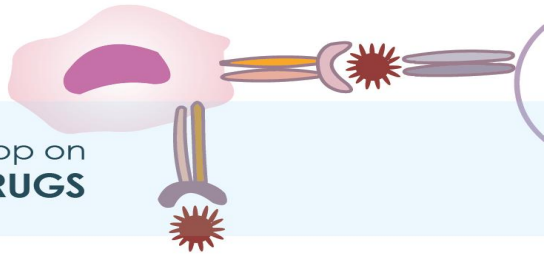
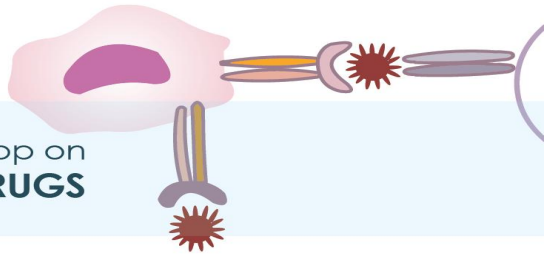


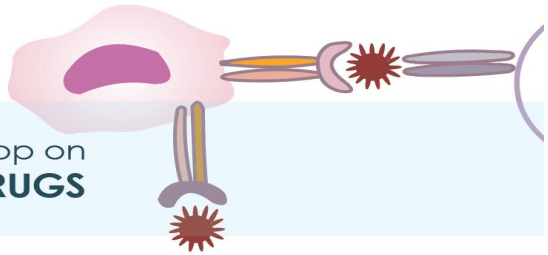
Professor Philip Walson, MD, USA/Germany

- Board Certified in Paediatrics, Clinical Pharmacology and Medical Toxicology
- Visiting Professor, Department of Laboratory Medicine at Georg-August-University Medical School, Göttingen, Germany



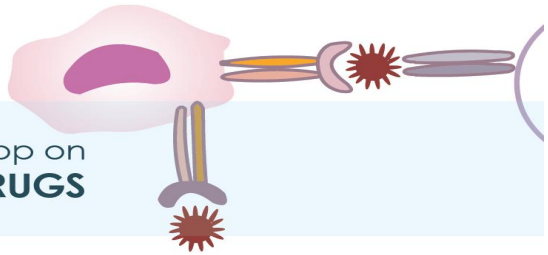
Best practices for the regulation, use and monitoring of follow-on non-biological complex drugs

Philip D Walson, MD
Editor-in-Chief, GaBI Journal
8 October 2013



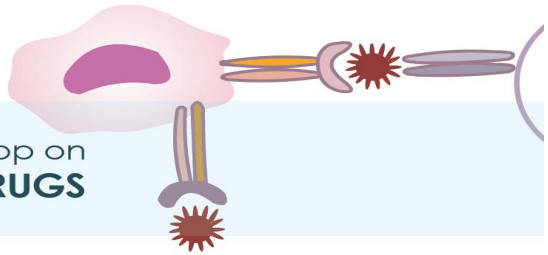
Patented/Follow-on Products

- Potential – lower cost/equivalent benefit
- Risk – no savings/less benefit or more risks
- Small Molecules – Generics
- Biologicals – Biosimilars
- NBCDs – ??



Regulatory Review Process

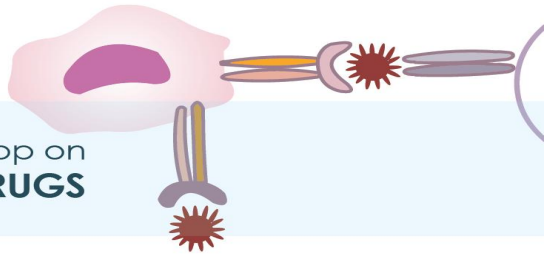
- Nomenclature
- Pre-clinical data
- Clinical data
  - Prior to approval
  - Post approval



Regulatory Approval

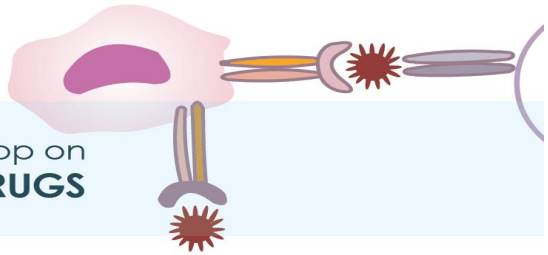
- Source – biologic product or not
- Ability to fully characterize
- Likelihood of performance differences
- Post-marketing surveillance*

*mandatory for biologicals



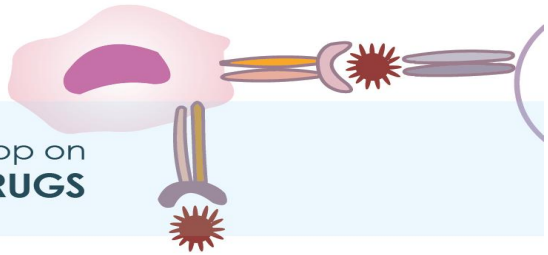
Generics/Biosimilars

- USP Nomenclature Perspective
- Name assumes single defined substance
- Analytical/Physiochemical characterization
- Same active ingredient(s)-others can matter
- Equal bioavailability-80-125% AUC, Cmax
- Biologics recognized as different, more difficult
- ??NBCDs??



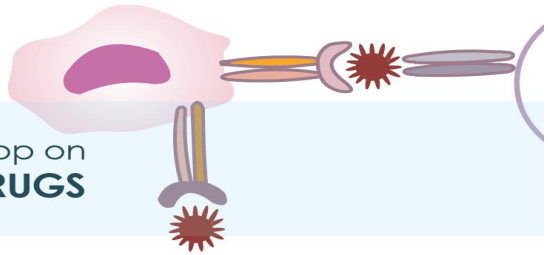
Some NBCD Examples

- Liposomal products
- Glatiramoids
- Low Molecular Weight Heparins (LMWHs)
- Intravenous Iron Preparations



Liposomal products: Amphotericin/generics

- Originally from streptomyces Nodosus
- Two amphoterics, A & B
- ? "simple"-**IUPAC Name:** (1S,3R,4E,6E,8E,10E,12E,14E,16E,18S,19R,20R,21S, 25R,27R,30R,31R,33S,35R, 37S,38R)-3-[(2R,3S,4S,5S,6R)-4-amino-3,5-dihydroxy-6-methyloxan-2-yl]oxy-19, 25,27,30,31,33,35,37-octahydroxy-18,20,21-trimethyl-23-oxo-22,39-dioxabicy-clo[33.3.1]nonatriaconta-4,6,8,10,12,14,16-heptaene-38-carboxylic acid
- Amphotericin B, AmBisome-liposomal products
- Fungisome/Amphotec-liposomal complex products
- Abelcet/Ampholip/Amfy-lipid complex products
- Amy-nanoparticles

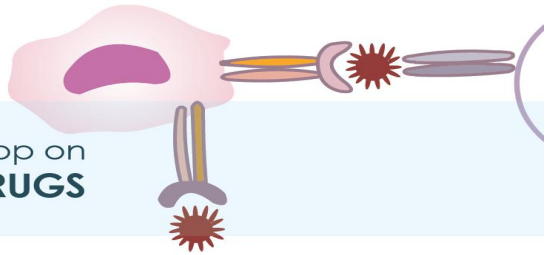


Glatiramoids

- Complex mixture of polypeptides
- Major pre-clinical differences based on manufacturing process

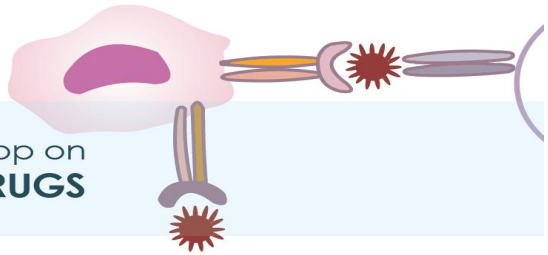
Low Molecular Weight Heparins (LMWHs)

- USA – regulated as generics
- EMA – regulated as biosimilars



Intravenous Iron Preparations

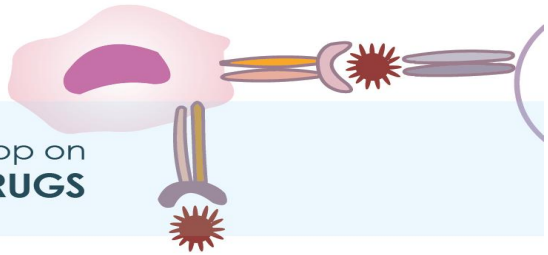
- Iron Dextrans
  - High Molecular weight
  - Low Molecular weight
- Iron gluconate
- Iron Carboxymaltose, Isomaltose, Saccharose
- Iron Sucrose



Iron Sucrose[USP]
Colloidal solution

Iron, Sucrose, MW range, Specific Gravity,

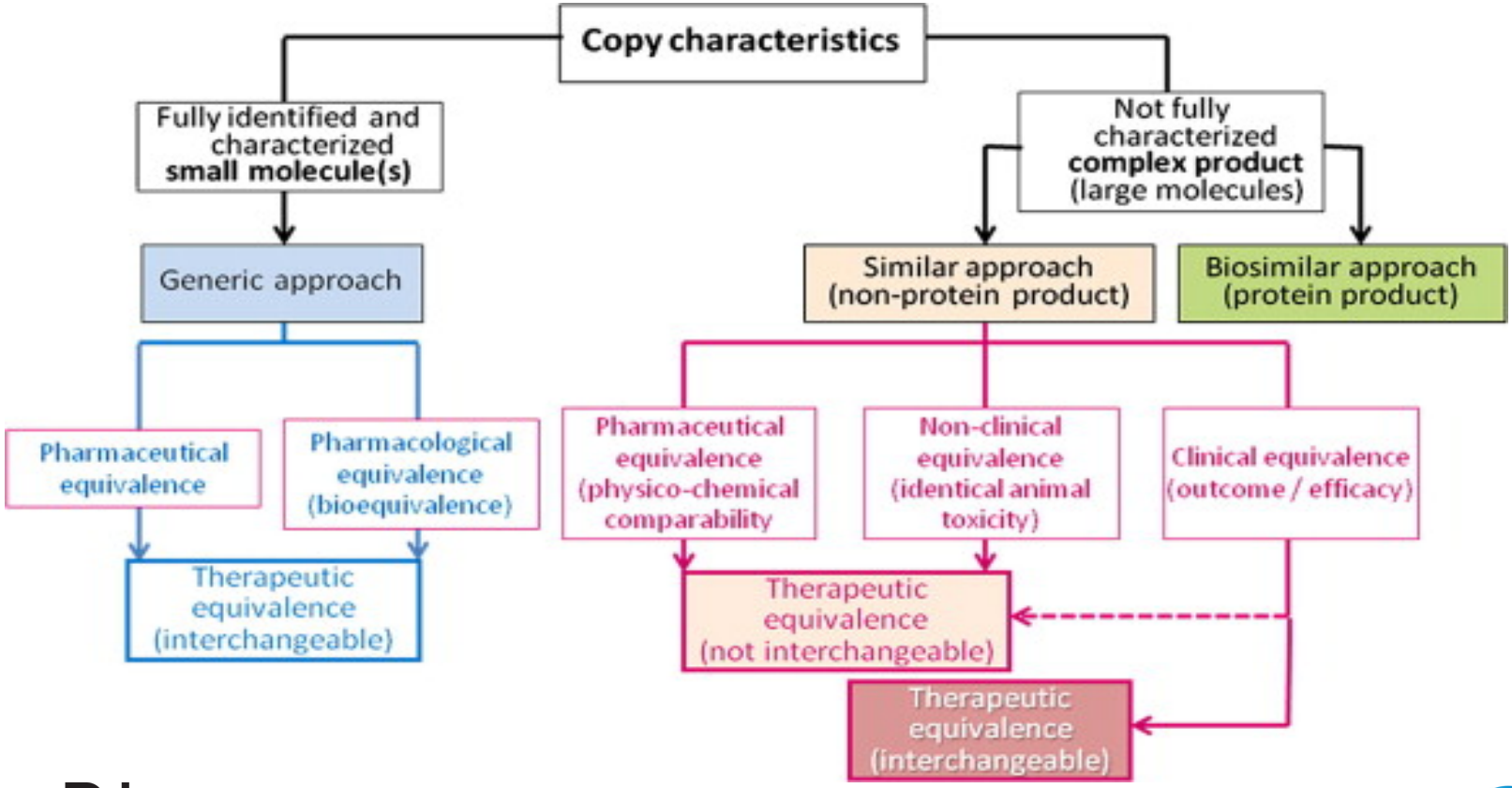
Endotoxins, pH, Osmolality, Particulates



Intravenous Iron Sucrose

- Complicated structure(s)
- Difficult to characterize
- Production method dependent
- Non-equivalent 'similars'
- Pre-clinical distribution studies
- Clinical trial outcomes
- Delayed, post-marketing recognition
- Impurities/storage containers

Algorithm for authorizations of copies (therapeutic equivalence): comparability of complex products by the similar pathway



Schellekens H, et al. Regul Toxicol Pharmacol. 2011;59(1):176-83.