BETTER REGULATION OF PHARMACEUTICALS:
TOWARDS A SIMPLER, CLEARER AND MORE FLEXIBLE FRAMEWORK ON VARIATIONS

Public consultation on the 'co-decision' part

What is the purpose of this consultation?

The Commission has announced its intention to make the regulatory framework covering changes to medicinal products (the 'Variations Regulations') simpler, clearer and more flexible. This initiative is the main contribution of this Commission to the 'Better Regulation' policy agenda in the field of pharmaceuticals.

With this public consultation, the Commission intends to consult all stakeholders on a proposal to modify the legal basis of the Variations Regulations, so that all authorised medicinal products are subject to the same criteria for the evaluation, approval and administrative handling of variations, regardless of the procedure under which those medicines have been initially authorised. With this public consultation, the Commission is committed to ensure that all stakeholders can make their views known on this important issue.

This public consultation **only** addresses the 'co-decision' part of this Better Regulation initiative. It does **not** address the aspects of the review which can be implemented through 'comitology'. These aspects will be addressed in another round of consultation.

Who is consulted?

Contributions are invited from all stakeholders dealing with medicines for human and/or veterinary use. Stakeholders who are not established within the European Union are equally invited to comment. Comments from Small and Medium-sized Enterprises (SMEs) involved in the pharmaceutical sector are especially welcomed.

How can I contribute?

Contributions should be sent by e-mail to nicolas.rossignol@ec.europa.eu, **before 21 September 2007**. Contributions should preferably not exceed 5 pages. An acknowledgement of receipt will be issued for each contribution received, within five working days. Contributions will be made publicly available on the 'Pharmaceuticals' website of the European Commission[1] once the consultation period is over, unless a specific request for confidentiality is made, in which case only an indication of the contributor will be disclosed. If you do not wish your contribution to be made public, please clearly indicate so.

What will happen next?

All contributions will be carefully analysed. A summary of the outcome of the consultation will be published on the 'Pharmaceuticals' website of the European Commission and also sent directly to all contributors. Any future proposal on the revision of the legal basis for the Variations Regulations will build on this consultation and will outline how its outcome was taken into account.

Any questions? Please contact at the European Commission:

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[1] http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm

COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, (Version 10 July 2007)
COM(2007)

xxx/xxx (COD)

DRAFT Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

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

(presented by the Commission)

This document does not represent an official position of the European Commission. It is a tool to explore the views of interested parties on a preliminary proposal. The suggestions contained in this document do not prejudge the form and content of any future proposal by the European Commission.

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DRAFT 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 handled either through national provisions or according to a specific Community legislative framework: the 'Variations Regulations'[2]. This framework applies both to medicines for human and veterinary use.

The Variations Regulations are implementing measures adopted by 'comitology' procedure. The legal basis for these implementing measures is laid down in Article 39 of Directive 2001/82/EC[3], Article 35 of Directive 2001/83/EC[4] and Articles 16 and 41 of Regulation (EC) No 726/2004[5]. This legal basis limits 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;

– medicinal products which have been considered within the scope of application of Directive 87/22/EEC[6] (so called 'ex-concertation' medicinal products).

However, the current Variations Regulations do not apply to changes to marketing authorisations for medicinal products granted at a national level by a Member State competent authority and which do not fall within the above categories (hereby referred to as "purely national" marketing authorisations). In the absence of Community harmonisation, changes affecting purely national authorisations are therefore handled according 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, the national rules vary from one country to the other, leading to disharmonised requirements and an unnecessary administrative burden.

The objective of this proposal is therefore to modify the legal basis of the Variations Regulations, so that all authorised medicinal products -including those authorised at purely

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2 Commission Regulation (EC) No 1084/2003, OJ L 159, 27.6.2003, p.1 and Commission Regulation (EC) No 1085/2003 OJ L 159, 27.6.2003, p.24.

3 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).

4 OJ L 311, 28.11.2001, p. 67. Directive as last amended by Directive 2004/27/EC (OJ L 136, 30.4.2004, p. 34).

5 OJ L 136, 30.4.2004, p. 1

6 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.

national level- are subject to the same criteria for the evaluation, approval and administrative handling of changes, regardless of the procedure under which those medicines have been initially authorised.

This proposal has been identified by the Commission as its main contribution in the field of pharmaceuticals to the overall simplification programme [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 are granted, like any other marketing authorisation for medicinal products within the European Community, 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 handled differently in Member States in terms of regulatory classification, administrative procedures, timelines and scientific criteria for assessment of the 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 why the scientific criteria for evaluating changes to medicinal products should be different from one Member State to the other.

From a legal perspective, does it make sense 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 burden both for pharmaceutical companies and for 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 countries. This legal uncertainty can 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 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.

[7] http://europa_eu.staging.entr.cec.eu.int/enterprise/regulation/better_regulation/simplification/entr.htm#2008

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;

– 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.

These 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 (hereinafter "the 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 respects Article 152(1) of the Treaty establishing the European Community, which lays down 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

Note: This Section 2 is preliminary only. It will be amended to take into account the results of the public consultation.

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' which is publicly available on: http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm

The results of the whole consultation process will be available on: http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm. Additional details on the consultations conducted by the Commission will be included in the Impact Assessment attached to the final proposal.

Summary of responses and how they have been taken into account

A summary of all the responses received as well as how they have been taken into account by the Commission when preparing this proposal will be provided in the Impact Assessment attached to the final proposal.

2.2. Impact assessment

Note: This section is to be completed once the results of the public consultation are known.

Once the public consultation is completed and the final Commission proposal is published, the detailed Impact Assessment carried out by the Commission will be accessible on: http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm.

3. LEGAL ELEMENTS OF THE PROPOSAL

3.1. Summary of the proposed action

The proposal modifies the legal basis of the Variations Regulations, so 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 establishing the European Community. Article 95, which prescribes the 'co-decision' procedure described in Article 251, is the main legal basis of the whole Community pharmaceutical legislation. The proposal amends Directive 2001/83/EC and Directive 2001/82/EC, which are also based on Article 95.

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.

EU action appears as 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 handling 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.

Finally, it should 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 whether they deal with a purely national authorisation, a mutual recognition procedure or a centralised authorisation. As a result, regulators' resources (and industry's, see above paragraph) are being diverted away from public health protection.

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 achieved 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 amendments 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. As the proposal concerns solely the exercise by the Commission of implementing powers, it does not require transposition by the Member States. Therefore it is not necessary to establish provisions for this purpose.

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 also part of the Commission Simplification Rolling Programme for 2006-2009[8].

The proposal provides for simplification of legislation, simplification of administrative procedures for public authorities, and simplification of administrative procedures for private parties.

The proposal is expected to simplify legislation by bringing harmonisation and exposing all operators within the European Community to the same rules for the evaluation and

[8] See "Commission Working Document: First progress report on the strategy for the simplification of the regulatory environment", COM(2006) 690 final, 14.11.2006. See also: http://europa_eu.staging.entr.cec.eu.int/enterprise/regulation/better_regulation/simplification/entr.htm#2008

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 harmonising 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.

[Note to the reader, for the purpose of the public consultation, 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.

Since the regulatory procedure with scrutiny has not yet been introduced in Directive 2001/82/EC and Directive 2001/83/EC, this proposal relies on the 'standard' regulatory procedure (without scrutiny). However, a Commission proposal adjusting Directive 2001/83/EC and introducing the regulatory procedure with scrutiny for a number of implementing measures, including the Variations Regulations, is currently in discussion in the European Parliament and in the Council[10]. The Commission intends to present other, similar proposals amending Directive 2001/82/EC, Regulation (EC) No 726/2004 and other legislative acts in the future. The present draft will be kept consistent with the developments on this issue.]

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9 OJ L 200, 22.7.2006, p. 11.

10 See COM(2006) 919 final, 22.12.2006, 2006/0295 (COD).

2005/0227 (COD)

DRAFT Proposal for a

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amending Directive 2001/82/EC and Directive 2001/83/EC as regards amendments 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 Commu nity, and in particular Article 95 thereof,

Having regard to the proposal from the Commission [11],

Having regard to the opinion of the European Economic and Social Committee [12],

Having regard to the opinion of the Committee of the Regions [13],

Acting in accordance with the procedure laid down in Article 251 of the Treaty [14],

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[15], 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[16] 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 [17] (hereinafter "the Agency"), lay

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11 OJ C , , p. .
12 OJ C , , p. .
13 OJ C , , p. .
14 OJ C , , p. .
15 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).
16 OJ L 311, 28.11.2001, p. 67. Directive as last amended by Directive 2004/27/EC (OJ L 136, 30.4.2004, p. 34).
17 OJ L 136, 30.4.2004, p. 1

down harmonised rules for the authorisation, supervision and pharmacovigilance of medicinal products within the Community.

(2) Since the granting of all marketing authorisations for medicinal products is subject to harmonised provisions within the Community, post-authorisation amendments to the terms of marketing authorisations should also, for reasons of consistency, be subject to harmonised rules.

(3) Article 39 of Directive 2001/82/EC, Article 35 of Directive 2001/83/EC and Articles 16 and 41 of Regulation (EC) No 726/2004 provide a legal basis for the establishment, in the form of implementing Regulations, of appropriate provisions concerning the examination of variations to the terms of certain marketing authorisations for medicinal products. However, this legal basis limits the scope of the implementing Regulations to medicinal products which have been granted a marketing authorisation in accordance with Regulation (EC) No 726/2004; to medicinal products which have been granted a marketing authorisation in accordance with the provisions of Chapter 4 of Directive 2001/83/EC or Chapter 4 of Directive 2001/82/EC; and to medicinal products which have been considered within the scope of application of Directive 87/22/EEC [18]. The implementing Regulations do not apply to changes to marketing authorisations for medicinal products granted at a national level by a Member State competent authority and which do not fall within the above categories.

(4) For reasons of public health, legal consistency and predictability for economic operators, the abovementioned legal basis should therefore be amended in order to provide for a harmonised regulatory framework covering all post-authorisation amendments to the terms of all marketing authorisations for medicinal products granted within the Community.

(5) In order to facilitate adaptation of all stakeholders to the new regulatory framework, a delay between the entry into force and the application of this Directive should be introduced.

(6) Directive 2001/82/EC and Directive 2001/83/EC should therefore be amended accordingly.

(7) Since the amendments made to Directive 2001/82/EC and Directive 2001/83/EC by this Directive concern solely the exercise by the Commission of implementing powers, they do not require transposition by the Member States. Therefore it is not necessary to establish provisions for this purpose,

HAVE ADOPTED THIS DIRECTIVE:

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[18] OJ L 15, 17.1.1987, p. 38.

Article 1

Amendments to Directive 2001/82/EC

Directive 2001/82/EC is amended as follows:

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

(2) The following Article 27aa is inserted:

"Article 27aa

The Commission shall adopt in the form of an implementing Regulation appropriate provisions for the examination of amendments to the terms of marketing authorisations granted in accordance with this Directive. This measure shall be adopted in accordance with the procedure referred to in Article 89(2)."

Article 2

Amendments to Directive 2001/83/EC

Directive 2001/83/EC is amended as follows:

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

(2) The following Article 23aa is inserted:

"Article 23aa

The Commission shall adopt in the form of an implementing Regulation appropriate provisions for the examination of amendments to the terms of marketing authorisations granted in accordance with this Directive. This measure shall be adopted in accordance with the procedure referred to in Article 121(2)."

Article 3

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

It shall apply from [*1 year after entry into force*].

Article 4

This Directive is addressed to the Member States.

Done at Brussels,

For the European Parliament
The President

For the Council
The President