REGULATION OF FOLLOW-ON PRODUCTS IN THE USA

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OUTLINE

U.S. STATUTES

FDA POLICIES

CURRENT ACTIVITIES

STATUTES

STATUTE	PRODUCTS
U.S. FOOD DRUG & COSMETIC ACT →	"TRADITIONAL" SMALL MOLECULE DRUGS AND SOME PROTEIN PRODUCTS
U.S. PUBLIC HEALTH SERVICE ACT →	BIOLOGICAL PRODUCTS

APPLICATIONS

STATUTE	APPLICATION
U.S. FOOD DRUG & COSMETIC ACT →	NEW DRUG APPLICATION (NDA) AND 505(b)(2) NDA
U.S. FOOD DRUG & COSMETIC ACT →	ABBREVIATED NDA (ANDA)
U.S. PUBLIC HEALTH SERVICE ACT →	BIOLOGIC LICENSE APPLICATION (BLA)
U.S. PUBLIC HEALTH SERVICE ACT → (prohibited)	ABBREVIATED BLA

CATEGORICAL EXAMPLES

NDA

h-GROWTH HORMONE

INSULIN

CALCITONIN

BLA

MONOCLONAL ANTIBODIES

INTERFERONS

INTERLEUKINS

GROWTH FACTORS

WHAT IS A FOLLOW-ON PRODUCT?

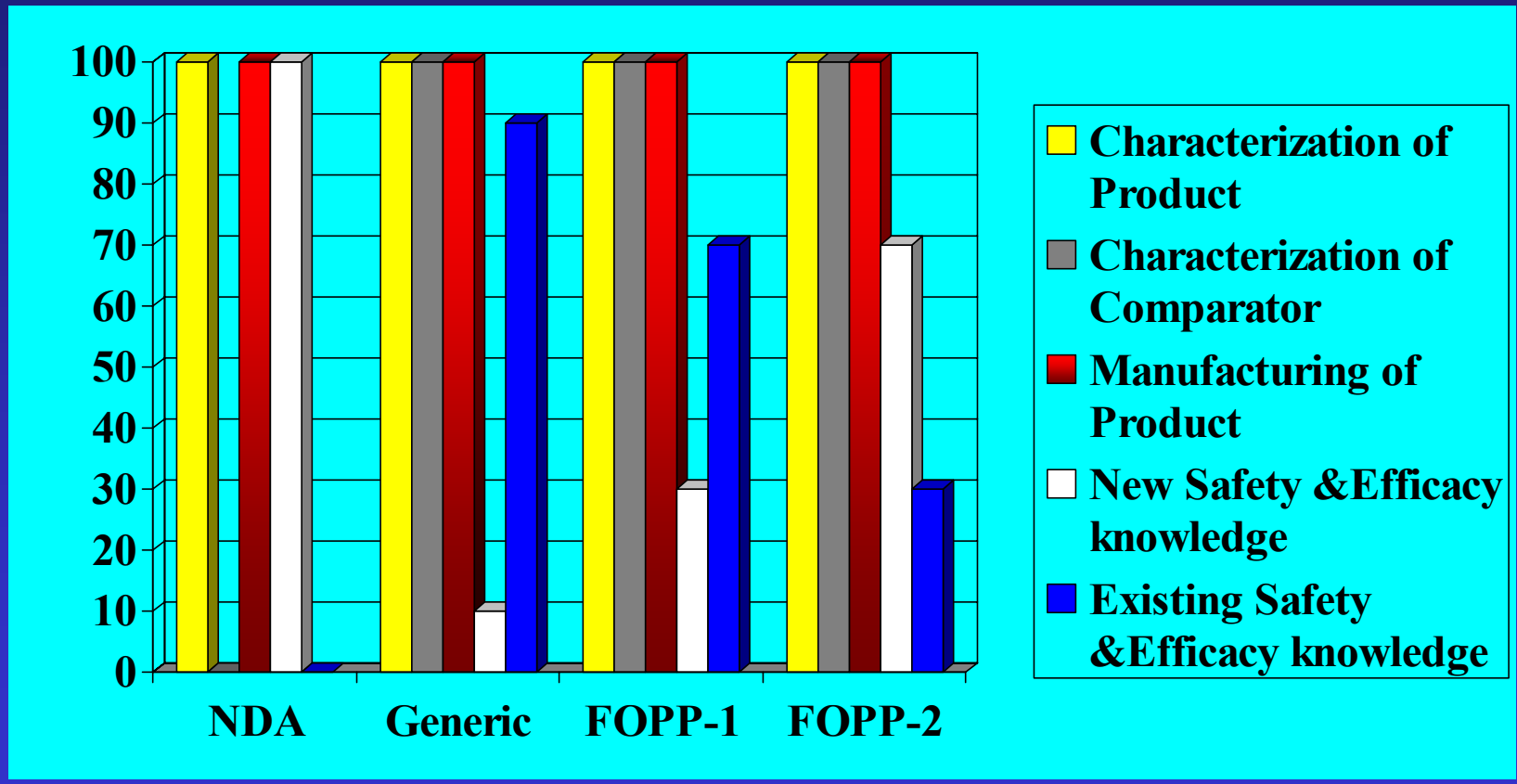
THESE ARE PRODUCTS INTENDED TO BE SUFFICIENTLY SIMILAR TO AN APPROVED PRODUCT TO PERMIT THE APPLICANT TO RELY ON CERTAIN EXISTING SCIENTIFIC KNOWLEDGE ABOUT THE SAFETY AND EFFICACY OF AN APPROVED REFERENCE PRODUCT.

WHAT IS A FOLLOW-ON PRODUCT?

NOT A SINGLE ANSWER…

- PRODUCT INTENDED TO BE IDENTICAL TO COMPARATOR PRODUCT
  - INTERCHANGEABLE
- PRODUCT INTENDED TO BE SIMILAR TO COMPARATOR PRODUCT
  - HIGHLY SIMILAR
  - IMPROVED (E.G., 2ND GENERATION PRODUCT)?

APPLICATION INFORMATION



COMPLEXITY

- COMPLEXITY IS MULTIFACTORIAL
- INTRINSIC PRODUCT COMPLEXITY
  - SIZE
  - SHAPE
  - NUMBER OF SUBUNITS
  - POST-TRANSLATIONAL MODIFICATIONS
- HETEROGENEITY
- IMPURITIES & CONTAMINANTS

FUNCTIONAL COMPLEXITY

- MECHANISM OF ACTION
  - ANTAGONIST
  - AGONIST
  - ENZYMATIC ACTIVITY
  - MULTIPLE FUNCTIONS
- CORRELATIONS TO SAFETY & EFFICACY
- MULTI-INDICATION PRODUCTS

EXAMPLES OF APPROVED FOLLOW-ON PRODUCTS

- HYALURONIDASE
- GLUCAGON
- CALCITONIN
- HUMAN GROWTH HORMONE

FDA POLICY

- SCIENCE-BASED
  - AVOID PRECEPTS
  - DATA-DRIVEN
  - FLEXIBLE TO CHANGING TECHNOLOGIES
- FOCUS ON PUBLIC HEALTH
  - PATIENT SAFETY
  - THERAPEUTIC EFFICACY
  - DRUG AVAILABILITY

NON-PROPRIETARY NAMES

- FOLLOW THE SAME RULES FOR NAMING OTHER PROTEINS
  - STRUCTURAL ATTRIBUTES
  - PHARMACOLOGICAL CLASS
- SAME NAME DOES NOT INDICATE CLINICAL INTERCHANGEABILITY

CURRENT ACTIVITIES

- FDA's Assessment of Follow-On Protein Products—An Historical Perspective on Scientific Evaluations – Nature Reviews April 13th, 2007
- Guidance for industry on scientific considerations in demonstrating the safety and effectiveness of follow-on protein products (under development)
- Guidance for industry on CMC issues for follow-on protein products (under development)
- Guidance for industry on immunogenicity studies (under development)

ADDITIONAL INFORMATION

CDER INTERNET SITE:

http://www.fda.gov/cder/index.html

INFORMATION AND PRESENTATIONS FROM THE FDA "FOLLOW-ON" WORKSHOPS:

http://www.fda.gov/cder/meeting/followOn/

OMNITROPE APPROVAL INFO:

http://www.fda.gov/cder/drug/infopage/somatropin/default.htm