area of biotherapeutics for the major chronic diseases*
- 2. Facilitate the strengthening of technical capacity in NRAs for biological therapeutics*
- 3. Collate information on standard or counterfeit biotherapeutic products*

– From 56th ECBS meeting decisions



Requests from ICDRA 2006

- *" WHO is requested to develop global regulatory consensus and guidance for biosimilars, which are a reality in several countries and will be a major regulatory challenge in the years to come"*
 - From 12th ICDRA recommendation in Workshop H, "Global challenges for regulation for vaccine and other biologicals"



INN ad hoc meeting for biosimilar products

- 1. It was concluded that biosimilar products do not require special considerations in terms of nomenclature.*
- 2. However, the importance of regulatory issues was emphasized.*

From WHO informal consultation on INN policy for biosimilar products, 4-5 September 2006



WHO Initiation of regulatory activity for biosimilar products



WHO informal consultation of working group on regulatory evaluation of therapeutic biological medicines

19~20 April 2007, WHO/HQ, Geneva

● Objective

- To review current regulatory directions and challenges in the regulatory evaluation of the quality, efficacy of biosimilar products
- To develop a plan of action for preparing guidance



WHO informal consultation of working group on regulatory evaluation of therapeutic biological medicines

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● Participants

– Regulatory authorities

- China, India, Iran, Japan, S.Korea, USA, EU, Australia, Canada, Germany, Switzerland, Brazil

– Academy

- Utrecht University

– Manufacturer's associations

- IFPMA, EGA, DCVMN

– WHO collaborating center for Biological Standardization

- NIBSC, UK



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- What WHO has identified from different regions
 - ‘Biosimilar products’ are here and WHO member states expressed a need for assistance to regulate them
 - Some authorities have recently established regulatory pathways for biosimilar products
 - Others, developing countries in particular do not have regulatory framework for such products
 - Generally the same issues have been highlighted but differences between regions do exist.

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● Issues that have been highlighted

- definitions
- Regulatory pathway for biosimilars (in many cases doesn't exist)
- scope of what types products should be addressed
- proof of similarity
 - quality - extensive studies
 - nonclinical and clinical studies
 - extent of comparability studies
 - PK/PD studies
 - Non-inferiority vs. clinical equivalence
- focus is on abridged studies
- the comparator/reference product
- extrapolation of indication
- high similarity vs. interchangeability vs. substitution
- the use of INNs



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● Suggestions from different regions

- International guidance for biosimilar products will be needed
 - General regulatory pathway
- Globally consented terminology and definition and regulatory principles should be given
- In developing guidance, concept of existing guidelines may applicable
 - EMEA's
 - ICH Q5E

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● Suggestions from different regions (cont)

- Collaboration on information sharing and scientific basis for decision making
- Collaboration for post-market surveillance may be needed for global framework
 - Safety database for possible adverse event collected from administration of biosimilar products
- Reference standard for quality control test



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● Conclusion and next step

- WHO should develop global regulatory guidance for biosimilar products.
- As a first step towards this goal, **working group** is to be set up to take this issue forward.
- Outcomes will be presented to the WHO Expert Committee on Biological Standardization in October 2007 for further consideration and advice.