The Revised SmPC Guideline

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DIA Regulatory Forum, London

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The Revised SmPC Guideline

Reasons for revising the Guideline

Changes, Implementation and Consequences

SmPC Guidance History

- **Directive 83/570/EEC… it is necessary from the point of view of public health and free movement of medicinal products for the competent authorities to have at their disposal all useful information on authorised medicinal products based in particular on summaries, adopted in other member states, of the characteristics of products.**

SmPC Guidance History

- **Sequence in SPC structured to highlight clinical orientation and the guideline on the sequence was found in III/9163: 89**
- **SPC is the basis of information for health professionals on how to use a product safely and effectively**
- **NOT there to give advice on treatment of particular medical conditions…. But specific aspects of treatment related to use of a product and it's effects should be mentioned**

SmPC Guidance Revision

- SmPC guideline revision: October 2005
- Consultation of CHMP, CMD(h) and WPs initiated June 2006
- Comments received from
  - BPWG, BWP, PGWP, PhWP, QWP, HMPC,
  - Ad-Hoc meetings with PEG members
  - QRD
  - EMEA staff, including Eudravigilance team
- Consultation of HCP WP on the existing guideline

European Medicines Agency

London, 14 December 2007
Doc. Ref. EMEA/299527/2007

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

DRAFT

PROPOSAL FOR A REVISION OF THE EUROPEAN COMMISSION GUIDELINE ON SUMMARY OF PRODUCT CHARACTERISTICS

This consultation applies to the proposed changes from Revision 1. These changes are highlighted in the text. This revision mainly aims to reflect new requirements in relation to the paediatric regulation and to further clarify guidance for some sections e.g. section 4.8 on undesirable effects.

TRANSMISSION TO CHMP	December 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	10 December 2007
END OF CONSULTATION ON PROPOSED CHANGES (DEADLINE FOR COMMENTS)	*28 March 2008*

Comments should be provided using this template and sent to MISecretariat@emea.europa.eu or by Fax: +44 20 75 23 71 29, by 28 March 2008.

To see the clean version of this draft revision of the SPC guideline, please follow this link

EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

Revision 2

NOTICE TO APPLICANTS

A GUIDELINE ON

SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC)

September 2009

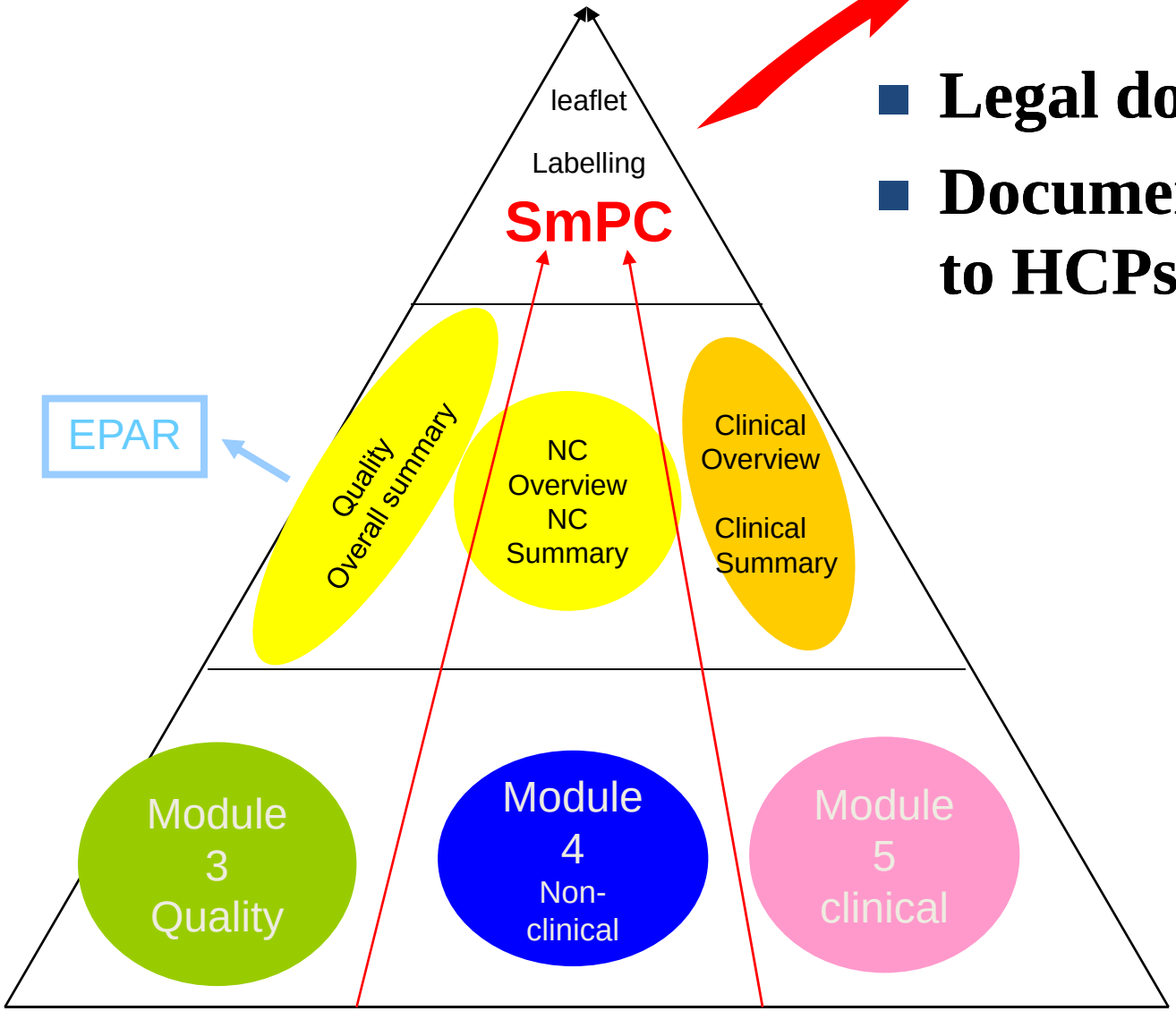
This guideline will be included in The Rules Governing Medicinal Products in the European Union Volume 2C Notice to Applicants

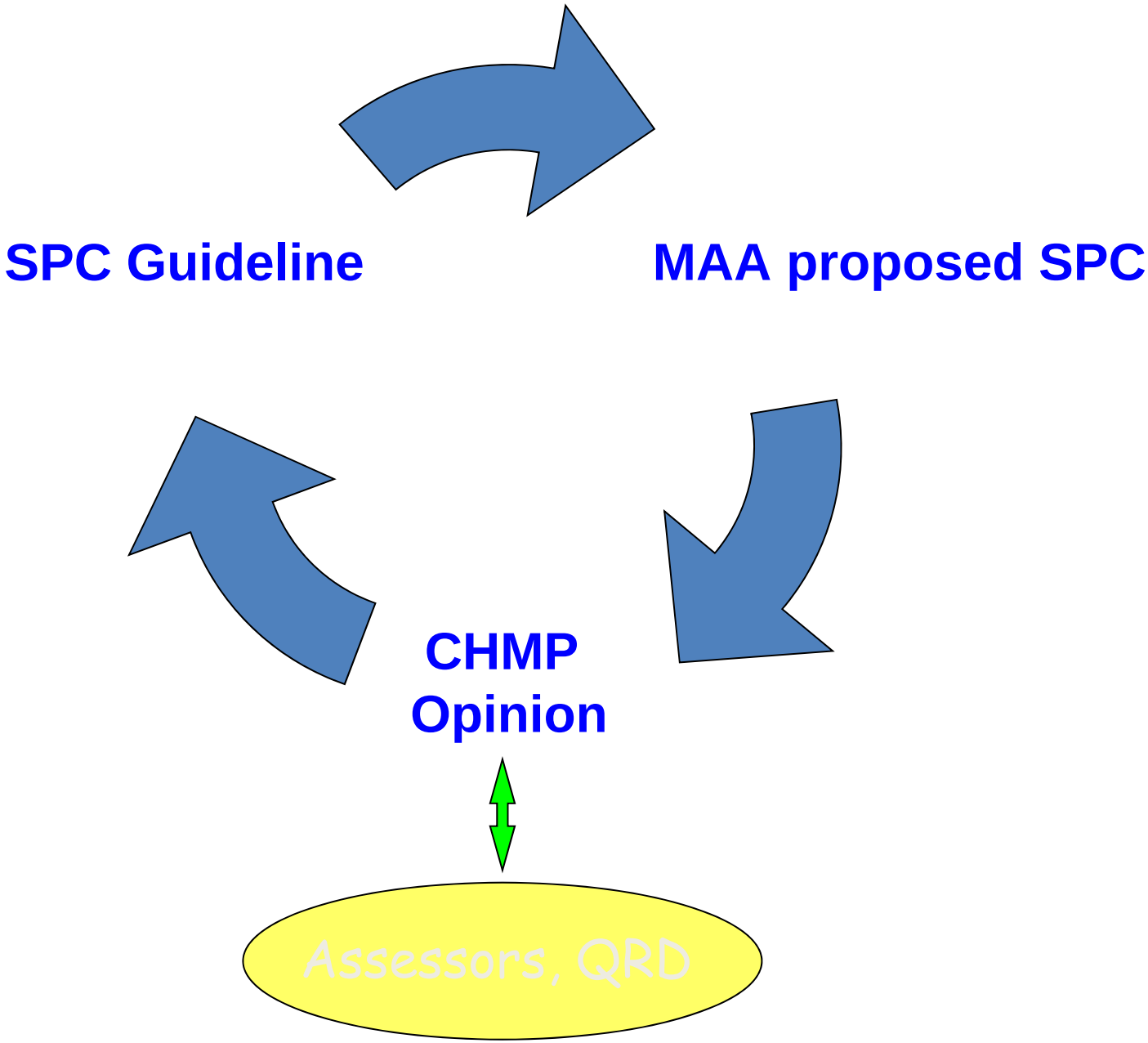
SmPC Guidance

- **Sets out the agreed position of the medicinal products as distilled during the course of assessment of the product.**
- **The definitive statement between the competent authority and the marketing authorisation holder; standardised presentation**
- **The common basis of communication between competent authorities of all member states**

Stakeholders

- **Legal document**
- **Document addressed to HCPs**



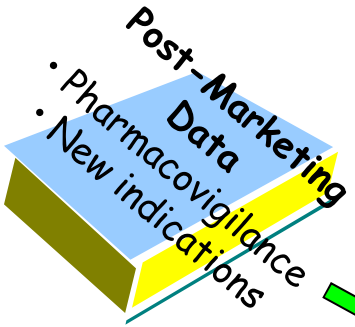

SPC Guideline
MAA proposed SPC
CHMP
Opinion
Assessors, QRD

Dir 2001/83/EC

Article 11

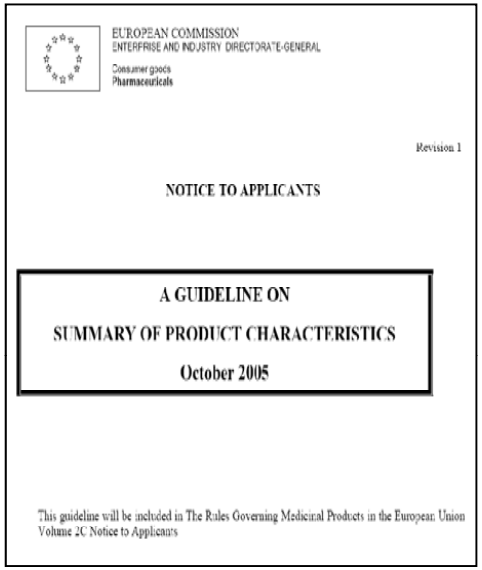
Future Regulation on advanced therapy medicinal products

Paediatric Regulation 1901/2006



SmPC

SmPC Guideline


EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL
Consumer goods
Pharmaceuticals

Revision 1

NOTICE TO APPLICANTS

A GUIDELINE ON
SUMMARY OF PRODUCT CHARACTERISTICS
October 2005

This guideline will be included in The Rules Governing Medicinal Products in the European Union Volume 2C Notice to Applicants

MA Application

EMEA Q, S&E Guidelines

"Core SmPC"

QRD Templates

HCP's needs

Disease concerned

SmPC: Legal and Scientific

- **Defined legal status under existing legislation**
- **Based on facts to provide prescribing and safety information and relevant background data to prescriber**
- **Basis for patient information leaflet**
- **Sets the limits for MAH marketing and promotion**

Why was the SmPC Guidance Revised?

- **Recent experience with SmPC Guidance**
- **Changes in legislation and guidance**
- **Changes in scientific and medical environment**

Why was the SmPC Guidance Revised?

Experience with existing SmPC Guidance

Previous revision October 2005

Last revision dealt with particular problems with sections 4.1 and 5.1

Since then, major problem areas identified were sections 4.6 and 4.8

Why SmPC Guidance Revision?

Changes in legislation and guidance

Paediatric Regulation

Advanced Therapies

Risk Management Plans

Pharmacovigilance

Why SmPC Guidance Revision?

Changes in scientific and medical environment

Medical and scientific progress

New therapies

SmPC Guidance Revision

- **Changes to Paediatric information**
- **Section 4.8**
- **Pharmacogenetic information**
- **Proprietary authentication factors “taggants”**

SmPC Guidance Revision

- S*m*PC
- Supplementary Protection Certificate

SmPC Guidance Revision

EC Paediatric Regulation (17)

To provide healthcare professionals and patients with *information on the safe and effective use of medicinal products in the paediatric population*, and as a transparency measure, information on the results of studies as well as on the status of the paediatric plans, waivers and deferrals, should be included in the product information

SmPC Guidance Revision

EC Paediatric Regulation

Article 28

Where authorisation is granted, the results of all those studies shall be included in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product, provided that the competent authority deems the information to be of use to patients, whether or not all the paediatric indications concerned were approved by the competent authority.

SmPC Guidance Revision

- Guidance for Paediatric Information in each SmPC section
  - Summary of available paediatric data,
  - Highlight of differences with adults or between paediatric subsets,
  - Information on waiver and deferral proposed in section 5.1

SmPC Guidance Revision

Guidance for Paediatric Information in many SmPC sections

Section 4.1 4.2 4.4 4.5 4.8 4.9 5.1 5.2

SmPC Revision: Section 4.1

Therapeutic Indications

- The indication should state *in which age groups the product is indicated, specifying* the age limits, e.g. ‘X is indicated in *<adults><neonates><infants>*<children> <adolescents> <aged x to y <years, months >

SmPC Revision: Section 4.2

- Specific subsection always included
- Information on subsets paediatric populations

4 possible overall conclusions :

- Indicated
- Contraindicated
- The <safety> <and> <efficacy> of X in children from the age of x to y <has><have> not <yet> been established; <no data are available> <currently available data are described in section <4.8><5.1><5.2>>.
- Not recommended because of a concern or no relevant use

SmPC Revision: Section 4.2

No indication in paediatric subset

- The <safety> <and> <efficacy> of X in children aged x to y <months, years> <*or any other relevant subsets e.g. weight, pubertal age, gender*> <*has*><*have*> *not* <*yet*> *been established.*

One of the following statements should be added:–

<No data are available>

or

<Currently available data are described in section <4.8><5.1> <5.2> but no recommendation on a posology can be made >

SmPC Revision: Section 4.2

No indication in paediatric subset

- X should not be used in children aged x to y <years, months><*or any other relevant subsets e.g. weight, pubertal age, gender> because of <safety> <efficacy> concern(s) <concern(s) to be stated* with cross-reference to sections detailing data (e.g. 4.8 or 5.1) >.
- There is no relevant use of X in <the paediatric population><in children aged x to y><years,months> <*or any other relevant subsets e.g. weight, pubertal age, gender> in the indication(s)*<specify indication(s)>.
- • X is contraindicated in children aged x to y <years, months> <*or any other relevant subsets e.g. weight, pubertal age, gender> <in the indication …> (cross-reference to section 4.3).*

SmPC Revision: Section 5.1

Paediatric population

- The results of all pharmacodynamic (clinically relevant) or efficacy studies conducted in children. Results should be stratified by age subsets.
- Where there is data but no indication, a cross-reference should be made to section 4.2, 4.4 or 4.3 as appropriate.
- For exploratory studies, the results of the main endpoints should be given with the main characteristics of the population studied and the doses used. However, explanatory studies should only be described in case of lack of confirmatory studies.

SmPC Revision: Section 5.1

Paediatric population

- For confirmatory studies, the objectives, the study duration, the doses used (and the formulation used if different from the marketed one), the main characteristics of the patient population studied (including age and numbers of patient), and the results regarding pre-specified primary endpoints should be provided, whether positive or negative. Outcomes if statistically compelling and relevant

- The objective and the main results or the conclusion of any specific clinical safety study should also be given.

SmPC Revision: Section 5.2

Paediatric population

- Results of pharmacokinetic studies in the different paediatric age group should be summarised, with a comparison to adults if available.
- If appropriate, the dose producing similar product exposure as in adults could be given.
- The pharmaceutical form(s) used for pharmacokinetic studies in children should be stated.
- Any uncertainties because of limited experience should be stated.

SmPC Guidance Revision

Section 4.8

Frequent discussions on how to present safety information

In practice, divergences with the principles of the guideline have been observed.

SmPC Revision: 4.8

In order to provide clear and readily accessible information, section 4.8 should be structured according to the following recommendations:

a. Summary of the safety profile

b. Tabulated summary of adverse reactions

c. Description of selected adverse reactions

d. Paediatric population

e. Other special population(s)

SmPC Guidance Revision: 4.8

- At authorisation, the content of this section must be justified in the Clinical Overview of the application on a best-evidence assessment of all observed adverse events and all facts relevant to the assessment of causality, severity and frequency.
- Should be **regularly reviewed** and if necessary, updated to ensure appropriate information to health care professionals on the safety profile of the product.
- Section could be **revised at renewal** of the marketing authorisation, where the safety profile of most products is likely to be well established, and thereafter at each of the three-yearly PSUR

SmPC Guidance Revision: 4.8

- Introduction: Summary of Safety Profile

The summary of the safety profile should inform on the most serious and/or most frequently occurring adverse reactions…..

Frequencies and timing

It should be consistent with the important identified risks mentioned in the Safety Specification of the Risk Management Plan and with the *Table* of Adverse Reactions.

SmPC Guidance Revision: 4.8

Table(s) of adverse reactions:

- A single table should list all adverse reactions with their respective frequency category. If necessary, for the clarity of the information, frequency figures may be presented in the table.
- Separate tables for separate indications are only acceptable in exceptional circumstances, e.g. when the underlying disease influences the adverse reaction profile markedly. For example, it might be the case for a product used in an oncology as well as in an non-oncology indication.
- The table should be introduced by a short paragraph stating the source and the extent of the safety database (e.g. from clinical trials, post-authorisation safety studies or spontaneous reporting).

SmPC Guidance Revision: 4.8

- Justified in the Clinical Overview

- R**egularly reviewed** and updated
- Table(s) of adverse reactions:
  - To be justified in clinical overview
  - Data from placebo-controlled studies
  - Data from other source
- Whole section **revised at renewal** and with each three-yearly PSUR

SmPC Guidance Revision

Principles of Presenting

- Clear and concise language
- To avoid duplication, each section should first describe information applicable to the general population to be treated followed by specific information necessary for any subset(s) of the population (e.g. children).
- Consistent terminology
- The SmPC provides information on a particular medicinal product; therefore it should not include reference to other medicinal product (e.g. through statement such as “Like other medicines of the same class …”) except when it is an official class warning recommended following a class review.
- Deviation from this guideline should be justified in the relevant Overview or Summary in the marketing authorisation application.

SmPC Guidance Revision: Others

Possibility to add **pharmacogenetic** information introduced for almost all sections

- 4.1: If the product's efficacy is related to a particular genotype, the expression of a gene or a particular phenotype, this should be stated in the indication.
- 4.2: Different dose recommendations based on genotype. Special population particular genotype
- 4.2: Situations where the medicinal product must not be given for safety reasons, i.e. contraindications, are the subject of this section. Such circumstances could include……. a particular genotype

SmPC Guidance Revision: Others

Add pharmacogenetic information

- 4.4:Subjects or patients with a specific genotype or phenotype might either not respond to the treatment or be at risk of a pronounced pharmacodynamic effect or adverse reaction. These may arise because of non-functioning enzyme alleles, alternative metabolic pathways (governed by specific alleles), or transporter deficiencies. Such situations should be clearly described if known.
- 4.8: Adverse reactions may be related to polymorphically determined product metabolism. Subjects or patients deficient in the specific enzyme may experience higher rate or severity of adverse reactions. This should be mentioned and where relevant correlated with data from clinical trials.

SmPC Guidance Revision: Others

- ***Section 6.1***:

  “In the case of a product containing a covert marker for the purpose of tracking, tracing and authentification, a general term such as “authentification factor” should be included in the list of excipients instead of the name of the excipient, unless the composition of the excipient is essential for safe administration of the medicinal product.”

SmPC Guidance Revision

- A visual description of the appearance of the product (colour, markings, etc.) *must* be given, in a separate paragraph to the standard term, including information on the actual size of a solid oral formulation,

SmPC Guidance Revision

Link to regulatory authority website

Public Assessment Reports provide detailed information on medicinal product and are available on the website of the European Medicines Agency or other National Competent Authorities. A link to the relevant website may be included in SmPCs.

SmPC Guidance Revision

Section 4.2

- In case of restricted medical prescription, this section should be started by specifying the conditions.
- *In case of specific safety or monitoring need, any recommended restriction to a particular type of clinical unit should also be stated.*

SmPC Guidance Revision

Section 4.4

- The conditions in which the use of the medicinal product could be acceptable, provided that special conditions for use are fulfilled.
- *In particular, specific risk minimisation measures requested as part of a Risk Management Plan to ensure safe and effective use should be described in this section*.

SmPC Guidance: implementation

- Prospectively.....

- Education of assessors

SmPC Guidance Revision: Consequences

Improved and consistent delivery of information

Adapted to legal and scientific changes

Incorporation safety information (RMP)

SmPC Guidance Revision

Follow the Guidance!

Thank you for your attention

Any questions?