EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

New Active Substance categorisation and Orphan Similarity

SME workshop: Focus on quality for medicines containing chemical entities

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New Active Substance

Macaroon

(French) Macaron

Background

NtA defines New chemical Active Substance as:

- a chemical substance not previously authorised as a medicinal product in the Union

or

- an isomer, mixture of isomers, a complex or derivative or salt of a chemical substance previously authorised as a medicinal product in the Union but significantly differing in properties with regard to safety and efficacy from that chemical substance previously authorised

Article 10(2)(b) of Directive 2001/83/EC:

"The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy."

Complex or derivative can still be classified as NAS if significant differences in safety and/or efficacy are demonstrated.

Part II, Annex 1 to Directive 2001/83/EC:

"Where the active substance of essentially similar medicinal product contains the **same therapeutic moiety** as the original authorised product associated with a different salt/ester complex/derivative evidence that there is no change in the pharmaco-kinetics of the moiety, pharmacodynamics and/or in toxicity which could change the safety/efficacy profile shall be demonstrated. Should this not to be the case, the association shall be considered as a new active substance."

NAS claim assessment

The spirit of the legislation is to encourage innovation whilst preventing from gaining rewards on the back of another's efforts.

Evaluation of the NAS status is envisaged if there is claim from the applicant.

Assessment of the claim is part of the evaluation procedure. Outcome is reflected in the CHMP AR and Opinion.

Confirmation of NAS status is used in the determination of data protection.

Challenges

How far do we go with assessment? (in case of substances falling under the second bullet point of the NtA definition)

Salts, esters, complexes, derivatives containing authorised therapeutic moiety – NAS status cannot be justified only on quality grounds. Additional studies such as PK/PD and/or toxicological data may be needed to support the claim, i.e. demonstrating significant differences in terms of efficacy and safety.

The common denominator in terms isomer, derivative, salt, complex, ester/ether is that all could potentially deliver exactly the **same therapeutic moiety.**

Derivatives

Concept of authorised therapeutic moiety versus derivatives

- where the original substance *in vivo* will be derived from the new applied substance and patients are exposed to the original substance (the applied substance is a prodrug).
- where the new applied substance is the same substance as the patients where exposed to when treated with the original substance. i.e. where the new substance is identical to what is in vivo derived from the original substance (the applied substance is a metabolite).

Complexes

Concept of authorised therapeutic moiety versus different types of complexes

- complexes intended to release an active substance entrapped by the complex, e.g. piroxicam betadex which will release piroxicam
- complexes not intended to release an active substance to the circulation but elsewhere in the body, e.g. complex consisting of iron surrounded by a carbohydrate layer.

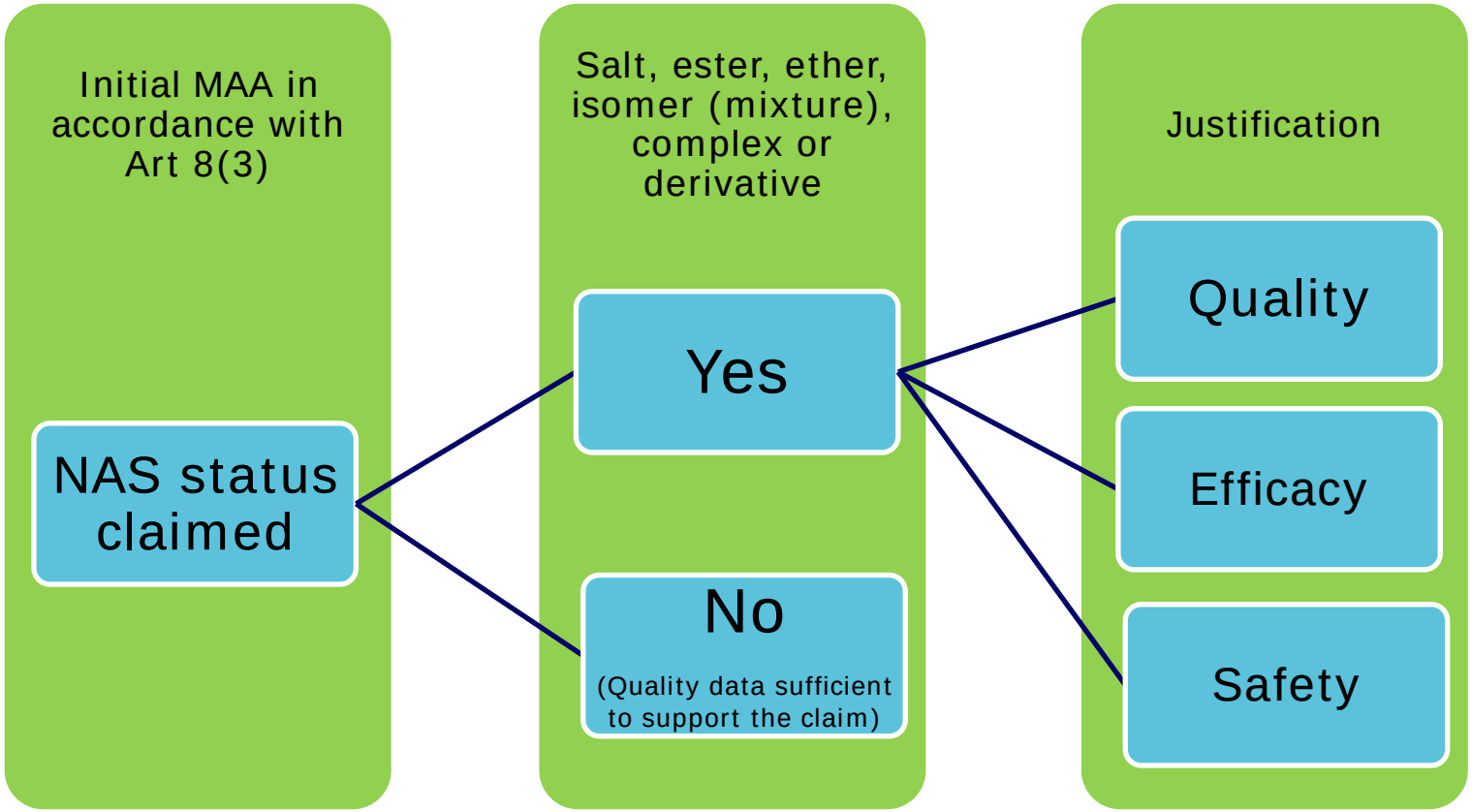
Assessment of the claim

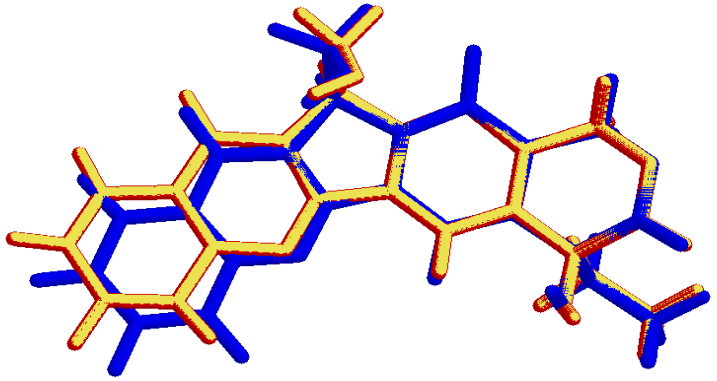
It is up to the applicant to provide sufficient evidence supporting the claim

The CHMP will assess only the data submitted in support of the claim, i.e. assessors will not actively look in public domain for relevant information

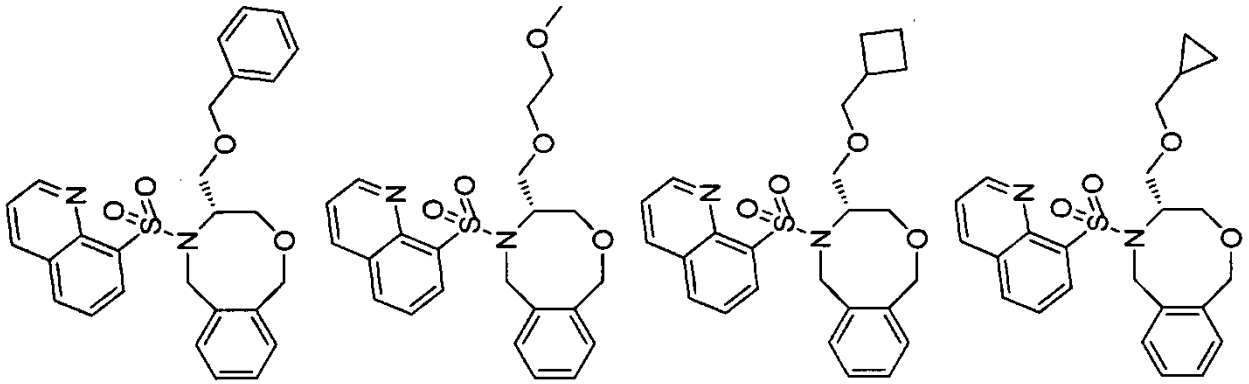
If information provided is considered insufficient, applicants may be requested to provide further evidence – possibilitv for LoQ/LoOI.

NAS assessment





Orphan similarity



Regulation EC No 141/2000 on orphan medicinal products

Art 8: Market exclusivity

1. “Where a marketing authorization in respect of an orphan medicinal product is granted (…) the Community and the Member States shall not, for a period of 10 years, accept another application for a marketing authorisation, or grant a marketing authorisation or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect to a **similar** medicinal product.”

4. “The Commission shall adopt definitions of ‘**similar medicinal product**’ and ‘**clinical superiority**’ (…)”

Regulation EC 847/2000 - Similarity

Art. 3 Definitions

b: "**Similar medicinal product**' means a medicinal product containing a ***similar active substance*** of substances as contained in a currently authorised Orphan Medicinal Product and which is intended for the ***same therapeutic indication***

c: **"Similar active substance'** means an identical active substance, or an active substance with the ***same principal molecular structural features*** but not necessarily all of the same molecular structural features) **and** which ***acts via the same mechanism***.

Similarity assessment principles

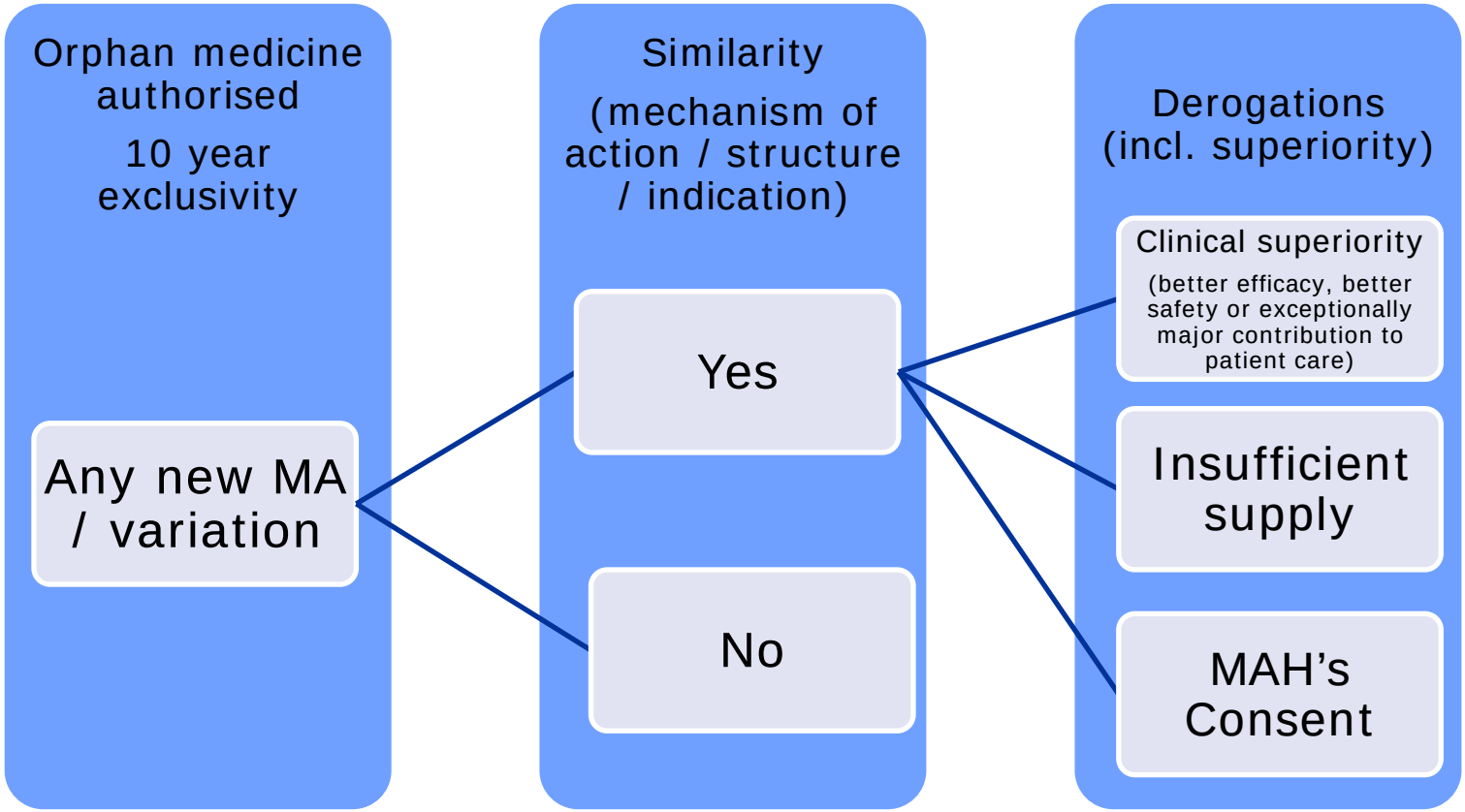
Based on definitions set out in article 3 of Regulation 847/2000, similarity assessment takes into consideration:

1) Principal molecular structural features

2) Mechanism of action

3) Therapeutic indication

Similarity assessment



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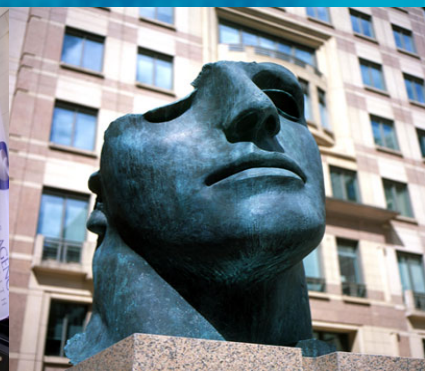

Thank you for your attention!

Questions?