# EU MARKETING AUTHORISATION SUBSEQUENT TO DISSOLUTION OF THE TRANSFEROR AND PRIOR TO EFFECTIVE TRANSFER

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**Abstract:**

Regulation (EC) No 2141/96 holds no explicit provision about the validity of a EU centralised marketing authorisation for a medicinal product during the time gap between dissolution of the transferor after granting of a favourable opinion by the EMA and effective authorisation by the European Commission. Marketing authorisations for medicinal products in terms of Article 3(1) of Regulation (EC) No 726/2004 are personal administrative acts, which, in principle, excludes a transfer unless otherwise and under exceptional terms allowed (*enumeratio ergo limitatio*). Regulation (EC) No 2141/96 constitutes such an exemption, laying down the procedural rules for a transfer of marketing authorisation. Though for this particular case the regulation holds no explicit provision about validity during the time gap. Despite the absence

of a provision about validity the time gap has to be filled by teleological interpretation to ensure that amongst several possible interpretations the one will prevail which best guarantees the practical effect of existing Community law. The examination of the objectives of the Regulations (EC) No 726/2004 and No 2141/96 indicate the validity of the marketing authorisation and consequently the transferee´s authorisation during that period of time.

**Keywords:** Centralised marketing authorisation, transfer, dissolution of the transferor

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## I. The Regulatory Issue

A stock corporation holds a marketing authorisation for a medicinal product in compliance with Article 3(1) of Regulation (EC) No 726/2004[1]. The marketing authorisation is granted for niche indication, for which the medicinal product is the sole vaccine in the European Union. However, the product does not qualify as an orphan drug.

The marketing authorisation holder and another stock corporation are to be merged. As a result of the merger the transferor will dissolve.

Prior to the merger, the holder will separate from its operative business and transfer all assets to a transferee, e.g. a wholly owned subsidiary.

The transferee will be equivalent to the transferor in regard to personnel as well as assets, premises, know-how and technology. The transferee will particularly meet any obligation and attend to all responsibilities of a marketing authorisation holder.

To facilitate the transfer of marketing authorisation, the transferor applied with European Medicines Agency ("EMA") for transfer of marketing authorisation under Regulation (EC) No 2141/96[2]. The EMA has issued a favourable opinion on the Transfer within 30 days of the receipt of the application, which has been sent to the Transferor, Transferee, and to the European Commission.

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[1] OJ L 136, 30.4.2004, p. 1.

[2] OJ L 286, 8.11.1996, p. 8.

The transfer might be authorised in terms of Article 7(1) of Regulation (EC) No 2141/96, after the initial marketing authorisation holder has dissolved due to the merger. The aforementioned time gap between dissolution of the transferor and authorisation of the transferee is expected to be no longer than a couple of days or weeks.

## II. As to the Law

### *1. Personal Nature of Marketing Authorisations for Medicinal Products*

Marketing authorisations for medicinal products in terms of Article 3(1) of Regulation (EC) No 726/2004 are personal administrative acts, which, in principle, excludes a transfer unless otherwise and under exceptional terms allowed (*enumeratio ergo limitatio*).[3] Regulation (EC) No 2141/96 constitutes such an exemption, laying down the procedural rules for a transfer of marketing authorisation.

Though for this particular case, in which the transferor has dissolved after granting of a favourable opinion by the EMA but prior to the Commission´s amendment of the marketing authorisation and its notification in terms of Article 6 of Regulation (EC) No 2141/96, the regulation holds no explicit provision about validity during the time gap.[4]

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[3] Looking at Article 2 of Regulations (EC) No 726/2004 and Annex of Regulation (EC) No 2141/96, especially number 5, the personal nature becomes obvious.

[4] Sec. 55 para. 7 German Telecommunications Act e.g. provides the right of use in a similar case:
"(7) Applications for a change in the frequency assignment are to be submitted without undue delay to the Regulatory Authority, in writing, with supporting documents, when

1. frequency usage rights are to be transferred by singular or universal succession;
2. frequencies are to be transferred to an affiliated undertaking as defined in section 15 of the Stock Corporation Act;
3. frequencies are to be transferred from a natural person to a legal entity in which the natural person holds a share; or
4. an heir intends to continue using the frequencies.

In these cases, the frequencies may continue to be used until such time as a decision is taken on the application for a change in the assignment [...]".

*2. Objectives of Marketing Authorisation and effet utile*

Despite the absence of a provision about validity[5] the time gap has to be filled by teleological interpretation to ensure that amongst several possible interpretations the one will prevail which best guarantees the practical effect of existing Community law.

The examination of the objectives of the Regulations (EC) No 726/2004 and No 2141/96 indicate the validity of the marketing authorisation and consequently the transferee´s authorisation during that period of time.

*a) Public Health and Safety, effective Surveillance*

The primary objective of the European centralised marketing authorisation procedure is to safeguard the public health, by ensuring quality, safety and efficacy of medicinal products[6] as stated in Recital 13 of Regulation (EC) No 726/2004:

> *In the interest of public health, authorisation decisions under the centralised procedure should be taken on the basis of the objective scientific criteria of quality, safety and efficacy of the medicinal product concerned [...]*

Further objective is the market surveillance as stated in Recital 30 of Regulation (EC) No 726/2004:

[5] As the above-mentioned Sec. 55 para. 7 German Telecommunications Act.

[6] Recital 13 of Regulation (EC) No 726/2004.

*In order to enhance the efficiency of market surveillance, the Agency should be responsible for coordinating Member States' pharmacovigilance activities. A number of provisions need to be introduced to put in place stringent and efficient pharmacovigilance procedures, to allow the competent authority to take provisional emergency measures, including the introduction of amendments to the marketing authorisation and, finally, to permit a reassessment to be made at any time of the risk-benefit balance of a medicinal product.*

The procedural rules for transfer of marketing authorisation under Regulation (EC) No 2141/96 are supposed to ensure efficient market surveillance and by that public health and safety. However, the risks resulting from the medicinal product itself are secondary under the procedure for transfer of marketing authorisation, as shown by the fact, that the market authorisation may be transferred and need not to be granted again under Regulation (EC) No 726/2004. The transfer procedure shall primarily guarantee the reliability of the marketing authorisation holder and the assignment of the already once approved medicinal product to its marketer.[7] In the given case both objectives will be met. The EMA has approved of the vaccine being in compliance with Regulations (EC) No 726/2004 and No 2141/96 and therefore no danger to the public health and safety exists. The objective of efficient surveillance, in particular with regard to efficient pharmacovigilance procedures, is hardly, if not, exposed to a risk of being negatively affected because the EMA, as well as the Commission, may establish the market authorisation holder at any time. Especially since the amendment of the Commission is to be expected latest in a couple of weeks, or as provided by Article 6 of Regulation (EC) No 2141/96, immediately.

[7] As shown by the enumeration of documents to be submitted to the EMA pursuant to Article 3 of Regulation (EC) No 2141/96 in the Annex of Regulation (EC) No 2141/96.

Also several procedural simplifications in the scope of medicinal product surveillance shall relieve the competent authorities, which e.g. has been explicitly stated in Regulation (EC) No 1234/2008 concerning the variation of medicinal products[8], and accelerate the transfer.[9]

*b) Niche indication and the Stage of the Transfer Procedure*

In this particular case the significance of the medicinal product has to be taken into consideration. The medicinal product is the sole obtainable vaccine for a niche indication in the EU and therefore irreplaceable, even if the product does not qualify as an orphan drug. Considering the objective of public health, prohibiting the marketing of a previously approved medicinal product seems contradictory since the transfer procedure is virtually completed.

A notified amendment is without question a necessary requirement for the transfer authorisation to come in effect but at the same time merely the final, formal act of the transfer procedure.

Once the favourable opinion of EMA has been granted, the most critical part of the transfer procedure has been completed as provided in Article 6 of Regulation (EC) No 726/2004:

> *In the case of a favourable opinion and without prejudice to the application of other provisions of Community law, the Commission shall immediately amend the decision taken in accordance with Articles 10 or 32 of Council Regulation (EEC) No 2309/93*.

[8] "In order to further reduce the overall number of variations procedures and to enable competent authorities to focus on those variations that have a genuine impact on quality, safety or efficacy [...]".

[9] Recital 6 of Regulation (EC) No 2141/96 "Whereas it is necessary in particular to institute an administrative procedure to enable the marketing authorization decision to be quickly amended in that event [...]."

Though the Commission may reject the transfer amendment due to inconsistence with other provisions of Community law, the amendment still is the regular course of action once a favourable opinion of the EMA has been granted.

*3. Article 14 of Regulation (EC) No 726/2004*

As mentioned, according to Article 3(1) of Regulation (EC) No 726/2004 a medicinal product may not be marketed without an effective marketing authorisation. Further according to Article 13 para. 4 sentence 2 of Regulation (EC) 726/2004 a market authorisation holder is obliged to notify EMA if a medicinal product permanently or temporarily ceases to be placed on the market:

> *The holder shall also notify the Agency if the product ceases to be placed on the market, either temporarily or permanently. Such notification shall, otherwise than in exceptional circumstances, be made no less than 2 months before the interruption in the placing on the market of the product.*

Hence, it is in the Community´s interest to oversee and predict the allocation of medicinal products in the EU.

If the vaccine were not marketed during the time gap, due to the actual transfer date agreed upon by the transferor and the transferee, the objective of predictable allocation, as safeguarded under Article 13 para. 4 sentence 2 of Regulation (EC) 726/2004, would not be met. This is especially critical since the vaccine is authorised for a niche indication.

In another constellation Article 14 para. 12 of Regulation (EC) No 726/2004 provides the option of an accelerated assessment procedure for medicinal products which are of major interest from the point of view of public health and therapeutic innovation:

*When an application is submitted for a marketing authorisation in respect of medicinal products for human use which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. The request shall be duly substantiated.*

Regulation (EC) No 726/2004 thereby considers the necessity of certain medicinal products entering the market quickly and being permanently placed there. In this case it seems contradictory to prohibit the marketing of a medicinal product, which, opposed to the constellation of Article 14, has already been approved in the EU for niche indication while the transfer procedure is virtually completed and since the last formal step of the transfer authorisation, i.e. the amendment issued by the Commission, is to be expected latest in a couple of weeks.

*4. Proportionality with special regard to the Relevance of the Modification*

The efficient surveillance demands less scrutiny in regard to procedural rules than public health or safety as expressed by the differentiation between the procedural obligations in case of Type I A, I B and II variations.

Recital 4 and 5 of Regulation (EC) No 1234/2008 clearly state the varying relevance of certain products and authorisation modifications resulting in corresponding higher or lower procedural scrutiny:

*(4) It should be clarified that certain changes which have the highest potential impact on the quality, safety or efficacy of medicinal products require a complete scientific assessment, in the same way as for the evaluation of new marketing authorisation applications.*

*(5) In order to further reduce the overall number of variations procedures and to enable competent authorities to focus on those variations that have a genuine impact on quality, safety or efficacy, an annual reporting system should be introduced for certain minor variations. Such variations should not require any prior approval and should be notified within 12 months following implementation. However, other types of minor variations whose immediate reporting is necessary for the continuous supervision of the medicinal product concerned should not be subject to the annual reporting system.*

The fact that the transfer of marketing authorisation is subject to Regulation (EC) No 2141/96, which provides an accelerated transfer procedure and reduced documentation obligations, as opposed to the initial granting of marketing authorisation, results from the minor risk significance of the transfer compared to other modifications.

*5. Similarity to Article 7(2) of Regulation (EC) No 2141/96:*

Article 7(2) of Regulation (EC) No 2141/96 provides for the option of the actual marketing transfer taking place another time than the effective marketing authorisation of the transferee:

*The date on which the transfer actually takes place shall be set by the Agency by mutual agreement with the holder of the marketing authorization and the person to whom the transfer is to be granted. The Agency shall immediately inform the Commission of this date*.

Naturally the provision has the opposing case in mind in which the authorisation is completed but the transfer is yet to be completed.

Still, the following explanation of EMA shows, that the release of batches which do not carry the name of the notified marketing authorisation holder, is in principle tolerable for a proportionate period of time. The EMA guidelines state on page 159 that the transitional period between authorisation and implementation of the transfer has to be proportionate:[10]

> *The transitional period between the notification of the Commission decision on the transfer of a marketing authorisation (Day B) and the implementation date (Day C) should be proportionate to the organisational activities that need to be performed by the Transferor and Transferee. Nevertheless, it should be noted that as of Day B, the Transferee becomes the new MAH of the medicinal product and the EMA will only deal with the new MAH for any further regulatory activity (e.g. variations applications).*

It can be concluded that Article 7(2) of Regulation (EC) No 2141/96 shall ensure consistency of the actual marketer, who bares the responsibility and the notified marketing authorisation holder. Contrary to this, the original authorisation holder will be the notified marketing authorisation holder but the transferee the actual marketer. Taking into account the lack of an alternative, the transferee has to be the actual marketer because the transferor is dissolved by then. The transferee would market shortly before its holder position is amended and notified but at a point where the authorisation and notification is a mere formality. This result will be the most in compliance with the objectives of Regulation (EC) No 2141/96 since the transferee will particularly meet any obligation and attend to all responsibilities of a marketing authorisation holder. This way the transferee may continue to place the vaccine, an irreplaceable medicinal product, on the European market.

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10 http://www.emea.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500003981.pdf

## III. Conclusion

Strong arguments point in favour of the efficacy of the authorisation. Despite the absence of a provision in Regulation (EC) No 2141/96 about validity, the time gap has to be filled by teleological interpretation to ensure that amongst several possible interpretations the one will prevail which best guarantees the practical effect of existing Community law.

Considering the objective of public health, prohibiting the marketing of a previously approved medicinal product, seems contradictory since the transfer procedure is virtually completed. If the vaccine were not marketed during the time gap, due to the actual transfer date agreed upon by the transferor and the transferee, the objective of predictable allocation, as safeguarded under Article 13 para. 4 sentence 2 of Regulation (EC) 726/2004, would not be met. This is especially critical in case a medicinal product is authorised for a niche indication. The objective of efficient surveillance, in particular with regard to efficient pharmacovigilance procedures, is hardly, if not, exposed to a risk of being negatively affected because the EMA, as well as the Commission, may establish the market authorisation holder at any time. Moreover, Article 14 of Regulation (EC) No 726/2004 explicitly provides for an accelerated assessment procedure for medicinal products which are of major interest from the point of view of public health and therapeutic innovation, thereby enabling a fast track market entry on a permanent basis.

And finally, due to the dissolution of the transferor and the completed transfer of its operative business and personnel as well as assets, premises, know-how and technology, merely the transferee may market the vaccine.

The (provisional) authorisation of the transferee will best guarantee the practical effect of existing Community law and its objectives. Hence, the transferee may provisionally market the vaccine in compliance with Article 3(1) of Regulation (EC) No 726/2004 during the time gap.