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From:	Presidency
To:	Delegations
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Subject:	Proposal for a Directive of the European Parliament and of the Council on the Union code relating to medicinal products for human use, and repealing Directive 2001/83/EC and Directive 2009/35/EC Proposal for a Regulation of the European Parliament and of the Council laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006 *- Exchange of views*

Delegations will find in Annex the cluster on procedures for national marketing authorisations to be discussed at the meeting of the Working Party on Pharmaceuticals and Medical Devices on 07-08 November 2024.

Changes compared to the Commission proposals are indicated in ~~strikethrough~~ for deletions and **bold/underline** for new text. In addition, changes compared to those made in document 13450/24 are highlighted in grey.

ANNEX

‘Procedures for national MA – Cluster’

REVISED DIRECTIVE

Chapter III

Procedures for national marketing authorisations

Section 1

General provisions

Article 29

Examination of marketing authorisation application

1. In order to examine an application submitted in accordance with Articles 6 and 9 to 14, the competent authority of the Member State:
   (a) shall verify whether the particulars and documentations submitted in support of the application comply with Articles 6 and 9 to 14 (‘validation’), and examine whether the conditions for issuing a marketing authorisation set out in Articles 43 to 45 are complied with;
   (b) may submit the medicinal product, its starting materials or ingredients and, if need be, its intermediate products or other **constituents** ~~**materials**~~, for testing by an Official Medicines Control Laboratory or a laboratory that a Member State has designated for that purpose in order to ensure that the control methods employed by the manufacturer of medicinal products and described in the particulars accompanying the application in accordance with Annex I are satisfactory;
   (c) may, where appropriate, require the applicant to supplement the particulars accompanying the application in respect of the items listed in the Articles 6 and 9 to 14;
   (d) may consider and decide upon additional evidence **that is** available **to the competent authority of that Member State**, independently from the data submitted by the marketing authorisation applicant.

~~2. Where the competent authority of the Member State avails itself of the option referred to in the first subparagraph, point (c), the time limits laid down in Article 30 shall be suspended until such time as the supplementary information required has been provided or for the time allowed to the applicant for giving oral or written explanations.~~

3. Where**, in the course of the validation referred to in paragraph 1, point (a),** the competent authority of the Member State considers that the marketing authorisation application is incomplete, or contains ~~critical~~ deficiencies **to the extent** ~~-~~that **this** may prevent the evaluation of the ~~medicinal product~~ **application,** it shall inform the applicant accordingly and shall set a time limit for submitting the missing information and documentation. If the applicant fails to provide the missing information and documentation within the time limit set, the application shall be considered to have been withdrawn.

3a. Where the competent authority of the Member State avails itself of the option referred to in ~~the first subparagraph~~ **paragraph 1**, point (c), the time limits laid down in Article 30 shall be suspended until such time as the supplementary information required has been provided or for the time allowed to the applicant for giving ~~oral or written~~ explanations.

4. In cases where on examination of an application for a marketing authorisation the competent authority of the Member State considers that the submitted data are not of sufficient quality or maturity for the completion of the examination of the application, the examination can be terminated within 90 days of the **date of** validation of the application.

Prior to the termination, t~~T~~he competent authority of the Member State shall summarise the deficiencies in writing. On this basis, the competent authority of the Member State shall inform the applicant accordingly and set a time limit to address the deficiencies. The application shall be suspended until the applicant addresses the deficiencies. If the applicant fails to address those deficiencies within the time limit set by the competent authority of the Member State, the **examination shall be terminated and the** application shall be considered as withdrawn.

5. ~~**In case of a potential serious risk to public health with regards to a reference medicinal product, Member States shall suspend the examination of marketing authorisation applications submitted under Articles 9 to12 that refer to that reference medicinal product, until the end of the procedure initiated under Article 39.**~~

In case a potential serious risk to public health related to the reference medicinal product is examined under a specific procedure under this Directive or [revised Regulation (EC) No 726/2004], the Member States shall suspend the examination of any marketing authorisation application that uses the same reference medicinal product until the end of the procedure related to the reference medicinal product.

6. **Where a competent authority of the Member State** ~~**notes**~~ **is informed that another marketing authorisation application for the same medicinal product is being examined by a competent authority of another Member State,** ~~**the competent authority of the Member States concerned**~~ **it shall decline to examine the application and advise the applicant to use the procedure referred to in Articles 34 or 36.**

7. **Where the competent authorities of the Member States are informed that another Member State has authorised** ~~**a**~~ **the same medicinal product** ~~**that is the subject of a marketing authorisation application in the Member State concerned**~~**, they shall reject the application unless it was submitted in compliance with the provisions referred to in Articles** ~~**34 or**~~ **36.**

Article 30

Duration of examination of marketing authorisation application

Member States shall take all appropriate measures to ensure that the procedure for granting a marketing authorisation for medicinal products is completed within a maximum of ~~180~~ **210** days after the submission of a valid application from the date of validation of a marketing authorisation application.

Article 31

Types of national marketing authorisation procedures

National marketing authorisations may be granted in accordance with the procedures laid down in Article 32 ('purely national marketing authorisation procedure'), Articles 33 and 34 ('decentralised procedure for national marketing authorisation') or Articles 35 and 36 ('mutual recognition procedure for national marketing authorisation').

Section 2

Marketing authorisations valid in a single Member State

Article 32

Purely national marketing authorisation procedure

1. An application for marketing authorisation ~~according to Article 6(2)~~ under the purely national marketing authorisation procedure shall be submitted to the competent authority in that Member State in which the marketing authorisation is applied.

2. The competent authority in the Member State concerned shall examine the application in accordance with Articles 29 and 30**, draw up an assessment report** and grant a marketing authorisation in accordance with Articles 43 to 45 and applicable national provisions.

3. A marketing authorisation granted under the purely national marketing authorisation procedure shall be valid only in the Member State of the competent authority that granted it.

Section 3

Marketing authorisations valid in several Member States

Article 33

Scope of decentralised procedure for national marketing authorisations

1. **~~In cases where the medicinal product has not been granted a marketing authorisation at the time of application, a~~**An application for marketing authorisation under the decentralised procedure for national marketing authorisation in several Member States in respect of the same medicinal product shall be submitted to the competent authorities in those Member States in which the marketing authorisation is applied.

2. The competent authorities in the Member State concerned shall examine the applications in accordance with Articles 29, 30 and 34 and grant a marketing authorisation in accordance with Articles 43 to 45.

~~3. Where a competent authority of the Member State notes that another marketing authorisation application for the same medicinal product is being examined by the competent authority in another Member State, the competent authorities of the Member States concerned shall decline to examine the application and shall advise the applicant that the provisions referred to in Articles 35 and 36 apply.~~

~~4. Where the competent authorities of the Member States are informed that another Member State has authorised a medicinal product that is the subject of a marketing authorisation application in the Member State concerned, they shall reject the application unless it was submitted in compliance with the provisions referred to in Articles 35 and 36.~~

5. Marketing authorisations granted under **the** decentralised procedure for national marketing authorisation shall be valid only in those Member States of the competent authorit**ies**~~y~~ that granted ~~it~~ **such authorisations**.

Article 34

Decentralised procedure for national marketing authorisations

1. With a view to obtain a national marketing authorisation for a medicinal product in several Member States in respect of the same medicinal product under the decentralised procedure for national marketing authorisation, an applicant shall submit a marketing authorisation application based on an identical dossier to the competent authority of the Member State chosen by the applicant, to prepare an assessment report on the medicinal product in accordance with Article 43(5) and to act in accordance with this Section ('reference Member State for the decentralised procedure'), and to the competent authorities in the other Member States concerned.

2. The application for marketing authorisation shall contain:
   (a) the particulars and documentations referred to **in** Articles 6, 9 to 14 ~~and 62~~ **and 62**;
   (b) a list of Member States concerned by the application.

3. The applicant shall inform all the competent authorities of all Member States of its application at the time of submission. **If necessary to meet the needs of patients in that Member State,** ~~T~~**t**he competent authority of a Member State may request ~~for justified public health reasons~~ to enter the procedure and shall inform the applicant and the competent authority of the reference Member State for the decentralised procedure of its request within 30 days from the date of submission**validation** of the application. The applicant shall provide the competent authorities of those Member States entering the procedure with the application without undue delay.

3a. Where, in the course of the validation referred to in Article 29, paragraph 1, point (a), the competent authority of the reference Member State for the decentralised procedure considers that the information in the submitted marketing authorisation application is incomplete or contains deficiencies to the extent that this may prevent the evaluation of the application ~~not of sufficient quality or maturity for the completion of the examination~~, it shall inform the applicant accordingly and shall set a time limit for submitting the missing information and documentation. If the applicant fails to provide the missing information and documentation within the time limit set, the application shall be considered to have been withdrawn.

4. In cases where on examination of an application for a marketing authorisation the competent authority of the reference Member State for the decentralised procedure considers that the submitted data are not of sufficient quality or maturity for the completion of the examination of the application, the examination can be terminated within ~~90~~ **70** days of **the** ~~completion~~ **date of** the validation of the application.

Prior to the termination, ~~T~~**t**he competent authority of the reference Member State for the decentralised procedure shall summarise the deficiencies in writing. On this basis, the competent authority of the reference Member State for the decentralised procedure shall inform the applicant and the competent authorities of the Member States concerned accordingly and set a time limit to address the deficiencies. The application shall be suspended until the applicant addresses the deficiencies. If the applicant fails to address those deficiencies within the time limit set by the competent authority of the reference Member State for the decentralised procedure, the **assessment shall be terminated and the** application shall be considered as withdrawn.

The competent authority of the reference Member State for the decentralised procedure shall inform the competent authorities of the Member States concerned and the applicant accordingly.

5. Within 120 days after **the** ~~completion~~ **date of the** validation of the application, the competent authority of the reference Member State for the decentralised procedure shall prepare an assessment report, a summary of product characteristics, the labelling and the package leaflet and shall send them to the Member States concerned and to the applicant.

6. Within ~~60~~ **90** days of receipt of the assessment report, the competent authorities of the Member States concerned shall approve the assessment report, the summary of product characteristics and the labelling and package leaflet and shall inform the competent authority of the reference Member State for the decentralised procedure accordingly. The competent authority of the reference Member State for the decentralised procedure shall record the agreement of all parties, close the procedure and inform the applicant accordingly.

6a. Within 7 days of the receipt of the information under paragraph 6 the applicant shall submit the high quality translations of the summary of product characteristics, the labelling and the package leaflet to the each of the competent authorities concerned.

7. Within ~~30~~ **23** days after ~~acknowledgement of the agreement and~~ **receipt of the translations ~~of the summary of product characteristics, the labelling and the package leaflet from the applicant~~referred to in paragraph 6a**, the competent authorities of all Member States concerned in which an application has been submitted in accordance with paragraph 1 shall adopt a decision according to Articles 43 to 45 and in conformity with the approved assessment report, the summary of product characteristics and the labelling and package leaflet as approved.

Section 4

Mutual recognition of national marketing authorisations

Article 35

*Scope of mutual recognition procedure for national marketing authorisation**s***

1. Where the medicinal product has already received a marketing authorisation in accordance with Articles 43 to 45 at the time of application, it shall be recognised in other Member States in accordance with the procedure laid down in Article 36.

2. An application for marketing authorisation for mutual recognition procedure for national marketing authorisation, granted under Articles 43 to 45 ~~and in accordance with Article 32~~, shall be submitted to the competent authorities of other Member States in accordance with the procedure laid down in Article 36.

Article 36

Mutual recognition procedure for national marketing authorisations

1. An application for mutual recognition of a marketing authorisation, granted under Articles 43 to 45 ~~and in accordance with Article 32~~, in several Member States in respect of the same medicinal product shall be submitted to the competent authority of **one of** the Member State**s** that granted the marketing authorisation ('reference Member State for the mutual recognition procedure') and to the competent authorities of the Member States concerned where the applicant seeks to obtain a national marketing authorisation.

2. Application shall include a list of Member States concerned by the application.

3. The competent authority of the reference Member State for the mutual recognition procedure shall ~~reject~~ **refuse the validation and assessment of** an application for mutual recognition of marketing authorisation of medicinal product within a year ~~**six months**~~ from the granting of that marketing authorisation, unless the competent authority of the Member State informs the competent authority of the reference Member State for the mutual recognition procedure of its interest in this medicinal product.

4. The applicant shall inform the competent authorities of all Member States of its application at the time of submission **referred to in paragraph 1**. **If necessary to meet the needs of patients in that Member State,** ~~T~~**t**he competent authority of a Member State may request ~~for justified public health reasons~~ to enter the procedure and shall inform the applicant and the competent authority of the reference Member State for the mutual recognition procedure of its request within 30 days from the date of submission ~~**validation**~~ of the application. The applicant shall provide the competent authorities of those Member States entering the procedure with the application without undue delay.

5. If **any of** the competent authorities of the Member States concerned so require~~, the marketing authorisation holder shall request~~ the competent authority of the reference Member State for the mutual recognition procedure to update the assessment report drawn on the medicinal concerned by the application. In that case, the reference Member State shall update the assessment report within 90 days after **the ~~completion~~ date of the** validation of the application. If **none of** the competent authorities of the Member States concerned ~~do not~~ require**~~s~~** the update of the assessment report, the reference Member State shall provide the assessment report within 30 days **after the ~~completion~~ date of the validation of the application**.

6. Within ~~60~~ **90** days of receipt of the assessment report, the competent authorities of the Member States concerned shall approve the assessment report, the summary of product characteristics, the labelling and package leaflet and shall inform the competent authority of the reference Member State accordingly.

7. The competent authority of reference Member State for the mutual recognition procedure shall record the agreement of all parties, close the procedure and inform the applicant accordingly. The assessment report together with the summary of product characteristics, labelling and package leaflet approved by the competent authority of the reference Member State for the mutual recognition procedure shall be sent to the Member States concerned and to the applicant.

7a. Within 7 days of the receipt of the information under paragrpaph 7 the applicant shall submit the high quality translations of the the summary of product characteristics, the labelling and the package leaflet to the each of the competent authorities concerned.

8. Within ~~30~~ **23** days after ~~acknowledgement of the agreement~~ **and the receipt of the ~~high quality translations of the summary of product characteristics, the labelling and the package leaflet from the~~ applicant translations referred to in paragraph 7a**, the competent authorities of all Member States concerned in which an application has been submitted in accordance with paragraph 1 shall adopt a decision according to Articles 43 to 45 in conformity with the approved assessment report, the summary of product characteristics, the labelling and package leaflet as approved.

Section 5

Coordination of national marketing authorisation

Article 37

Coordination group for decentralised and mutual recognition procedures

1. A coordination group for decentralised and mutual recognition procedures ('coordination group') shall be set up for the following purposes:
   (a) the examination of any question relating to a national marketing authorisation of a medicinal product in two or more Member States in accordance with the procedures laid down in Sections 3, 4 and 5 of this Chapter, and Article 95;
   (b) the examination of questions related to the pharmacovigilance of medicinal products covered by national marketing authorisations, in accordance with Articles 108, 110, 112, 116 and 121;
   (c) the examination of questions relating to variations of national marketing authorisations, in accordance with Article 93(1)
   (d) the establishment and publication of a list of medicinal products for which a harmonised summary of product characteristics is to be drawn up, in accordance with Article 40.

   For the fulfilment of its pharmacovigilance tasks contemplated under first subparagraph, point (b), including approving risk management systems and monitoring their effectiveness, the coordination group shall rely on the scientific assessment and the recommendations of the Pharmacoigilance Risk Assessment Committee referred to in Article 149 of [revised Regulation (EC) No 726/2004].

2. The coordination group shall be composed of one representative per Member State appointed for a renewable period of three years. Member States may appoint an alternate for a renewable period of three years. Members of the coordination group may arrange to be accompanied by experts.

Members of the coordination group and experts shall, for the fulfilment of their tasks, rely on the scientific and regulatory resources available to competent authorities of the Member States. Each competent authority of the Member State shall monitor the level of expertise of the evaluations carried out and facilitate the activities of nominated coordination group members and experts.

Article 147 of [revised Regulation (EC) No 726/2004] shall apply to the coordination group as regards transparency and the independence of its members.

3. The Agency shall provide the secretariat of this coordination group. The coordination group shall draw up its own Rules of Procedure, which shall enter into force after a favourable opinion has been given by the Commission. These Rules of Procedure shall be made publicly available.

4. The Executive Director of the Agency or the representative of the Executive Director and representatives of the Commission shall be entitled to attend all meetings of the coordination group.

5. The members of the coordination group shall ensure that there is appropriate coordination between the tasks of that group and the work of competent authorities of the Member States, including the consultative bodies concerned with the marketing authorisation.

6. Where otherwise provided for in this Directive, within the coordination group, all Member States representatives shall use their best endeavours to reach a position by consensus on the action to be taken. If such a consensus cannot be reached, the position of the majority of the Member States represented within the coordination group shall prevail.

7. Members of the coordination group shall be required, even after their duties have ceased, not to disclose information of the kind covered by the obligation of professional secrecy.

Article 38

Divergent positions of Member States in decentralised or mutual recognition procedure

1. If, at the end of the period laid down in Articles 34(6) or 36(6), there is disagreement between Member States on whether the marketing authorisation can be issued, on the grounds of potential serious risk to public health, the disagreeing Member State concerned shall give a detailed explanation of the points of disagreement and the reasons for its position to the reference Member State, to the other Member States concerned and to the applicant. The points of disagreement shall be referred to the coordination group without undue delay.

2. Guidelines to be adopted by the Commission shall define a potential serious risk to public health.

3. Within the coordination group, ~~all disagreeing~~ Member States ~~concerned~~ shall use their best endeavours to reach agreement on the action to be taken. They shall allow the applicant the opportunity to make its point of view known orally or in writing. If, within 60 days of the communication of the points of disagreement, the Member States reach an agreement by consensus, the reference Member State shall record the agreement, close the procedure and inform the applicant accordingly. The procedure laid down in Articles 34(7) or 36(8) shall apply.

4. If within the 60-day period laid down in paragraph 3, an agreement by consensus cannot be reached, the position of the majority of the Member States represented within the coordination group**, with a detailed description of the matters on which the other Member States have been unable to reach an agreement and of all the divergent positions of Member States presented,** shall be forwarded to the Commission, which shall apply the procedure laid down in Article~~s 41 and~~ 42. **Where a Member State or the Commission considers that the matter shall be referred to the Committee for Medicinal Products for Human Use, Article 41 shall also apply.**

5. In the circumstances referred to in paragraph 4, Member States that have approved the assessment report, the summary of product characteristics, the labelling and package leaflet of the reference Member State may, at the request of the applicant, authorise the medicinal product without waiting for the outcome of the procedure laid down in Article 4~~1~~**2**. In that event, the national marketing authorisation granted shall be without prejudice to the outcome of that procedure.

Article 39

Referral procedure of divergent decisions of Member States

If applications for a national marketing authorisation have been submitted in accordance with Articles 6 and 9 to 14 for a particular medicinal product, and if Member States have adopted divergent decisions concerning the national marketing authorisation, its variation, suspension or revocation or the summary of product characteristics, the competent authority of the Member State, the Commission ~~or the marketing authorisation holder~~ may refer the matter to the Committee for Medicinal Products for Human Use for the application of the procedure laid down in Articles 41 and 42.

Article 40

Harmonisation of summary of product characteristics

1. In order to promote the harmonisation of national marketing authorisations for medicinal products throughout the Union, the competent authorities of the Member States ~~shall~~**may**, each year, forward to the coordination group referred to in Article 37 a list of medicinal products for which a harmonised summary of product characteristics is to be drawn up.

2. The coordination group ~~shall~~ **may** lay down a list of medicinal products for which a harmonised summary of product characteristics is to be drawn up, taking into account the proposals from the competent authorities of all Member States, and shall forward that list to the Commission.

3. The Commission or the competent authority of a Member State, in agreement with the Agency and taking into account the views of interested parties, may refer the matter concerning the harmonisation of summary of products characteristics of those medicinal products to the ~~Committee for Medicinal Products for Human Use for the application of the procedure laid down in Articles 41 and 42~~ **coordination group**.

Article 41

Scientific evaluation by the Committee for Medicinal Products for Human Use in a referral procedure

1. When reference is made to the procedure laid down in this Article, the Committee for Medicinal Products for Human Use referred to in Article 148 of [revised Regulation (EC) No 726/2004] shall consider the matter concerned and shall issue a reasoned opinion within 60 days from the date when the matter was referred to it.

   However, in cases submitted to the Committee for Medicinal Products for Human Use in accordance with Articles 39, 40 and 95, this period may be extended by the Committee for Medicinal Products for Human Use for a further period of up to 90 days.

On a proposal from its chairperson, the Committee for Medicinal Products for Human Use may agree to a shorter deadline.

2. In order to consider the matter, the Committee for Medicinal Products for Human Use shall appoint one of its members to act as rapporteur. The Committee may also appoint individual experts to advise it on specific questions. When appointing experts, the Committee for Medicinal Products for Human Use shall define their tasks and specify the time limit for the completion of these tasks.

3. Before issuing its opinion, the Committee for Medicinal Products for Human Use shall provide the applicant or the marketing authorisation holder with an opportunity to present written or oral explanations within a time limit which it shall specify.

The opinion of the Committee for Medicinal Products for Human Use shall be accompanied by a summary of product characteristics, the labelling and package leaflet.

If necessary, the Committee for Medicinal Products for Human Use may call upon any other person to provide information relating to the matter before it or consider a public hearing.

The Agency shall, in consultation with the parties concerned, draw up Rules of Procedure on the organisation and conduct of public hearings, in accordance with Article 163 of [revised Regulation (EC) No 726/2004].

The Committee for Medicinal Products for Human Use may suspend the time limits referred to in paragraph 1 in order to allow the applicant or the marketing authorisation holder to prepare explanations.

4. The Agency shall without undue delay inform the applicant or the marketing authorisation holder where the opinion of the Committee for Medicinal Products for Human Use provides that:

   (a) the application does not satisfy the criteria for a marketing authorisation;

   (b) the summary of product characteristics proposed by the applicant or the marketing authorisation holder in accordance with Article 62 is to be amended;

   (c) the marketing authorisation is to be granted subject to certain conditions, that are considered essential for the safe and effective use of the medicinal product, including pharmacovigilance;

   (d) a marketing authorisation is to be suspended, varied or revoked;

   (e) the medicinal product satisfies the conditions set out in Article 83 regarding medicinal products addressing an unmet medical need.

   Within 12 days after receipt of the opinion, the applicant or the marketing authorisation holder may notify the Agency in writing of its intention to request a re-examination of the opinion. In that case, they shall forward to the Agency the detailed grounds for the request within 60 days after receipt of the opinion.

   Within 60 days following receipt of the grounds for the request, the Committee for Medicinal Products for Human Use shall re-examine its opinion in accordance with Article 12(2), third subparagraph, of [revised Regulation (EC) No 726/2004]. The reasons for the conclusion reached further to its re-examination shall be annexed to the assessment report referred to in Article 12(2), third subparagraph, of [revised Regulation (EC) No 726/2004].

5. Within 12 days after its adoption, the Agency shall forward the final opinion of the Committee for Medicinal Products for Human Use to the competent authorities of the Member States, to the Commission and to the applicant or the marketing authorisation holder, together with a report describing the assessment of the medicinal product and stating the reasons for its conclusions.

In the event of an opinion in favour of granting or maintaining a marketing authorisation to place the medicinal product concerned on the market, the following documents shall be annexed to the final opinion:

(a) a summary of product characteristics, as referred to in Article 62;

(b) the details of any conditions affecting the marketing authorisation within the meaning of paragraph 4, first subparagraph, point (c);

(c) the details of any recommended conditions or restrictions with regard to the safe and effective use of the medicinal product;

(d) the labelling and package leaflet.

Article 42

Commission decision

1. Within 12 days of receipt of the opinion of the Committee for Medicinal Products for Human Use~~,~~ **or the position of the majority of the Member States represented within the coordination group, as set out in Article 38 (4),** the Commission shall submit to the Standing Committee on Medicinal Products for Human Use referred to in Article 214(1) a draft of the decision on the application, on the basis of the requirements set out in this Directive.

In duly justified cases, the Commission may return the opinion to the Agency **or the coordination group, as applicable,** for further consideration.

Where a draft decision envisages the granting of a marketing authorisation, it shall include or make reference to the documents referred to in Article **38(5) or** 41(5), second subparagraph.

Where a draft decision differs from the opinion of the Agency **or of the coordination group**, the Commission shall provide a detailed explanation of the reasons for the differences.

The Commission shall send the draft decision to the competent authorities of the Member States and the applicant or the marketing authorisation holder.

2. The Commission shall, by means of implementing acts, adopt a final decision within 12 days after obtaining the opinion of the Standing Committee on Medicinal Products for Human Use.

Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 214(2) and (3).

3. Where a Member State raises important new questions of a scientific or technical nature that have not been addressed in the opinion delivered by the Agency **or by the coordination group**, the Commission may refer the application back to the Agency **or to the coordination group, as applicable,** for further consideration. In that case, the procedures set out in paragraphs 1 and 2 shall start again upon reception of the reply of the Agency **or of the coordination group**.

4. The decision referred to in paragraph 2 shall be addressed to all Member States and forwarded for information to the applicant or the marketing authorisation holder. The Member States concerned and the reference Member State shall adopt a decision to either grant**, suspend, refuse** or revoke the marketing authorisation, or vary its terms as necessary to comply with the decision referred to in paragraph 2 within 30 days following its notification. In the decision to grant, suspend, **refuse,** revoke or vary the marketing authorisation, the Member States shall refer to the decision adopted pursuant to paragraph 2. They shall inform the Agency **or the coordination group** accordingly**, as applicable**.

5. Where the scope of the procedure initiated under Article 95 includes medicinal products covered by centralised marketing authorisation pursuant to Article 95(2), third subparagraph, the Commission shall, where necessary, adopt decisions to vary, suspend or revoke the marketing authorisations or to refuse the renewal of the marketing authorisations concerned in accordance with this Article.

Section 6

Results of examination of a national marketing authorisation application

Article 43

Granting of the national marketing authorisation

1. When a competent authority of the Member State grants a national marketing authorisation, it shall inform the applicant of the marketing authorisation of the summary of product characteristics, the package leaflet, the labelling as well as any conditions established in accordance with Articles 44 and 45 together with any deadlines for the fulfilment of those conditions.

2. The competent authorities of the Member States shall take all necessary measures to ensure that the information given in the summary of product characteristics is in conformity with that accepted when the national marketing authorisation is granted or subsequently.

~~3. The competent authorities of the Member States shall, without undue delay, make publicly available the national marketing authorisation together with the summary of product characteristics,~~ **~~the labelling,~~** ~~the package leaflet as well as any conditions established in accordance with Articles 44, 45 and any obligations imposed subsequently in accordance with Article 87, together with any deadlines for the fulfilment of those conditions and obligations for each medicinal product that they have authorised.~~

4. The competent authority of the Member State may consider and decide upon additional evidence available, independently from the data submitted by the marketing authorisation holder. On that basis, **if the additional evidence has an impact on the benefit-risk balance of a medicinal product,** the summary of product characteristics shall be updated. **Such updates shall be made by the variation procedure or the application of the procedures laid down in Arfticle 40 or 41. For medicinal products authorised in accordance with Articles 34 or -36, the reference Member State and all concerned member States shall be involved.** ~~in accordance with t~~**The procedure referred to in Articles 38, 39 or 40 shall apply as appropriate.** ~~if the additional evidence has an impact on the benefit-risk balance of a medicinal product.~~ **If the summary of product characteristics has been updated in accordance with this paragraph, the Member State shall inform the reference Member State or the Member States concerned if the procedure referred to in Articles 34 and or 36 was applied.**

~~5. The competent authorities of the Member States shall draw up an assessment report and make comments on the file as regards the results of the pharmaceutical and non-clinical tests, the clinical studies, the risk management system, the environmental risk assessment and the pharmacovigilance system of the medicinal product concerned.~~

6. The competent authorities of the Member States shall make the assessment report publicly available without undue delay, together with the reasons for their opinion, after deletion of any information of a commercially confidential nature. The justification shall be provided separately for each therapeutic indication applied for.

7. The public assessment report referred to in paragraph **6**~~5~~ shall include a summary written in a manner that is understandable to the public. The summary shall contain, in particular, a section relating to the conditions of use of the medicinal product.

8. The competent authorities of the Member States shall, without undue delay, make publicly available the national marketing authorisation together with the summary of product characteristics, the package leaflet as well as any conditions established in accordance with Articles 44, 45 and any obligations imposed subsequently in accordance with Article 87, together with any deadlines for the fulfilment of those conditions and obligations for each medicinal product that they have authorised.

Article 44

National marketing authorisation subject to conditions

1. A marketing authorisation for a medicinal product may be granted subject to one or more of the following conditions:
   (a) to take certain measures for ensuring the safe use of the medicinal product to be included in the risk management system;
   (b) to conduct post-authorisation safety studies;
   (c) to comply with obligations on the recording or reporting of suspected adverse reactions that are stricter than those referred to in Chapter IX;
   (d) any other conditions or restrictions with regard to the safe and effective use of the medicinal product;
   (e) the existence of an adequate pharmacovigilance system;
   (f) to conduct post-authorisation efficacy studies where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed;
   (g) in case of medicinal products for which there is ~~substantial~~ **specific** uncertainty as to the surrogate endpoint relation to the expected health outcome, where appropriate and relevant for the benefit-risk balance, a post-authorisation obligation to substantiate the clinical benefit;

   (ga) in case of the environmental risk assessment suffering from deficiencies at the time of application, or if the risk identified in the environmental risk assessment has not been sufficiently addressed by the applicant, to implement appropriate risk mitigation measures;

(h) to conduct post-authorisation environmental risk assessment studies, collection of monitoring data or information on use, where identified or potential concerns about risks to the environment or public health, including antimicrobial resistance need to be further investigated after the medicinal product has been marketed;

(i) to conduct post-authorisation studies to improve the safe and effective use of the medicinal product;

(j) where appropriate, to carry out medicinal product-specific validation studies to replace animal-based control methods with non-animal-based control methods.

An obligation to conduct post authorisation efficacy studies referred to in the first subparagraph, point (f), shall be based on the delegated acts adopted pursuant to Article 88.

2. The marketing authorisation shall lay down deadlines for the fulfilment of the conditions referred to in paragraph 1, first subparagraph, where necessary.

Article 45

National marketing authorisation under exceptional circumstances

1. In exceptional circumstances where, in an application under Article 6 for a marketing authorisation of a medical product, or in an application under Article 92 for a new therapeutic indication of an existing marketing authorisation, an applicant is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use, the competent authority of the Member State may, by derogation to Article 6, grant an authorisation under Article 43, subject to specific conditions, where the following requirements are met:

(a) the applicant has demonstrated, in the application file, that there are objective and verifiable reasons not to be able to submit comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use based on one of the grounds set out in Annex II;

(b) except for the data referred to in point (a), the application file is complete and satisfies all the requirements of this Directive;

(c) specific conditions are included in the decision of the competent authorities of the Member States, in particular to ensure the safety of the medicinal product as well to ensure that the marketing authorisation holder notifies to the competent authorities of the Member States any incident relating to its use and takes appropriate action where necessary.

2. The maintenance of the authorised new therapeutic indication and the validity of the national marketing authorisation shall be linked to the reassessment of the conditions set out in paragraph 1 after **the deadline specified by the competent authority or** two years from the date when the new therapeutic indication was authorised or the marketing authorisation was granted, and thereafter at a risk-based frequency to be det~~va~~ermined by the competent authorities of the Member State and specified in the marketing authorisation.

This reassessment shall be conducted on the basis of an application by the marketing authorisation holder to maintain the authorised new therapeutic indication or renew the marketing authorisation under exceptional circumstances.

Article 46

Validity and renewal of marketing authorisation

1. Without prejudice to paragraph 4, a marketing authorisation for a medicinal product shall be valid for an unlimited period.

By way of derogation from the first subparagraph, a national marketing authorisation granted in accordance with Article 45(1) shall be valid for five years and be subject to renewal in accordance with paragraph 2.

By way of derogation from the first subparagraph, a competent authority of the Member State may decide at the time of granting the national marketing authorisation, on objectively and duly justified grounds relating to safety of the medicinal product, to limit the validity of the national marketing authorisation to five years.

2. The marketing authorisation holder may submit an application for a renewal of a national marketing authorisation granted under paragraph 1, second or third subparagraph. Such application shall be submitted at least nine months before the national marketing authorisation ceases to be valid.

3. Once the application for a renewal has been submitted within the time limit provided for in paragraph 2, the national marketing authorisation shall remain valid until the competent authority of the Member State adopts a decision.

4. The competent authority of the Member State may renew the national marketing authorisation on the basis of a re-evaluation of the benefit-risk balance. Once renewed, the marketing authorisation shall be valid for an unlimited period.

Article 47

Refusal of a national marketing authorisation

1. The national marketing authorisation shall be refused if, after verification of the particulars and documentations referred to in Article 6 and subject to the specific requirements laid down in Articles 9 to 14, the view is taken that:
   (a) the benefit-risk balance is not considered to be favourable;
   (b) that the applicant has not properly or sufficiently demonstrated the quality, safety or efficacy of the medicinal product;
   (c) its qualitative and quantitative composition is not as declared;
   (d) **the data for** the environmental risk assessment **submitted by the applicant suffers from major deficiencies, unless it is considered, taking into account the benefit of the immediate availability of the medicinal product concerned, that those deficiencies shall be addressed with post-authorisation environmental risk assessment studies;** ~~is incomplete or insufficiently substantiated by the applicant or if the risks identified in the environmental risk assessment have not been sufficiently addressed by the applicant;~~
   (e) the **summary of product characteristics,** labelling and package leaflet proposed by the applicant ~~are not in accordance~~ **do not comply with** with Chapter VI **or they are not in accordance with the particulars listed in the summary of product characteristics**.

2. The national marketing authorisation shall also be refused if any particulars or documentations submitted in support of the application do not comply with Article 6, paragraphs 1 to 6, and Articles 9 to 14.

3. The applicant or the marketing authorisation holder shall be responsible for the accuracy of the particulars and documentations submitted.

Section 7
Specific requirements for paediatric medicinal products

Article 48

Compliance with the paediatric investigation plan

1. The competent authority of the Member State for which an application for marketing authorisation or variation of a marketing authorisation is submitted under the provisions of this Chapter or of the Chapter VIII, shall verify whether it complies with the requirements laid down in Article 6(5).

2. Where the application is submitted in accordance with the procedure set out in this Chapter, Sections 3 and 4, the verification of compliance, including, as appropriate, requesting an opinion of the Agency in accordance with paragraph 3, point (b), shall be conducted by the reference Member State.

3. The Committee for Medicinal Products for Human Use, as referred to in Article 148 of [revised Regulation (EC) No 726/2004] may, in the following cases, be requested to give its opinion as to whether studies conducted by the applicant are in compliance with the agreed paediatric investigation plan as defined in Article 74 of [revised Regulation (EC) No 726/2004]:
   (a) by the applicant, prior to submitting an application for a marketing authorisation or for a variation of a marketing authorisation;

(b) by the competent authority of the Member State, when validating an application for a marketing authorisation or for a variation of a marketing authorisation that does not already include such an opinion.

4. In the case of a request in accordance with paragraph 3, point (a), the applicant shall not submit its application until the Committee for Medicinal Products for Human Use has provided its opinion, and a copy thereof shall be annexed to the application.

5. Member States shall take due account of an opinion drawn up in accordance with paragraph 3.

6. When the competent authority of the Member State, during the scientific assessment of a valid application for a marketing authorisation or a variation of a marketing authorisation, concludes that the studies are not in conformity with the agreed paediatric investigation plan, the medicinal product shall not be eligible for the rewards and incentives provided for in Article 86.

Article 49

Data deriving from a paediatric investigation plan

1. Where a marketing authorisation or a variation of a marketing authorisation, is granted in accordance with the provisions under this Chapter or of the provisions under Chapter VIII:
   (a) the results of all clinical **and non-clinical** studies, conducted in compliance with an agreed paediatric investigation plan as referred to in Article 6(5), point (a), shall be included in the summary of product characteristics and, if appropriate, in the package leaflet, or
   (b) any agreed waiver as referred to in Article 6(5), points (b) and (c), shall be recorded in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product concerned.

2. If the application complies with all the measures contained in the agreed completed paediatric investigation plan and if the summary of product characteristics reflects the results of studies conducted in compliance with that agreed paediatric investigation plan, the competent authority of the Member State shall include within the marketing authorisation a statement indicating compliance of the application with the agreed completed paediatric investigation plan.

3. An application for new therapeutic indications, including paediatric indications, new pharmaceutical forms, new strengths and new routes of administration of medicinal products authorised in accordance with the provisions under this Chapter or of the provisions under Chapter VIII and which are protected either by a supplementary protection certificate under [Regulation (EC) No 469/2009 - OP please replace reference by new instrument when adopted], or by a patent which qualifies for the granting of the supplementary protection certificate, may be submitted under the procedure laid down in Articles 41 and 42.

4. The procedure referred to in paragraph 3 shall be limited to the assessment of the specific section of the summary of product characteristics to be varied.

Chapter I:

Subject matter, scope and definitions

Article 4

Definitions

(9) ‘competent authorities’ means the Agency and the competent authorities of the Members States;

(10) ‘Agency’ means the European Medicines Agency;

(11) ‘non-clinical’ means a study or a test conducted in vitro, in silico, or in chemico, or a non-human in vivo test related to the investigation of the safety and efficacy of a medicinal product. Such test may include simple and complex human cell-based assays, microphysiological systems including organ-on-chip, computer modelling, other non-human or human biology-based test methods, and animal-based tests;

(37) ‘paediatric investigation plan’ means a research and development programme aimed at ensuring that the necessary data are generated determining the conditions in which a medicinal product may be authorised to treat the paediatric population;

(38) ‘paediatric population’ means that part of the population aged between birth and 18 years;

(41) ‘benefit-risk balance’ means an evaluation of the positive therapeutic effects of the medicinal product in relation to the risks referred to in point (35), subpoint (a);