II

(Information)

INFORMATION FROM EUROPEAN UNION INSTITUTIONS, BODIES, OFFICES AND AGENCIES

EUROPEAN COMMISSION

Commission Notice

Handling of duplicate marketing authorisation applications of pharmaceutical products under Article 82(1) of Regulation (EC) No 726/2004

(2021/C 76/01)

Foreword

Requests for duplicate marketing authorisations under Article 82(1) of Regulation (EC) No 726/2004 of the European Parliament and of the Council (1) have increased steadily, and this trend is likely to continue as the use of the centralised procedure rises.

To ensure a smooth application of Article 82(1) and to create more transparency and predictability for the stakeholders concerned, the Commission published a document in March 2010 (updated in 2011 (2)) on the criteria it would use when assessing a request for an application for a duplicate marketing authorisation. The Commission will continue to update this document to address new questions of interpretation of Article 82(1). Section III of the Annex lists the dates and content of the updates that have been made so far.

This notice aims to provide guidance to those who wish to submit a request for an application for a duplicate marketing authorisation. While guidance documents are not legally binding, this Notice is based on the Commission's interpretation of Article 82(1) of Regulation (EC) No 726/2004. In case of doubt, reference should be made to the appropriate EU directives and regulations. In addition, only the European Court of Justice can give an authentic interpretation of the EU law.

1. General considerations

A marketing authorisation granted under Regulation (EC) No 726/2004 allows the holder to market the medicinal product in the entire EU. In light of the unique nature and EU dimension of marketing authorisations granted under the centralised procedure, Regulation (EC) No 726/2004 requires that a single name is used to identify a medicinal product authorised under the centralised procedure (3). The Regulation also limits the ability of applicants/holders to obtain more than one marketing authorisation per medicinal product ('duplicate marketing authorisations'). In particular, Article 82(1) of Regulation (EC) No 726/2004 provides that:

‘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 of whether the conditions of Article 82(1) have been met must be done on a case-by-case basis, looking at the facts of each application. Nevertheless, prospective applicants should note that the second subparagraph of Article 82(1) is an exception to the general rule set out in the first subparagraph and should be therefore subject to restrictive interpretation. The overall objectives of preserving public health and the harmonisation of centrally authorised products must also play an important role.

2. Marketing authorisation applications under the scope of Article 82(1)

Article 82(1) of Regulation (EC) No 726/2004 concerns marketing authorisation applications submitted by an applicant for a medicinal product for which they have already been granted a marketing authorisation under the centralised procedure.

Note that a marketing authorisation for a medicinal product that differs from a previously authorised product is not considered a duplicate and therefore does not need to be assessed under Article 82(1). This also means that any such application cannot benefit from any fee reduction that applies to duplicates.

By contrast, a marketing authorisation application for a medicinal product that has already been granted a marketing authorisation under the centralised procedure does fall under Article 82(1) if the applicant is the same (4) as the one that holds the original marketing authorisation. Such an application could qualify for a fee reduction that may be applicable for duplicates but, in turn, could only be granted if the conditions under Article 82(1) are met.

When assessing whether an application concerns a specific medicinal product that has already been granted a marketing authorisation, and therefore falls under the scope of Article 82(1), the Commission will consider the composition in active substance(s) and the pharmaceutical form. This is in line with the ‘Communication on the Community marketing authorisation procedures for medicinal products’ (5), which states that any medicinal product with the same qualitative and quantitative composition in active substance (i.e. the same strength) and the same pharmaceutical form is to be considered as the same product.

In addition, Article 10(2)(b) of Directive 2001/83/EC of the European Parliament and of the Council (6) 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 when assessing differences under Article 82(1).

When a separate marketing authorisation application is required by law, it falls outside the scope of Article 82(1), meaning that the applicant does not have to submit a request for a duplicate marketing authorisation to the Commission.

Sections 2.1 and 2.2 below set out practical cases that fall outside and inside the scope of Article 82(1) respectively.

2.1. Applications outside the scope of Article 82(1)

Applications that fall outside the scope of Article 82(1) include the following cases:

— The active substance(s) is not the same.

— The active substance is a different salt, ester, ether, isomer, mixture of isomers, complex or derivative that differs significantly in properties regarding safety or efficacy.

— The medicinal product contains different excipients that result in significant differences in safety or efficacy.

— The manufacturer or manufacturing site is different and may, as a result of the characteristics of the product (notably in the case of biological products), lead to significant differences in safety or efficacy.

— Applications submitted under Article 7(3) of Regulation (EC) No 141/2000: that provision provides that an orphan and non-orphan indication cannot be covered by the same marketing authorisation.

(4) Cf. Section 5.1 below.


— Applications submitted under Article 30 of Regulation (EC) No 1901/2006 or applications for marketing authorisations for other indications where the initial marketing authorisation has been submitted under Article 30 of Regulation (EC) No 1901/2006. Article 30 provides for a new, self-standing type of marketing authorisation called the Paediatric Use Marketing Authorisation.

2.2. Applications under the scope of Article 82(1)

Applications that fall under the scope of Article 82(1) include the following cases:

— The active substance is a different salt, ester, ether, isomer, mixture of isomers, complex or derivative that does not differ significantly in properties regarding safety or efficacy.

— The medicinal product contains different excipients that do not result in significant differences in safety or efficacy.

— Different manufacturer or manufacturing site, unless this leads to significant differences in 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 in terms of safety or efficacy.

— In addition, the fact that one marketing authorisation application is submitted in accordance with Article 8(3) of Directive 2001/83/EC and the other marketing authorisation application is submitted under an abridged procedure (e.g. generic, biosimilar or hybrid application, 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 fewer 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 Summary of Product Characteristics (SmPCs), the applicant should provide a commitment letter undertaking to extend the indication(s)/pharmaceutical form(s) of the duplicate marketing authorisation when the patent restrictions no longer exist. Alternatively, the applicant may also commit to withdrawing the marketing authorisation with restricted indications/pharmaceutical forms after the relevant patents are no longer in force. Given that the harmonisation of SmPCs across the EU is 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 accompany the marketing authorisation application dossier.

The Commission considers it necessary to emphasize 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 that Article are met. Prospective applicants are therefore advised to inform the European Medicines Agency (the Agency) when an application falls under Article 82(1) and to seek advice in case of doubt (e.g. if a different manufacturing site is used 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 fall outside the scope of this document.

3. Validation of duplicate marketing authorisation applications by the Agency

Applications for marketing authorisations, including duplicates, are submitted to the Agency. For the validation of a duplicate marketing authorisation, the Agency checks:

— That the duplicate application is submitted by the same applicant that has submitted the marketing authorisation/application that is being duplicated (the ‘original marketing authorisation/application’). See Section 5.1 for further clarifications.

(7) Articles 10 and 10(c) of Directive 2001/83/EC refer to different types of abridged procedures, where a company may refer to data included in other marketing authorisation dossiers.
— That the original marketing authorisation is valid. See Section 5.2 for further clarifications. This step does not apply to 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, as is the case for applications submitted under Article 10c of Directive 2001/83/EC. See Section 5.3 for further clarifications.

— That an authorisation by the Commission to submit a duplicate marketing authorisation application has been granted. See Section 5.3 for further clarifications.

4. The Commission’s authorisation to submit a duplicate marketing authorisation

Before granting an authorisation to submit a duplicate marketing authorisation application under Article 82(1), the Commission must be satisfied that the relevant conditions are met. It must therefore verify that:

— the applicant is the ‘same applicant’ as explained in Section 5.1; and

— the public health reasons or co-marketing reasons are met (see criteria laid down in the Annex to this Notice).

The letter of authorisation should specify:

— the name of the marketing authorisation holder relevant for the duplicate application;

— the name of the medicinal product for the duplicate application (*)

— if co-marketing reasons are being invoked, the evidence of such co-marketing (contract or letter of agreement between the companies) should be provided to the Commission at least 1 month prior to the Committee for Medicinal Products for Human Use (CHMP) issuing its opinion on the duplicate marketing authorisation application; and

— if duplicates are requested 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 no longer exist. Alternatively, the applicant can commit to withdrawing the marketing authorisation with restricted indications/pharmaceutical forms after the relevant patents are no longer in force. Given that the harmonisation of SmPCs across the EU is 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 accompany the marketing authorisation application dossier.

5. Requirements to be checked for all duplicate marketing authorisation applications

5.1. ‘Same applicant’

When the Agency receives an application for a marketing authorisation, it should verify if the applicant has already applied for or been granted a marketing authorisation for that product. If so, the Agency will process their application as a duplicate application in line with Article 82(1). Before issuing an authorisation letter under Article 82(1), the Commission should also verify that the applicant for the duplicate marketing authorisation is the same applicant that applied for or holds the original marketing authorisation. In either case, the applicant may be asked to provide the appropriate evidence.

Assessment of requests for authorisation under Article 82(1) should use the same criteria as:

— the ‘1998 Communication on the Community marketing authorisation procedures for medicinal products’ to define ‘same entity’; and

— Chapter 2 of the Notice to Applicants to define ‘same applicant’.

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 with the applicant of the original marketing authorisation as regards the marketing of the relevant medicinal product can apply for a duplicate.

(*) If the proposed name is not accepted by the Agency’s Name Review Group, the letter of authorisation may be updated as appropriate.
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Under the scope of Article 82(1)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applicant is the same that applied for the original marketing authorisation.</td>
<td>yes</td>
</tr>
<tr>
<td>Applicant belongs to the same group of companies as the applicant of the original marketing authorisation.</td>
<td>yes (1)</td>
</tr>
<tr>
<td>Applicant is an independent company that has agreed with the applicant of the original marketing authorisation (license agreement or other agreement that can be identified) to place the product on the market.</td>
<td>yes</td>
</tr>
<tr>
<td>Applicant is an independent company. It has licence agreements with the marketing authorisation holder of the product for which the duplicate is asked but not to place that product on the market (e.g. company A and B have an agreement to place products x1 and x2 on the market, but the requested duplicate is for product x3).</td>
<td>no (2)</td>
</tr>
<tr>
<td>Applicant is an independent company that has an agreement to purchase and/or use the data of the company that has applied for a marketing authorisation for the product for the first time. However, there is no agreement to place the product on the market.</td>
<td>no (2)</td>
</tr>
</tbody>
</table>

(1) Unless the request for the duplicate marketing authorisation is on grounds of co-marketing (see Annex, section I B).

(2) This application is to be treated in accordance with Article 6 of Regulation (EC) No 726/2004.

5.2. Original marketing authorisation is valid

The duplicate application must relate to an original marketing authorisation that is still valid. It is not possible to submit a duplicate application for a marketing authorisation: (i) that has not been renewed; (ii) that has been withdrawn/revoked or suspended; or (iii) that has ceased to be valid according to Article 24(5) of Directive 2001/83/EC. The Agency may ask the applicant to provide evidence that the original marketing authorisation is valid.

5.3. Letter of consent in the case of an ‘informed consent application’

A duplicate application requested in the form of an informed consent application in accordance with Article 10c of Directive 2001/83/EC must be accompanied by a letter of consent from the marketing authorisation holder that owns the dossier that is referred to, as it is the case for every application submitted under Article 10c.

5.4. Authorisation by the Commission to submit a duplicate marketing authorisation

Companies requesting a duplicate marketing authorisation can initiate pre-submission activities with the Agency prior to having the Commission’s agreement as required under Article 82(1). They should note, however, that the duplicate marketing authorisation cannot be granted if the Commission has not issued an authorisation letter prior to the CHMP opinion, or if any requirements stated therein have not been complied with prior to the CHMP opinion.
It is therefore extremely important that applicants apply for an authorisation letter and provide any relevant information that may be requested promptly and at least 1 month prior to the CHMP opinion.

Applicants should also complete the information template provided in Section II of the Annex to this Notice and submit it with their request letter. The template should be used for all applications submitted from 1 April 2021 onwards.
ANNEX

SECTION I

Commission assessment of public health and co-marketing reasons

A. Public health reasons

Under Article 82(1) of Regulation (EC) No 726/2004, the Commission can grant a duplicate marketing authorisation if there are objective, verifiable reasons relating to public health that show an increased availability of medicinal products to healthcare professionals and/or patients.

Having more than one authorisation does not necessarily increase the availability of a particular product, as this would deprive of purpose the principle in Article 82(1) which provides that only one single marketing authorisation should be granted per product to the same applicant/holder. Therefore, any claim that a duplicate marketing authorisation would increase a product’s availability should be assessed on a case-by-case basis by examining the justification and evidence provided by the applicant.

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 Summary of Product Characteristics (SmPCs) of the original application/marketing authorisation that is protected by patent law in one or more Member States. In this context, Article 11 of Directive 2001/83/EC 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) can also apply to duplicate applications.

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

The commitment letter should accompany the marketing authorisation application dossier.

For any other case, the applicant should demonstrate how the duplicate marketing authorisation increases availability and patient access, based on objective and verifiable evidence, including but not limited to the following information:

i) the Member States where the original medicinal product is actually marketed;

ii) the Member States where the duplicate medicinal product is intended to be marketed;

iii) the Member States in which the duplicate is not to be placed on the market: the applicant should explain the reasons for not marketing the product in these countries.

In the past, the Commission has granted duplicate marketing authorisations to the holder of the marketing authorisation of the original medicinal product in order to increase availability. However, experience shows (1) that there is no automatic link between the introduction of a duplicate marketing authorisation by the holder of the original medicinal product (be it a chemical or a biological medicinal product) and increased availability. Taking into account that a duplicate marketing authorisation can only be granted exceptionally, the applicant should provide the Commission with specific evidence that demonstrates that the duplicate marketing authorisation is likely to increase availability.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>In compliance with Article 82(1)?</th>
</tr>
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<tbody>
<tr>
<td>Patents on indications or pharmaceutical forms</td>
<td>yes</td>
</tr>
<tr>
<td>Pricing and reimbursement considerations</td>
<td>no</td>
</tr>
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### Classification (prescription/non-prescription) considerations

<table>
<thead>
<tr>
<th>Classification (prescription/non-prescription) considerations</th>
<th>no</th>
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<tbody>
<tr>
<td>Considerations based on national legislation deemed</td>
<td>no</td>
</tr>
<tr>
<td>incompatible with EU law (e.g. names)</td>
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</tbody>
</table>

### B. Co-marketing reasons

Under Article 82(1), the Commission can grant a duplicate marketing authorisation for co-marketing reasons when the marketing authorisation holder can prove that he will stipulate a co-marketing agreement with one or more companies for the product for which the duplicate is requested. A co-marketing arrangement is generally understood as an agreement between two parties to commercialise a specific medical product under different trademarks.

Note that co-marketing requires the existence of two parties, i.e. a request for authorisation under Article 82(1) on co-marketing grounds will 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.

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 least 1 month before the CHMP issues its opinion.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>In compliance with Article 82(1)?</th>
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<tbody>
<tr>
<td>Co-marketing with a company of the same group?</td>
<td>no</td>
</tr>
<tr>
<td>Co-marketing with another independent company?</td>
<td>yes</td>
</tr>
</tbody>
</table>

Data required

Name of the co-marketing partner and proof that the envisaged co-marketing for that product will actually take place (e.g. contract or letter of agreement between the companies).

The required evidence must have been received at least 1 month prior to the adoption of an opinion by the CHMP.

### SECTION II

**Template**

**Information an applicant must provide to the European Commission for a request to submit a duplicate marketing authorisation under Article 82(1) of Regulation (EC) No 726/2004**

<table>
<thead>
<tr>
<th>Name of the marketing authorisation holder (1) relevant for the duplicate marketing authorisation application</th>
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<tbody>
<tr>
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<tr>
<td>Name of the original product for which the duplicate is requested</td>
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</tbody>
</table>
In case of co-marketing, the name of the co-marketer

In case of co-marketing, the proof that the envisaged co-marketing for that product will actually take place (e.g. contract or letter of agreement between the companies)

In case of public health reasons related to intellectual property that impact indications or pharmaceutical forms in the SmPC of the original application/marketing authorisation:
— the number and name(s) of indication(s)/pharmaceutical forms claimed for each duplicate marketing authorisation product(s) relevant for the application
— the list of Member States where the duplicate is intended to be marketed, clarifying the patent situation (in force or not in force) and the patent expiry date by Member State for each patented indication/pharmaceutical form. This information should be provided in a table:

<table>
<thead>
<tr>
<th>Member State</th>
<th>Patent situation</th>
<th>Patent expiry date</th>
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— a commitment letter undertaking to
  ✓ extend the therapeutic indication(s)/pharmaceutical form(s) of the duplicate marketing authorisation as soon as the patent restrictions no longer exist, OR
  ✓ withdraw the marketing authorisation with restricted indication(s)/pharmaceutical form(s) after the relevant patent is no longer in force
— a commitment letter stating that the applicant will not market two products with different indications/strengths/pharmaceutical forms in the same country

In case of public health reasons not related to intellectual property, the specific evidence demonstrating that the duplicate marketing authorisation are likely to increase availability, including but not limited to the following information:
— the list of Member States where the 'first' medicinal product is actually marketed, AND
— the list of Member States where the duplicate medical product is intended to be marketed, AND
— the list of Member States in which the duplicate is not to be placed on the market and the reasons for not marketing the product in these countries.
### History of the document

<table>
<thead>
<tr>
<th>Version</th>
<th>Main changes</th>
<th>Date</th>
</tr>
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<tbody>
<tr>
<td>First Communication</td>
<td></td>
<td>March 2010</td>
</tr>
<tr>
<td>Update 1</td>
<td>— Addition of the ‘General Considerations’ section.</td>
<td>October 2011</td>
</tr>
<tr>
<td></td>
<td>— Addition of a section regarding the Clarification of the scope of Article 82(1).</td>
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<tr>
<td></td>
<td>— Clarification of the ‘public health reasons’ relevant for authorising the submission of a duplicate application.</td>
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</tr>
<tr>
<td>Update 2 (Current version)</td>
<td>— Clarification of the scope of Article 82(1).</td>
<td>February 2021</td>
</tr>
<tr>
<td></td>
<td>— Clarification of the ‘public health reasons’ relevant for authorising the submission of a duplicate application.</td>
<td></td>
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<tr>
<td></td>
<td>— New Annex ‘Template: Information an applicant must provide to the European Commission for a request to submit a duplicate marketing authorisation under Article 82(1) of Regulation (EC) No 726/2004’.</td>
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