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Follow-On Biologics

Overview

- BIO's Position on Follow-On Biologics (FOBs)
- Biological Products vs. Chemical "Small-Molecule" Drugs
- Generics vs. Follow-Ons
- Immunogenicity
- Naming of FOBs
- Conclusions

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BIO's Position on FOBs

- **Ensuring Patient Safety**
  - Patients should not have to accept greater risks or uncertainties in using a follow-on product than when they use an innovator's product.
  - A clinical trial remains a fundamental principle for evaluating the safety and effectiveness of a follow-on biotechnology product
- **Protecting Incentives for Innovation, including Intellectual Property Rights**
  - Any approval of a follow-on biologic must be carefully crafted so that it does not create disincentives to research and development of innovative biotechnology products
  - FDA cannot rely on an innovator's unpublished proprietary data, including trade secrets, to approve a follow-on biologic

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Biological products are different from chemical drugs

- Generally larger
- Made in living systems (e.g. yeast or mammalian cells)
- More complicated
  - Elaborate folding
  - Sugars may be attached (“glycosylation”)
  - Several forms of the active molecule may be present
- More sensitive to temperature and shear forces
- Analytical methods, while advancing, may not detect important variations that affect safety and effectiveness, so clinical trials are essential.

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Biological Products are Different

Product	Molecular Weight
CHEMICAL	
Aspirin	180
Ranitidine (Zantac®)	351
Atorvastatin (Lipitor®)	1209
BIOLOGICAL	
Insulin	~5800*
Epoetin	~30000*
Factor VIII	~266000*

*depends on brand

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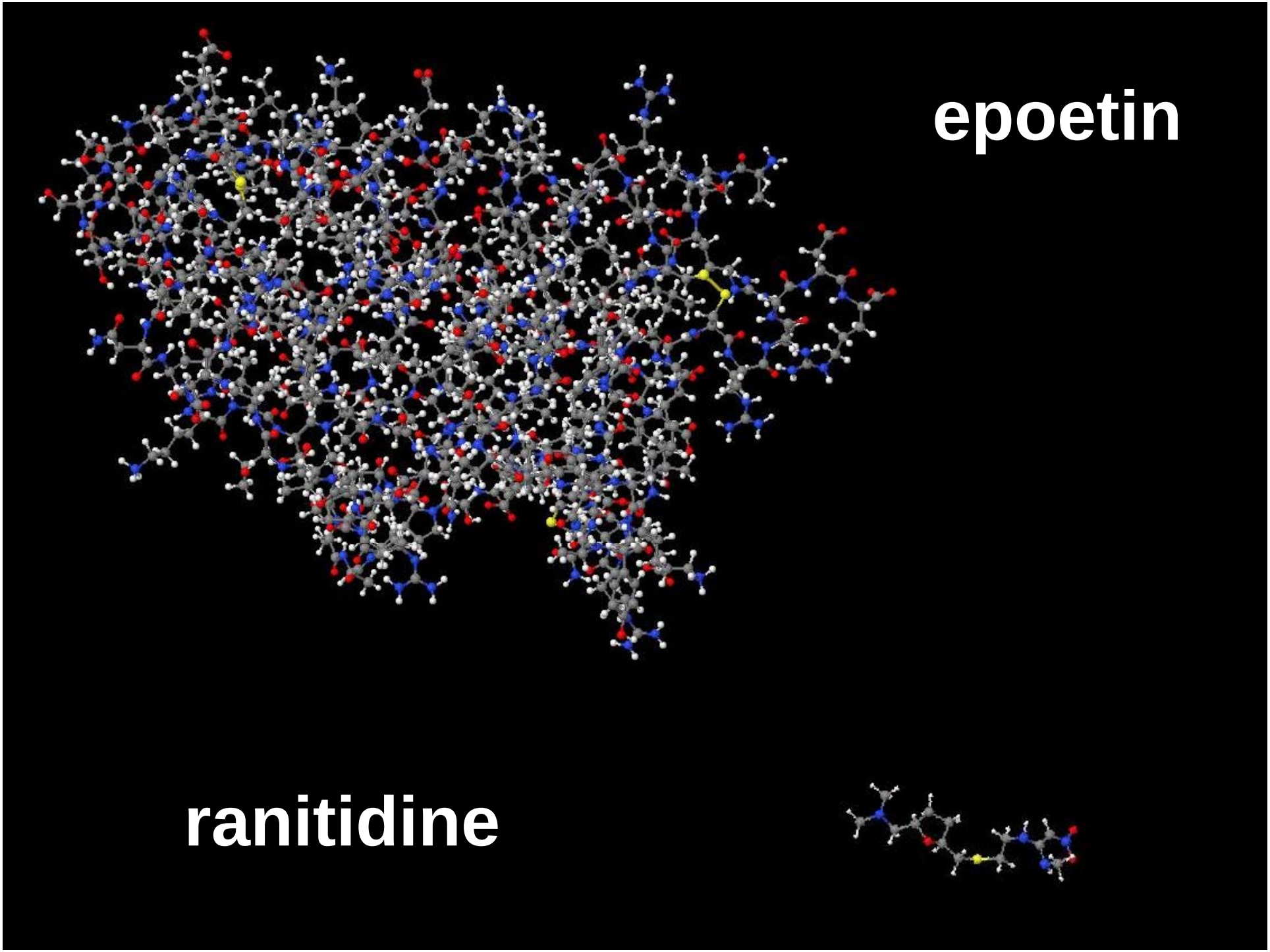
epoetin
ranitidine

Generics vs. Follow-Ons

- A generic is a product that is shown to be the *same* as an innovative product.
  - But each biological product, and its associated manufacturing process, are unique and cannot be exactly duplicated by another manufacturer
  - The methods used to show that one chemical drug is the same as another are not sufficient for biologics.
  - Only the innovator has the information necessary to show comparability of a biological product after a manufacturing change
- A follow-on (or "biosimilar") is a product that is *similar to* but *not the same* as an innovator product
- EMEA has stated that the generic pathway is not appropriate for biologics
- FDA has stated (September 2006) that it "has not determined how interchangeability can be established for complex proteins"

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Immunogenicity

- Many biologics cause an immune reaction
- Usually, this immunogenicity is benign and does not affect clinical safety
- Sometimes, immunogenic reactions can
  - inactivate the biological product, resulting in disease progression
  - inactivate the body's naturally occurring protein, resulting in side-effects that can be very serious
- To protect patients, all biological products must be tested in clinical trials

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Naming of Biological Products, including FOBs

- To help ensure patient safety, each biological product should have a distinct International Nonproprietary Name (INN)
- Many prescribing, dispensing, and payment systems were developed for interchangeable small molecule generic drugs. If FOBs have the same INN as the respective innovator product, application of these systems to FOBs may result in unplanned and potentially dangerous switching among biological products that are not interchangeable.
- Unique identification of biological products would
  - help to prevent inadvertent or inappropriate product substitution
  - facilitate safety surveillance ("pharmacovigilance")
  - facilitate product traceability

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Conclusions

- Biological products are very different from chemical ("small-molecule") drugs
- There is no such thing as a "biogeneric," and to date interchangeability cannot be demonstrated
- Patient safety requires that standards for approval of biologics remain high
- Each biological product, including FOBs, should have a distinct nonproprietary name

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