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## **HANDLING OF DUPLICATE MARKETING AUTHORISATION APPLICATIONS**

The requests for duplicate marketing authorisations under Article 82(1) of Regulation (EC) No 726/2004 have increased steadily and this is a trend that is likely to continue in the future as the use of the centralised procedure rises.

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, a document on the criteria applied regarding the handling of duplicate marketing authorisation applications was made public by the Commission services in March 2010.

That publication has made a very important contribution to transparency and predictability when dealing with requests for authorisations to submit a duplicate marketing authorisation application in the application of Article 82(1) of the Regulation.

The Commission services consider that it is important to maintain the transparency effort and therefore will continue using that document as an instrument to address new questions of interpretation regarding Article 82(1).

The history of the document in Annex II facilitates the identification of the updates.

### **I. General considerations**

A marketing authorisation granted under Regulation 726/2004 empowers the holder to market the medicinal product in the entire EU. In the light of the unique nature and EU dimension of marketing authorisations granted under the centralised procedure, Regulation 726/2004 requires that a single name is used to identify a medicinal product authorised under the centralised procedure.<sup>1</sup> In addition, the Regulation limits the ability of applicants/holders to obtain more than one marketing authorisation per medicinal product (hereafter, "duplicate marketing authorisations"). In particular, Article 82(1) of Directive Regulation 726/2004 provides that

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<sup>1</sup> Article 6(1) of Regulation 726/2004.

*"Only one authorisation may be granted to an applicant for a specific medicinal product.*

*However, the Commission shall authorise the same applicant to submit more than one application to the Agency for that 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."*

The assessment whether the conditions of Article 82(1) are met must be done case-by-case, having regard to the facts of each application. Nevertheless, prospective applicants should note that the second subparagraph of Article 82(1) constitutes a derogation from the general rule contained in the first subparagraph and should be therefore subject to a restrictive interpretation. In addition, the overall objectives of preserving public health and the harmonisation of centrally authorised products must also play an important role.

## **II. Marketing authorisation applications under the scope of Article 82(1).**

Article 82(1) of Regulation 726/2004 concerns marketing authorisation applications submitted by an applicant regarding a medicinal product in respect of which a marketing authorisation has already been granted to him under the centralised procedure.

A marketing authorisation for a medicinal product that is different to a previously authorised product is outside the scope of Article 82(1) and, therefore, cannot be considered as a duplicate. This means that any such application could not benefit from any fee reduction that may be applicable for duplicates but, in turn, it would not need to be assessed under Article 82(1).

In contrast, a marketing authorisation application for a medicinal product that has already been granted a marketing authorisation under the centralised procedure falls under Article 82(1) if the applicant is the same that holds that marketing authorisation. This application could qualify for a fee reduction that may be applicable for duplicates but, in turn, it could only be granted if the conditions under Article 82(1) are met.

To assess whether an application refers to a specific medicinal product that has already been granted a marketing authorisation, and therefore whether an application for a marketing authorisation falls under the scope of Article 82(1), the composition in active substance(s) and the pharmaceutical form should be considered. In particular, the Communication on the Community marketing authorisation procedures for medicinal products<sup>2</sup> provides that any medicinal product 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.

In addition, Article 10(2)(b) of Directive 2001/83 states that "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". While Article 10 deals with the assessment of generic applications, it is appropriate to apply the same principle in the context of the assessment of differences under Article 82(1).

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

In the light of the above principles, it is appropriate to illustrate with practical examples cases that fall under Article 82(1) and cases that are outside Article 82(1).

### **3.1 Applications outside the scope of Article 82(1).**

Examples of applications that fall outside the scope of Article 82(1) include but are not limited to the following cases:

- The active substance(s) is not the same.
- The active substance is a different salt that differs significantly in properties regarding safety or efficacy.
- The medicinal product contains different excipients, and this results in significant differences regarding safety or efficacy.
- The manufacturer or manufacturing site is different and this may, as a result of the characteristics of the product (notably in the case of biological products), lead to significant differences regarding safety or efficacy.

### **3.2 Applications under the scope of Article 82(1).**

Examples of applications that fall under the scope of Article 82(1) include but are not limited to the following cases:

- The active substance is a different salt that does not differ significantly in properties regarding safety or efficacy.
- The medicinal product contains different excipients but this does not result in significant differences regarding safety or efficacy.
- Different manufacturer or manufacturing site, unless this leads to significant differences regarding safety or efficacy.
- Differences in the data submitted in connection with the marketing authorisation application for a medicinal product with the same composition in active substance(s) and pharmaceutical form (*e.g.* data to show bioequivalence), provided that the product does not significantly differ regarding safety or efficacy.

In addition, the fact that one marketing authorisation application is done as a full submission in accordance with Article 8(3) and the other is done under an abridged legal base (*e.g.* informed consent) is irrelevant provided that both applications relate to a medicinal product with the same qualitative and quantitative composition in active substances and the same pharmaceutical form

- A duplicate application may contain less indications or pharmaceutical forms than the original application/marketing authorisation when this is necessary to market the product in Member States where a specific indication or pharmaceutical form is protected by patent law.

However, in order to maintain the harmonisation of the SmPCs, the applicant should provide a commitment letter undertaking to extend the indication(s)/ pharmaceutical

form(s) of the duplicate marketing authorisation as soon as the patent restrictions do not longer exist. Alternatively, the applicant may also commit to withdraw the marketing authorisation with restricted indications/pharmaceutical forms after the relevant patents are no longer in force. The commitment letter should be provided with the marketing authorisation application dossier.

In the previous document on the handling of duplicate marketing authorisations, reference was made to the term "true duplicate". This term captured the characteristics of applications that had been typically processed as duplicates and that, therefore, had benefited from the relevant fee reductions due to the fact that the related assessment by the Agency was less extensive given the similarity to a previous application of the same applicant.

However, since the publication of the document on the handling of duplicate marketing authorisations, the Commission services have identified a trend for applicants to submit applications for the authorisation of a medicinal product having the same pharmaceutical form and the same composition in active substance as a previously authorised product of the applicant without requesting the authorisation provided under for under Article 82(1) on grounds that the application was not a "true duplicate".

In the light of this misinterpretation, the Commission services consider it necessary to clarify that applications falling under the scope of Article 82(1) can only lead to the granting of a marketing authorisation if the conditions set out in Article 82(1) are met. Prospective applicants are therefore advised to signal to the Agency when an application falls under Article 82(1) and to seek advice in case of doubt (*e.g.* different manufacturing site for a biological medicinal product).

For the sake of clarity, the extent of the scientific assessment required from the Agency and any possible consequences in terms of fees should be left outside the scope of the present document.

#### **A. Validation of duplicate marketing authorisation applications by the Agency.**

Applications for marketing authorisations, including duplicates, are submitted to the European Medicines Agency. In connection with the validation of a duplicate marketing authorisation, the following elements should be checked by the Agency:

- That the duplicate application is submitted by the same applicant that has submitted the marketing authorisation/application that is being duplicated (hereafter "original marketing authorisation/application"). Further clarifications of this requirement are laid down in Section C.1.
- That the original marketing authorisation is valid. Further clarifications of this requirement are laid down in Section C.2. This step does not apply in case of duplicate applications that are submitted in parallel with the original marketing authorisation application (*i.e.* in cases where the application for the original marketing authorisation is still pending).
- In cases where the duplicate marketing authorisation is submitted on the basis of an informed consent application, that there is a letter of consent from the marketing authorisation holder that owns the dossier that is referred to. Further clarifications of this requirement are laid down in Section C.3.

- That an authorisation by the Commission to submit a duplicate marketing authorisation application has been granted. Further clarifications of this requirement are laid down in Section C.4.

## **B. The Commission’s authorisation to submit a duplicate marketing authorisation.**

Before an authorisation is granted in accordance with Article 82(1), the Commission services must be satisfied that the relevant conditions are met. It is therefore for the Commission services to verify that:

- the applicant is the “same applicant” as explained in Section C.1; and
- the public health reasons or co-marketing reasons are met. The criteria that are applied are laid down in the Annex to this note.

The letter of authorisation shall specify the following:

- the name of the marketing authorisation holder relevant for the duplicate application;
- the name of the product relevant for the duplicate application;<sup>2</sup>
- in the case of co-marketing reasons, that the evidence of such co-marketing (contract or letter of agreement between the companies) is provided to the Commission at least one month prior to the CHMP issuing its opinion; and
- in the case of duplicates asked on grounds of the existence of patents protecting certain therapeutic indications or pharmaceutical forms, the applicant should provide a commitment letter undertaking to extend the therapeutic indication(s) / pharmaceutical form(s) of the duplicate marketing authorisation as soon as the patent restrictions do not longer exist. Alternatively, the applicant may also commit to withdraw the marketing authorisation with restricted indications/pharmaceutical forms after the relevant patents are no longer in force. The harmonisation of SmPCs across the Union being one of the basic pillars of the centralised procedure, applicants of duplicate marketing authorisations should not market the two products with different indications/ strengths/ pharmaceutical forms in the same country. The commitment letter should be provided with the Marketing Authorisation Application Dossier.

## **C. Requirements to be checked in any duplicate application.**

### **1. “Same applicant”**

When it receives an application for a marketing authorisation, the Agency should verify if the applicant has already applied for a marketing authorisation for that product or if it has already been granted a marketing authorisation for that product. In the affirmative, the Agency will process this application as a duplicate application as provided for under Article 82(1) of Regulation 726/2004. Before issuing an authorisation letter in the framework of Article 82(1) of the Regulation, the Commission services shall also verify that the applicant for the

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<sup>2</sup> If the proposed name is not accepted by the Name Review Group of the Agency, the letter of authorisation may be updated as appropriate.

duplicate marketing authorisation is the same applicant that applied for/holds the original marketing authorisation. In both cases, appropriate evidence may be requested to the applicant.

The criteria laid down in the 1998 Communication on the Community marketing authorisation procedures for medicinal products regarding the definition of “same entity” and the criteria laid down in Chapter 2 of the Notice to Applicants in connection with the interpretation of “same applicant” should be followed also in the context of Article 82(1).

Specifically, this means that a company that belongs to the same group of companies, or companies that have entered into a license agreement or have otherwise agreed to the marketing of the relevant medicinal product can apply for a duplicate.

Scenario	Under the scope of Article 82(1)?
Applicant is the same that applied for the original marketing authorisation.	yes
Applicant belongs to the <u>same group</u> of companies as the applicant of the original marketing authorisation.	yes
Applicant is an <u>independent company that has agreed</u> (license agreement or other agreement that can be identified) <u>to placing on the market the product</u> with the applicant of the original marketing authorisation.	yes
Applicant is an independent company. There are licence agreements with the marketing authorisation holder of the product in respect of which the duplicate is asked but <u>not for the placing on the market of that product</u> (e.g. company A and B have an agreement for the placing on the market of products x1, and x2 but duplicate is asked for product x3).	no <sup>3</sup>
Applicant is an independent company that has got an agreement to purchase and/or use data from the company that has applied for a marketing authorisation for the product for the first time but there is <u>not an agreement regarding the placing on the market of the</u>	no <sup>2</sup>

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<sup>3</sup> This application is to be treated in the framework of Article 6 of Regulation 726/2004.

<u>product.</u>	
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**2. Original marketing authorisation is valid.**

The original marketing authorisation to which the duplicate application relates has to be valid at the time of the submission of the duplicate application. Thus, there cannot be a duplicate application in respect of a marketing authorisation that has not been renewed, that has been withdrawn/revoked or that has been suspended, or that has ceased to be valid in accordance with Article 24(5) of Directive 2001/83. Evidence that the original marketing authorisation is valid may be requested to the applicant by the Agency.

**3. Letter of consent in the case of an "informed consent application".**

In cases where the duplicate application is asked in the form of an informed consent application in accordance with Article 10c, there must be a letter of consent from the marketing authorisation holder that owns the dossier that is referred to.

**4. Authorisation by the Commission to submit a duplicate marketing authorisation**

While it should be possible for companies requesting a duplicate marketing authorisation to initiate pre-submission activities with the Agency prior to having the Commission's agreement as required under Article 82, prospective applicants are reminded that the duplicate marketing authorisation cannot be granted if an authorisation letter has not been issued by the Commission prior to the CHMP opinion or if any requirements stated therein have not been complied with prior to the CHMP opinion.

It is therefore of the utmost importance that applicants apply for an authorisation letter and provide any information that may be requested in this context in a timely manner and at the latest one month prior to the CHMP opinion.

## Annex I

### **Assessment of public health and co-marketing reasons by the Commission**

#### **1. Public health reasons.**

Under Article 82(1), the Commission shall agree to the application for a duplicate if there are objective verifiable reasons relating to public health regarding the availability of medicinal products to health-care professionals and/or patients.

This requires a case by case assessment but arguments that are not linked to the availability of the product cannot be considered. In addition, having more than one authorisation for the same product cannot, *per se*, be considered to increase availability as this would be void of purpose the principle in Article 82(1) that a single marketing authorisation should be granted per product to the same applicant/holder.

The most common case in which a duplicate is justified on public health grounds is when there is an indication or pharmaceutical form in the SmPC of the original application/marketing authorisation that is protected by patent law in one or more Member States. In this context it is noted that Article 11 of Directive 2001/83 specifically allows for the submission of different SmPCs on grounds related to patent law. While this article refers to generic applications the same considerations (*i.e.* the need to ensure availability of the product in the Member States where there is patent protection) are applicable in the case of duplicate applications.

In such cases and in order to maintain the harmonisation of the SmPCs, the applicant should be required to provide a commitment letter undertaking to extend the indication/pharmaceutical form of the duplicate marketing authorisation as soon as the patent restrictions do not longer exist. Alternatively, the applicant may also commit to withdraw the marketing authorisation with restricted indications/pharmaceutical forms after the relevant patents are no longer in force. The harmonisation of SmPCs across the Union being one of the basic pillars of the centralised procedure, applicants of duplicate marketing authorisations should not to market two products with different indications/ pharmaceutical forms in the same country. The commitment letter should be provided with the marketing authorisation application dossier.

The first introduction of a generic product by the holder of the reference medicinal product can also improve the availability of a medicinal product. This is because the first entry of a generic to the market has an impact on availability as it usually increases accessibility. Any subsequent application of the holder of the reference medicinal product would need to be justified by further arguments, and could not be based solely on the fact that the second authorisation for the same product concerns a generic.

<b>Scenario</b>	<b>In compliance with Article 82(1)?</b>
Patents on indications or pharmaceutical forms.	yes

Pricing and reimbursement considerations.	no
Classification (prescription/ non prescription) considerations.	no
Considerations based on national legislation deemed incompatible with EC law ( <i>e.g.</i> names).	no
First introduction of a generic by the holder of the reference medicinal product.	yes

## 2 Co-marketing reasons

Under Article 82(1), the Commission shall agree to the application for a duplicate if there are co-marketing reasons. A co-marketing arrangement is generally understood as an agreement between two parties to commercialise a specific medical product under different trademarks. It is noted that co-marketing requires the existence of two parties; *i.e.* a request for authorisation under Article 82(1) on co-marketing grounds shall not be accepted when the two marketing entities belong to the same company group. Likewise an application for a duplicate cannot be accepted if the co-marketing partners are already co-marketing (together) the product in the EU (*i.e.* product A is co-marketed by company X and Y and company Y applies for a duplicate marketing authorisation of product A on grounds of co-marketing with company X).

Co-marketing can be limited to one or more Member States or cover the entire EU. It must, however, not lead to partition of the internal market.

In order to grant a duplicate marketing authorisation for co-marketing reasons, it is necessary that the evidence of such co-marketing (contract or letter of agreement between the companies) is provided to the Commission at the latest one month before the CHMP issues its opinion.

Scenario	In compliance with Article 82(1)?
Co-marketing with a company of the same group?	no
Co-marketing with another independent company?	yes
Data required.	Name of the co-marketing partner and proof that the envisaged co-marketing <u>for that product</u> will actually take place ( <i>e.g.</i> contract or letter of agreement between the companies).  At the latest, the required evidence must have been received one month prior to the

	adoption of an opinion by the CHMP.
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## Annex II

### History of the document

<b>Version</b>	<b>Comment</b>	<b>Date</b>
First Communication		March 2010
Update 1	<ul style="list-style-type: none"><li>• Addition of the section "General Considerations".</li><li>• Addition of a section regarding the Clarification on the scope of Article 82(1).</li><li>• Clarification on the "public health reasons" relevant for the authorisation of the submission of a duplicate application.</li></ul>	October 2011