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EGA Position on INN Naming of Biosimilar Products

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Marcy Macdonald
Director, Global Regulatory Affairs
Hospira, Inc

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Introduction

Why are INNs for Biosimilar Products suddenly an Issue?

- There is current discussion whether biosimilar molecules are "similar enough" to originator molecules such that the same INN as the reference product can be used
- There have been attempts to modify the WHO INN nomenclature system to achieve objectives such as drug safety, interchangeability and pharmacovigilance for which it was never intended
- Currently, originator companies are using comparative analytical technology and at times, clinical testing to support changes made to their processes. For the first time, other organizations are using the same techniques to create biosimilar products and to claim the same INN identity to the originator product
- WHO meetings convened in 2006 and 2007

Purpose of INN

Is …	Is Not …
Identification of drug substance	Identification of a medicinal product or its impurities
Nomenclature: means of classifying and cataloguing pharmacological classes	Statement of therapeutic equivalence and/or substitution
Means of communication between health care professionals etc…	Means of managing the practice of medicine
	Means of establishing traceability or for pharmacovigilance

INN is a nomenclature system for a drug substance.
The INN has never been the primary means for managing clinical decisions by physicians, more than one of several components that together make up a robust track and trace system for medicinal products

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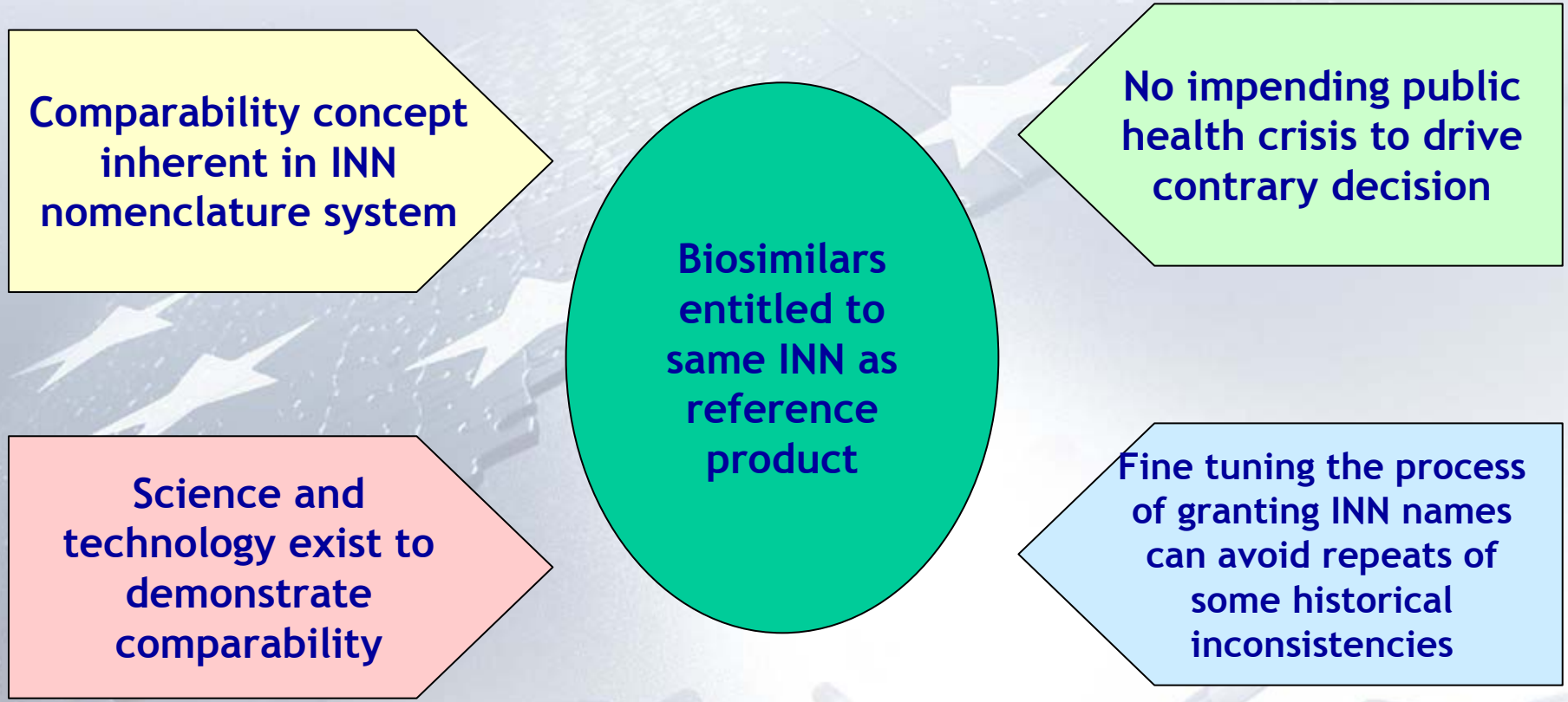
EGA Position and Recommendations

Biosimilars and Originator product: same INN is justified



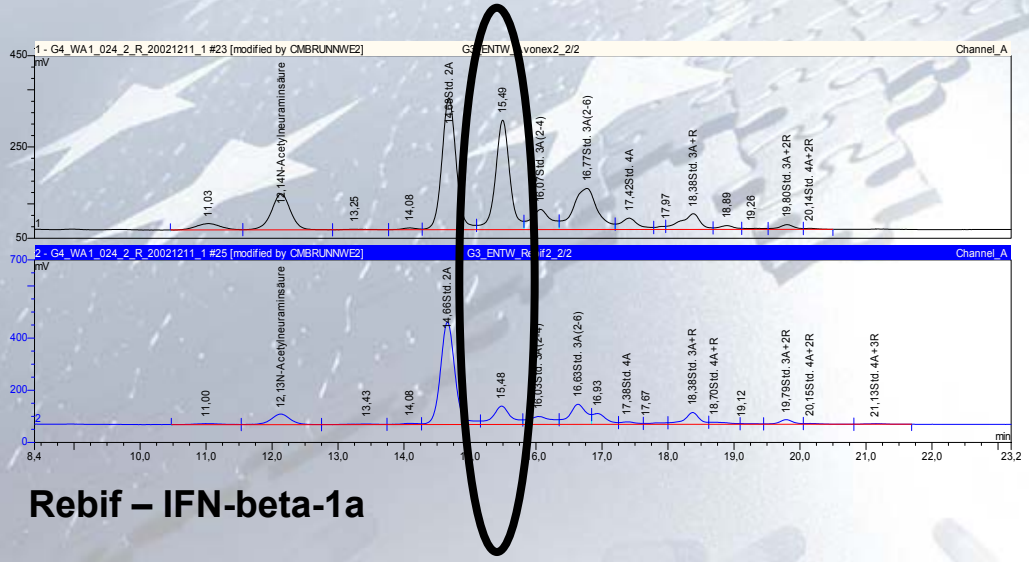
Same INN for Originator Protein Products

- **The same INN for originator protein based products has often been granted by regulators**
  - To multiple manufacturers with no comparability exercises
  - Changes in manufacturing site/process (leading to different glycosylation pattern/same INN)
- **Currently, originator companies are using comparative analytical technology and at times, clinical testing to support changes made to their processes**

Examples: Same INN

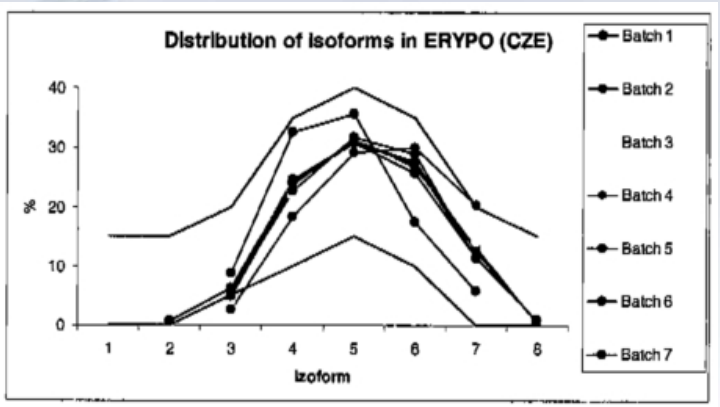
- **Purpose of INN is characterization of active substance, not impurities or finished product**
  - Major ‘safety’ concerns pertaining to impurities – never been a reason for changing INN for small molecules eg paclitaxel extracted from different yew sources by different processes

Avonex – IFN-beta-1a

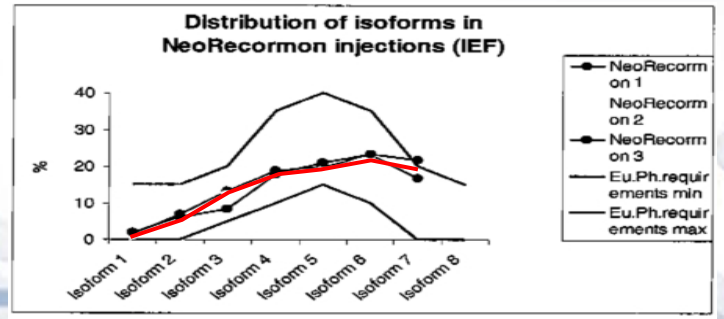


Rebif – IFN-beta-1a

Eprex – EPO alpha

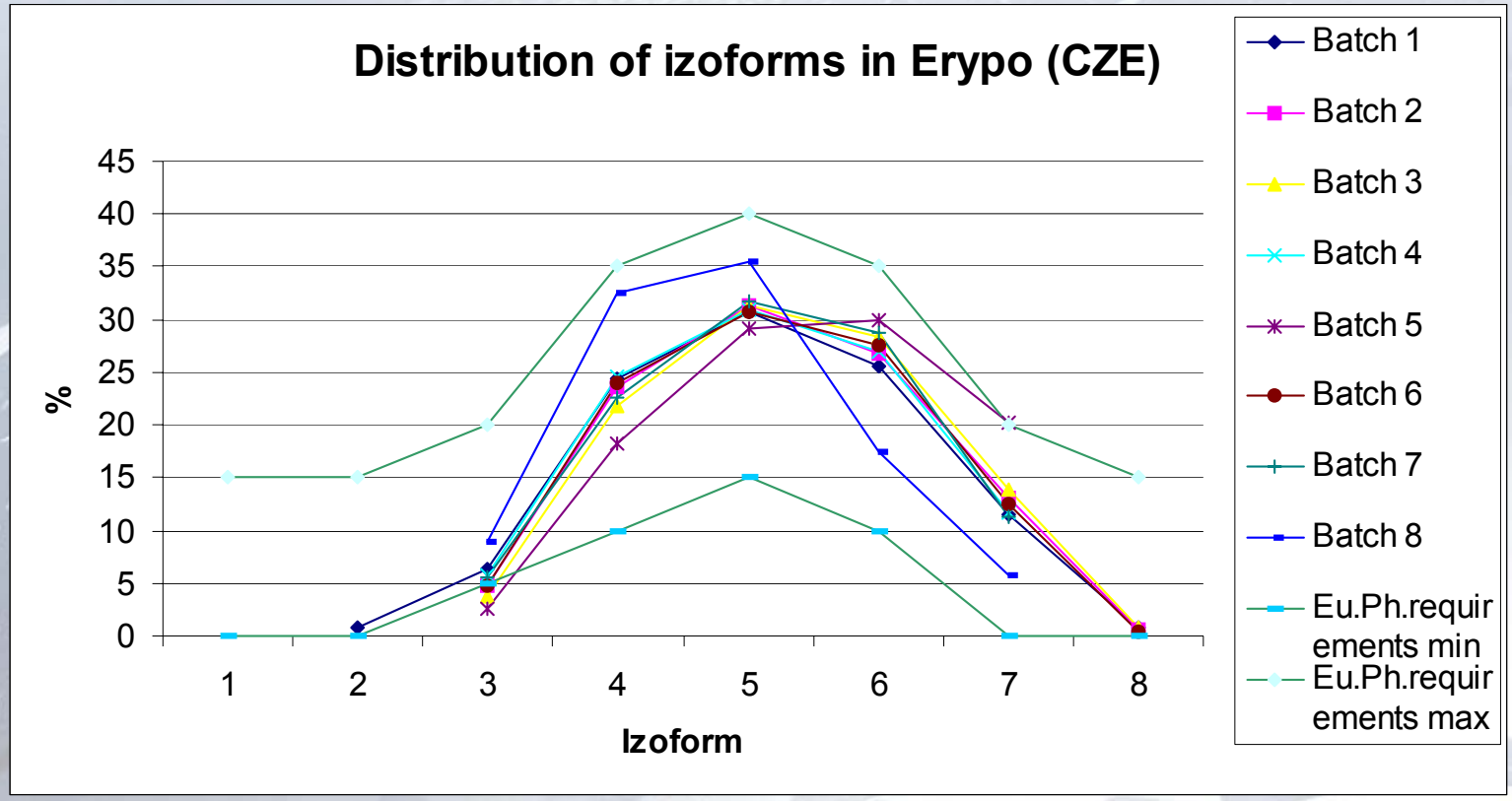


Neorecormon – EPO beta



Different Glycosylation- Same INN

- **Reference product displays variability**
  - INN assigned to reference product actually refers to some sort of average structure



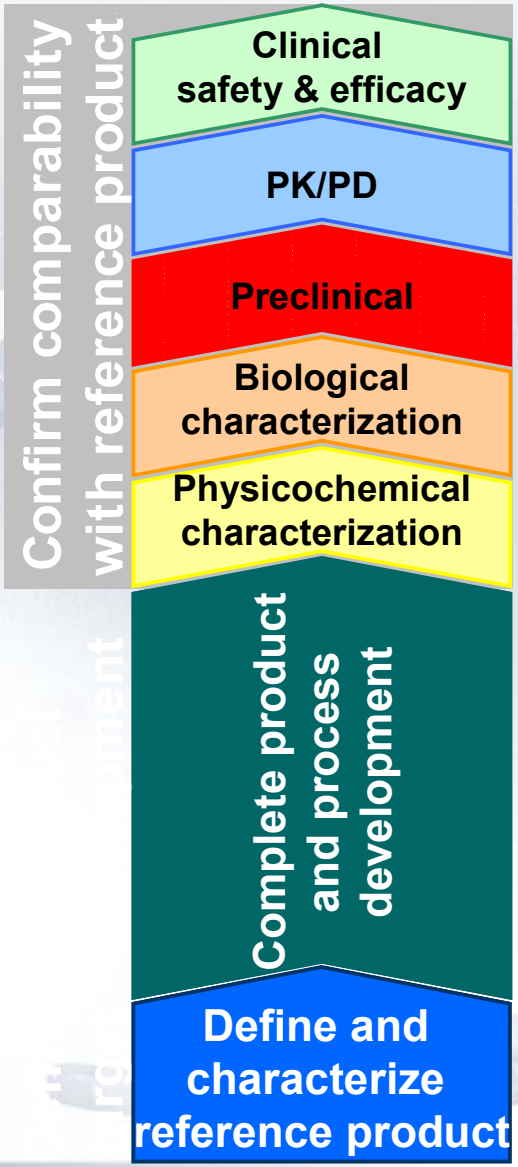
Source: Pliva dd

EU Variations Regulation (Annex II) Supports Same INN

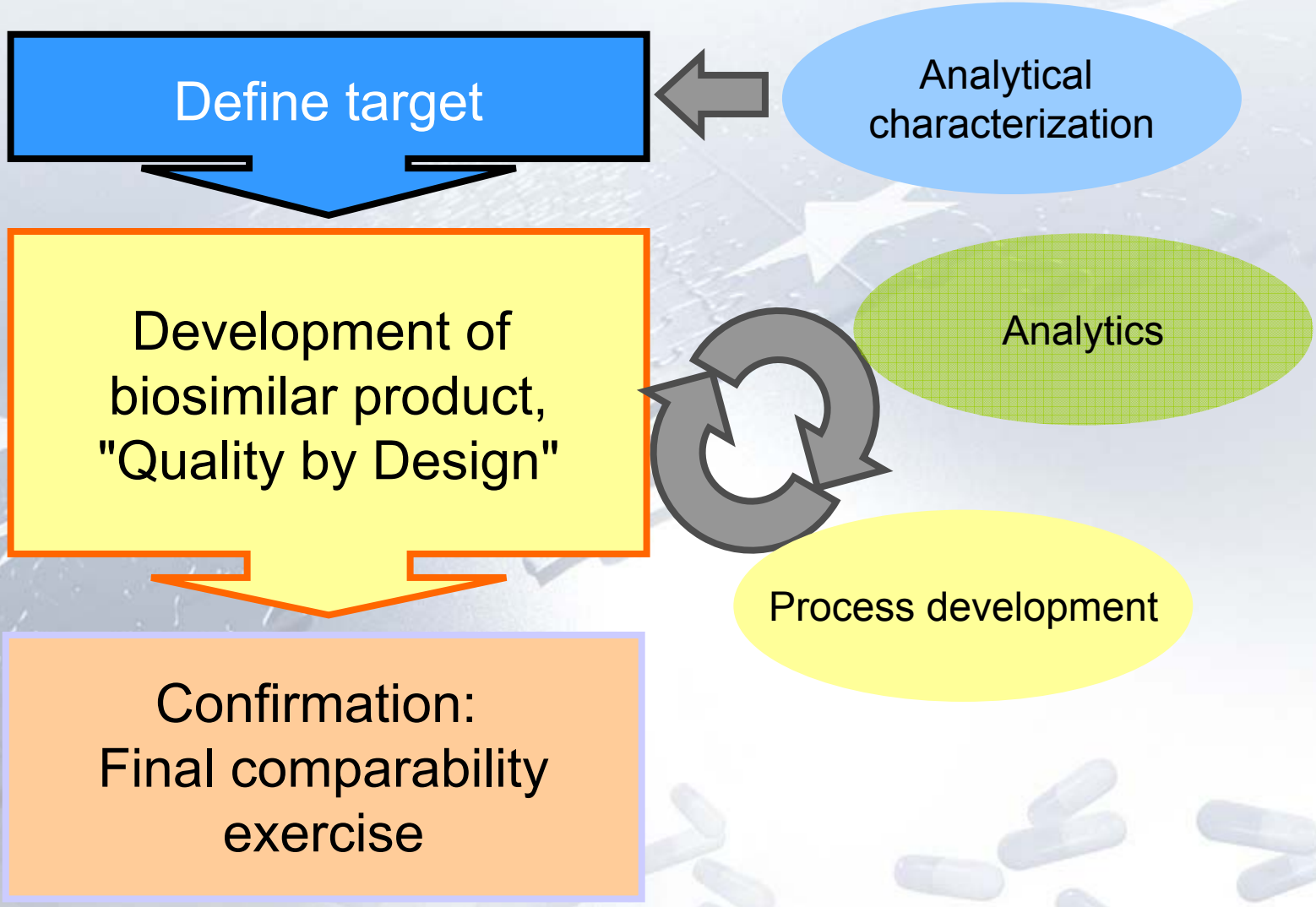
- **Changes to the active substance(s):**
  - (iii) replacement of a biological substance or product of biotechnology with one of a slightly different molecular stucture. Modification of vector used to produce the antigen/source material, including a new master cell bank from a different source where the efficacy/safety characteristics are not significantly different
  - **Same INN is retained**
- Same scientific principles and criteria apply to biosimilar comparability

Biosimilars are Biologics Too

- **The goals of drug development for both originator and biosimilar products are**
  - Safety
  - Efficacy
  - Quality
  - Reproducibility
- **Biosimilars also require**
  - Thorough characterization
  - Extensive comparability to an approved reference product
- The development of a biosimilar product is targeted to match the reference medicinal product through the application of state-of-the-art science and technology in head-to-head studies



Biosimilars:
The Reference Product Defines the Target



How Close is Close Enough? Demonstrating Comparability

- **The criteria for the comparison of the biosimilar candidate and the reference product are based on**
  - Understanding batch-to-batch variability of the reference medicinal product
  - Classification of the process related impurities and/or degradation products
  - Level of understanding in the relevance of subtle differences of safety/efficacy
- **The manufacturing process for the biosimilar is systematically designed to meet the required comparability criteria**

Comparability can be Shown

- Comparability can be demonstrated today applying state-of-the-art technologies
- The decision as to whether a sponsor has demonstrated comparability is a regulatory determination
- If a sponsor fails to demonstrate comparability at the level of quality, safety and efficacy, that product will not be approved or the applicant may be requested to apply for a different INN

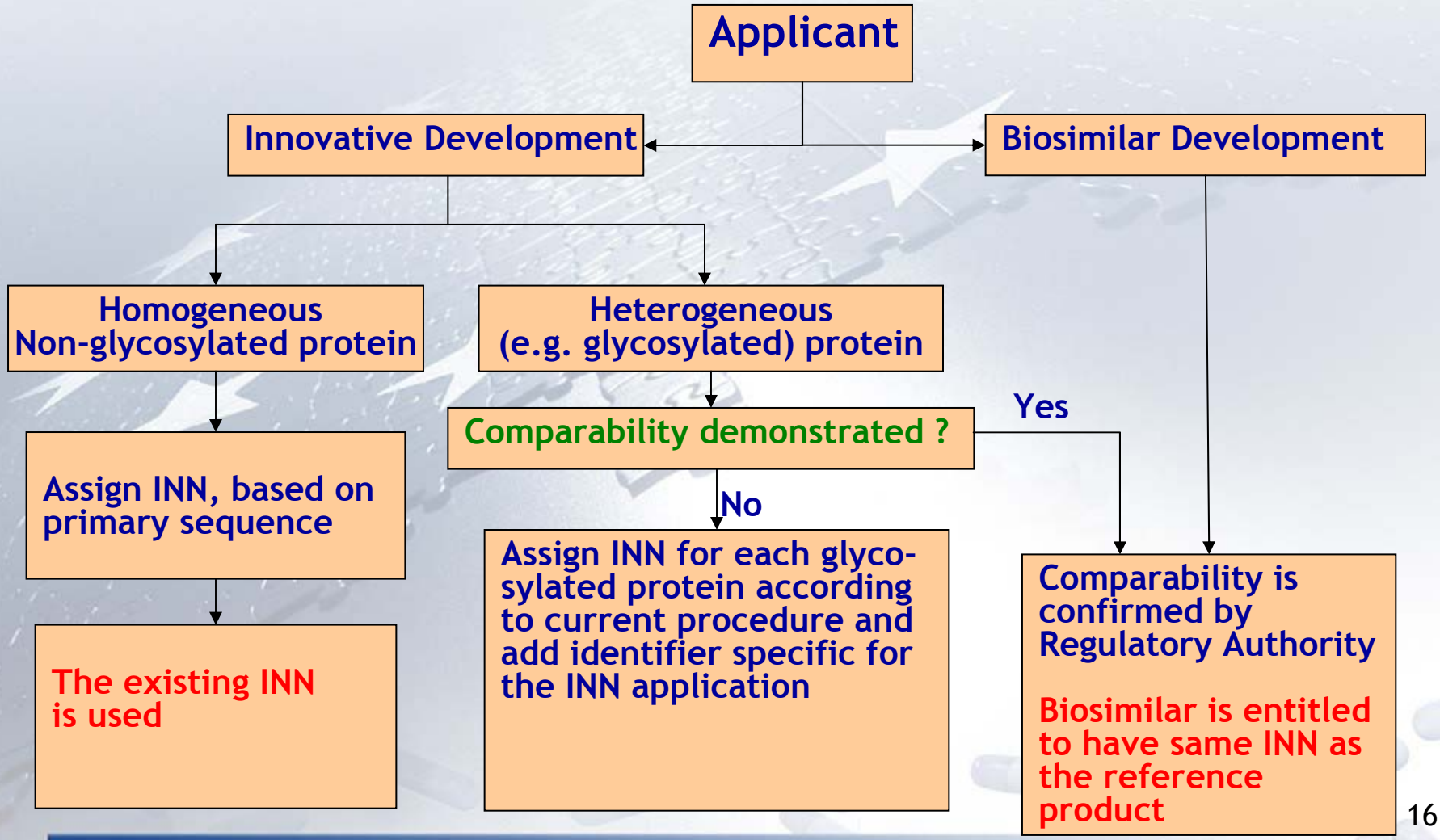
Recommendation to WHO INN Expert Committee

‘Standard WHO process’ has to acknowledge the

concept of comparability

Recommendation:

- Incorporation of Comparability Assessment



Recommendations to WHO

- Establish a WHO working group on regulatory evaluation of therapeutic biological medicines

- WHO Guidance should clearly state that biosimilar INN naming is part of the regulatory process rather than an INN nomenclature issue

Recommendation to EMEA/European Commission

Clarification added to appropriate guidelines that the biosimilar INN is part of the regulatory process rather than an INN nomenclature issue

Summary

- Biosimilars are entirely compatible with WHO's existing INN rules
- There is no basis for expecting a "public health crisis" to emerge from biosimilars carrying the INNs of the originator products
- State-of-the art analytical technologies allow a detailed physicochemical and biological characterization and a sound scientific judgment on comparability
- Regulatory Authorities can decide if comparability has been demonstrated or not:
  - If product is comparable, it is entitled to have the same INN
- WHO does not evaluate comparability data and thus cannot assign an INN for a biosimilar prior to the regulatory authority's decision
- Assessment and approval of biosimilar medicinal products should proceed independently from WHO's naming process

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Thank You