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# Follow-on Biologics Workshop

*Scientific Issues in  
Assessing the Similarity  
of Follow-on Protein Products*

A New York Academy of Sciences Meeting  
December 12 - 14, 2005  
New York Marriott at the Brooklyn Bridge  
Brooklyn, New York



Co-sponsored with the  
US Food and Drug Administration

In collaboration with the  
National Institute of Standards and Technology

<http://www.nyas.org/follow-on>

# Results

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- **Need battery of orthogonal methods to determine structure, function, and purity**
  - **Primary, Secondary, Tertiary, Quaternary, Aggregates**
  - **Multiple techniques available and should be used**
- **Stress (temp, pH, ionic) to characterize product**
- **Do side-by-side comparisons to the comparator or a common reference standard**
- **Show results of all primary tests and algorithm to determine degree of similarity**

# BIOASSAYS

- Essential for correct and consistent dosing (units; S.A.)
- Principle means for assessing potency
- Correct and comparable **function** confirms higher-order structure of the protein
  - *Tests for 2<sup>e</sup> and 3<sup>e</sup> structure not substitutes for functional bioassay*

# BIOASSAYS AND POTENCY

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- **Multiple bioassays usually necessary, especially if**
  - **Clinical mechanism of action not known**
  - **Protein is pleiotropic**
- **Relevant**

# Manipulation of drug product

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- **Manipulate purchased product for some analyses (*e.g.*, purify, co-formulate)**
- **Effect of formulation/excipients on analyses**
  - **Protein stabilizers, polysorbate, sugar, buffers**
- **Verify validity of the approach and impact of manipulations on the results**

# Major Challenges

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Protein products can be highly characterized.

How much difference from an innovator product is acceptable?

Identify, quantify *critical* product quality attributes to determine which are clinically important