



SANDOZ

What Should Congress Do about Generic or Follow-On Biologic Drugs?

Ajaz S. Hussain, Ph.D.

**Vice President & Global Head for Biopharmaceutical
Development**

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a Novartis company

Novartis: An broad portfolio for a dynamically changing healthcare environment



- Aging
- New diseases
- Lifestyle
- Access / costs



- Better medicines (efficacy, side effects)
- Prevention
- Less expensive drugs
- Simple and readily available self-treatment



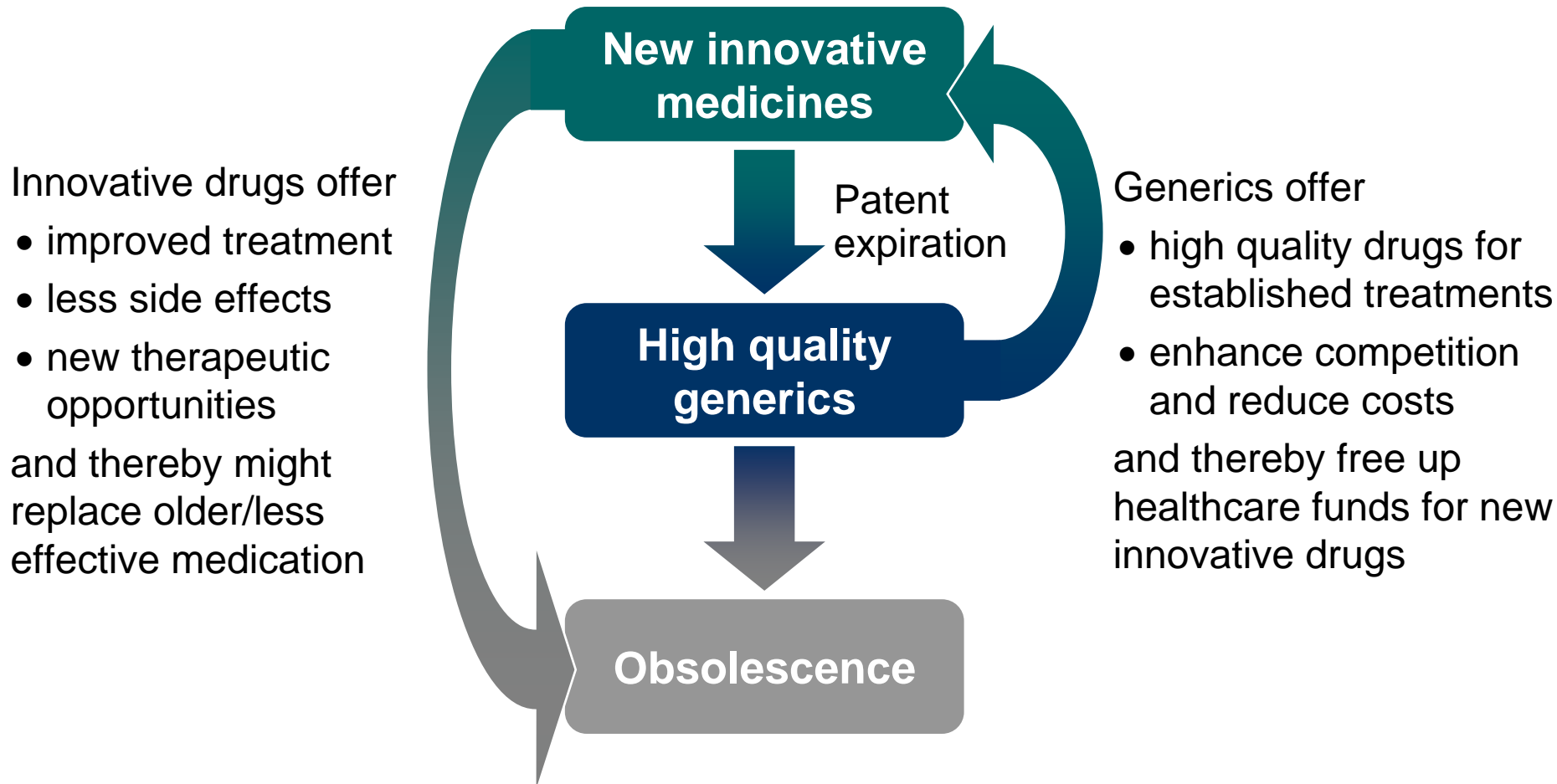
Pharma

Vaccines &
Diagnostics

Sandoz

Consumer
Health

Innovative drugs and generics are complementary



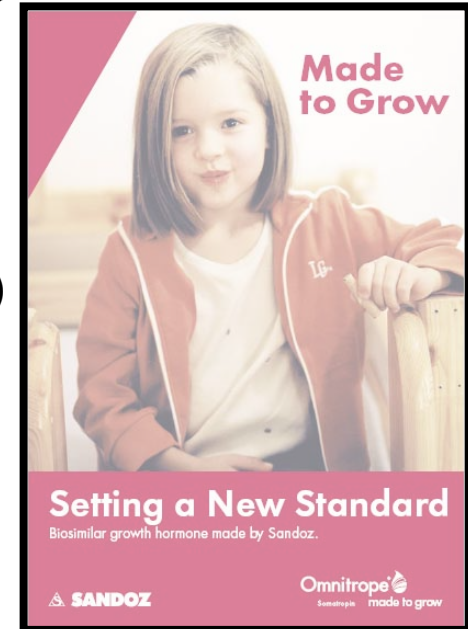
FOBs: Public, Scientific Debate & Discussions in US

- **FDA Workshop: Scientific Considerations Related to Developing Follow-On Protein Products, September 14-15, 2004**
- **Follow-On Protein Pharmaceuticals, February 14-16, 2005**
 - **Co-sponsored by FDA and the Drug Information Association**
- **Scientific Issues in Assessing the Similarity of Follow-on Protein Products, December 12-14, 2005**
 - **Co-sponsored by FDA, in collaboration with the National Institute for Standards and Technology, and the New York Academy of Sciences**

¹ http://www.fda.gov/cder/regulatory/follow_on/default.htm

Impact of Omnitrope® Approval?

- **Citizen Petitions and Responses¹**
 - **2003P-0176: Follow-On Approval of Therapeutic Protein Products**
 - **2004P-0171: Standards for 'Similarity' or 'Sameness' of Biotechnology-Derived Products**
 - **2004P-0231: Deny Approval of NDA 21-426 (Omnitrope)**
- **Omnitrope®: “Is this FDA's first approval of a follow-on protein product?”²**
 - **“No. FDA has approved other follow-on protein products under section 505 of the Food, Drug, and Cosmetic Act.”**
 - **How is Omnitrope different?**



Does approval of Omnitrope create a new pathway for follow-on versions of all protein products?²

- No.
- There is no abbreviated approval pathway analogous to 505(b)(2) or 505(j) of the Act for protein products licensed under section 351 of the Public Health Service Act.
- Such a pathway for the approval or licensure of follow-on protein products under the Public Health Service Act would require new legislation.

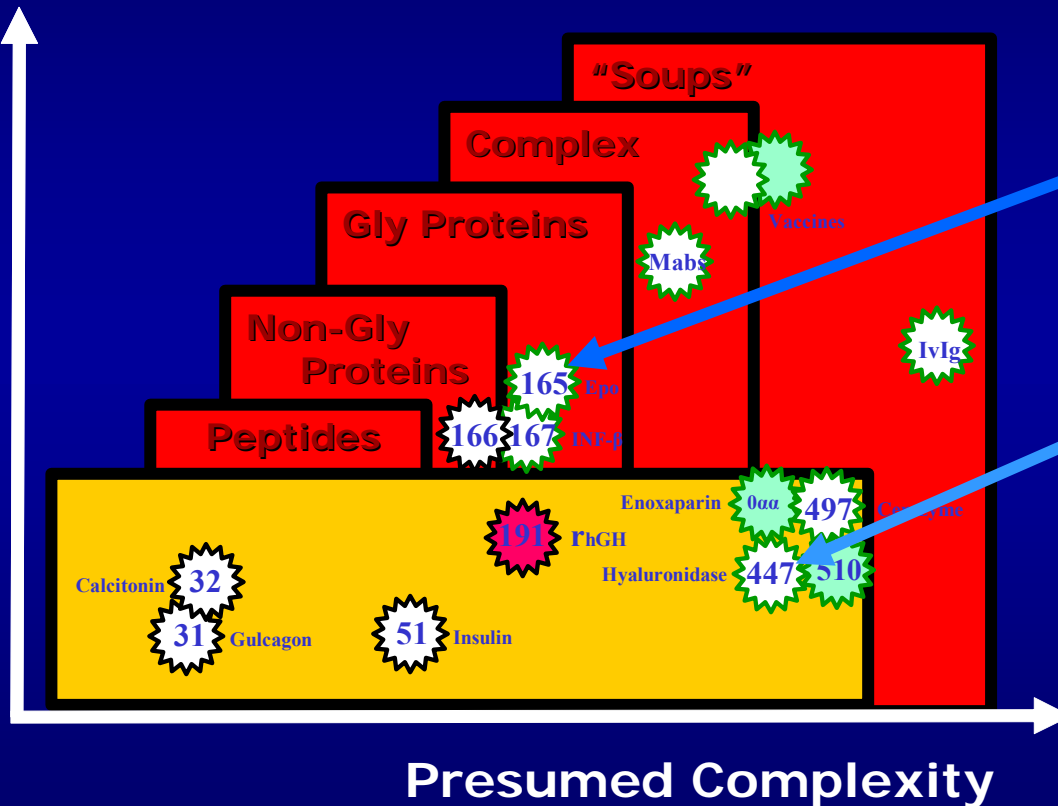
**Congress needs to give FDA the authority
to approve BLAs for FOBs!**

² <http://www.fda.gov/cder/drug/infopage/somatropin/qa.htm>

FOB Drugs: Different Regulatory Pathways, but the Same Scientific Foundation and Standards

No Bright Lines...

**Cost of Development
[= Data]**



PHS Act

FDC Act

ENGL& NORT LLP - THE LAW FIRM FARKNOW'S SCIENCE

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Source: Courtesy Gillian Woollett

711 June 2007, AEI Washington, D.C.

The FDA journey: Convergence to a harmonized regulatory approach for drugs and biologics

- **The Biologics Control Act (1902), The Pure Food and Drug Act (1906), The Federal Food, Drug, and Cosmetic Act (1938), The Insulin Amendments (1941), The Public Health Service Act (1944), The Kefauver-Harris Amendments to FD&C Act (1962)**
 - **In 1972 the authority over biologics products transferred from NIH to FDA**
 - **1980's – the first wave of products" based on rDNA technology**
 - **Reinventing the Regulation of Drugs Made From Biotechnology Washington D.C.: National Performance Review, 1995, U.S. Gov. Doc: PRVP 42.2: D 84/2.**

The FDA journey: Convergence to a harmonized regulatory approach for drugs and biologics

- **FDA Guidance - Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-derived Products, April 1996**
- **The FDA Modernization Act of 1997 (Modernization Act)—
Modernization of the Regulation of Biological Products**
- **FDA guidance for industry *Providing Clinical Evidence of Effectiveness for Drug and Biological Products*, (1998)**
- **Transfer of Therapeutic Biological Products to the Center for Drug Evaluation and Research (2003) --- Office of Biotechnology Products/OPS**
- **The FDA Initiatives – PAT, CGMP for the 21st Century, and the Critical Path Initiative**

The FDA journey: Convergence to a harmonized regulatory approach for drugs and biologics

- “Biological products subject to the *PHS Act* also meet the definition of *drugs* under the *Federal Food, Drug and Cosmetic Act (FDC Act)*.”
- “Biological products are a subset of drugs; therefore both are regulated under provisions of the FDC Act. However, only biological products are licensed under section 351 of the PHS Act.” (Note: some therapeutic protein products are approved under section 505 of the FDC Act, not under the PHS Act.)

Mature Regulatory System to Ensure Quality, Safety and Efficacy of all Biological Drugs

- **Examples of available regulatory guidelines for approval of biopharmaceuticals and for their post-approval manufacturing process changes**
 - **Content and Format of INDs for Phase I Studies of Drugs Including Well-Characterized, Therapeutic, Biotechnology-derived products"**
<http://www.fda.gov/cder/guidance/clin2.pdf>
 - **"Providing Clinical Effectiveness of Human Drugs and Biological Products"**
<http://www.fda.gov/cber/gdlns/clineff.pdf>
 - **ICH Q5A Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin, Posted 9/1998**
 - **ICH Q5B Quality of Biotechnological Products: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Final 2/1996**
 - **ICH Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Final 7/1996**
 - **ICH Q5D Quality of Biotechnological/Biological Products: Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products; Availability, Posted 9/21/1998**
 - **ICH Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process, Final 6/2005 (based on FDA's 1996 guidance)**

EMEA Framework: FOB's Manufactured & controlled according to their own development; demonstration of "extensive comparability" required.

Quality

Comparability supported by sufficiently sensitive analytical systems; may allow a reduction of non-clinical and clinical requirements

Non-Clinical

Comparative, designed to detect differences. Clear understanding of product characteristics Emerging technologies.

Clinical

Stepwise, begin with PK/PD then clinical efficacy and safety trial's). In certain cases, PK/PD for clinical comparability. Clinical safety & pharmacovigilance

Source: <http://www.emea.eu.int/pdfs/human/biosimilar/26819505en.pdf>

What Should Congress Do?

- **Require the same scientific standards be applied to approval of all biologic drugs**
- **How? Amend section 351 of PHS Act**
 - **Subparagraph (C)(i)(I) of section 351(a)(2) of the PHS Act**
 - **The biological product that is the subject of the application is safe, pure, and potent based upon**
 - **the applicant's demonstration that its biological product is comparable to biological product for which the Secretary has previously approved a biologics license application.....; and**
 - **the Secretary's assessment of comparability of the biological product based upon the Secretary's prior finding of safety, purity, and potency of the previously approved biological license application....**

What Should Congress Do?

- **Recognize “Interchangeability” as a public health objective**
 - **Based on demonstration of equivalent identity, strength, quality, purity, and potency; and**
 - **Demonstration of no clinically-meaningful differences from the previously-licensed product in terms of safety, purity, and potency.**
- **Recognize the need for appropriate incentives for future innovation**
 - **Market exclusivity**
- **Ensure proper protection of intellectual property**
 - **“Decouple” patent litigation from FDA approval process**
 - **Provision for post-approval patent notification system**

What Should Congress Do?

- **Recognize rapid advancements of science and technology that will continually provide more effective means to address increasing complexity to reduce uncertainty**
 - **Require the same scientific standards be applied to approval of all biologic drugs**
 - **Recognize “Interchangeability” as a public health objective**
 - **Recognize the need for appropriate incentives for future innovation**
 - **Ensure proper protection of intellectual property and “decouple” patent litigation from FDA approval process**