COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 4.3.2008
COM(2008) 123 final

2008/0045 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending Directive 2001/82/EC and Directive 2001/83/EC as regards variations to the terms of marketing authorisations for medicinal products

(presented by the Commission)

{SEC(2008)273}
{SEC(2008)274}

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE PROPOSAL

1.1. Grounds for and objectives of the proposal

Within the European Community, medicinal products are regulated throughout their entire lifetime. Changes subsequent to their placing on the market, such as change in the production process, change in the packaging or change in the address of the manufacturer, are governed either by national provisions or by Community rules: Commission Regulations (EC) Nos 1084/2003 and 1085/2003[1] (hereinafter referred to as the "Variations Regulations"). This framework applies to medicines for both human and veterinary use.

The Variations Regulations are implementing measures adopted by 'comitology' regulatory procedure. The legal bases for these implementing measures are laid down in Article 39 of Directive 2001/82/EC[2], Article 35 of Directive 2001/83/EC[3] and Articles 16 and 41 of Regulation (EC) No 726/2004[4]. Those legal bases limit the scope of the Variations Regulations to the following medicinal products:

– medicinal products which have been granted a Community ('centralised') marketing authorisation in accordance with Regulation (EC) No 726/2004;

– medicinal products which have been granted a marketing authorisation in accordance with the provisions of Chapter 4 of Directive 2001/83/EC or Directive 2001/82/EC ('mutual recognition' and 'decentralised' procedure);

– medicinal products which have been considered within the scope of application of Directive 87/22/EEC[5] (so called 'ex-concertation' medicinal products).

However, the current Variations Regulations do not apply to changes to marketing authorisations for medicinal products which have been granted at a national level by a Member State competent authority under a national procedure and which do not fall within the above categories (hereinafter referred to as 'purely national' marketing authorisations). In the absence of Community harmonisation, changes affecting purely national authorisations are therefore subject to national rules. In some Member States, national requirements on changes to purely national authorisations nevertheless follow the Variations Regulations, by analogy. But in the majority of Member States there is no such alignment on Community legislation, which results in discrepancies between the rules of those Member States.

The objective of this proposal is therefore to amend Directives 2001/82/EC and 2001/83/EC in order to empower the Commission to extend the scope of the corresponding Variations Regulation, namely Regulation (EC) No 1084/2003. This would ensure that all medicinal products, regardless of the procedure under which they have been authorised, are subject to the same criteria for the evaluation, approval and administrative treatment of variations. This

---

1 OJ L 159, 27.6.2003, p.1 and OJ L 159, 27.6.2003, p. 24 respectively.

2 OJ L 311, 28.11.2001, p. 1. Directive as last amended by Directive 2004/28/EC (OJ L 136, 30.4.2004, p. 58).

3 OJ L 311, 28.11.2001, p. 67. Directive as last amended by Regulation (EC) No 1394/2007 (OJ L 324, 10.12.2007, p. 121).

4 OJ L 136, 30.4.2004, p. 1. Regulation as last amended by Regulation (EC) No 1394/2007 (OJ L 324, 10.12.2007, p. 121).

5 Directive 87/22/EEC on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology, OJ L 15, 17.1.1987, p. 38.

proposal is part of the Commission Legislative and Work Programme for 2008, under Annex 2 (simplification initiatives)[6]. It is also part of a broader 'Better Regulation' initiative to review the content of the Variations Regulations in order to make the framework simpler, clearer and more flexible, without compromising public and animal health[7].

1.2. General context

Purely national marketing authorisations represent the vast majority of authorisations in the European Community (more than 80%), both in the human and in the veterinary sector. Although purely national authorisations, like any other marketing authorisation for medicinal products within the European Community, are granted in accordance with the harmonised requirements laid down in Directive 2001/82/EC and Directive 2001/83/EC, changes to purely national authorisations are at present not subject to harmonised Community rules. For example, critical changes such as the introduction of a new therapeutic indication, or of a new method of administration, may be treated differently in the Member States as regards regulatory classification, administrative procedures, timelines and scientific criteria for the assessment of changes.

This situation has negative consequences in terms of public health, administrative burden and overall functioning of the internal market in pharmaceuticals.

From a public health perspective, there appears to be no justification for Member States applying different scientific criteria for evaluating changes to medicinal products.

From a legal perspective, it does not seem justified that the requirements for the granting of the initial marketing authorisation are fully harmonised at Community level, whereas the post-authorisation requirements are not.

From a practical perspective, the current situation increases the administrative and financial burden for both pharmaceutical companies and Member States competent authorities:

– Undertakings, which very often operate globally but on the basis of purely national authorisations, may be confronted with different rules in different Member States. This legal uncertainty may delay, impair or even prevent the introduction of certain changes, including changes which may benefit patients by improving the safety/efficacy profile of the concerned product(s). It also raises logistical issues for the actual implementation of changes;

– Member States competent authorities must follow different legal requirements, depending on whether they are dealing with changes to a purely national authorisation or not.

Finally, discrepancies amongst Member States as regards purely national variations may also affect the functioning of the internal market, by hindering the free movement of medicinal products initially authorised at a purely national level but subsequently undergoing mutual recognition.

1.3. Existing provisions in the area of the proposal

The proposal amends the two main pieces of Community legislation in the area of pharmaceuticals, namely:

– Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products;

---

6 http://ec.europa.eu/atwork/programmes/docs/clwp2008_en.pdf (see page 32)

7 http://ec.europa.eu/enterprise/pharmaceuticals/varreg/index.htm

– Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

Those two legislative acts, together with Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, lay down harmonised rules for the authorisation, supervision and pharmacovigilance of medicinal products within the Community.

1.4. Consistency with the other policies and objectives of the Union

The proposal is consistent with the overall objective of the Community pharmaceutical legislation, which is to remove disparities between national provisions in order to ensure the proper functioning of the internal market for medicinal products, while at the same time safeguarding a high level of protection of public, human and animal health. The proposal also complies with Article 152(1) of the Treaty establishing the European Community, which provides that a high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities.

2. CONSULTATION OF INTERESTED PARTIES AND IMPACT ASSESSMENT

2.1. Consultation of interested parties

Consultation methods, main sectors targeted and general profile of respondents

All interested parties, in particular patients associations, Member States competent authorities and industry associations, have been widely consulted on this proposal. Various means of consultation have been used, namely internet-based public consultation, dedicated workshops, questionnaires and bilateral meetings. In particular:

– a targeted consultation was conducted in October 2006-January 2007 with industry associations and Member States competent authorities, on the basis of an 'Issue paper';

– a public consultation was conducted in July-September 2007, on the basis of a draft proposal.

The detailed results of the public consultation process, including a summary of the outcome, are available on http://ec.europa.eu/enterprise/pharmaceuticals/varreg/index.htm. Additional details on the consultations conducted by the Commission can be found in the Impact Assessment attached to this proposal.

Summary of responses and how they have been taken into account

The Impact Assessment attached to this proposal contains a summary of all the responses received and explains how those responses have been taken into account by the Commission when preparing this proposal.

2.2. Impact assessment

The details of the impact assessment are provided in the Commission Staff Working Document 'Impact Assessment' attached to this proposal.

Several policy options have been considered by the Commission when preparing this proposal. The 'status quo' option (*i.e.* no change to the scope of application of the Community Variations Regulations) would leave the situation as it is today and would not address the harmonisation issue faced both by industry and by Member States competent authorities. The issue is all the more important as purely national authorisations are the vast majority of authorisations, both in the human and veterinary sector.

A 'partial harmonisation' option was envisaged, whereby only the technical requirements would be harmonised, while procedural aspects such as the timelines for evaluation of changes would remain subject to specific national rules. However, this would not address the main practical issue for economic operators, which is precisely related to the logistical complications that disharmonised procedures across various Member States can entail (*e.g.* different timelines for evaluation of changes).

A 'full harmonisation, no transitional period' option was envisaged. This option would readily address the harmonisation issue. However, it was recognised that a number of Member States competent authorities and companies have been working under national, sometimes diverging frameworks for many years already, and are actually used to these frameworks. Any proposal to modify the scope of the Regulation (EC) No 1084/2003 and to bring changes to purely national authorisations within this scope should therefore take into account the workload that such a regulatory 'shift' would entail for stakeholders. For this reason, a 'full harmonisation, with a period of transition' option appeared preferable.

It is important to note that since this legal proposal only concerns the legal base empowering the Commission to act at 'comitology' level, the abovementioned transitional period will be introduced only once the subsequent 'comitology' modification of the scope of Regulation (EC) No 1084/2003 is adopted. The transitional period will be introduced through a delay of application of this subsequent 'comitology' modification.

3. LEGAL ELEMENTS OF THE PROPOSAL

3.1. Summary of the proposed action

The proposal is of purely legal nature. It only modifies the legal basis of Regulation (EC) No 1084/2003, thereby empowering the Commission to modify subsequently the scope of that Regulation by 'comitology' procedure. Enlarging the scope of Regulation (EC) No 1084/2003 will ensure that all medicinal products placed on the Community market -including those authorised at purely national level - are subject to the same criteria for the approval and administrative handling of changes, regardless of the procedure under which those medicines have been authorised.

3.2. Legal basis

The proposal is based on Article 95 of the Treaty, which provides for the use of the 'co-decision' procedure referred to in Article 251 of the Treaty. Article 95 is the main legal basis of the whole Community pharmaceutical legislation, including Directive 2001/83/EC and Directive 2001/82/EC which this proposal seeks to amend.

3.3. Subsidiarity principle

The subsidiarity principle applies insofar as the proposal does not fall under the exclusive competence of the Community.

The proposal seeks to harmonise an area where, by definition, action of Member States alone is not sufficient to bring full harmonisation and currently leads to divergent approaches for the evaluation and supervision of changes to medicinal products. Action by Member States alone is therefore not expected to be sufficient to bring full harmonisation in this area. This issue is important from a quantitative point of view, since purely national authorisations are the vast majority of marketing authorisations within the Community.

Community action appears to be the most efficient way to achieve a genuine harmonisation and to ensure that all authorised medicinal products are subject to the same criteria for the

approval, administrative treatment and supervision of changes, regardless of the legal procedure under which those medicinal products have been authorised.

It is important to note that most of the purely national authorisations are related to relatively 'old' products which have often been authorised before the 'centralised' authorisation procedure was established (1995), but which are actually authorised in a large number of Community Member States (one product=one authorisation in Germany, one authorisation in Poland, one in Italy etc.). As a result, changes to these products simultaneously affect a large number of marketing authorisations in several Member States. The administrative burden and logistical complications caused by the current lack of harmonisation of the rules governing these changes are hence very high for industry operators.

It should also be borne in mind that the current situation also increases the administrative burden for Member States competent authorities, who have to apply different rules depending on whether they deal with a purely national authorisation, a mutual recognition procedure or a centralised authorisation. As a result, resources of the regulators (and the industry, see above paragraph) are being diverted away from public health protection.

Finally, the feedback gathered during the consultation phase demonstrates that the vast majority of stakeholders, including the authorities of Member States where a national system is in place, support harmonisation in this field.

3.4. Proportionality principle

The proposal has been carefully designed with all stakeholders, in order to avoid imposing an unnecessary regulatory burden. The proposal does not go beyond what is necessary to achieve the objective pursued, *i.e.* harmonisation of requirements for the evaluation and supervision of changes to medicinal products.

3.5. Choice of instruments

The proposal aims at laying down a proper legal basis for the examination, approval and supervision of variations to the terms of marketing authorisations for all medicinal products. Since the proposal amends two existing Directives, a Directive is considered as the most appropriate legal instrument.

4. BUDGETARY IMPLICATION

The proposal has no implication for the Community budget.

5. ADDITIONAL INFORMATION

5.1. Simplification

This project is referenced in the Commission Agenda Planning as 2008/ENTR/016. It is part of the Commission Legislative and Work Programme for 2008, under Annex 2 (simplification initiatives)[8].

This proposal is intended to allow the simplification of legislation and of administrative procedures for public authorities and private parties, as it provides the Commission with the power to modify the scope of Regulation (EC) No 1084/2003.

The proposal is expected to simplify legislation by allowing harmonisation, so that all operators within the European Community are subject to the same rules for the evaluation and

[8] http://ec.europa.eu/atwork/programmes/docs/clwp2008_en.pdf (see page 32)

supervision of changes to medicinal products, thereby eliminating diverging, redundant or contradicting requirements.

The proposal is expected to simplify the administrative procedures for Member States competent authorities by allowing harmonisation of the requirements for evaluation and supervision of all changes to all medicinal products. Thus, competent authorities will no longer have to follow different requirements depending on the legal status of the product.

The proposal is expected to simplify the administrative procedures for private parties, as companies, which very often operate globally but on the basis of purely national authorisations, will no longer be confronted with different rules in different Member States.

5.2. European Economic Area

The proposed act concerns an EEA matter and should therefore extend to the European Economic Area.

5.3. Note on comitology

Decision 1999/468/EC laying down the procedures for the exercise of implementing powers conferred on the Commission has been amended by Decision 2006/512/EC[9], which introduces the regulatory procedure with scrutiny. This procedure is applicable to implementing measures of general scope intended to amend non-essential elements of a basic instrument adopted in accordance with the procedure referred to in Article 251 of the Treaty (i.e. 'co-decision'), including by deleting some of those elements or by supplementing them by the addition of new non-essential elements.

As regards Directive 2001/83/EC, a Commission proposal amending this Directive and introducing the regulatory procedure with scrutiny for a number of implementing measures, including Article 35 of Directive 2001/83/EC concerning variations, has recently been agreed by the European Parliament and the Council[10]. For reasons of consistency, the regulatory procedure with scrutiny should therefore be kept in the amendments to Directive 2001/83/EC which this proposal lays down.

As regards Directive 2001/82/EC, a Commission proposal amending this Directive and introducing the regulatory procedure with scrutiny for a number of implementing measures, including Article 39 of Directive 2001/82/EC concerning variations, has recently been adopted by the Commission. For reasons of legal consistency, the amendments to Directive 2001/82/EC laid down in the referred Commission proposal should be outlined in this proposal as well.

---

9 OJ L 200, 22.7.2006, p. 11.

10 COM(2006)0919 – C6-0030/2007 – 2006/0295(COD)

2008/0045 (COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

amending Directive 2001/82/EC and Directive 2001/83/EC as regards variations to the terms of marketing authorisations for medicinal products

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission[1],

Having regard to the opinion of the European Economic and Social Committee[2],

Having regard to the opinion of the Committee of the Regions[3],

Acting in accordance with the procedure laid down in Article 251 of the Treaty[4],

Whereas:

(1) Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products[5], Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use[6] and Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[7], lay down harmonised rules for the authorisation, supervision and pharmacovigilance of medicinal products within the Community.

(2) Under those rules, marketing authorisations may be granted in accordance with harmonised Community procedures. The terms of those marketing authorisations may subsequently be varied where, for instance, the production process or the address of the manufacturer has changed.

(3) Article 39 of Directive 2001/82/EC and Article 35 of Directive 2001/83/EC empower the Commission to adopt an implementing Regulation as regards variations

---

1 OJ C […], […], p. […].
2 OJ C […], […], p. […].
3 OJ C […], […], p. […].
4 OJ C […], […], p. […].
5 OJ L 311, 28.11.2001, p. 1. Directive as last amended by Directive 2004/28/EC (OJ L 136, 30.4.2004, p. 58).
6 OJ L 311, 28.11.2001, p. 67. Directive as last amended by Regulation (EC) No 1394/2007 (OJ L 324, 10.12.2007, p. 121).
7 OJ L 136, 30.4.2004, p. 1. Regulation as last amended by Regulation (EC) No 1394/2007 (OJ L 324, 10.12.2007, p. 121).

subsequently made to marketing authorisations granted in accordance with the provisions of Chapter 4 of Title III of Directive 2001/82/EC and Chapter 4 of Title III of Directive 2001/83/EC, respectively. The Commission therefore adopted Regulation (EC) No 1084/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products granted by a competent authority of a Member State[8].

(4) However, the majority of medicinal products for human or veterinary use currently on the market have been authorised under purely national procedures and, as such, fall outside the scope of Regulation (EC) No 1084/2003. Variations to marketing authorisations granted under purely national procedures are thus subject to national rules.

(5) It results therefrom that while the granting of all marketing authorisations for medicinal products is subject to harmonised rules within the Community, this is not the case for variations to the terms of marketing authorisations.

(6) For reasons of public health, legal consistency and predictability for economic operators, variations to all types of marketing authorisations should be subject to harmonised rules.

(7) As regards Directive 2001/82/EC power should be conferred on the Commission in particular to adapt certain provisions and annexes, and to lay down specific conditions of application. Since those measures are of general scope and are designed to amend non-essential elements of that Directive and/or to supplement it by the addition of new non-essential elements, they must be adopted in accordance with the regulatory procedure with scrutiny provided for in Article 5a of Decision 1999/468/EC.

(8) Directive 2001/82/EC and Directive 2001/83/EC should therefore be amended accordingly,

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Amendments to Directive 2001/82/EC

Directive 2001/82/EC is amended as follows:

(1) Article 10(3) is replaced by the following:

"3. By way of derogation from Article 11, the Commission shall establish a list of substances essential for the treatment of equidae and for which the withdrawal period shall be not less than six months according to the control mechanisms laid down in Decisions 93/623/EEC and 2000/68/EC.

This measure, designed to amend non-essential elements of this Directive, by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a)."

(2) In Article 11(2), the third subparagraph is replaced by the following:

"However, the Commission may modify these specific withdrawal periods. Those measures**,** designed to amend non-essential elements of this Directive, shall be

[8] OJ L 159, 27.6.2003, p. 1.

adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a).”

(3) In Article 13(1), the fourth subparagraph is replaced by the following:

“However, the ten-year period provided for in the second subparagraph shall be extended to 13 years in the case of veterinary medicinal products for fish or bees or other species designated by the Commission.

That measure designed to amend non-essential elements of this Directive, by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a).”

(4) In Article 17(1), the second subparagraph is replaced by the following:

“If it appears justified in the light of new scientific evidence, the Commission may adapt points (b) and (c) of the first subparagraph. Those measures, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a).”

(5) The following Article 27b is inserted:

"Article 27b

The Commission shall adopt appropriate arrangements for the examination of variations to the terms of marketing authorisations granted in accordance with this Directive.

The Commission shall adopt these arrangements in the form of an implementing regulation. That regulation, measure designed to amend non-essential elements of this Directive, by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a)."

(6) In Article 39(1), the second and third subparagraphs are deleted.

(7) Article 50a (2) is replaced by the following:

“2. The Commission shall adopt any amendments which may be necessary to adapt the provisions of Paragraph 1 to take account of scientific and technical progress.

Those measures, designed to amend non-essential elements of this directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a).”

(8) In Article 51, the first subparagraph is replaced by the following:

“The principles and guidelines of good manufacturing practice for veterinary medicinal products referred to in Article 50(f) shall be adopted by the Commission in the form of a Directive addressed to the Member States. Those measures, designed to amend non-essential elements of this Directive, by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a).”

(9) In Article 67, point (aa) is replaced by the following:

“(aa) veterinary medicinal products for food-producing animals.

However, Member States may grant exemptions from this requirement according to criteria established by the Commission. The establishment of those criteria, measure designed to amend non-essential elements of this Directive, by supplementing it,

shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a).

Member States may continue to apply national provisions until either:

– the date of application of the decision adopted in accordance with the first subparagraph; or

– 1 January 2007, if no such decision has been adopted by 31 December 2006;"

(10) Article 68(3) is replaced by the following:

"3. The Commission shall adopt any amendments to the list of substances referred to in paragraph 1.

Those measures, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a)."

(11) Article 75(6) is replaced by the following:

"6. The Commission may amend paragraph 5 in the light of the experience gained from its operation.

Those measures, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a)."

(12) Article 79 is replaced by the following:

"Article 79

The Commission shall adopt any amendments which may be necessary to update Articles 72 to 78 to take account of scientific and technical progress.

Those measures, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a)."

(13) Article 88 is replaced by the following:

"Article 88

The Commission shall adopt any changes which are necessary in order to adapt Annex I to take account of technical progress.

Those measures, designed to amend non-essential elements of this Directive, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 89(2a)."

(14) Article 89 is amended as follows:

(a) The following paragraph 2a is inserted:

"2a. Where reference is made to this paragraph, Article 5a (1) to (4) and Article 7 of Decision No 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof".

(b) Paragraph 4 is replaced by the following:

"4. The rules of procedure of the Standing Committee shall be made public."

Article 2

Amendments to Directive 2001/83/EC

Directive 2001/83/EC is amended as follows:

(1) The following Article 23b is inserted:

"Article 23b

The Commission shall adopt appropriate arrangements for the examination of variations to the terms of marketing authorisations granted in accordance with this Directive.

These arrangements shall be adopted by the Commission in the form of an implementing regulation. This measure, designed to amend non-essential elements of this Directive, by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 121(2a)."

(2) In Article 35(1), the second and third subparagraphs are deleted.

Article 3

Transposition

1. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by [12 months after entry into force] at the latest. They shall forthwith communicate to the Commission the text of those provisions and a correlation table between those provisions and this Directive.

When Member States adopt those provisions, they shall contain a reference to this Directive or be accompanied by such a reference on the occasion of their official publication. Member States shall determine how such reference is to be made.

2. Member States shall communicate to the Commission the text of the main provisions of national law which they adopt in the field covered by this Directive.

Article 4

This Directive shall enter into force on the [twentieth] day following that of its publication in the Official Journal of the European Union.

Article 5

This Directive is addressed to the Member States.

Done at Brussels, […]

For the European Parliament	*For the Council*
The President	*The President*
[…]	*[…]*