

## European Commission's Update of Guideline on Duplicate Marketing Authorizations to Cover Biosimilars

On May 18, 2018, the European Commission (“Commission”) launched a public consultation on “Duplicate Marketing Authorisation for Biological Medicinal Products” (“Consultation”) in relation to updating its “Note on Handling of Duplicate Marketing Authorisation Applications” (“[Note on Duplicate MAs](#)”).<sup>1</sup> The Commission wants to learn about the potential impact of duplicate marketing authorizations (“MAs”) for “friendly” biosimilars, i.e., biosimilars developed by the innovators of the reference biological medicinal products. Comments are due by September 10, 2018.

Article 82(1) of Regulation 726/2004 expressly prohibited more than one MA for centrally authorized medicinal products, with two exceptions: (i) when there are objective verifiable reasons relating to public health regarding the availability of medicinal products to healthcare professionals and/or patients (“public health”) or (ii) for co-marketing. The prohibition of duplicate MAs and its exceptions apply to both chemical and biological medicinal products. The Commission is entrusted with applying the exceptions and authorizing duplicate MAs. The Note on Duplicate MAs concerns the application of Article 82(1) – see below.

The Note on Duplicate MAs gives friendly generics as an example of the public health exception. While friendly biosimilars should logically benefit from this exception as well, the Commission seems to have found that they should not because they may not increase the availability of medicinal products. If this finding is confirmed by the public consultation, obtaining duplicate MAs for friendly biosimilars would be more difficult than for friendly generics.

### Article 82(1) of Regulation 726/2004

The objective of the centralized marketing authorization procedure is to have, for each medicinal product, one authorization and one name valid throughout the European Union. Article 82(1), first indent of Regulation 726/2004, thus limits to one the number of MAs that may be granted to medicinal products authorized through the centralized marketing authorization procedure.

The second indent, however, empowers the Commission to authorize more than one MA for a specific medicinal product “*when there are objective verifiable reasons relating to public health regarding the availability of medicinal products to health-care professionals and/or patients, or for co-marketing reasons.*”

### Commission's Note on Duplicate Marketing Authorizations

For a long time, companies were basically left without guidance with regard to duplicate MAs. A few explanations had been given by the European Medicines Agency on the procedure to follow for requesting the Commission's authorization, but the criteria for obtaining such authorization remained unclear. The Commission was deciding on a case-by-case basis, and the grounds for allowing or refusing duplicate MAs were not publicly disclosed. On March 30, 2010, the Commission finally issued the Note on Duplicate MAs, which it updated about one year later.

**Basic Principles and Conditions.** Before defining the scope of application of Article 82(1) and detailing the authorization criteria, the Commission “sets the scene” by stressing the basic principles, i.e., (i) assessment of each request on a case-by-case basis,

<sup>1</sup> [https://ec.europa.eu/health/sites/health/files/files/latest\\_news/2011\\_09\\_duplicates\\_note\\_upd\\_01.pdf](https://ec.europa.eu/health/sites/health/files/files/latest_news/2011_09_duplicates_note_upd_01.pdf)

taking into account the factual circumstances of each case; (ii) restrictive interpretation of Article 82(1), second indent, because it constitutes an exception from the general rule of a single MA per medicinal product and per MA holder; and (iii) importance of the objectives of preserving public health and harmonizing centrally authorized products.

***Scope of Application – Same Medicinal Product and Same Applicant.*** Article 82(1), second indent, only concerns an MA application (“MAA”) submitted by an applicant regarding a medicinal product for which he was already granted an MA under the centralized procedure. This provision thus concerns a “same medicinal product” (material scope) and a “same applicant” (personal scope).

“*Same Medicinal Product*” – For determining whether the medicinal product is the “same,” the Commission refers to:

- its 1998 Communication on the Community marketing authorization procedures for medicinal products:<sup>2</sup> any medicinal products with the same qualitative and quantitative composition in active substance (i.e., the same strength) and the same pharmaceutical form are to be considered as the same relevant product; and
- Article 10(2)(b) of Directive 2001/83/CE: the different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance are to be considered to be the same active substance unless they differ significantly in properties with regard to safety and/or efficacy.

This means that an MAA for the following medicinal products does not require a prior Commission authorization under Article 82(1): a medicinal product with a different active substance; a medicinal product with a different salt of an approved active substance that differs significantly in properties regarding safety or efficacy; a medicinal product with different excipients resulting in significant differences with regard to safety or efficacy; or a medicinal product with a different manufacturer or manufacturing site resulting in its characteristics (notably in the case of biological products) leading to significant differences regarding safety or efficacy.

On the other hand, a duplicate MA for a different therapeutic indication requires a prior Commission authorization even in the case of an orphan indication for a medicinal product that is not orphan (i.e., in cases where a separate MA is mandatory). So also do MAAs for generic medicinal products, hybrid medicinal products or “informed consent” medicinal products. The key criterion is whether both MAAs relate to a medicinal product with the same qualitative and quantitative composition in active substances and the same pharmaceutical form.

A duplicate MA may contain less therapeutic indications or pharmaceutical forms than the original MA when this is necessary to market the product in EU member states where a specific indication or pharmaceutical form is protected by patent law. However, the applicant must commit to extend the indication(s)/pharmaceutical form(s) of the duplicate MA or to withdraw the duplicate MA once the remaining patent protection expires, and the commitment letter should be provided with the MAA dossier. The harmonization of summary of product characteristics (“SmPCs”) across the European Union being one of the basic pillars of the centralized procedure, applicants of duplicate MAs should not market two products with different indications/strengths/pharmaceutical forms in the same country.

“*Same applicant*” – For determining whether an applicant is the same, the Commission applies again the 1998 Communication on the Community marketing authorization procedures for medicinal products, which defines “same entity” as a company that belongs to the same group of companies or as a company that has entered into a license agreement or has otherwise agreed to the marketing of the medicinal product.

By way of examples, the Commission stresses that Article 82(1) does not apply where an applicant is an independent company that entered into a license agreement, purchase agreement or data agreement with the MA holder of the product but not for the placing of that product on the market.

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<sup>2</sup> 1998 OJ C229/4.

**Criteria for Duplicate MA.** Article 82(1) provides for a derogation from the general rule of a single MA under two limited circumstances: public health or co-marketing.

**Public Health** – The Commission considers that arguments that are linked to public health but not to the availability of the product cannot be considered. Moreover, having more than one MA for the same product cannot, per se, be considered to increase availability.

The Note on Duplicate MAs gave two examples that both concern generics:

- According to the Commission, the most common case in which a duplicate is justified on public health grounds is when a therapeutic indication or pharmaceutical form in the SmPC of the original MA is patent protected in one or more member states. The second example is the introduction of the first friendly generic product, as the first entry of a generic to the market usually increases accessibility. Any subsequent MAA of the innovator would need to be justified by further arguments and could not be based solely on the fact that the second MA for the same product concerns a generic. The Note on Duplicate MA does not indicate whether the justification holds in cases where the “friendly generic” is not the first generic on the market or whether the MAA for the friendly generic must be based on Article 10 rather than Article 10(3) or Article 10(c).

On the other hand, neither pricing and reimbursement considerations nor classification (prescription/ non-prescription) considerations nor considerations based on national legislation deemed incompatible with EC law (e.g., names) are considered as relevant.

**Co-Marketing** – Co-marketing refers to an agreement between two parties to commercialize a specific medical product under different trademarks. Evidence of the co-marketing (contract or letter of agreement between the companies) must be provided to the Commission.

The Commission indicates that co-marketing requires the existence of two parties so that a request for a duplicate MA cannot be accepted when the two marketing entities belong to the same company group or if the co-marketing partners are already co-marketing (together) the product in the European Union. This exclusion, however, has no legal basis. Article 82(1) being only triggered by an MAA by the same company, and co-marketing being an express ground for parallel MAs, co-marketing should logically be accepted intra-group.

Co-marketing can be limited to one or more member states or cover the entire European Union, but it must not lead to partition of the internal market.

Update to the Note on Duplicate MA – Biosimilars as “First Generics”

The rules on duplicate MA also apply to biological medicinal products. The Commission, however, has identified potential issues related to the granting of a duplicate MA for a “first biosimilar.” With regard to biological medicines, a duplicate MA may, but does not always, improve the availability of a specific medicinal product due to the potential impact of the friendly biosimilar on the biosimilar market (including anticompetitive effects) and on the number of treatment options for patients. Accordingly, the Commission wants to gain knowledge on this potential impact directly from the stakeholders.

As a side comment, we note that the Commission expressly adds that a request for authorization of a duplicate MAA “*need[s] to be properly substantiated and based on sound evidence.*”

Stakeholders have until September 10, 2018 to submit their comments to the Commission. Until then, requests for duplicate MAs for biologicals will be assessed on a case-by-case basis, taking into account the evidence provided by the applicant company.

## Comments

The Commission does not expect comments other than information on the potential impact of a first biosimilar on the availability of the biological medicinal product and number of treatment options. Yet, other comments can always be made if they are relevant.

The Commission allegedly adopted the Note on Duplicate MA *“in order to ensure a smooth application of Article 82(1) of the Regulation and to create more transparency and predictability for the stakeholders concerned.”*

Three modifications to the updated Note on Duplicate MA can be suggested that would contribute to transparency and predictability.

First, the updated wording proposed by the Commission does not provide examples of situations where a friendly biosimilar does/does not increase the availability of the biological product. Such examples however would be very useful for transparency and predictability purposes.

Second, a section on the authorization procedure could be added in the Note on Duplicate MAs.

However, no guideline or the like has been adopted with regard to the authorization procedure.

Companies know that they have to obtain the Commission’s authorization before submitting the MAA dossier for a duplicate MA to the EMA, but they do not know to whom send the request, how long it takes to obtain such a decision, etc.

Furthermore, the Commission’s authorizations are not publicly available, which means that companies cannot determine the justifications that have been accepted or rejected by the Commission for authorizing a duplicate MA. Publication of the Commission’s reasoned decisions would also increase transparency and predictability.

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