SAHPRA Approach To Biosimilars: *Assessment & Approval*

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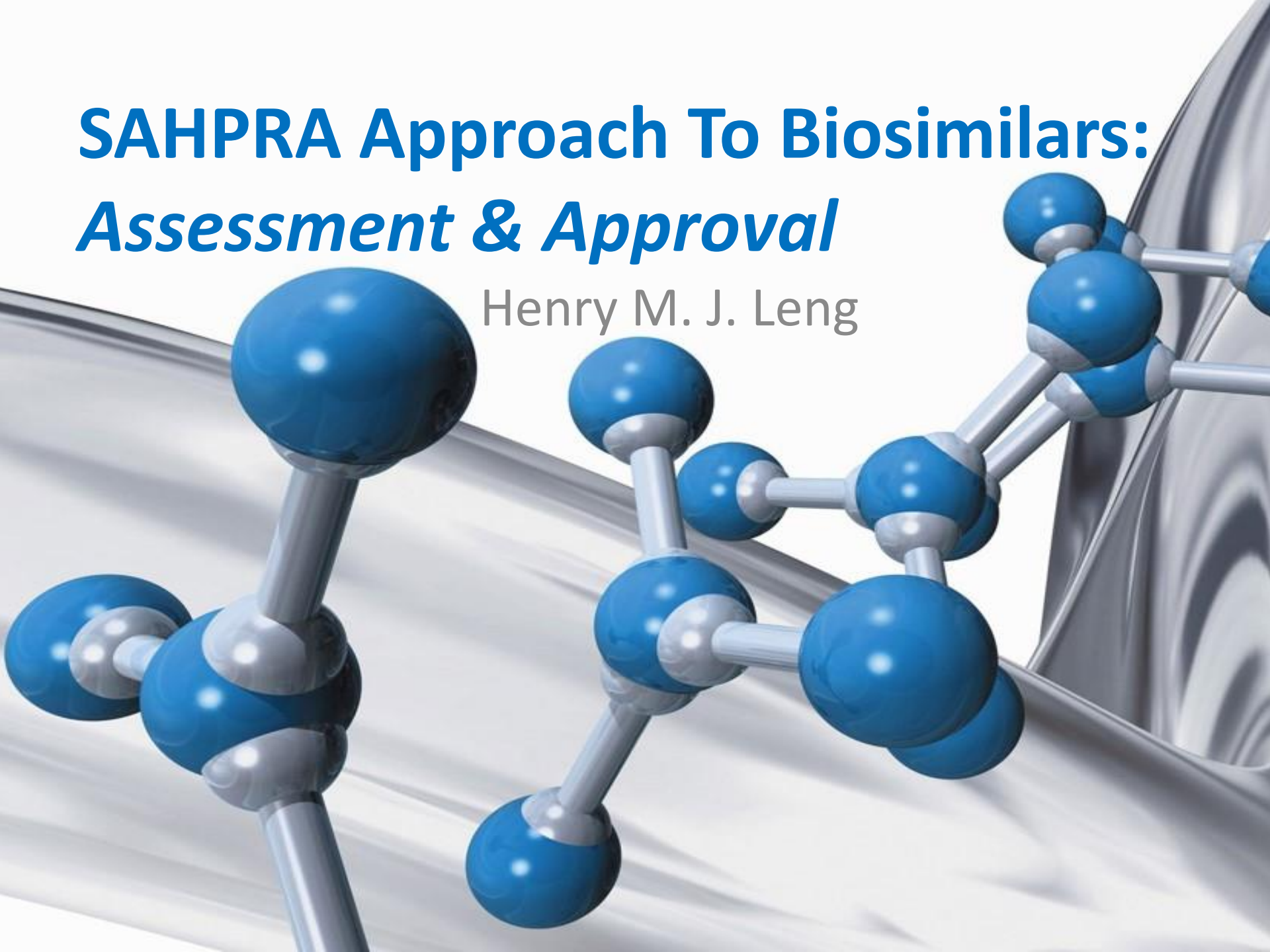

Outline

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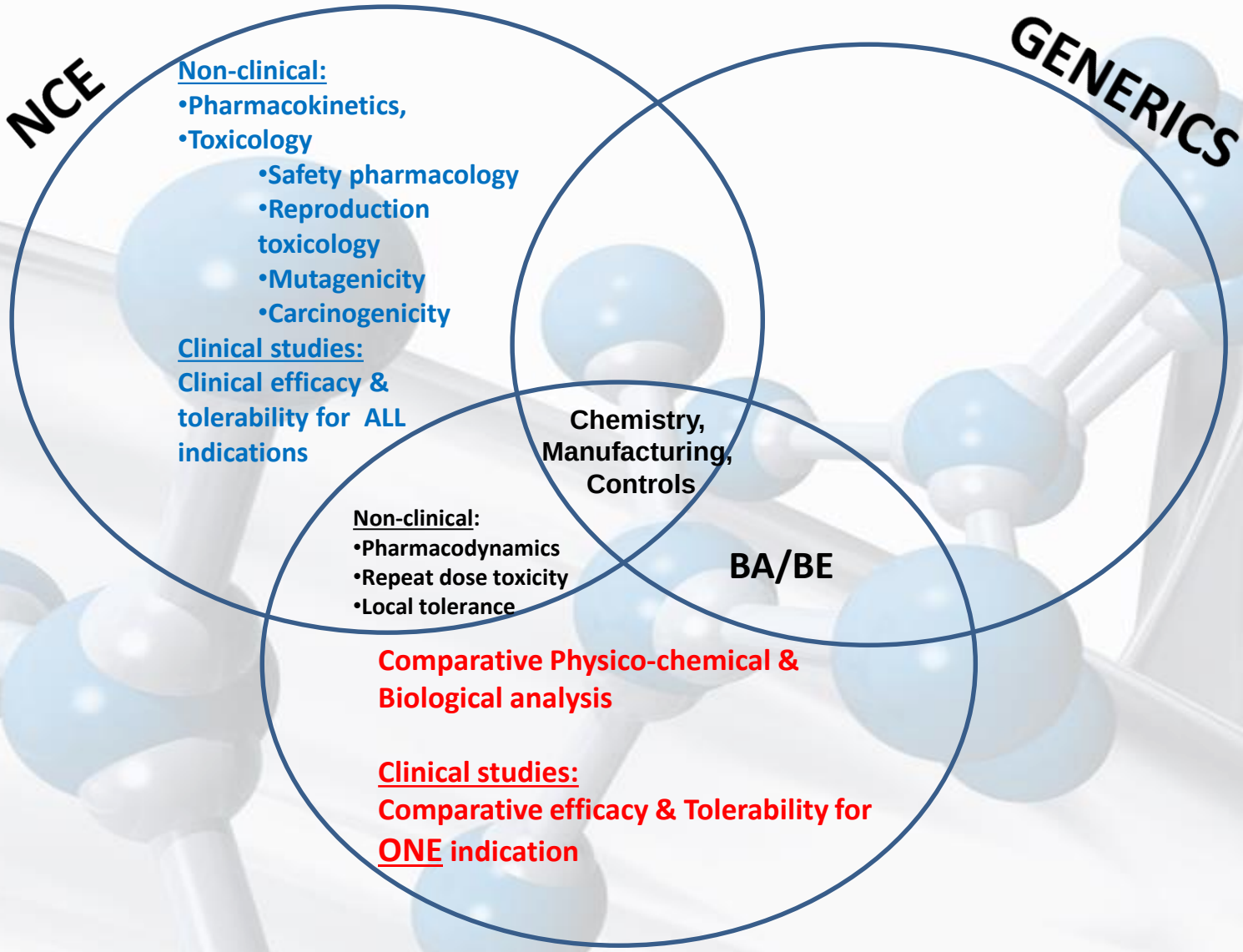
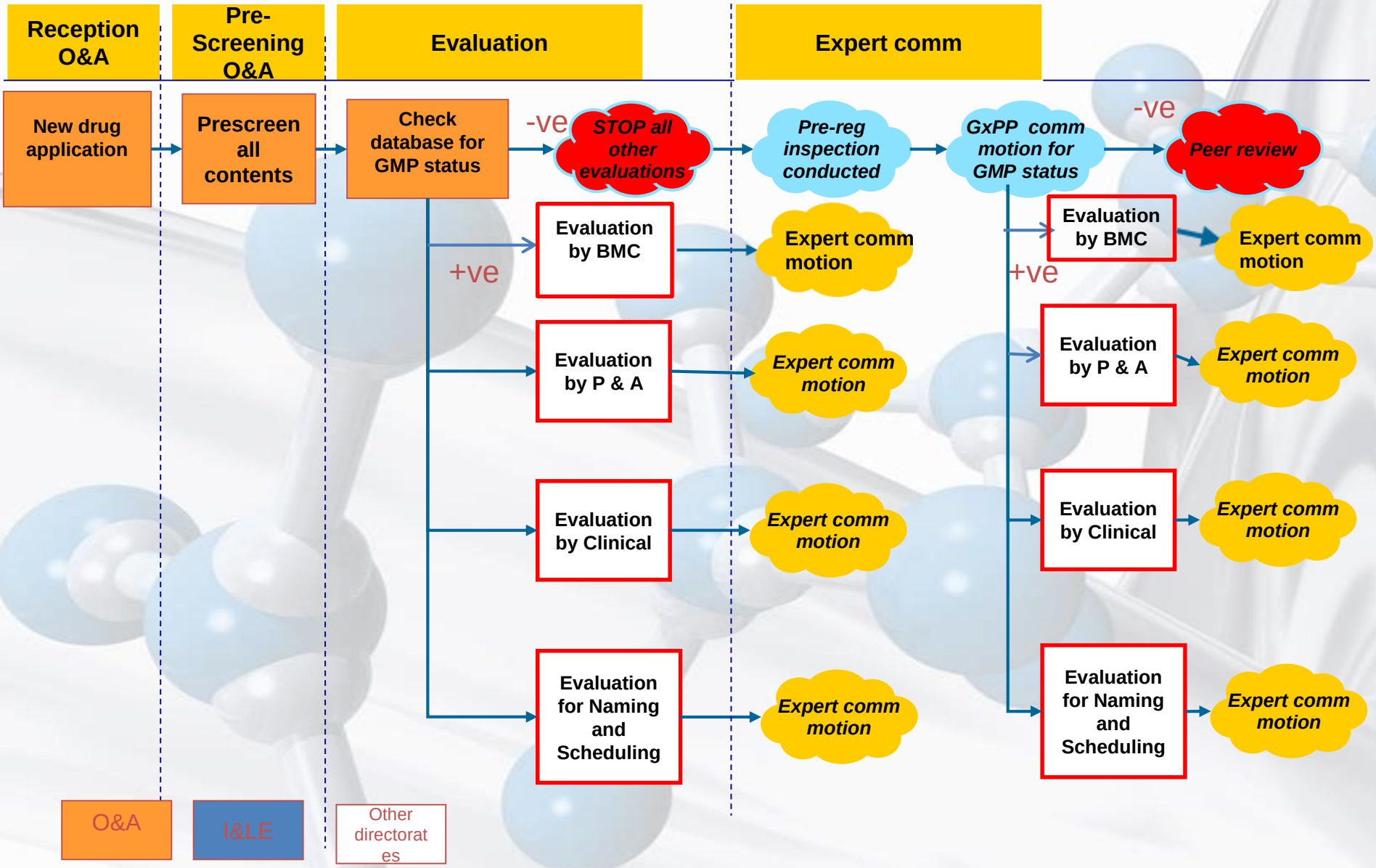
Introduction
Definitions

Innovator	Generic	Biosimilar
The first product that contains a specific active pharmaceutical ingredient (or unique combination of APIs) that have been registered by a medicine regulatory authority on the basis of **full** quality, safety and clinical data, and for which the company has received a **patent** that protects the medicine from market competition for a defined period of time.	A **pharmaceutical** product, intended to be interchangeable with the innovator, manufactured without a license from the **innovator** company and marketed **after** the expiry date of the patent. Because the active ingredient is **identical** to that of the innovator the **clinical performance** of the generic medicine is accepted to be the **same** as that of the innovator. Consequently, the data required to *register a generic* are substantially **less** than that for an innovator.	It is a **biological** medicine that is **highly similar** to the reference/innovator product in terms of quality (purity and potency), safety and efficacy. Any **structural differences** have been **shown** to be clinically inactive.

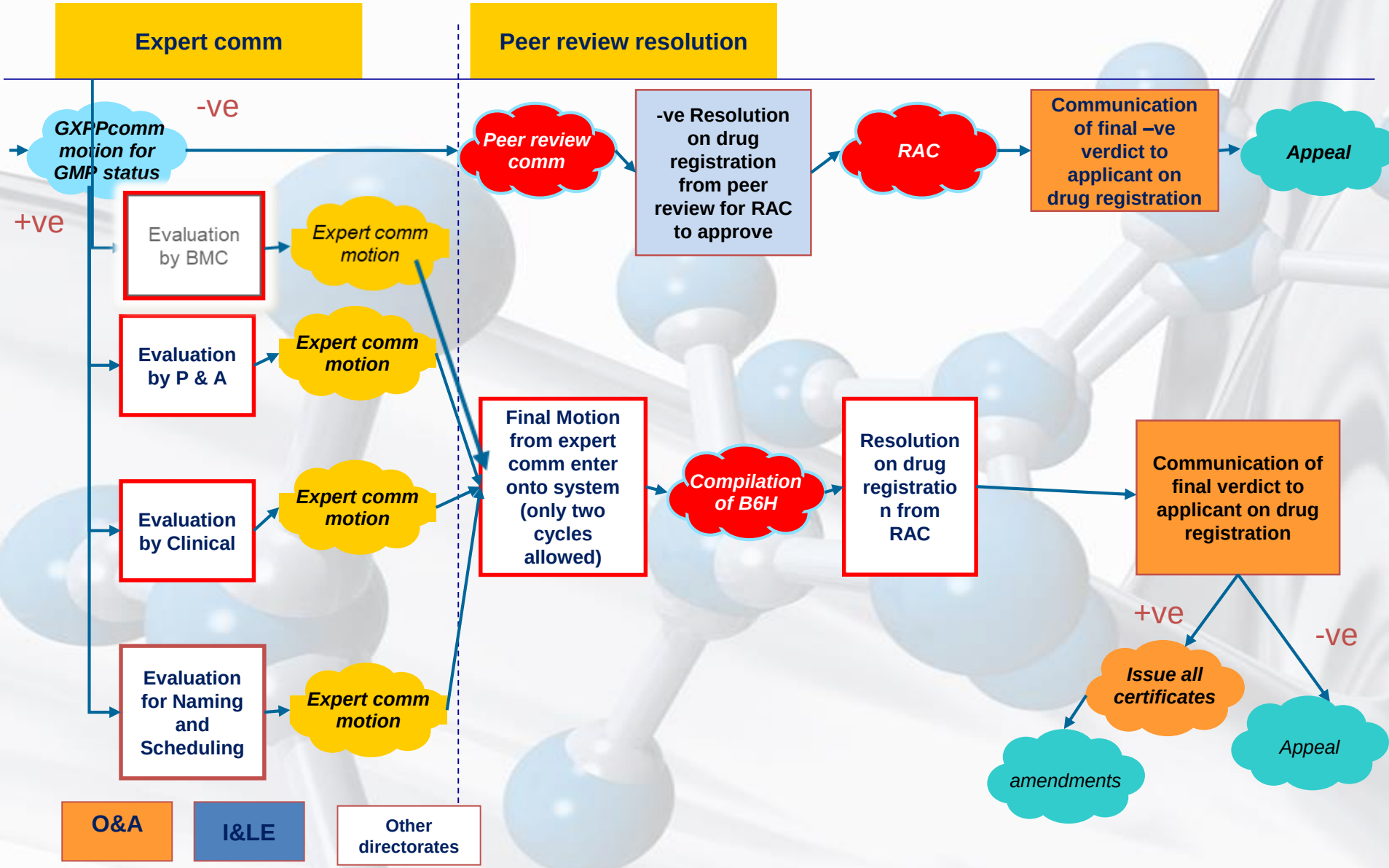
Comparison of Data Requirements for Registration of NCEs, Generics & Biosimilars



Medicine registration Process

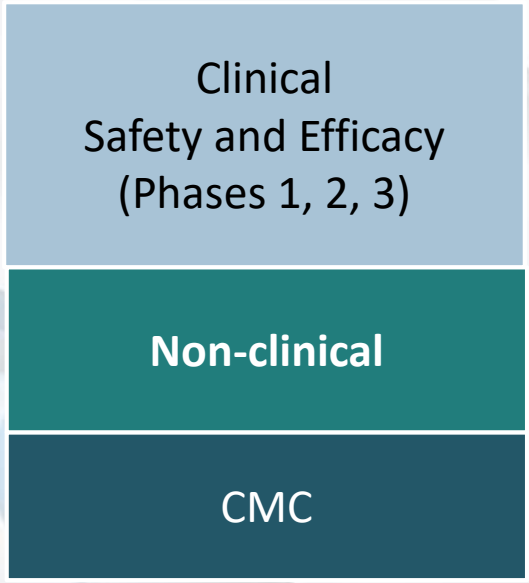


Medicine registration Process

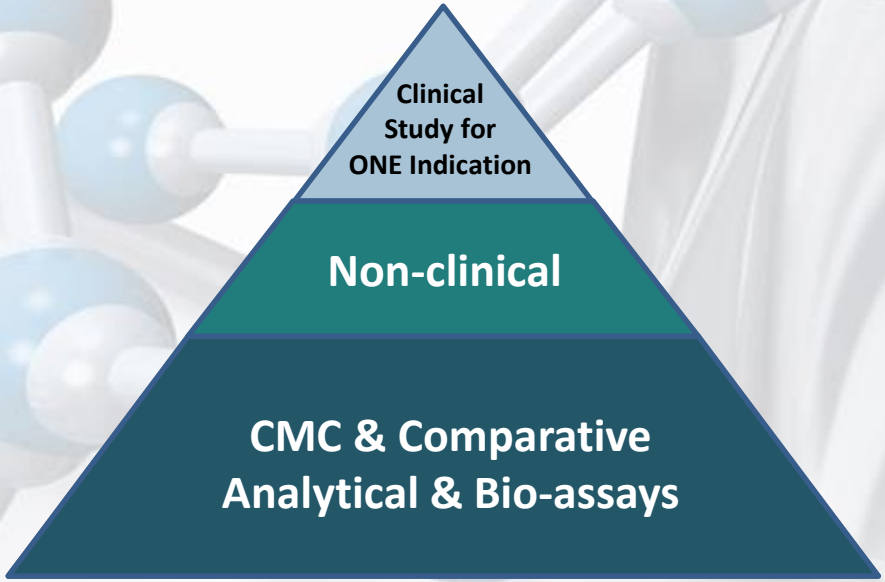


Goals of "Stand-Alone" and Biosimilar Development are Different

"Stand-alone"
Goal: To establish **safety** and **efficacy** of a new product (incl. quality)



"Biosimilar"
Goal: To demonstrate **biosimilarity**



The goal is not to independently establish safety and effectiveness of the Biosimilar product.

This has already been done with the RBP!!

Biosimilarity

It is the demonstration that a candidate SBP is highly similar to a reference biotherapeutic product (RBP) in terms of structure, function, purity and potency and that any structural or functional differences in the SBP, from that of the reference product, are not clinically meaningful.

This implies that biosimilarity is demonstrated at a physico-chemical level first and is then confirmed with non-clinical and clinical studies.

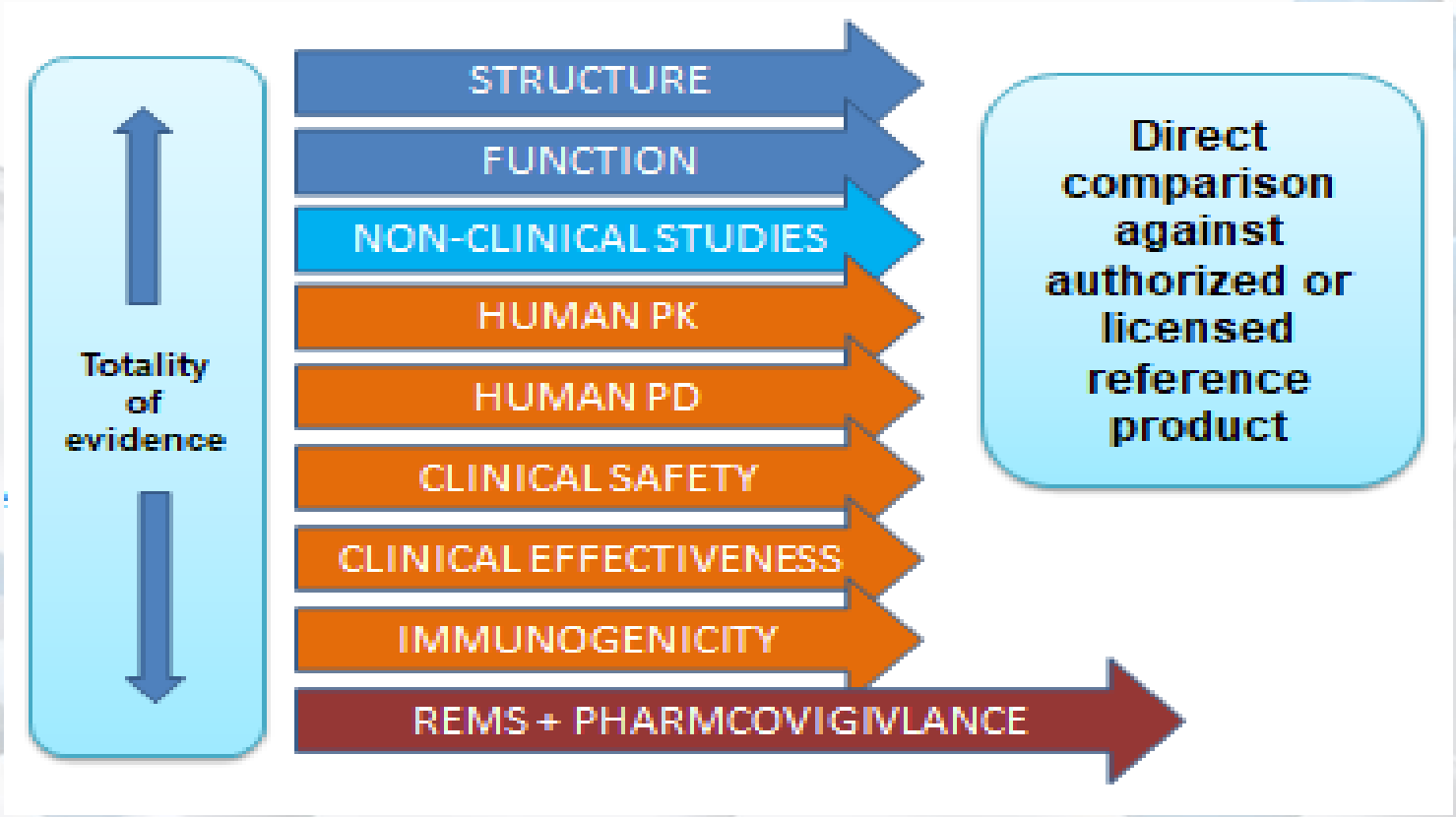
Any uncertainty of biosimilarity at the physico-chemical level between the SBP and RBP must be thoroughly addressed by clinical studies – **the more uncertainty, the greater the amount of clinical data that will be required to confirm biosimilarity .**

Totality of Evidence

- SAHPRA has now realised that the best approach is to consider **ALL** the data – quality, non-clinical and clinical data and especially the comparability data between the SBP and RBP – in the evaluation of biosimilars.
- This means that all of the evidence submitted by an applicant will be considered collectively by **ONE Expert Committee** in order to determine whether a high degree of biosimilarity exists between the Applicant's product and the RBP.
- This approach, commonly referred to as the **Totality of Evidence Approach,** is also used by other regulatory authorities such as the FDA .
- The current fragmented approach in which the Clinical, Biological and Pharmaceutical & Analytical Committees assess a biosimilar application separately and make recommendations based only on the scope of data packages that each committee reviewed, will cease.
- It is highly likely that one or more biosimilar applications that have been rejected by one committee could have been registered if all the data the applicant submitted were taken into consideration before such a decision was made. Usually when one committee rejects, the other committees stop their evaluation of the dossier.
- With the **Totality of Evidence Approach** the non-clinical and clinical data packages will now be assessed at the same time as the quality data to determine if they sufficiently address any uncertainties of high similarity at the structural and functional level – **before** a recommendation is made.

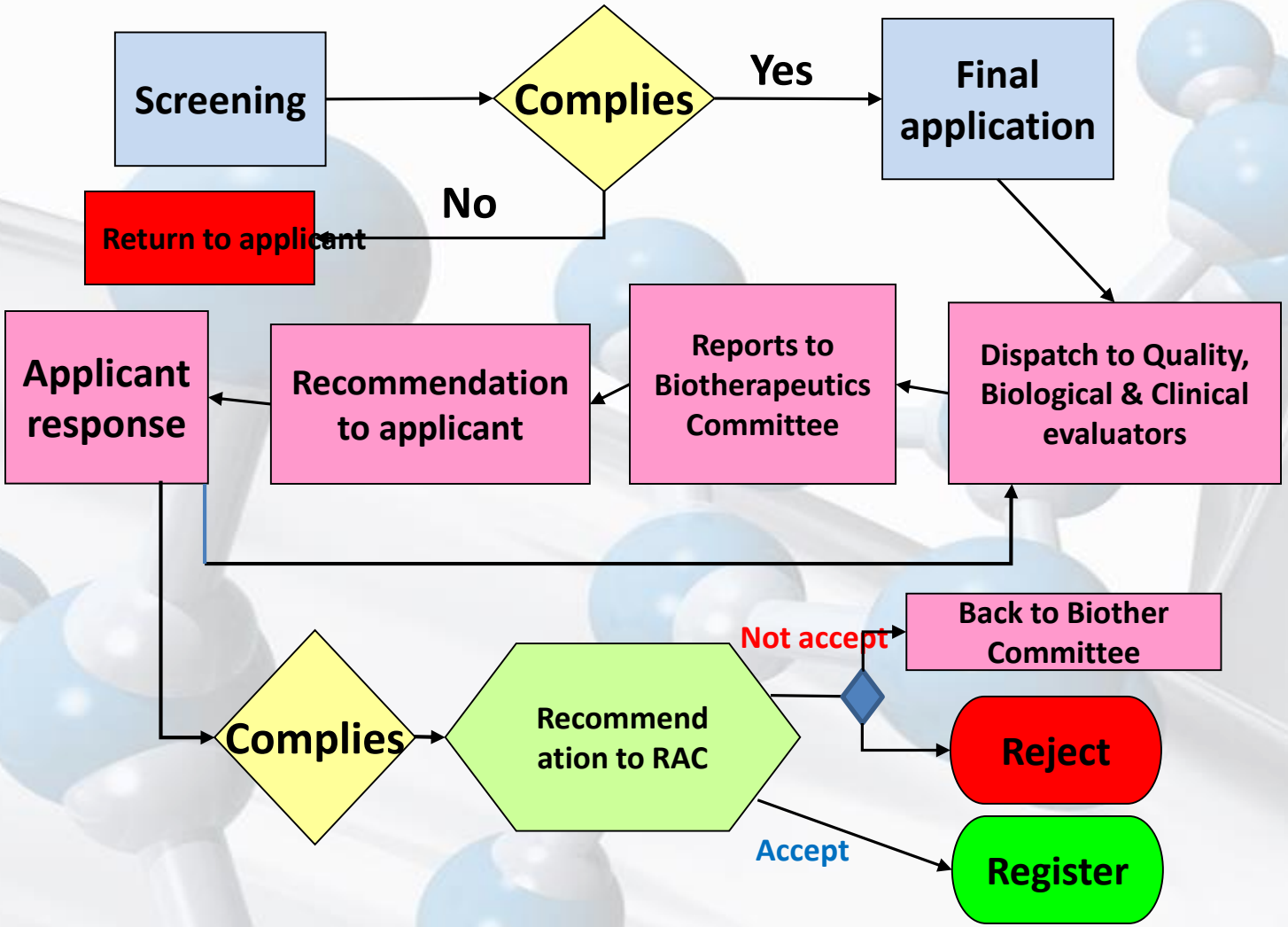
The New Evaluation Model For Biosimilars

Totality of Evidence Approach



PK = pharmacokinetics
PD = pharmacodynamics
REMS = Risk Evaluation and Mitigation Strategy

Registration Process For Biosimilars




Thank You