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Price: EUR 4

(Continued overleaf)

⁽¹⁾ Text with EEA relevance

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Acts whose titles are printed in light type are those relating to day-to-day management of agricultural matters, and are generally valid for a limited period.

The titles of all other acts are printed in bold type and preceded by an asterisk.

This issue closes the L series for 2010.

DIRECTIVES

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⁽¹⁾ Text with EEA relevance

I

(Legislative acts)

REGULATIONS

**REGULATION (EU) No 1235/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 15 December 2010****amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products****(Text with EEA relevance)**

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee ⁽¹⁾,

Having regard to the opinion of the Committee of the Regions ⁽²⁾,

Having regard to the opinion of the European Data Protection Supervisor ⁽³⁾,

Acting in accordance with the ordinary legislative procedure ⁽⁴⁾,

Whereas:

(1) Regulation (EC) No 726/2004 ⁽⁵⁾ creates a Union-wide marketing authorisation procedure for certain categories of medicinal products (the 'centralised procedure'), lays down rules for the pharmacovigilance of those products and establishes the European Medicines Agency (the 'Agency').

(2) Pharmacovigilance rules are necessary for the protection of public health in order to prevent, detect and assess

adverse reactions to medicinal products for human use placed on the Union market, as the full safety profile of medicinal products for human use can be known only after they have been placed on the market.

(3) The pollution of waters and soils with pharmaceutical residues is an emerging environmental problem. Member States should consider measures to monitor and evaluate the risk of environmental effects of such medicinal products for human use, including those which may have an impact on public health. The Commission should, based, inter alia, on data received from the Agency, the European Environment Agency, and Member States, produce a report on the scale of the problem, along with an assessment on whether amendments to Union legislation on medicinal products for human use or other relevant Union legislation are required.

(4) In the light of the experience acquired and following an assessment by the Commission of the Union system of pharmacovigilance, it has become clear that it is necessary to take measures in order to improve the operation of Union law on the pharmacovigilance of medicinal products for human use.

(5) The main tasks of the Agency in the area of pharmacovigilance laid down in Regulation (EC) No 726/2004 should be maintained and further developed, in particular as regards the management of the Union pharmacovigilance database and data-processing network (the 'Eudravigilance database'), the coordination of safety announcements by the Member States and the provision to the public of information regarding safety issues.

⁽¹⁾ OJ C 306, 16.12.2009, p. 22.

⁽²⁾ OJ C 79, 27.3.2010, p. 50.

⁽³⁾ OJ C 229, 23.9.2009, p. 19.

⁽⁴⁾ Position of the European Parliament of 22 September 2010 (not yet published in the Official Journal) and Council Decision of 29 November 2010.

⁽⁵⁾ OJ L 136, 30.4.2004, p. 1.

- (6) In order to allow all competent authorities to receive, access simultaneously and share pharmacovigilance information for medicinal products for human use authorised in the Union, the Eudravigilance database should be maintained and strengthened as the single point of receipt of such information. Member States should therefore not impose any additional reporting requirements on marketing authorisation holders. The database should be fully and permanently accessible to the Member States, the Agency and the Commission, and accessible to an appropriate extent to marketing authorisation holders and the public.
- (7) In order to increase transparency as regards pharmacovigilance issues, a European medicines web-portal should be created and maintained by the Agency.
- (8) In order to ensure the availability of the necessary expertise and resources for pharmacovigilance assessments at Union level, it is appropriate to create a new scientific committee within the Agency: the Pharmacovigilance Risk Assessment Committee. That committee should be composed of members appointed by Member States who are competent in the safety of medicines including the detection, assessment, minimisation and communication of risk, and in the design of post-authorisation safety studies and pharmacovigilance audits, and of members appointed by the Commission, who are independent scientific experts, or representatives of healthcare professionals and patients.
- (9) The rules on Scientific Committees of the Agency laid down in Regulation (EC) No 726/2004 should apply to the Pharmacovigilance Risk Assessment Committee.
- (10) In order to ensure harmonised responses across the Union to safety concerns regarding medicinal products for human use, the Committee for Medicinal Products for Human Use and the coordination group established by 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⁽¹⁾ should rely on the recommendations of the Pharmacovigilance Risk Assessment Committee with regard to any question relating to the pharmacovigilance of medicinal products for human use. However, for the sake of consistency and continuity of the safety assessments, the final responsibility for issuing an opinion on the risk-benefit assessment of medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004 should remain with the Committee for Medicinal Products for Human Use and with the authorities competent for the granting of marketing authorisations.
- (11) It is appropriate that the Pharmacovigilance Risk Assessment Committee should give a recommendation as part of any Union-wide post-authorisation assessment based on pharmacovigilance data relating to medicinal products for human use and it should be responsible for making recommendations on risk management systems and monitoring their effectiveness. Such Union-wide assessments should follow the procedures laid down in Directive 2001/83/EC also for medicinal products for human use that were authorised through the centralised procedure.
- (12) In accordance with Directive 2001/83/EC the Agency provides the secretariat to the coordination group. In view of the enlarged mandate of the coordination group in the area of pharmacovigilance, the technical and administrative support by the secretariat of the Agency to the coordination group should be reinforced. Provision should be made for the Agency to ensure appropriate coordination between the coordination group and the Agency's Scientific Committees.
- (13) In order to protect public health, the pharmacovigilance activities of the Agency should be adequately funded. It should be ensured that adequate funding is possible for pharmacovigilance activities by empowering the Agency to charge fees to marketing authorisation holders. However, the management of those collected funds should be under the permanent control of the Management Board in order to guarantee the independence of the Agency.
- (14) To ensure the highest levels of expertise and the functioning of the Pharmacovigilance Risk Assessment Committee, rapporteurs providing assessments for Union pharmacovigilance procedures, periodic safety update reports, post-authorisation safety study protocols and risk management systems should receive payment through the Agency.
- (15) Therefore, the Agency should be empowered to charge fees in return for performing the activities of the coordination group within the Union system of pharmacovigilance, as provided for in Directive 2001/83/EC, and the rapporteurs within the coordination group should, in turn, be paid by the Agency.
- (16) It is necessary, from a public health perspective, to complement the data available at the time of authorisation with additional data about the safety and, in certain cases, also about the efficacy of medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004. The Commission should therefore be empowered to impose on the marketing authorisation holder the obligation to conduct post-authorisation studies on safety and on efficacy. It should be

⁽¹⁾ OJ L 311, 28.11.2001, p. 67.

possible to impose that obligation at the time of granting the marketing authorisation or later, and it should be a condition of the marketing authorisation. Such studies may be aimed at collecting data to enable the assessment of safety or efficacy of medicinal products for human use in everyday medical practice.

(17) It is essential that a strengthened system of pharmacovigilance not lead to the premature granting of marketing authorisations. However, some medicinal products for human use are authorised subject to additional monitoring. This includes all medicinal products for human use with a new active substance and biological medicinal products, including biosimilars, which are priorities for pharmacovigilance. Competent authorities may also require additional monitoring for specific medicinal products for human use that are subject to the obligation to conduct a post-authorisation safety study or to conditions or restrictions with regard to the safe and effective use of the medicinal product that will be specified in the risk management plan. Risk management plans are normally required for new active substances, biosimilars, medicinal products for paediatric use and for medicinal products for human use involving a significant change in the marketing authorisation, including a new manufacturing process of a biotechnologically-derived medicinal product. Medicinal products for human use subject to additional monitoring should be identified as such by a black symbol, which will be selected by the Commission on the basis of a recommendation by the Pharmacovigilance Risk Assessment Committee, and an appropriate standardised explanatory sentence in the summary of product characteristics and in the package leaflet. The Agency should keep an up-to-date, publicly available list of such medicinal products.

(18) Experience has shown that the responsibilities of marketing authorisation holders with regard to pharmacovigilance of authorised medicinal products for human use should be clarified. The marketing authorisation holder should be responsible for continuously monitoring the safety of its medicinal products for human use, for informing the authorities of any changes that might have an impact on the marketing authorisation, and for ensuring that the product information is kept up to date. As medicinal products for human use could be used outside the terms of the marketing authorisation, the marketing authorisation holder's responsibilities should include providing all available information, including the results of clinical trials or other studies, as well as reporting any use of the medicinal product which is outside the terms of the marketing authorisation. It is also appropriate to ensure that all relevant information collected on the safety of the medicinal product for human use is taken into account when the marketing authorisation is being renewed.

(19) Scientific and medical literature is an important source of information on suspected adverse reaction case reports.

Currently, for active substances included in more than one medicinal product for human use, literature cases are reported in adverse reaction case reports in a duplicative way. In order to enhance the efficiency of reporting, the Agency should monitor a defined list of literature for a defined list of active substances used in medicinal products for which there are several marketing authorisations.

(20) As a result of the submission of all suspected adverse reaction data for medicinal products for human use authorised by the Member States directly to the Eudra-vigilance database, it is not necessary to provide for different reporting rules for medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004. The rules on suspected adverse reaction recording and reporting laid down in Directive 2001/83/EC should therefore apply to medicinal products for human use authorised in accordance with Regulation (EC) No 726/2004.

(21) It is necessary to increase the shared use of resources between competent authorities for the assessment of periodic safety update reports. The assessment procedures provided for in Directive 2001/83/EC should therefore apply for the single assessment of periodic safety update reports for different medicinal products for human use containing the same active substance or the same combination of active substances, including joint assessments of medicinal products for human use authorised both nationally and through the centralised procedure.

(22) It is appropriate to strengthen the supervisory role for medicinal products for human use authorised through the centralised procedure by providing that the supervisory authority for pharmacovigilance should be the competent authority of the Member State in which the pharmacovigilance system master file of the marketing authorisation holder is located.

(23) This Regulation shall apply without prejudice to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data⁽¹⁾ and Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on

⁽¹⁾ OJ L 281, 23.11.1995, p. 31.

the free movement of such data⁽¹⁾. In order to detect, assess, understand and prevent adverse reactions, and to identify and take actions to reduce the risks of, and increase the benefits from, medicinal products for human use for the purpose of safeguarding public health, it should be possible to process personal data within the Eudravigilance system while respecting the Union legislation relating to data protection. The purpose of safeguarding public health constitutes a substantial public interest and consequently the processing of personal data can be justified if identifiable health data are processed only when necessary and only when the parties involved assess this necessity at every stage of the pharmacovigilance process.

(24) This Regulation and Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use⁽²⁾ widen the tasks of the Agency with regard to pharmacovigilance, including the monitoring of literature cases, the improved use of information technology tools and the provision of more information to the general public. The Agency should be enabled to fund these activities from fees charged to marketing authorisation holders. These fees should not cover tasks carried out by national competent authorities for which such authorities charge fees in accordance with Directive 2001/83/EC.

(25) The pharmacovigilance activities provided for in this Regulation require that uniform conditions be established as concerns the contents and maintenance of the pharmacovigilance system master file, as well as the minimum requirements for the quality system for the performance of pharmacovigilance activities by the Agency, the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities, and the minimum requirements for the monitoring of the data contained in the Eudravigilance database to determine whether there are new risks or whether risks have changed. The format and content of the electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders, the format and content of electronic periodic safety update reports and risk management plans as well as the format of protocols, abstracts and final study reports for the post-authorisation safety studies should also be established. In accordance with Article 291 of the Treaty on the Functioning of the European Union (TFEU), rules and general principles concerning mechanisms for the control by Member States of the Commission's exercise of implementing powers are to be laid down in advance by a regulation adopted in accordance with the ordinary legislative procedure. Pending the adoption of that new regulation, Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission⁽³⁾ continues to

apply, with the exception of the regulatory procedure with scrutiny, which is not applicable.

(26) The Commission should be empowered to adopt delegated acts in accordance with Article 290 TFEU in order to supplement the provisions in point (cc) of Article 9(4) and in point (b) of Article 10a(1) of Regulation (EC) No 726/2004. The Commission should be empowered to adopt supplementary measures laying down the situations in which post-authorisation efficacy studies may be required. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level.

(27) The provisions on the monitoring of medicinal products for human use in Regulation (EC) No 726/2004 constitute specific provisions in the meaning of Article 15(2) of Regulation (EC) No 765/2008 of the European Parliament and of the Council of 9 July 2008 setting out the requirements for accreditation and market surveillance relating to the marketing of products⁽⁴⁾.

(28) Proper coordination between the newly established Pharmacovigilance Risk Assessment Committee and the other Committees of the Agency, in particular the Committee for Medicinal Products for Human Use, the Committee for Orphan Medicinal Products and the Committee for Advanced Therapies established under Regulation (EC) No 1394/2007⁽⁵⁾ should be ensured.

(29) Regulations (EC) No 726/2004 and (EC) No 1394/2007 should therefore be amended accordingly,

HAVE ADOPTED THIS REGULATION:

Article 1

Amendments to Regulation (EC) No 726/2004

Regulation (EC) No 726/2004 is hereby amended as follows:

1. in Article 5(2) the following sentence is added:

'For the fulfilment of its pharmacovigilance tasks, including the approval of risk management systems and monitoring their effectiveness provided for under this Regulation, the Committee for Medicinal Products for Human Use shall rely on the scientific assessment and recommendations of the Pharmacovigilance Risk Assessment Committee referred to in Article 56(1)(aa).';

2. Article 9(4) is amended as follows:

(a) the following point is inserted:

'(aa) a recommendation on the frequency of submission of periodic safety update reports';

⁽¹⁾ OJ L 8, 12.1.2001, p. 1.

⁽²⁾ See page 74 of this Official Journal.

⁽³⁾ OJ L 184, 17.7.1999, p. 23.

⁽⁴⁾ OJ L 218, 13.8.2008, p. 30.

⁽⁵⁾ OJ L 324, 10.12.2007, p. 121.

(b) the following points are inserted:

‘(ca) details of any recommended measures for ensuring the safe use of the medicinal product to be included in the risk management system;

(cb) if appropriate, details of any recommended obligation to conduct post-authorisation safety studies or to comply with obligations on the recording or reporting of suspected adverse reactions which are stricter than those referred to in Chapter 3;

(cc) if appropriate, details of any recommended obligation 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. Such an obligation to conduct such studies shall be based on the delegated acts adopted pursuant to Article 10b while taking into account the scientific guidance referred to in Article 108a of Directive 2001/83/EC;’

(c) point (e) is replaced by the following:

‘(e) the assessment report as regards the results of the pharmaceutical and pre-clinical tests and of the clinical trials, and as regards the risk management system and the pharmacovigilance system for the medicinal product concerned;’

3. Article 10 is amended as follows:

(a) paragraph 1 is replaced by the following:

‘1. Within 15 days after receipt of the opinion referred to in Article 5(2), the Commission shall prepare a draft of the decision to be taken in respect of the application.

Where a draft decision envisages the granting of a marketing authorisation, it shall include or make reference to the documents mentioned in points (a) to (d) of Article 9(4).

Where a draft decision envisages the granting of a marketing authorisation subject to the conditions referred to in points (c), (ca), (cb), or (cc) of Article 9(4), it shall lay down deadlines for the fulfilment of the conditions, where necessary.

Where the draft decision differs from the opinion of the Agency, the Commission shall attach a detailed explanation of the reasons for the differences.

The draft decision shall be forwarded to Member States and the applicant;’

(b) paragraph 6 is replaced by the following:

‘6. The Agency shall disseminate the documents referred to in points (a) to (d) of Article 9(4),

together with any deadlines laid down pursuant to the third subparagraph of paragraph 1 of this Article;’

4. the following Articles are inserted:

‘Article 10a

1. After the granting of a marketing authorisation, the Agency may impose an obligation on the marketing authorisation holder:

(a) to conduct a post-authorisation safety study if there are concerns about the risks of an authorised medicinal product. If the same concerns apply to more than one medicinal product, the Agency shall, following consultation with the Pharmacovigilance Risk Assessment Committee, encourage the marketing authorisation holders concerned to conduct a joint post-authorisation safety study;

(b) to conduct a post-authorisation efficacy study when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly. The obligation to conduct the post-authorisation efficacy study shall be based on the delegated acts adopted pursuant to Article 10b while taking into account the scientific guidance referred to in Article 108a of Directive 2001/83/EC.

The imposition of such an obligation shall be duly justified, notified in writing, and shall include the objectives and timeframe for submission and conduct of the study.

2. The Agency shall provide the marketing authorisation holder with an opportunity to present written observations in response to the imposition of the obligation within a time limit which it shall specify, if the marketing authorisation holder so requests within 30 days of receipt of the written notification of the obligation.

3. On the basis of the written observations submitted by the marketing authorisation holder, and of the opinion of the Agency, the Commission shall withdraw or confirm the obligation. Where the Commission confirms the obligation, the marketing authorisation shall be varied to include the obligation as a condition of the marketing authorisation and the risk management system shall be updated accordingly.

Article 10b

1. In order to determine the situations in which post-authorisation efficacy studies may be required under point (cc) of Article 9(4) and point (b) of Article 10a(1) of this Regulation, the Commission may adopt, by means of delegated acts in accordance with Article 87b, and subject to the conditions of Articles 87c and 87d, measures supplementing the provisions in point (cc) of Article 9(4) and point (b) of Article 10a(1).

2. When adopting such delegated acts, the Commission shall act in accordance with the provisions of this Regulation.;

5. Article 14 is amended as follows:

(a) the second subparagraph of paragraph 2 is replaced by the following:

‘To this end, the marketing authorisation holder shall provide the Agency with a consolidated version of the file in respect of quality, safety and efficacy, including the evaluation of data contained in suspected adverse reactions reports and periodic safety update reports submitted in accordance with Chapter 3, and information on all variations introduced since the marketing authorisation was granted, at least 9 months before the marketing authorisation ceases to be valid in accordance with paragraph 1.’;

(b) paragraph 3 is replaced by the following:

‘3. Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the Commission decides, on justified grounds relating to pharmacovigilance, including exposure of an insufficient number of patients to the medicinal product concerned, to proceed with one additional five-year renewal in accordance with paragraph 2.’;

(c) paragraph 8 is replaced by the following:

‘8. In exceptional circumstances and following consultation with the applicant, the marketing authorisation may be granted subject to certain conditions, in particular relating to the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. The marketing authorisation may be granted only when the applicant can show that he is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use, for objective, verifiable reasons and must be based on one of the grounds set out in Annex I to Directive 2001/83/EC. Continuation of the marketing authorisation shall be linked to the annual reassessment of these conditions.’;

6. the following Article is inserted:

‘Article 14a

The marketing authorisation holder shall incorporate any conditions referred to in points (c), (ca), (cb) and (cc) of Article 9(4) or in Article 10a, or in Article 14(7) and (8) in his risk management system.’;

7. Article 16 is replaced by the following:

‘Article 16

1. After a marketing authorisation has been granted in accordance with this Regulation, the marketing authorisation holder shall, in respect of the methods of manufacture and control provided for in points (d) and (h) of Article 8(3) of Directive 2001/83/EC, take account of scientific and technical progress and introduce any changes that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods. He shall apply for approval of corresponding variations in accordance with this Regulation.

2. The marketing authorisation holder shall forthwith provide the Agency, the Commission and the Member States with any new information which might entail the amendment of the particulars or documents referred to in Article 8(3), Article 10, 10a, 10b and 11, or Article 32(5) of Directive 2001/83/EC, in Annex I thereto, or in Article 9(4) of this Regulation.

In particular, the marketing authorisation holder shall forthwith inform the Agency and the Commission of any prohibition or restriction imposed by the competent authorities of any country in which the medicinal product is marketed and of any other new information which might influence the evaluation of the benefits and risks of the medicinal product concerned. The information shall include both positive and negative results of clinical trials or other studies in all indications and populations, whether or not included in the marketing authorisation, as well as data on the use of the medicinal product where such use is outside the terms of the marketing authorisation.

3. The marketing authorisation holder shall ensure that the product information is kept up to date with the current scientific knowledge including the conclusions of the assessment and recommendations made public by means of the European medicines web-portal established in accordance with Article 26.

4. In order to be able to continuously assess the risk-benefit balance, the Agency may at any time ask the marketing authorisation holder to forward data demonstrating that the risk-benefit balance remains favourable. The marketing authorisation holder shall answer fully and promptly any such request.

The Agency may at any time ask the marketing authorisation holder to submit a copy of the pharmacovigilance system master file. The marketing authorisation holder shall submit the copy at the latest 7 days after receipt of the request.’;

8. Article 18 is amended as follows:

(a) paragraph 1 is replaced by the following:

‘1. In the case of medicinal products manufactured within the Union, the supervisory authorities for manufacturing shall be the competent authorities of the Member State or Member States which granted the manufacturing authorisation provided for in Article 40(1) of Directive 2001/83/EC in respect of the medicinal product concerned.’;

(b) in paragraph 2, the first subparagraph is replaced by the following:

‘In the case of medicinal products imported from third countries, the supervisory authorities for imports shall be the competent authorities of the Member State or Member States that granted the authorisation provided for in Article 40(3) of Directive 2001/83/EC to the importer, unless appropriate agreements have been made between the Union and the exporting country to ensure that those controls are carried out in the exporting country and that the manufacturer applies standards of good manufacturing practice at least equivalent to those laid down by the Union.’;

(c) the following paragraph is added:

‘3. The supervisory authority for pharmacovigilance shall be the competent authority of the Member State in which the pharmacovigilance system master file is located.’;

9. Article 19 is amended as follows:

(a) paragraph 1 is replaced by the following:

‘1. The supervisory authorities for manufacturing and imports shall be responsible for verifying on behalf of the Union that the marketing authorisation holder for the medicinal product or the manufacturer or importer established within the Union satisfies the requirements concerning manufacturing and imports laid down in Titles IV and XI of Directive 2001/83/EC.

The supervisory authorities for pharmacovigilance shall be responsible for verifying on behalf of the Union that the marketing authorisation holder for the medicinal product satisfies the pharmacovigilance requirements laid down in Titles IX and XI of Directive 2001/83/EC. They may, if this is considered necessary, conduct pre-authorisation inspections to verify the accuracy and

successful implementation of the pharmacovigilance system as it has been described by the applicant in support of his application.’;

(b) in paragraph 3, the second subparagraph is replaced by the following:

‘The inspection shall be undertaken by inspectors from the Member States who possess the appropriate qualifications. They may be accompanied by a rapporteur or expert appointed by the Committee referred to in paragraph 2. The report of the inspectors shall be made available electronically to the Commission, the Member States and the Agency.’;

10. Article 20 is amended as follows:

(a) paragraph 3 is replaced by the following:

‘3. Following an opinion by the Agency, the Commission shall adopt the necessary provisional measures, which shall be applied immediately.

A final decision in respect of the medicinal product concerned shall be adopted within 6 months, in accordance with the regulatory procedure referred to in Article 87(2).

The Commission may also adopt a decision addressed to the Member States pursuant to Article 127a of Directive 2001/83/EC.’;

(b) the following paragraphs are added:

‘8. Notwithstanding paragraphs 1 to 7 of this Article, the Union procedures laid down in Article 31 and Article 107i of Directive 2001/83/EC shall apply, as appropriate, where the reason for the Member State or the Commission to consider taking decisions or measures referred to in this Article is based on the evaluation of data resulting from pharmacovigilance activities.

9. By way of derogation from paragraphs 1 to 7 of this Article, where a procedure under Article 31 or Articles 107i to 107k of Directive 2001/83/EC concerns a range of medicinal products or a therapeutic class, medicinal products that are authorised in accordance with this Regulation and that belong to that range or class shall only be included in the procedure under Article 31, or Articles 107i to 107k of that Directive.’;

11. Chapter 3 of Title II is replaced by the following:

‘CHAPTER 3

PHARMACOVIGILANCE

Article 21

1. The obligations of marketing authorisation holders laid down in Article 104 of Directive 2001/83/EC shall apply to marketing authorisation holders for medicinal products for human use authorised in accordance with this Regulation.

Without prejudice to paragraphs 2, 3 and 4 of this Article, holders of marketing authorisations granted before 2 July 2012 shall, by way of derogation from Article 104(3)(c) of Directive 2001/83/EC not be required to operate a risk management system for each medicinal product.

2. The Agency may impose an obligation on a marketing authorisation holder to operate a risk management system, as referred to in point (c) of Article 104(3) of Directive 2001/83/EC, if there are concerns about the risks affecting the risk-benefit balance of an authorised medicinal product. In that context, the Agency shall also oblige the marketing authorisation holder to submit a detailed description of the risk-management system which he intends to introduce for the medicinal product concerned.

The imposition of such obligations shall be duly justified, notified in writing, and shall include the timeframe for submission of the detailed description of the risk-management system.

3. The Agency shall provide the marketing authorisation holder with an opportunity to present written observations in response to the imposition of the obligation within a time limit which it shall specify, if the marketing authorisation holder so requests within 30 days of receipt of the written notification of the obligation.

4. On the basis of the written observations submitted by the marketing authorisation holder, and of the opinion of the Agency, the Commission shall withdraw or confirm the obligation. Where the Commission confirms the obligation, the marketing authorisation shall be varied accordingly, to include the measures to be taken as part of the risk management system as conditions of the marketing authorisation referred to in point (ca) of Article 9(4).

Article 22

The obligations of marketing authorisation holders laid down in Article 106a(1) of Directive 2001/83/EC, and the obligations of the Member States, the Agency and the Commission laid down in paragraphs 2, 3 and 4 of that Article shall apply to the safety announcements referred to in point (e) of Article 57(1) of this Regulation concerning

medicinal products for human use authorised in accordance with this Regulation.

Article 23

1. The Agency shall, in collaboration with the Member States, set up, maintain and make public a list of medicinal products that are subject to additional monitoring.

That list shall include the names and active substances of:

(a) medicinal products authorised in the Union that contain a new active substance which, on 1 January 2011, was not contained in any medicinal product authorised in the Union;

(b) any biological medicinal product not covered by point (a) that was authorised after 1 January 2011.

2. At the request of the Commission, following consultation with the Pharmacovigilance Risk Assessment Committee, medicinal products that are authorised pursuant to this Regulation subject to conditions referred to in points (c), (ca), (cb) and (cc) of Article 9(4), or in Articles 10a, Article 14(7) and (8) and in Article 21(2), may also be included in the list.

At the request of a national competent authority, following consultation with the Pharmacovigilance Risk Assessment Committee, medicinal products that are authorised pursuant to Directive 2001/83/EC, subject to the conditions referred to in Articles 21a, 22, 22a and 104a of that Directive, may also be included in the list.

3. The list shall include an electronic link to the product information and to the summary of the risk management plan.

4. The Agency shall remove a medicinal product from the list 5 years after the Union reference date referred to in Article 107c(5) of Directive 2001/83/EC.

However, the Commission or the national competent authority, as appropriate, may, following a recommendation of the Pharmacovigilance Risk Assessment Committee, extend that period until such time as they conclude that the conditions referred to in Article 14a and Article 21(2) of this Regulation or referred to in Articles 22b and 104a of Directive 2001/83/EC have been fulfilled.

5. For medicinal products included in that list, the summary of product characteristics and the package leaflet shall include the statement “This medicinal product is subject to additional monitoring”. That statement shall be preceded by a black symbol which shall be selected by the Commission following a recommendation of the Pharmacovigilance Risk Assessment Committee by 2 January 2012, and shall be followed by an appropriate standardised explanatory sentence.

Article 24

1. The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a database and data processing network (hereinafter the “Eudravigilance database”) to collate pharmacovigilance information regarding medicinal products authorised in the Union and to allow competent authorities to access that information simultaneously and to share it.

The Eudravigilance database shall contain information on suspected adverse reactions in human beings arising from use of the medicinal product within the terms of the marketing authorisation as well as from uses outside the terms of the marketing authorisation, and on those occurring in the course of post-authorisation studies with the medicinal product or associated with occupational exposure.

2. The Agency shall, in collaboration with the Member States and the Commission, draw up the functional specifications for the Eudravigilance database, together with a timeframe for their implementation.

The Agency shall prepare an annual report on the Eudravigilance database and send it to the European Parliament, the Council and the Commission. The first annual report shall be prepared by 2 January 2013.

The Management Board of the Agency shall on the basis of an independent audit report that takes into account the recommendation of the Pharmacovigilance Risk Assessment Committee confirm and announce when the Eudravigilance database has achieved full functionality and the system meets the functional specifications drawn up pursuant to the first subparagraph.

Any substantial change to the Eudravigilance database and the functional specifications shall take into account the recommendations of the Pharmacovigilance Risk Assessment Committee.

The Eudravigilance database shall be fully accessible to the competent authorities of the Member States and to the Agency and the Commission. It shall also be accessible to marketing authorisation holders to the extent necessary for them to comply with their pharmacovigilance obligations.

The Agency shall ensure that healthcare professionals and the public have appropriate levels of access to the Eudravigilance database, while guaranteeing personal data protection. The Agency shall work together with all stakeholders, including research institutions, healthcare professionals, and patient and consumer organisations, in order to define the “appropriate level of access” for healthcare professionals and the public to the Eudravigilance database.

The data held on the Eudravigilance database shall be made publicly accessible in an aggregated format together with an explanation of how to interpret the data.

3. The Agency shall, in collaboration either with the marketing authorisation holder or with the Member State that submitted an individual suspected adverse reaction report to the Eudravigilance database, be responsible for operating procedures that ensure the quality and integrity of the information collected in the Eudravigilance database.

4. Individual suspected adverse reaction reports and follow-ups submitted to the Eudravigilance database by marketing authorisation holders shall be transmitted electronically upon receipt to the competent authority of the Member State where the reaction occurred.

Article 25

The Agency shall, in collaboration with the Member States, develop standard web-based structured forms for the reporting of suspected adverse reactions by healthcare professionals and patients in accordance with the provisions referred to in Article 107a of Directive 2001/83/EC.

Article 25a

The Agency shall, in collaboration with the national competent authorities and the Commission, set up and maintain a repository for periodic safety update reports (hereinafter the “repository”) and the corresponding assessment reports so that they are fully and permanently accessible to the Commission, the national competent authorities, the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use and the coordination group referred to in Article 27 of Directive 2001/83/EC (hereinafter the “coordination group”).

The Agency shall, in collaboration with the national competent authorities and the Commission, and after consultation with the Pharmacovigilance Risk Assessment Committee, draw up the functional specifications for the repository.

The Management Board of the Agency shall, on the basis of an independent audit report that takes into account the recommendations of the Pharmacovigilance Risk Assessment Committee, confirm and announce when the repository has achieved full functionality and meets the functional specifications drawn up pursuant to the second paragraph.

Any substantial change to the repository and the functional specifications shall always take into account the recommendations of the Pharmacovigilance Risk Assessment Committee.

Article 26

1. The Agency shall, in collaboration with the Member States and the Commission, set up and maintain a European medicines web-portal for the dissemination of information on medicinal products authorised in the Union. By means of that portal, the Agency shall make public at least the following:

- (a) the names of members of the Committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and the members of the coordination group, together with their professional qualifications and with the declarations referred to in Article 63(2) of this Regulation;
- (b) agendas and minutes from each meeting of the Committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and of the coordination group as regards pharmacovigilance activities;
- (c) a summary of the risk management plans for medicinal products authorised in accordance with this Regulation;
- (d) the list of medicinal products referred to in Article 23 of this Regulation;
- (e) a list of the locations in the Union where pharmacovigilance system master files are kept and contact information for pharmacovigilance enquiries, for all medicinal products authorised in the Union;
- (f) information about how to report to national competent authorities suspected adverse reactions to medicinal products and the standard structured forms referred to in Article 25 for their web-based reporting by patients and healthcare professionals, including links to national websites;
- (g) Union reference dates and frequency of submission of periodic safety update reports established in accordance with Article 107c of Directive 2001/83/EC;
- (h) protocols and public abstracts of results of the post-authorisation safety studies referred to in Articles 107n and 107p of Directive 2001/83/EC;
- (i) the initiation of the procedure provided for in Articles 107i to 107k of Directive 2001/83/EC, the active substances or medicinal products concerned and the issue being addressed, any public hearings pursuant to that procedure and information on how to submit information and to participate in public hearings;
- (j) conclusions of assessments, recommendations, opinions, approvals and decisions taken by the Committees referred to in points (a) and (aa) of Article 56(1) of this Regulation and by the coordination group, the national competent authorities and the

Commission in the framework of the procedures of Articles 28, 28a and 28b of this Regulation and of sections 2 and 3 of Chapter 3 and Chapter 4 of Title IX of Directive 2001/83/EC.

2. Before the launch of this portal, and during subsequent reviews, the Agency shall consult relevant stakeholders, including patient and consumer groups, healthcare professionals and industry representatives.

Article 27

1. The Agency shall monitor selected medical literature for reports of suspected adverse reactions to medicinal products containing certain active substances. It shall publish the list of active substances being monitored and the medical literature subject to this monitoring.

2. The Agency shall enter into the Eudravigilance database relevant information from the selected medical literature.

3. The Agency shall, in consultation with the Commission, Member States and interested parties, draw up a detailed guide regarding the monitoring of medical literature and the entry of relevant information into the Eudravigilance database.

Article 28

1. The obligations of marketing authorisation holders and of Member States laid down in Articles 107 and 107a of Directive 2001/83/EC shall apply to the recording and reporting of suspected adverse reactions for medicinal products for human use authorised in accordance with this Regulation.

2. The obligations of marketing authorisation holders laid down in Article 107b of Directive 2001/83/EC and the procedures under Article 107b and Article 107c of that Directive shall apply to the submission of periodic safety update reports, the establishment of Union reference dates and changes to the frequency of submission of periodic safety update reports for medicinal products for human use authorised in accordance with this Regulation.

The provisions applicable to the submission of periodic safety update reports laid down in the second subparagraph of Article 107c(2) of that Directive shall apply to holders of marketing authorisations which were granted before 2 July 2012 and for which the frequency and dates of submission of the periodic safety update reports are not laid down as a condition to the marketing authorisation until such time as another frequency or other dates of submission of the reports are laid down in the marketing authorisation or are determined in accordance with Article 107c of that Directive.

3. The assessment of the periodic safety update reports shall be conducted by a rapporteur appointed by the Pharmacovigilance Risk Assessment Committee. The rapporteur shall closely collaborate with the rapporteur appointed by the Committee for Medicinal Products for Human Use or the Reference Member State for the medicinal products concerned.

The rapporteur shall prepare an assessment report within 60 days of receipt of the periodic safety update report and send it to the Agency and to the members of the Pharmacovigilance Risk Assessment Committee. The Agency shall send the report to the marketing authorisation holder.

Within 30 days of receipt of the assessment report, the marketing authorisation holder and the members of the Pharmacovigilance Risk Assessment Committee may submit comments to the Agency and to the rapporteur.

Following the receipt of the comments referred to in the third subparagraph, the rapporteur shall within 15 days update the assessment report taking into account any comments submitted, and forward it to the Pharmacovigilance Risk Assessment Committee. The Pharmacovigilance Risk Assessment Committee shall adopt the assessment report with or without further changes at its next meeting and issue a recommendation. The recommendation shall mention the divergent positions with the grounds on which they are based. The Agency shall include the adopted assessment report and the recommendation in the repository set up under Article 25a, and forward both to the marketing authorisation holder.

4. In the case of an assessment report that recommends any action concerning the marketing authorisation, the Committee for Medicinal Products for Human Use shall, within 30 days of receipt of the report by the Pharmacovigilance Risk Assessment Committee, consider the report and adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisation concerned, including a timetable for the implementation of the opinion. Where this opinion of the Committee for Medicinal Products for Human Use differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences together with the recommendation.

Where the opinion states that regulatory action concerning the marketing authorisation is necessary, the Commission shall adopt a decision to vary, suspend or revoke the marketing authorisation. Article 10 of this Regulation shall apply to the adoption of that decision. Where the Commission adopts such a decision, it may also adopt a decision addressed to the Member States pursuant to Article 127a of Directive 2001/83/EC.

5. In the case of a single assessment of periodic safety update reports concerning more than one marketing authorisation in accordance with Article 107e(1) of Directive 2001/83/EC which includes at least one marketing authorisation granted in accordance with this Regulation, the procedure laid down in Articles 107e and 107g of that Directive shall apply.

6. The final recommendations, opinions and decisions referred to in paragraphs 3 to 5 of this Article shall be made public by means of the European medicines web-portal referred to in Article 26.

Article 28a

1. Regarding medicinal products for human use authorised in accordance with this Regulation, the Agency shall, in collaboration with the Member States, take the following measures:

- (a) monitor the outcome of risk minimisation measures contained in risk management plans and of conditions referred to in points (c), (ca), (cb) and (cc) of Article 9(4) or in points (a) and (b) of Article 10a(1), and in Article 14(7) and (8);
- (b) assess updates to the risk management system;
- (c) monitor the data in the Eudravigilance database to determine whether there are new risks or whether risks have changed and whether those risks impact on the risk-benefit balance.

2. The Pharmacovigilance Risk Assessment Committee shall perform the initial analysis and prioritisation of signals of new risks or risks that have changed or changes to the risk-benefit balance. Where it considers that follow-up action may be necessary, the assessment of those signals and agreement on any subsequent action concerning the marketing authorisation shall be conducted in a timescale commensurate with the extent and seriousness of the issue.

3. The Agency and national competent authorities and the marketing authorisation holder shall inform each other in the event of new risks or risks that have changed or changes to the risk-benefit balance being detected.

Article 28b

1. For non-interventional post-authorisation safety studies concerning medicinal products for human use authorised in accordance with this Regulation which fulfil one of the requirements referred to in Articles 10 and 10a of this Regulation, the procedure provided for in paragraphs 3 to 7 of Article 107m, Articles 107n to 107p and Article 107q(1) of Directive 2001/83/EC shall apply.

2. Where, in accordance with the procedure referred to in paragraph 1 of this Article, the Pharmacovigilance Risk Assessment Committee issues recommendations for the variation, suspension or revocation of the marketing authorisation, the Committee on Medicinal Products for Human Use shall adopt an opinion taking into account the recommendation, and the Commission shall adopt a decision in accordance with Article 10.

Where the opinion of the Committee on Medicinal Products for Human Use differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee on Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences, together with the recommendation.

Article 28c

1. The Agency shall collaborate with the World Health Organisation in matters of pharmacovigilance and shall take the necessary steps to submit to it, promptly, appropriate and adequate information regarding the measures taken in the Union which may have a bearing on public health protection in third countries.

The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the World Health Organisation.

2. The Agency and the European Monitoring Centre for Drugs and Drug Addiction shall exchange information that they receive on the abuse of medicinal products including information related to illicit drugs.

Article 28d

At the request of the Commission, the Agency shall participate in collaboration with the Member States in international harmonisation and standardisation of technical measures in relation to pharmacovigilance.

Article 28e

The Agency and the Member States shall cooperate to continuously develop pharmacovigilance systems capable of achieving high standards of public health protection for all medicinal products, regardless of the routes of marketing authorisation, including the use of collaborative approaches, to maximise use of resources available within the Union.

Article 28f

The Agency shall perform regular independent audits of its pharmacovigilance tasks and report the results to its Management Board on a 2-yearly basis.

Article 29

The Commission shall make public a report on the performance of pharmacovigilance tasks by the Agency on 2 January 2014 at the latest and subsequently every 3 years thereafter.;

12. Article 56(1) is amended as follows:

(a) the following point is inserted:

‘(aa) the Pharmacovigilance Risk Assessment Committee, which shall be responsible for providing recommendations to the Committee for Medicinal Products for Human Use and the coordination group on any question relating to pharmacovigilance activities in respect of medicinal products for human use and on risk management systems and it shall be responsible for monitoring the effectiveness of those risk management systems.;;’

(b) point (f) is replaced by the following:

‘(f) a Secretariat, which shall provide technical, scientific and administrative support for the Committees and ensure appropriate coordination between them, and which shall provide technical and administrative support for the coordination group and ensure appropriate coordination between it and the Committees.;;’

13. Article 57 is amended as follows:

(a) in paragraph 1, points (c) to (f) are replaced by the following:

‘(c) coordinating the monitoring of medicinal products for human use which have been authorised within the Union and providing advice on the measures necessary to ensure the safe and effective use of these medicinal products for human use, in particular by coordinating the evaluation and implementation of pharmacovigilance obligations and systems and the monitoring of such implementation;

(d) ensuring the collation and dissemination of information on suspected adverse reactions to medicinal products for human use authorised in the Union by means of a database permanently accessible to all Member States;

(e) assisting Member States with the rapid communication of information on pharmacovigilance concerns to healthcare professionals and coordinating the safety announcements of the national competent authorities;

- (f) distributing appropriate information on pharmacovigilance concerns to the general public, in particular by setting up and maintaining a European medicines web-portal;;

- (b) in paragraph 2, the following subparagraph is inserted after the first subparagraph:

‘For the purposes of the database, the Agency shall set up and maintain a list of all medicinal products for human use authorised in the Union. To this effect the following measures shall be taken:

- (a) the Agency shall, by 2 July 2011 at the latest, make public a format for the electronic submission of information on medicinal products for human use;
- (b) marketing authorisation holders shall, by 2 July 2012 at the latest, electronically submit to the Agency information on all medicinal products for human use authorised or registered in the Union, using the format referred to in point (a);
- (c) from the date set out in point (b), marketing authorisation holders shall inform the Agency of any new or varied marketing authorisations granted in the Union, using the format referred to in point (a).’;

14. the following Article is inserted:

‘Article 61a

1. The Pharmacovigilance Risk Assessment Committee shall be composed of the following:

- (a) one member and one alternate member appointed by each Member State, in accordance with paragraph 3 of this Article;
- (b) six members appointed by the Commission, with a view to ensuring that the relevant expertise is available within the Committee, including clinical pharmacology and pharmacoepidemiology, on the basis of a public call for expressions of interest;
- (c) one member and one alternate member appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament, in order to represent healthcare professionals;
- (d) one member and one alternate member appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament, in order to represent patient organisations.

The alternate members shall represent and vote for the members in their absence. The alternate members referred

to in point (a) may be appointed to act as rapporteurs in accordance with Article 62.

2. A Member State may delegate its tasks in the Pharmacovigilance Risk Assessment Committee to another Member State. Each Member State may represent no more than one other Member State.

3. The members and alternate members of the Pharmacovigilance Risk Assessment Committee shall be appointed on the basis of their relevant expertise in pharmacovigilance matters and risk assessment of medicinal products for human use, in order to guarantee the highest levels of specialist qualifications and a broad spectrum of relevant expertise. For this purpose, Member States shall liaise with the Management Board and the Commission in order to ensure that the final composition of the Committee covers the scientific areas relevant to its tasks.

4. The members and alternate members of the Pharmacovigilance Risk Assessment Committee shall be appointed for a term of 3 years, which may be prolonged once and thereafter renewed following the procedures referred to in paragraph 1. The Committee shall elect its Chairman from among its members for a term of 3 years, which may be prolonged once.

5. Paragraphs 3, 4, 6, 7 and 8 of Article 61 shall apply to the Pharmacovigilance Risk Assessment Committee.

6. The mandate of the Pharmacovigilance Risk Assessment Committee shall cover all aspects of the risk management of the use of medicinal products for human use including the detection, assessment, minimisation and communication relating to the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product for human use, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit.’;

15. Article 62 is amended as follows:

(a) paragraph 1 is amended as follows:

- (i) the first subparagraph is replaced by the following:

‘Where, in accordance with this Regulation, any of the Committees referred to in Article 56(1) is required to evaluate a medicinal product for human use, it shall appoint one of its members to act as rapporteur, taking into account existing expertise in the Member State. The Committee concerned may appoint a second member to act as co-rapporteur.

A rapporteur appointed for this purpose by the Pharmacovigilance Risk Assessment Committee shall closely collaborate with the rapporteur appointed by the Committee for Medicinal Products for Human Use or the Reference Member State for the medicinal product for human use concerned.;

- (ii) the fourth subparagraph is replaced by the following:

'If there is a request for re-examination of one of its opinions where this possibility is provided for in Union law, the Committee concerned shall appoint a different rapporteur and, where necessary, a different co-rapporteur from those appointed for the initial opinion. The re-examination procedure may deal only with the points of the opinion initially identified by the applicant and may be based only on the scientific data available when the Committee adopted the initial opinion. The applicant may request that the Committee consult a scientific advisory group in connection with the re-examination.;

- (b) in paragraph 2, the first subparagraph is replaced by the following:

'Member States shall transmit to the Agency the names of national experts with proven experience in the evaluation of medicinal products for human use who, taking into account Article 63(2), would be available to serve on working parties or scientific advisory groups of any of the Committees referred to in Article 56(1), together with an indication of their qualifications and specific areas of expertise.;

- (c) in paragraph 3, the following subparagraph is added:

'The first and second subparagraphs shall also apply to the work of rapporteurs in the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.;

16. Article 64(2) is amended as follows:

- (a) point (b) is replaced by the following:

'(b) for managing all the Agency resources necessary for conducting the activities of the Committees referred to in Article 56(1), including making

available appropriate scientific and technical support to those Committees, and for making available appropriate technical support to the coordination group.;

- (b) point (d) is replaced by the following:

'(d) for ensuring appropriate coordination between the Committees referred to in Article 56(1) and, where necessary, between the Committees and the coordination group.;

17. in Article 66(g), the words 'Article 67' are replaced by the words 'Article 68';

18. Article 67 is amended as follows:

- (a) in paragraph 3, the first subparagraph is replaced by the following:

'The Agency's revenue shall consist of a contribution from the Union and fees paid by undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency, or by the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.;

- (b) paragraph 4 is replaced by the following:

'4. Activities relating to pharmacovigilance, to the operation of communications networks and to market surveillance shall be under the permanent control of the Management Board in order to guarantee the independence of the Agency. This shall not preclude the Agency from charging fees to marketing authorisation holders for performing these activities by the Agency on the condition that its independence is strictly guaranteed.;

19. Article 82(3) is replaced by the following:

'3. Without prejudice to the unique, Union nature of the content of the documents referred to in points (a) to (d) of Article 9(4) and in points (a) to (e) of Article 34(4), this Regulation shall not prohibit the use of two or more commercial designs for a given medicinal product for human use covered by a single marketing authorisation.;

20. in Article 83(6), the second sentence is replaced by the following:

'Article 28(1) and (2) shall apply *mutatis mutandis*.;

21. the following Articles are inserted:

‘Article 87a

In order to harmonise the performance of the pharmacovigilance activities provided for in this Regulation, the Commission shall adopt implementing measures as provided for in Article 108 of Directive 2001/83/EC covering the following areas:

- (a) the content and maintenance of the pharmacovigilance system master file kept by the marketing authorisation holder;
- (b) the minimum requirements for the quality system for the performance of pharmacovigilance activities by the Agency;
- (c) the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities;
- (d) the minimum requirements for the monitoring of data included in the Eudravigilance database to determine whether there are new risks or whether risks have changed;
- (e) the format and content of electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders;
- (f) the format and content of electronic periodic safety update reports and risk management plans;
- (g) the format of protocols, abstracts and final study reports of the post-authorisation safety studies.

Those measures shall take account of the work on international harmonisation carried out in the area of pharmacovigilance and shall, where necessary, be revised to take account of technical and scientific progress. Those measures shall be adopted in accordance with the regulatory procedure referred to in Article 87(2).

Article 87b

1. The power to adopt the delegated acts referred to in Article 10b shall be conferred on the Commission for a period of 5 years from 1 January 2011. The Commission shall draw up a report in respect of the delegated powers not later than 6 months before the end of the 5 year period. The delegation of powers shall be automatically extended for periods of an identical duration, unless the European Parliament or the Council revokes it in accordance with Article 87c.

2. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.

3. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in Articles 87c and 87d.

Article 87c

1. The delegation of powers referred to in Article 10b may be revoked at any time by the European Parliament or by the Council.

2. The institution which has commenced an internal procedure for deciding whether to revoke the delegation of powers shall endeavour to inform the other institution and the Commission within a reasonable time before the final decision is taken, indicating the delegated powers which could be subject to revocation and possible reasons for a revocation.

3. The decision of revocation shall put an end to the delegation of the powers specified in that decision. It shall take effect immediately or at a later date specified therein. It shall not affect the validity of the delegated acts already in force. It shall be published in the *Official Journal of the European Union*.

Article 87d

1. The European Parliament or the Council may object to a delegated act within a period of 2 months from the date of notification.

At the initiative of the European Parliament or the Council that period shall be extended by 2 months.

2. If, on expiry of the period referred to in paragraph 1, neither the European Parliament nor the Council has objected to the delegated act, it shall be published in the *Official Journal of the European Union* and shall enter into force on the date stated therein.

The delegated act may be published in the *Official Journal of the European Union* and enter into force before the expiry of that period if the European Parliament and the Council have both informed the Commission of their intention not to raise objections.

3. If either the European Parliament or the Council objects to the delegated act within the period referred to in paragraph 1, it shall not enter into force. The institution which objects shall state the reasons for objecting to the delegated act.’

*Article 2***Amendments to Regulation (EC) No 1394/2007**

Article 20(3) of Regulation (EC) No 1394/2007 is replaced by the following:

‘3. The Executive Director of the Agency shall ensure appropriate coordination between the Committee for Advanced Therapies and the other Committees of the Agency, in particular the Committee for Medicinal Products for Human Use, the Pharmacovigilance Risk Assessment Committee and the Committee for Orphan Medicinal Products, their working parties and any other scientific advisory groups.’.

*Article 3***Transitional provisions**

1. The obligation on the part of the marketing authorisation holder to maintain and make available on request a pharmacovigilance system master file in respect of one or more medicinal products for human use provided for in Article 104(3)(b) of Directive 2001/83/EC as amended by Directive 2010/84/EU, which applies to medicinal products for human use authorised pursuant to Regulation (EC) No 726/2004 by virtue of Article 21 of Regulation (EC) No 726/2004 as amended by this Regulation, shall apply to marketing authorisations granted before 2 July 2012 as from either:

(a) the date on which those marketing authorisations are renewed; or

(b) the expiry of a period of 3 years starting from 2 July 2012,

whichever is the earlier.

2. The procedure provided for in Articles 107m to 107q of Directive 2001/83/EC as amended by Directive 2010/84/EU, which apply by virtue of Article 28b of Regulation (EC) No 726/2004 as amended by this Regulation, shall apply only to studies which have commenced after 2 July 2012.

3. The obligation of the Agency under the second subparagraph of Article 28c(1) of Regulation (EC) No 726/2004 as amended by this Regulation shall apply once the full functionality of Eudravigilance has been announced by the Management Board.

*Article 4***Entry into force and application**

This Regulation shall enter into force on the day following its publication in the *Official Journal of the European Union*.

It shall apply from 2 July 2012.

Done at Strasbourg, 15 December 2010.

For the European Parliament

The President

J. BUZEK

For the Council

The President

O. CHASTEL

REGULATION (EU) No 1236/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 15 December 2010

laying down a scheme of control and enforcement applicable in the area covered by the
Convention on future multilateral cooperation in the North-East Atlantic fisheries and repealing
Council Regulation (EC) No 2791/1999

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 43(2) thereof,

Having regard to the proposal from the European Commission,

Having regard to the opinion of the European Economic and Social Committee ⁽¹⁾,

Acting in accordance with the ordinary legislative procedure ⁽²⁾,

Whereas:

- (1) The Convention on future multilateral cooperation in the North-East Atlantic fisheries (the Convention), was approved by the Council in Decision 81/608/EEC ⁽³⁾ and entered into force on 17 March 1982.
- (2) The Convention provides for an appropriate framework for multilateral cooperation on the rational conservation and management of fishery resources in the Area defined by the Convention (the Convention Area).
- (3) The North-East Atlantic Fisheries Commission (NEAFC), at its Annual Meeting on 15 November 2006, adopted a recommendation establishing a scheme of control and enforcement (the Scheme) applicable to fishing vessels operating in the waters of the Convention Area which lie beyond the waters under the fisheries jurisdiction of the Contracting Parties (the Regulatory Area). The Scheme, which came into force on 1 May 2007, was amended by several recommendations at the Annual Meetings in November 2007, 2008 and 2009.
- (4) Under Articles 12 and 15 of the Convention, these recommendations came into force on 9 February 2008, 6 and 8 January 2009, and 6 February 2010 respectively.

(5) The Scheme provides for control and enforcement measures applicable to vessels flying the flag of Contracting Parties and operating in the Regulatory Area, and arrangements for inspection at sea which include inspection and surveillance procedures and infringement procedures which must be implemented by the Contracting Parties.

(6) The Scheme provides for a new Port State Control system which will effectively close European ports to landings and transshipments of frozen fish which have not been verified to be legal by the flag state of fishing vessels flying the flag of a Contracting Party other than the port state.

(7) Certain control provisions adopted by NEAFC have been incorporated into Union law by way of the yearly TAC and quotas Regulation, and most recently by Council Regulation (EC) No 43/2009 of 16 January 2009 fixing for 2009 the fishing opportunities and associated conditions for certain fish stocks and groups of fish stocks, applicable in Community waters and, for Community vessels, in waters where catch limitations are required ⁽⁴⁾. For the sake of legal certainty, such provisions which are not of a temporary nature should be the subject of a new separate regulation.

(8) The Scheme also comprises provisions to promote compliance by vessels flying the flag of a non-Contracting Party with the control and enforcement measures in order to ensure full respect of conservation and management measures adopted by NEAFC. NEAFC recommended removing a number of vessels from the list of vessels that have been confirmed to have engaged in illegal, unreported and unregulated fisheries. The incorporation of those recommendations into Union law should be ensured.

(9) Article 5(2) of Council Regulation (EC) No 1224/2009 of 20 November 2009 establishing a Community control system for ensuring compliance with the rules of the common fisheries policy ⁽⁵⁾ provides that Member States shall control access to waters and resources and control activities outside EU waters carried out by vessels flying their flag. Provision should therefore be made for Member States whose vessels are authorised to fish in the Regulatory Area to assign inspectors to the Scheme to undertake monitoring and surveillance as well as adequate resources for inspection.

⁽¹⁾ Opinion of 17 March 2010 (not yet published in the Official Journal).

⁽²⁾ Position of the European Parliament of 19 October 2010 (not yet published in the Official Journal) and decision of the Council of 29 November 2010.

⁽³⁾ OJ L 227, 12.8.1981, p. 21.

⁽⁴⁾ OJ L 22, 26.1.2009, p. 1.

⁽⁵⁾ OJ L 343, 22.12.2009, p. 1.

- (10) In order to ensure the monitoring of fishing activities in the Convention Area, it is necessary for Member States to cooperate with one another and with the Commission and the body designated by it in applying the Scheme.
- (11) It is the responsibility of Member States to ensure that their inspectors comply with the inspection procedures laid down by NEAFC.
- (12) The Commission should be empowered to adopt delegated acts in accordance with Article 290 of the Treaty on the Functioning of the European Union (TFEU) in respect of detailed rules concerning lists of the fishery resources to be notified, procedures for prior notification of entry into port and for the cancellation thereof as well as authorisation to land or tranship. The Commission should also be empowered to adopt delegated acts in respect of the incorporation into Union law of future amendments of those measures of the Scheme which form the subject matter of certain expressly defined non-essential elements of this Regulation and which become binding upon the Union in accordance with the terms of the Convention. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level.
- (13) The measures necessary for the implementation of this Regulation should be adopted by the Commission by means of implementing acts in accordance with Article 291 TFEU. According to that Article, rules and general principles concerning mechanisms for the control by Member States of the Commission's exercise of implementing powers are to be laid down in advance by a regulation adopted in accordance with the ordinary legislative procedure. Pending the adoption of that new regulation, Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission⁽¹⁾ continues to apply, with the exception of the regulatory procedure with scrutiny, which is not applicable.
- (14) As this Regulation will establish new rules concerning control and enforcement in the Convention Area, Council Regulation (EC) No 2791/1999 of 16 December 1999 laying down certain control measures applicable in the area covered by the Convention on future multilateral cooperation in the North-East Atlantic fisheries⁽²⁾ should be repealed,

HAVE ADOPTED THIS REGULATION:

CHAPTER I

GENERAL PROVISIONS

Article 1

Subject matter

This Regulation lays down the general rules and conditions for the application by the Union of the Scheme adopted by NEAFC.

Article 2

Scope

Unless otherwise stated, this Regulation shall apply to all EU vessels used or intended for use for fishing activities carried out in respect of fishery resources in the Regulatory Area.

Article 3

Definitions

For the purpose of this Regulation, the following definitions shall apply:

1. 'Convention' means the Convention on future multilateral cooperation in North-East Atlantic fisheries, as amended;
2. 'Convention Area' means the Convention Area as defined in Article 1(1) of the Convention;
3. 'Regulatory Area' means the waters of the Convention Area which lie beyond the waters under the fisheries jurisdiction of the Contracting Parties;
4. 'Contracting Parties' means the Contracting Parties to the Convention;
5. 'NEAFC' means the North-East Atlantic Fisheries Commission;
6. 'fishing activities' means fishing, including joint fishing operations, fish processing operations, the transshipment or landing of fish or fish products and any other commercial activity in preparation for or related to fishing;
7. 'fishery resources' means the resources referred to in Article 1(2) of the Convention;
8. 'regulated resources' means those fishery resources which are subject to recommendations under the Convention and are listed in the Annex;
9. 'fishing vessel' means any vessel used or intended for use for the purposes of the commercial exploitation of fishery resources, including fish processing vessels and vessels engaged in transhipment;

⁽¹⁾ OJ L 184, 17.7.1999, p. 23.

⁽²⁾ OJ L 337, 30.12.1999, p. 1.

10. 'non-Contracting Party vessel' means any fishing vessel not flagged in a Contracting Party, including vessels for which there are reasonable grounds for suspecting them to be without nationality;
11. 'joint fishing operation' means any operations between two or more vessels where catch is taken from the fishing gear of one fishing vessel to another;
12. 'transhipment operation' means the unloading of all or any fishery products on board a fishing vessel onto another fishing vessel;
13. 'port' means any place used for landing or a place close to the shore designated by a Contracting Party for transhipping fishery resources.

Article 4

Contact points

1. Member States shall designate the competent authority which shall act as the contact point for the purposes of receiving surveillance and inspection reports in accordance with Articles 12, 19, 20 and 27 and for receiving notifications and issuing authorisations in accordance with Articles 24 and 25.
2. Contact points for receiving notifications and issuing authorisations in accordance with Articles 24 and 25 shall be available 24 hours a day.
3. Member States shall send to the Commission or to the body designated by it and to the NEAFC Secretary the telephone number, e-mail address and fax number of the designated contact point.
4. Any subsequent changes to the information concerning the contact points referred to in paragraphs 1 and 3 shall be notified to the Commission or the body designated by it and to the NEAFC Secretary no later than 15 days before the change comes into force.
5. The format for transmission of the information referred to in paragraphs 1 and 3 shall be established in accordance with Article 50(2).

CHAPTER II

MONITORING MEASURES

Article 5

Union participation

1. Member States shall send to the Commission, in a computer-readable form, a list of all vessels flying their flag and registered in the Union which are authorised to fish in

the Regulatory Area, in particular the vessels authorised to fish directly for one or more regulated resources together with any amendments to the list. This information shall be sent no later than 15 December each year or no later than 5 days before the vessel enters the Regulatory Area. The Commission shall forward the information promptly to the NEAFC Secretary.

2. The format for transmission of the list referred to in paragraph 1 shall be determined in accordance with Article 50(2).

Article 6

Marking of gear

1. Member States shall ensure that gear used by their fishing vessels in the Regulatory Area is marked in accordance with Commission Regulation (EC) No 356/2005 of 1 March 2005 laying down detailed rules for the marking and identification of passive fishing gear and beam trawls ⁽¹⁾.

2. Member States may remove and dispose of fixed gear that is not marked in accordance with Regulation (EC) No 356/2005 or that contravenes in any other way recommendations adopted by NEAFC, as well as fish that are found in the gear.

Article 7

Retrieval of lost gear

1. The competent authority of the flag Member State shall send without delay to the NEAFC Secretary the information provided to it pursuant to Article 48(3) of Regulation (EC) No 1224/2009 as well as the call sign of the vessel that has lost the gear.
2. Member States shall undertake to retrieve on a regular basis lost gears belonging to vessels flying their flag.

Article 8

Recording of catches

1. In addition to the information specified in Article 6 of Council Regulation (EEC) No 2847/93 of 12 October 1993 establishing a control system applicable to the common fisheries policy ⁽²⁾, the masters of EU fishing vessels shall record, either in a bound paginated fishing logbook or by electronic means, the following:

- (a) each entry into and exit from the Regulatory Area;
- (b) on a daily basis and/or for each haul the estimated cumulative catches retained on board since the last entry into the Regulatory Area;

⁽¹⁾ OJ L 56, 2.3.2005, p. 8.

⁽²⁾ OJ L 261, 20.10.1993, p. 1.

- (c) on a daily basis and/or for each haul the amount of fish discarded;
- (d) immediately after each communication pursuant to Article 9, the date and time, according to Universal Coordinated Time (UTC), of transmission of a report and, in the case of radio transmission, the name of the radio station through which the report was transmitted;
- (e) the fishing depth, where appropriate.

2. The masters of EU fishing vessels engaged in fishing activities carried out in respect of regulated resources and which process and/or freeze their catch shall:

- (a) record their cumulative production by species and product form in a production logbook; and
- (b) stow in the hold all processed catch in such a way that the location of each species can be identified from a stowage plan maintained on board the fishing vessel.

3. By way of derogation from paragraph 1, Member States may exempt from the obligation to record in a fishing logbook or electronically a vessel engaged in transshipment operations which on-loads quantities on board. Vessels benefiting from this derogation shall specify in a stowage plan the location in the hold of frozen fish referred to in Article 14(1) and record in a production logbook:

- (a) the date and time, according to UTC, of transmission of a report referred to in Article 9;
- (b) in the case of radio transmission, the name of the radio station through which the report was transmitted;
- (c) the date and time, according to UTC, of the transshipment operation;
- (d) the location (latitude/longitude) of the transshipment operation;
- (e) the quantities of each species on-loaded;
- (f) the name and international radio call sign of the fishing vessel from which the catch has been off-loaded.

4. Detailed rules for the implementation of this Article shall be determined in accordance with Article 50(2).

Article 9

Reporting of catches of regulated resources

1. The masters of EU fishing vessels engaged in fishing activities carried out in respect of regulated resources shall communicate catch reports by electronic means to their

Fisheries Monitoring Centre, as defined in point (15) of Article 4 of Regulation (EC) No 1224/2009. The data contained in such reports shall be accessible to the Commission on request. Reports shall include the following:

- (a) reports on the quantities held on board when entering the Regulatory Area. Such reports shall be transmitted no earlier than 12 hours and no later than 2 hours before each entry into the Regulatory Area;
- (b) reports on weekly catches. Such reports shall be transmitted for the first time no later than the end of the seventh day following the entry of the vessel into the Regulatory Area or, when fishing trips take more than 7 days, no later than Monday noon for catches taken in the Regulatory Area during the preceding week ending at midnight on Sunday. This report shall include the number of fishing days since the start of fishing, or since the last catch report;
- (c) reports on catches on board when exiting the Regulatory Area. Such reports shall be transmitted no earlier than 8 hours and no later than 2 hours before each departure from the Regulatory Area. Such reports shall include, where appropriate, the number of fishing days and the catch taken in the Regulatory Area since the start of fishing, or since the last catch report;
- (d) reports on the quantities on-loaded and off-loaded for each transshipment of fish during the vessel's stay in the Regulatory Area. Donor vessels shall make this report no later than 24 hours before the transshipment, and receiving vessels no later than 1 hour after the transshipment. The report shall include the date, time and geographical position of the planned transshipment as well as the total round weight by species which are to be off-loaded or which have been on-loaded in kilograms and the call signs of the donor and receiving vessels. Without prejudice to Chapter IV, at least 24 hours before any landing, the receiving vessel shall report the total catch on board, the total weight to be landed, the name of the port and the estimated date and time of landing.

2. The reports on catches referred to in this Article shall be expressed in kilograms (rounded to the nearest 100 kg). The total round weight shall be reported by species, using the FAO codes. The total quantity of species for which the total round weight by species is less than 1 tonne may be reported under the 3-alpha code MZZ (marine fish not specified).

3. Member States shall record the data contained in the catch reports in the database referred to in Article 109(1) of Regulation (EC) No 1224/2009.

4. The detailed rules for the implementation of this Article and in particular the format and the specifications for the transmissions shall be determined in accordance with Article 50(2).

*Article 10***Global reporting of catches and fishing effort**

1. Member States shall inform the Commission by computer transmission before the 15th day of each month of the quantities of fishery resources caught in the Regulatory Area by vessels flying their flag which have been landed or transhipped during the preceding month.

2. Without prejudice to Article 33(2) of Regulation (EC) No 1224/2009, Member States shall also inform the Commission by computer transmission before the 15th day of each month of the quantities of regulated resources caught in areas under the national fisheries jurisdiction of third countries and in EU waters of the Convention Area by vessels flying their flag which have been landed or transhipped during the preceding month.

3. The format for transmission of the data pursuant to paragraphs 1 and 2 shall be determined in accordance with Article 50(2).

The list of the fishery resources referred to in paragraph 1 shall be adopted in accordance with the procedure laid down in Articles 46 to 49.

4. The Commission shall compile the data referred to in paragraphs 1 and 2 for all Member States and forward them to the NEAFC Secretary within 30 days following the calendar month in which the catches were landed or transhipped.

*Article 11***Vessel Monitoring System**

Member States shall ensure the automatic and electronic transmission to the NEAFC Secretary of information obtained by the vessel monitoring system (VMS) concerning vessels flying their flag which fish or plan to fish in the Regulatory Area. The format and the specifications of these transmissions shall be determined in accordance with Article 50(2).

*Article 12***Communication of information**

1. Member States shall communicate the reports and the information referred to in Articles 9 and 11 without delay to the NEAFC Secretary. In the event of technical malfunction, however, such reports and information shall be transmitted to the NEAFC Secretary within 24 hours of receipt. Member States shall ensure that all reports and messages forwarded by them are numbered sequentially.

2. Member States shall ensure that the reports and information transmitted to the NEAFC Secretary are in accordance with the data exchange formats and protocols determined in accordance with Article 50(2).

*Article 13***Transshipments and joint fishing operations**

1. EU fishing vessels shall engage in transshipment activities in the Regulatory Area only if they have received prior authorisation from the competent authorities in their flag Member State.

2. EU fishing vessels may only engage in transshipment operations or joint fishing operations with vessels flying the flag of a Contracting Party and vessels of a non-Contracting Party granted the status of a cooperating non-Contracting Party by NEAFC.

3. EU fishing vessels engaged in transshipment operations which on-load quantities on board shall not engage in other fishing activities, including joint fishing operations, during the same trip, with the exception of fish-processing operations and landings.

*Article 14***Separate stowage**

1. EU fishing vessels which carry on board frozen fishery resources caught in the Convention Area by more than one fishing vessel may stow the fish from each of those vessels in more than one part of the hold but shall keep it clearly separate from fish caught by other vessels, in particular by using plastic, plywood or netting.

2. All catches taken inside the Convention Area shall be stowed separately from all catches taken outside the area.

*Article 15***Labelling of frozen fish**

When frozen, all fish caught in the Convention Area shall be identified with a clearly legible label or stamp. The label or stamp shall be placed at the time of stowage on each box or block of frozen fish and shall indicate the species, the production date, the ICES sub-area and division where the catch was taken and the name of the vessel which caught the fish.

CHAPTER III

INSPECTIONS AT SEA*Article 16***NEAFC inspectors**

1. Member States whose fishing vessels are authorised to fish in the Regulatory Area shall assign inspectors to the Scheme to carry out surveillance and inspection (NEAFC inspectors).

2. Member States shall issue a special identity document to each NEAFC inspector. The form of this document shall be determined in accordance with Article 50(2).

3. Each NEAFC inspector shall carry and produce the special identity document when boarding a fishing vessel.

Article 17

General provisions for inspection and surveillance

1. The Commission or the body designated by it shall coordinate the surveillance and inspection activities for the Union and shall draw up each year, in concert with the Member States concerned, a joint deployment plan for Union participation in the Scheme in the following year. This deployment plan shall, inter alia, determine the number of inspections to be carried out.

Where at any time more than ten EU fishing vessels are engaged in fishing activities carried out in respect of regulated resources in the Regulatory Area, the Commission or the body designated by it shall ensure that an inspection vessel from a Member State is present during that time in the Regulatory Area or that an agreement has been concluded with another Contracting Party to ensure the presence of an inspection vessel.

2. Member States shall ensure that the inspections by their NEAFC inspectors are carried out in a non-discriminatory manner and in accordance with the Scheme. The number of inspections shall be based on fleet size, taking into account the time spent by fishing vessels in the Regulatory Area.

3. The Commission or the body designated by it shall seek to ensure, through an equitable distribution of inspections, equal treatment of all Contracting Parties with fishing vessels operating in the Regulatory Area.

4. Member States shall take steps to ensure that NEAFC inspectors from another Contracting Party are permitted to carry out inspections on board vessels flying their flag.

5. NEAFC inspectors shall avoid the use of force except in cases of legitimate self-defence. When carrying out inspections on board fishing vessels, NEAFC inspectors shall not carry firearms. This paragraph shall be without prejudice to national provisions concerning the prohibition of the use of force.

6. NEAFC inspectors shall avoid causing any inconvenience to the fishing vessel or interfering with its activities and the catch retained on board, except when and to the degree necessary to carry out their mandates.

Article 18

Means to carry out inspection

1. Member States shall make available to their NEAFC inspectors adequate means to enable them to carry out their surveillance and inspection tasks. To that end they shall assign inspection vessels and aircraft to the Scheme.

2. The Commission or the body designated by it shall send to the NEAFC Secretary before 1 January each year details of the plan together with the names of the NEAFC inspectors and special inspection vessels as well as the types of aircraft and their identification details (registration number, name, radio call-sign) which Member States are assigning to the Scheme during that year. Where appropriate, this information shall be taken from the list of inspectors referred to in Article 79(1) of Regulation (EC) No 1224/2009. Member States shall send changes to this list to the Commission or the body designated by it which in turn shall forward them to the NEAFC Secretary and the other Member States 1 month before the changes are due to come into effect.

3. Any vessel assigned to the Scheme and carrying NEAFC inspectors, as well as the boarding craft deployed by that vessel, shall display the NEAFC inspection special signal to indicate that NEAFC inspectors on board may carry out inspection duties in accordance with the Scheme. Aircraft assigned to the Scheme shall have their international radio call-sign clearly displayed. The form of the special signal shall be determined in accordance with Article 50(2).

4. For each Union inspection vessel or aircraft assigned to the Scheme, the Commission or the body designated by it shall keep a record of the date and hour of the start and termination of their duties under the Scheme as set out in the form determined in accordance with Article 50(2).

Article 19

Surveillance procedure

1. Surveillance shall be based on sightings of fishing vessels by NEAFC inspectors from a vessel or aircraft assigned to the Scheme. NEAFC inspectors shall forward a copy of each sighting report for every vessel without delay, by electronic transmission in the form set out in accordance with Article 50(2), to the flag state of the vessel concerned, to the Commission or the body designated by it and to the NEAFC Secretary. A hard copy of each sighting report and any photographs shall be forwarded on request to the flag state of the vessel concerned.

2. NEAFC inspectors shall record their sightings in a surveillance report using a form established in accordance with Article 50(2).

Article 20

Inspection procedure

1. NEAFC inspectors shall not board any fishing vessel without prior notice being transmitted by radio to that vessel or without that vessel being given the appropriate signal using the International Code of Signals, including the identity of the inspection platform; however, it shall not be necessary for such notice to be acknowledged as received.

2. NEAFC inspectors shall have the authority to examine all relevant areas, decks and rooms of the fishing vessels, catch (whether processed or not), nets or other gear, equipment, and any relevant documents which they deem necessary to verify compliance with the conservation and management measures adopted by NEAFC and to question the master or a person designated by the master.

3. The fishing vessel to be boarded shall not be required to stop or manoeuvre when fishing, shooting or hauling. The NEAFC inspectors may order that the hauling of the fishing gear be interrupted or delayed until they have boarded the fishing vessel but may not do so in any event more than 30 minutes after the fishing vessel has received the signal referred to in paragraph 1.

4. Masters of inspection platforms shall ensure that they manoeuvre at a safe distance from the fishing vessels in accordance with good seamanship.

5. NEAFC inspectors may instruct a fishing vessel to delay its entry into or exit from the Regulatory Area for up to 6 hours from the time of transmission by the fishing vessel of the reports referred to in Article 9(1)(a) and (c).

6. The duration of an inspection shall not exceed 4 hours, or the time it takes to haul in the net and to inspect the net and the catch, whichever is longer. Where an infringement is detected the NEAFC inspectors may stay on board for the time necessary for the completion of the measures provided for in Article 29(1)(b).

7. In special circumstances relating to the size of a fishing vessel and the quantities of fish retained on board, the duration of the inspection may exceed the limits laid down in paragraph 6. In such a situation, NEAFC inspectors shall under no circumstances stay on board the fishing vessel longer than the time required to complete the inspection. The reasons for exceeding the limit laid down in paragraph 6 shall be recorded in the inspection report referred to in paragraph 9.

8. No more than two NEAFC inspectors assigned by a Member State shall board a fishing vessel of another Contracting Party. In carrying out their inspection, the NEAFC inspectors may request the master to provide any assistance which is required. NEAFC inspectors shall not interfere with the master's ability to communicate with the authorities of the flag state during the boarding and inspection.

9. Each inspection shall be documented by the completion of an inspection report in the format established in accordance with Article 50(2). The master may add his comments to the inspection report which shall be signed by the NEAFC inspectors at the end of the inspection. A copy of the inspection report shall be given to the master of the fishing vessel. A copy of each inspection report shall be transmitted without delay to

the flag state of the inspected vessel and to the Commission or the body designated by it. The Commission or the body designated by it shall forward the copy promptly to the NEAFC Secretary. The original or a certified copy of each inspection report shall be forwarded on request to the flag state of the inspected vessel.

Article 21

Obligations of the master of the vessel during the inspection procedure

The master of a fishing vessel shall:

- (a) facilitate prompt and safe boarding and disembarkation pursuant to specifications adopted in accordance with Article 50(2);
- (b) cooperate with and assist in the inspection of the fishing vessel conducted pursuant to this Regulation, not obstruct, intimidate or interfere with the NEAFC inspectors in the performance of their duties and ensure their safety;
- (c) allow the NEAFC inspectors to communicate with the authorities of the flag state and the inspecting state;
- (d) provide access to any areas, decks and rooms of the fishing vessel, catch (whether processed or not), nets or other gear, equipment, and to any relevant information or documents which the NEAFC inspectors deem necessary in accordance with Article 20(2);
- (e) provide copies of documents as required by the NEAFC inspectors; and
- (f) provide NEAFC inspectors with reasonable facilities, including, where appropriate, food and accommodation when they remain on board the vessel in accordance with Article 32(3).

CHAPTER IV

PORT STATE CONTROL OF FISHING VESSELS FLYING THE FLAG OF ANOTHER CONTRACTING PARTY

Article 22

Scope

Without prejudice to Regulation (EC) No 1224/2009 and to Council Regulation (EC) No 1005/2008 of 29 September 2008 establishing a Community system to prevent, deter and eliminate illegal, unreported and unregulated fishing⁽¹⁾, the provisions set out in this Chapter shall apply to landing or transshipping in ports of Member States of fishery resources frozen after being caught in the Convention Area by fishing vessels flying the flag of another Contracting Party.

⁽¹⁾ OJ L 286, 29.10.2008, p. 1.

*Article 23***Designated ports**

Member States shall designate and notify the Commission of ports where the landing or transshipment of fishery resources frozen after being caught in the Convention Area by fishing vessels flying the flag of another Contracting Party are permitted. The Commission shall notify the NEAFC Secretary of these ports and of any changes to the list of ports designated at least 15 days before the change comes into force.

Landings and transshipments of fish frozen after being caught in the Convention Area by fishing vessels flying the flag of another Contracting Party shall be allowed only in designated ports.

*Article 24***Prior notification of entry into port**

1. In accordance with Article 6 of Regulation (EC) No 1005/2008, when the master of a fishing vessel carrying fish referred to in Article 22 of this Regulation intends to call into a port to land or transship fish, the master of the vessel, or his representative, shall notify the competent authorities of the Member State of the port he wishes to use no later than three working days before the estimated time of arrival.

However, a Member State may make provision for another notification period, taking into account, in particular, the distance between the fishing grounds and its ports. In such a case, the Member State shall inform the Commission, or the body designated by it, and the NEAFC Secretary thereof without delay.

2. Masters or their representatives may cancel a prior notification by notifying the competent authorities of the port they wish to use no later than 24 hours before the notified estimated time of arrival in that port. The notification shall be accompanied by a copy of the original notification form with the word 'CANCELLED' written across it.

However, a Member State may make provision for another notification period for cancellation. In such a case, the Member State shall inform the Commission, or the body designated by it, and the NEAFC Secretary thereof without delay.

3. The competent authorities of the port Member State shall forward without delay a copy of the notifications referred to in paragraphs 1 and 2 to the flag state of the fishing vessel and to the flag state or states of the donor vessels when the fishing vessel has engaged in transshipment operations. A copy of the notification referred to in paragraph 2 shall also be forwarded without delay to the NEAFC Secretary.

4. The format and the specifications of the notifications shall be determined in accordance with Article 50(2).

As far as necessary, further detailed rules on the notification and cancellation procedures under this Article, including periods, shall be adopted in accordance with the procedure laid down in Articles 46 to 49.

*Article 25***Authorisation to land or tranship**

1. The flag state of the fishing vessel intending to land or tranship or, where the fishing vessel has engaged in transshipment operations outside EU waters, the flag state or states of the donor vessels, shall, by returning a copy of the prior notification referred to in Article 24 to the competent authorities of the port Member State, confirm that:

- (a) the fishing vessel which declared having caught the fish had sufficient quota for the species declared;
- (b) the quantities of fish on board have been duly reported and taken into account for the calculation of any catch or effort limitations that may be applicable;
- (c) the fishing vessel which declared having caught the fish had authorisation to fish in the areas declared;
- (d) the presence of the fishing vessel in the area of catch declared has been verified according to VMS data.

2. Landing or transshipment operations may only start after authorisation has been given by the competent authorities of the port Member State. Such authorisation shall only be given if the confirmation from the flag state referred to in paragraph 1 has been received.

3. By way of derogation from paragraph 2, the competent authorities of the port Member State may authorise all or part of a landing in the absence of the confirmation referred to in paragraph 1, but in such cases they shall keep the fish concerned in storage under their control. The fish shall only be released to be sold, taken over or transported once the confirmation referred to in paragraph 1 has been received. If the confirmation has not been received within 14 days of the landing the competent authorities of the port Member State may confiscate and dispose of the fish in accordance with national rules.

4. The competent authorities of the port Member State shall without delay notify their decision on whether or not to authorise the landing or transshipment to the master and shall inform the NEAFC Secretary thereof.

5. Detailed rules on the authorisation to land or tranship under this Article shall be adopted in accordance with the procedure laid down in Articles 46 to 49.

*Article 26***Port inspections**

1. Each Member State shall carry out inspections of at least 15 % of landings or transshipments in its ports during each reporting year.

2. Inspections shall involve the monitoring of the entire discharge or transshipment and include a cross-check between the quantities by species recorded in the prior notification of landing and the quantities by species landed or transhipped. When the landing or transshipment has been completed, the inspector shall verify and note the quantities by species of fish remaining on board.

3. National inspectors shall make all possible efforts to avoid delaying a vessel unduly and to ensure that the vessel suffers the minimum interference and inconvenience and that degradation of the quality of the fish is avoided.

4. The port Member State may invite inspectors of other Contracting Parties to accompany their own inspectors and observe the inspection of landings or transshipment operations of fishery resources caught by fishing vessels flying the flag of another Contracting Party.

*Article 27***Inspection reports**

1. Each inspection shall be documented by the completion of an inspection report using the form established in accordance with Article 50(2).

2. The master may add his comments to the inspection report, which shall be signed by the inspector and the master at the end of the inspection. A copy of the inspection report shall be given to the master of the fishing vessel.

3. A copy of each inspection report shall be transmitted without delay to the flag state of the inspected fishing vessel, to the flag state or states of the donor vessels where the vessel has engaged in transshipment operations, to the Commission or the body designated by it and to the NEAFC Secretary. The original or a certified copy of each inspection report shall be forwarded on request to the flag state of the inspected vessel.

CHAPTER V

INFRINGEMENTS*Article 28***Scope**

Without prejudice to Regulation (EC) No 1224/2009 and to Regulation (EC) No 1005/2008 the provisions set out in this Chapter shall apply to EU fishing vessels and to fishing vessels

flying the flag of another Contracting Party used or intended for use for fishing activities carried out in respect of fishery resources in the Regulatory Area.

*Article 29***Infringement procedures**

1. Where inspectors find that there are clear grounds for believing that a fishing vessel has engaged in any activity contrary to the conservation and management measures adopted by NEAFC they shall:

(a) record the infringement in the report referred to in Articles 19(2), 20(9) or 27;

(b) take all necessary measures to ensure security and continuity of the evidence. An identification mark may be affixed securely to any part of the fishing gear which appears to the inspector to be or to have been in contravention of applicable measures;

(c) attempt immediately to communicate with an inspector or designated authority of the flag state of the inspected fishing vessel;

(d) transmit the inspection report promptly to the Commission or the body designated by it.

2. The Member State carrying out the inspection shall communicate in writing the details of the infringement to the designated authority of the flag state of the inspected vessel and to the Commission or the body designated by it and, whenever possible, shall do so during the first working day following the start of the inspection.

3. The Member State carrying out the inspection shall send without delay the original of the surveillance or inspection report with any supporting documents to the competent authorities of the flag state of the inspected fishing vessel as well as a copy to the Commission or the body designated by it, which shall forward a copy to the NEAFC Secretary.

*Article 30***Follow-up in the case of infringement**

1. Where a Member State is notified by another Contracting Party or another Member State of an infringement committed by a fishing vessel flying its flag, it shall take prompt action in conformity with its national law to obtain and consider the evidence of the infringement and to conduct any further investigation necessary for the follow-up to the infringement and, whenever possible, to inspect the fishing vessel concerned.

2. Member States shall designate the competent authorities which are to receive evidence of infringement and shall inform the Commission or the body designated by it of the address of those authorities and of any change in this information. The Commission or the body designated by it shall subsequently forward the information to the NEAFC Secretary.

Article 31

Serious infringements

For the purpose of this Regulation, the following infringements shall be considered to be serious:

- (a) fishing without a valid authorisation issued by the flag state;
- (b) fishing without quota or after its exhaustion;
- (c) use of prohibited fishing gear;
- (d) serious misrecording of catches;
- (e) repeated failure to comply with Articles 9 or 11;
- (f) landing or transshipping in a port not designated in accordance with Article 23;
- (g) failure to comply with Article 24;
- (h) landing or transshipment without authorisation of the port state as referred to in Article 25;
- (i) preventing an inspector from carrying out his duties;
- (j) directed fishing for a stock which is subject to a moratorium or for which fishing is prohibited;
- (k) falsifying or concealing the markings, identity or registration of a fishing vessel;
- (l) concealing, tampering with or disposing of evidence relating to an investigation;
- (m) multiple violations which together constitute a serious disregard of conservation and management measures;
- (n) engaging in transshipment or joint fishing operations with vessels of a non-Contracting Party which has not been accorded the status of a cooperating non-Contracting Party by NEAFC;
- (o) supplying any provisions, fuel or other services to vessels that have been placed on the list referred to in Article 44.

Article 32

Follow-up in the case of serious infringements

1. If an inspector considers that there are clear grounds for believing that a fishing vessel has committed a serious infringement under Article 31, that inspector shall promptly notify that infringement to the Commission or the body

designated by it, the competent authorities of the flag state of the inspected fishing vessel and the flag state or states of the donor vessels where the inspected vessel has engaged in transshipment operations, in accordance with Article 29(3), and shall also transmit a copy to the NEAFC Secretary.

2. In order to preserve the evidence, the inspector shall take all necessary measures to ensure the security and continuity thereof whilst minimising inconvenience to the vessel and interference with its operation.

3. The inspector shall be entitled to remain on board the fishing vessel for the period necessary to provide information on the infringement to the duly authorised inspector referred to in Article 33, or until receiving a reply from the flag state requesting him to leave the fishing vessel.

Article 33

Follow-up in the case of serious infringements by an EU fishing vessel

1. Flag Member States shall respond to the notification referred to in Article 32(1) without delay and shall ensure that the fishing vessel concerned is inspected within 72 hours by an inspector duly authorised in relation to the infringement. The duly authorised inspector shall board the fishing vessel concerned and examine the evidence of the suspected infringement established by the inspector, and forward the results of the examination as quickly as possible to the competent authority in the flag Member State and to the Commission or the body designated by it.

2. Following notification of the results of the examination referred to in paragraph 1, flag Member States shall, if the evidence so warrants, require the fishing vessel to proceed immediately, and in any case within 24 hours, to a port designated by that flag Member State, for a thorough inspection under its authority.

3. The flag Member State may authorise the inspecting state to bring without delay the fishing vessel to a port designated by the flag Member State.

4. If the fishing vessel is not called to port, the flag Member State must provide due justification in a timely manner to the Commission or the body designated by it and to the inspecting state. The Commission or the body designated by it shall forward such justification to the NEAFC Secretary.

5. Where a fishing vessel is required to proceed to port for a thorough inspection pursuant to paragraphs 2 or 3, a NEAFC inspector from another Contracting Party may, subject to the consent of the flag Member State of the fishing vessel, board and remain on board the fishing vessel as it proceeds to port, and may be present during the inspection of the fishing vessel in port.

6. Flag Member States shall inform promptly the Commission or the body designated by it of the outcome of the thorough inspection and of the measures that they have adopted as a result of the infringement.

7. The detailed rules for the implementation of this Article shall be determined in accordance with Article 50(2).

Article 34

Reporting and follow-up of infringements

1. By 15 February each year, Member States shall report to the Commission or the body designated by it on the status of the proceedings concerning infringements of the conservation and management measures adopted by NEAFC which were committed during the previous calendar year. The infringements shall continue to be listed in each subsequent report until the proceedings are concluded in accordance with the relevant provisions of national law. The Commission or the body designated by it shall forward the reports to the NEAFC Secretary before 1 March of the same year.

2. The report referred to in paragraph 1 shall indicate the current status of the proceedings and in particular whether the case is pending, under appeal or still under investigation. The report shall describe in specific terms any sanctions imposed, stating in particular the level of fines, the value of forfeited fish and/or gear and any written warnings given and, if no action has been taken, it shall state the reasons thereof.

Article 35

Treatment of inspection reports

Without prejudice to Article 77 of Regulation (EC) No 1224/2009, Member States shall collaborate with each other and with other Contracting Parties in order to facilitate judicial or other proceedings arising from a report submitted by an inspector under the Scheme, subject to the rules governing the admissibility of evidence in domestic judicial or other systems.

Article 36

Reports on surveillance and inspection activities

1. Each Member State shall report to the Commission or the body designated by it by 15 February each year for the previous calendar year:

- (a) the number of inspections it has carried out under Articles 19, 20 and 26, specifying the number of inspections on the vessels of each Contracting Party and, where an infringement has been committed, the date and position of the inspection of the individual vessel concerned and the nature of the infringement;
- (b) the number of hours flown and the number of days at sea on NEAFC patrols, the number of sightings of both Contracting Party vessels and non-Contracting Party vessels, and the list of individual vessels for which a surveillance report has been completed.

2. The Commission or the body designated by it shall compile a Union report on the basis of the reports of the Member States. It shall send the Union report to the NEAFC Secretary by 1 March each year.

CHAPTER VI

MEASURES TO PROMOTE COMPLIANCE BY NON-CONTRACTING PARTY FISHING VESSELS

Article 37

Scope

1. This Chapter shall apply to non-Contracting Parties' fishing vessels used or intended for use for fishing activities carried out in respect of fishery resources in the Convention Area.

2. This Chapter shall be without prejudice to Regulation (EC) No 1224/2009 and to Regulation (EC) No 1005/2008.

Article 38

Sightings and identifications of non-Contracting Party vessels

1. Member States shall transmit without delay to the Commission or the body designated by it any information regarding non-Contracting Party vessels sighted or otherwise identified as engaging in fishing activities in the Convention Area. The Commission or the body designated by it shall inform promptly the NEAFC Secretary and all other Member States of each sighting report it receives.

2. The Member State which sighted the non-Contracting Party vessel shall attempt to inform that vessel without delay that it has been sighted or otherwise identified as engaging in fishing activities in the Convention Area and is consequently presumed, unless its flag state has been accorded the status of cooperating non-Contracting Party by NEAFC, to be undermining the NEAFC conservation and management measures.

3. In the case of a non-Contracting Party vessel sighted or otherwise identified as engaging in transshipment activities, the presumption of undermining the NEAFC conservation and management measures shall apply to any other non-Contracting Party vessel that has been identified as having engaged in such activities with that vessel.

Article 39

Inspections at sea

1. NEAFC inspectors shall request permission to board and inspect non-Contracting Party vessels sighted or otherwise identified by a Contracting Party as engaging in fishing activities in the Convention Area. If the master consents to the boarding and inspection of the vessel, the inspection shall be documented by the completion of an inspection report, as referred to Article 20(9).

2. NEAFC inspectors shall without delay transmit a copy of the inspection report to the Commission or the body designated by it, to the NEAFC Secretary and to the master of the non-Contracting Party vessel. Where the evidence in that report so warrants, a Member State may take such action as may be appropriate in accordance with international law. Member States are encouraged to examine whether their national measures are appropriate for the exercise of jurisdiction over such vessels.

3. If the master does not consent to the boarding and inspection of his vessel or does not fulfil any one of the obligations laid down in Article 21(a) to (d), the vessel shall be presumed to have engaged in illegal, unreported and unregulated fishing activities (IUU activities). The NEAFC Inspector shall inform without delay the Commission or the body designated by it thereof. In turn the Commission or the body designated by it shall promptly inform the NEAFC Secretary thereof.

Article 40

Entry into port

1. The master of a non-Contracting Party fishing vessel may only call into a port designated in accordance with Article 23. The master intending to call into a port of a Member State shall notify the competent authorities of the port Member State in accordance with the provisions of Article 24. The port Member State concerned shall forward this information without delay to the flag state of the vessel and to the Commission or the body designated by it. In turn, the Commission or the body designated by it shall forward this information to the NEAFC Secretary.

2. The port Member State shall prohibit the entry into its ports of vessels that have not given the required prior notification of entry into port as referred to in Article 24.

Article 41

Inspections in port

1. Member States shall ensure that all non-Contracting Party vessels entering one of their ports are inspected. The vessel shall not be allowed to land or tranship any fish until this inspection has been completed. Each inspection shall be documented by the completion of an inspection report as provided for in Article 27. Where the master of the vessel has failed to fulfil any one of the obligations laid down in Article 21(a) to (d), the vessel shall be presumed to have engaged in IUU activities.

2. Information on the results of all inspections of non-Contracting Party vessels conducted in the ports of Member States, and concerning subsequent action, shall immediately be transmitted to the Commission or the body designated by it, which shall forward such information to the NEAFC Secretary.

Article 42

Landings and transhipments

1. Landings and transhipments may only start after authorisation has been given by the competent authorities of the port state.

2. Landings and transhipments from a non-Contracting Party vessel which has been inspected pursuant to Article 41 shall be prohibited in the ports and waters of all Member States if such an inspection reveals that the vessel has species on board which are subject to recommendations established under the Convention, unless the master of the vessel provides satisfactory evidence to the competent authorities proving that the fish were caught outside the Regulatory Area or in compliance with all relevant recommendations established under the Convention.

3. The vessel shall not be authorised to engage in landings or transhipments if the flag state of the vessel, or the flag state or states of the donor vessels, where the vessel has engaged in transhipment operations, does not provide the confirmation referred to in Article 25.

4. Furthermore, landings and transhipments shall be prohibited where the master of the vessel has failed to fulfil any one of the obligations laid down in Article 21(a) to (d).

Article 43

Reports on non-Contracting Parties activities

1. Each Member State shall report to the Commission or the body designated by it by 15 February each year for the previous calendar year:

(a) the number of inspections of non-Contracting Party vessels that it conducted under this Scheme at sea or in its ports, the names of the vessels inspected and their respective flag states, the dates of the inspections and the names of any ports where the inspections were conducted, and the results of such inspections; and

(b) where fish are landed or transhipped following an inspection pursuant to this Scheme, the evidence provided pursuant to Article 42.

2. In addition to surveillance reports and information on inspections, Member States may at any time submit to the Commission or the body designated by it any further information which might be relevant for the identification of non-Contracting Party vessels that might be carrying out IUU activities in the Convention Area.

3. On the basis of this information, the Commission or the body designated by it shall send a global report on non-Contracting Parties' activities to the NEAFC Secretary by 1 March each year.

*Article 44***Vessels engaged in IUU activities**

1. Member States shall ensure that vessels appearing in the provisional list of vessels engaged in IUU activities established by NEAFC ('A' list) are:

- (a) inspected in accordance with the provisions of Article 41 when they enter their ports;
- (b) not authorised to land or tranship in their ports or in the waters under their jurisdiction;
- (c) not given assistance by fishing vessels, support vessels, refuel vessels, the mother-ship and cargo vessels flying their flag or permitted to participate in any transshipment or joint fishing operation with such vessels;
- (d) not supplied with provisions, fuel or other services.

2. The provisions laid down in paragraph 1(b) and (d) shall not be applied to any vessel appearing on the 'A' list where a recommendation has been made to NEAFC that the vessel in question should be removed from the 'A' list.

CHAPTER VII

FINAL PROVISIONS

*Article 45***Confidentiality**

1. In addition to the obligations laid down in Articles 112 and 113 of Regulation (EC) No 1224/2009, Member States shall ensure confidential treatment of electronic reports and messages transmitted to and received from the NEAFC Secretary pursuant to Articles 11, 12 and 19(1).

2. The detailed rules for the implementation of this Article shall be determined in accordance with Article 50(2).

*Article 46***Delegation of powers**

1. The Commission may adopt, by means of delegated acts in accordance with Article 47 and subject to the conditions of Articles 48 and 49 the detailed rules for the application of Article 25, as well as the list of fishery resources referred to in Article 10(1) and detailed rules on the notification and cancellation procedures, including periods, as referred to in the second subparagraph of Article 24(4).

2. When adopting such delegated acts, the Commission shall act in accordance with the provisions of this Regulation.

*Article 47***Exercise of the delegation**

1. The power to adopt delegated acts referred to in Article 46 shall be conferred on the Commission for a period of 3 years from 1 January 2011. The Commission shall make a report in respect of the delegated powers at the latest 6 months before the end of the three-year period. The delegation of power shall be automatically extended for periods of an identical duration, unless the European Parliament or the Council revokes it in accordance with Article 48.

2. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.

3. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in Articles 48 and 49.

*Article 48***Revocation of the delegation**

1. The delegation of power referred to in Article 46 may be revoked at any time by the European Parliament or by the Council.

2. The institution which has commenced an internal procedure for deciding whether to revoke the delegation of power shall endeavour to inform the other institution and the Commission within a reasonable time before the final decision is taken, indicating the delegated powers which could be subject to revocation and possible reasons for a revocation.

3. The decision of revocation shall put an end to the delegation of the powers specified in that decision. It shall take effect immediately or at a later date specified therein. It shall not affect the validity of the delegated acts already in force. It shall be published in the *Official Journal of the European Union*.

*Article 49***Objections to delegated acts**

1. The European Parliament or the Council may object to a delegated act within a period of 2 months from the date of notification.

At the initiative of the European Parliament or the Council this period shall be extended by 2 months.

2. If, on expiry of that period, neither the European Parliament nor the Council has objected to the delegated act it shall be published in the *Official Journal of the European Union* and shall enter into force at the date stated therein.

The delegated act may be published in the *Official Journal of the European Union* and enter into force before the expiry of that period if the European Parliament and the Council have both informed the Commission of their intention not to raise objections.

3. If the European Parliament or the Council objects to a delegated act, it shall not enter into force. The institution which objects shall state the reasons for objecting to the delegated act.

Article 50

Implementation

1. The Commission shall be assisted by a Management Committee for Fisheries and Aquaculture.

2. Where reference is made to this paragraph, Articles 4 and 7 of Decision 1999/468/EC shall apply. The period referred to in Article 4(3) of Decision 1999/468/EC shall be set at 3 months.

Article 51

Procedure for amendments

As far as is necessary, in order to incorporate into Union law amendments to the existing provisions of the Scheme which become obligatory for the Union, the Commission may amend the provisions of this Regulation by means of delegated acts in accordance with Article 47 and subject to the conditions set out in Articles 48 and 49, concerning:

(a) participation of Contracting Parties in the fishery in the Regulatory area as referred to in Article 5;

(b) removal and disposal of fixed gear and the retrieval of lost gear as referred to in Articles 6 and 7;

(c) use of VMS as referred to in Article 11;

(d) cooperation and communication of information to the NEAFC Secretary as referred to in Article 12;

(e) requirements for separate stowage and labelling of frozen fishery resources as referred to in Articles 14 and 15;

(f) assignment of NEAFC inspectors as referred to in Article 16;

(g) measures to promote compliance with the Scheme by non-Contracting Party fishing vessels under Chapter VI;

(h) the list of regulated resources set out in the Annex.

When adopting such delegated acts, the Commission shall act in accordance with the provisions of this Regulation.

Article 52

Repeal

Regulation (EC) No 2791/1999 is hereby repealed.

Article 53

Entry into force

This Regulation shall enter into force on the day following its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg, 15 December 2010.

For the European Parliament
The President
J. BUZEK

For the Council
The President
O. CHASTEL

ANNEX

REGULATED RESOURCES

A) Pelagic and oceanic species

Stock (common name)	FAO code	Scientific Name	ICES subareas and divisions
Redfish	REB	<i>Sebastes mentella</i>	I, II, V, XII, XIV
Norwegian Spring Spawning Herring (Atlanto Scandian)	HER	<i>Clupea harengus</i>	I, II
Blue whiting	WHB	<i>Micromesistius poutassou</i>	Ila, IVa, Vb, VI, VII, XII, XIV
Mackerel	MAC	<i>Scomber scombrus</i>	Ila, IV, V, VI, VII, XII
Haddock	HAD	<i>Melanogrammus aeglefinus</i>	Vlb

B) Deep-Sea Species

Stock (common name)	FAO code	Scientific Name	ICES subareas
Baird's smoothhead	ALC	<i>Alepocephalus bairdii</i>	I to XIV
Risso's smoothhead	PHO	<i>Alepocephalus rostratus</i>	I to XIV
Blue antimora (Blue hake)	ANT	<i>Antimora rostrata</i>	I to XIV
Black scabbardfish	BSF	<i>Aphanopus carbo</i>	I to XIV
Iceland catshark	API	<i>Apristurus</i> spp.	I to XIV
Greater silver smelt	ARG	<i>Argentina silus</i>	I to XIV
Alfonsinos	ALF	<i>Beryx</i> spp.	I to XIV
Tusk	USK	<i>Brosme brosme</i>	I to XIV
Gulper shark	GUP	<i>Centrophorus granulosus</i>	I to XIV
Leafscale gulper shark	GUQ	<i>Centrophorus squamosus</i>	I to XIV
Black dogfish	CFB	<i>Centroscyllium fabricii</i>	I to XIV
Portuguese dogfish	CYO	<i>Centroscyrnus coelolepis</i>	I to XIV
Longnose velvet dogfish	CYP	<i>Centroscyrnus crepidater</i>	I to XIV
Deep-water red crab	KEF	<i>Chaceon (Geryon) affinis</i>	I to XIV
Rabbit fish (Rattail)	CMO	<i>Chimaera monstrosa</i>	I to XIV
Frilled shark	HXC	<i>Chlamydoselachus anguineus</i>	I to XIV
Conger eel	COE	<i>Conger conger</i>	I to XIV
Roundnose grenadier	RNG	<i>Coryphaenoides rupestris</i>	I to XIV
Kitefin shark	SCK	<i>Dalatias licha</i>	I to XIV
Birdbeak dogfish	DCA	<i>Deania calceus</i>	I to XIV

Stock (common name)	FAO code	Scientific Name	ICES subareas
Black (Deep-water) cardinal fish	EPI	<i>Epigonus telescopus</i>	I to XIV
Greater lanternshark	SHL	<i>Etmopterus princeps</i>	I to XIV
Velvet belly	SHL	<i>Etmopterus spinax</i>	I to XIV
Blackmouth dogfish	SHO	<i>Galeus melastomus</i>	I to XIV
Mouse catshark	GAM	<i>Galeus murinus</i>	I to XIV
Bluemouth (Blue mouth redfish)	BRF	<i>Helicolenus dactylopterus</i>	I to XIV
Bluntnose six-gilled shark	SBL	<i>Hexanchus griseus</i>	I to XIV
Orange roughy	ORY	<i>Hoplostethus atlanticus</i>	I to XIV
Silver roughy (Pink)	HPR	<i>Hoplostethus mediterraneus</i>	I to XIV
Large-eyed rabbit fish (Ratfish)	CYH	<i>Hydrolagus mirabilis</i>	I to XIV
Silver scabbard fish (Cutlass fish)	SFS	<i>Lepidopus caudatus</i>	I to XIV
Eelpout	ELP	<i>Lycodes esmarkii</i>	I to XIV
Roughhead grenadier (Rough rattail)	RHG	<i>Macrourus berglax</i>	I to XIV
Blue ling	BLI	<i>Molva dypterygia</i>	I to XIV
Ling	LIN	<i>Molva molva</i>	I to XIV
Common mora	RIB	<i>Mora moro</i>	I to XIV
Sailfin roughshark (Sharpback shark)	OXN	<i>Oxynotus paradoxus</i>	I to XIV
Red (blackspot) seabream	SBR	<i>Pagellus bogaraveo</i>	I to XIV
Forkbeards	GFB	<i>Phycis</i> spp.	I to XIV
Wreckfish	WRF	<i>Polyprion americanus</i>	I to XIV
Round skate	RJY	<i>Raja fyllae</i>	I to XIV
Arctic skate	RJG	<i>Raja hyperborea</i>	I to XIV
Norwegian skate	JAD	<i>Raja nidarosiensis</i>	I to XIV
Greenland halibut	GHL	<i>Rheinhardtius hippoglossoides</i>	I to XIV
Straightnose rabbitfish	RCT	<i>Rhinochimaera atlantica</i>	I to XIV
Knifetooth dogfish	SYR	<i>Scymnodon ringens</i>	I to XIV
Small redfish (Norway haddock)	SFV	<i>Sebastes viviparus</i>	I to XIV
Greenland shark	GSK	<i>Somniosus microcephalus</i>	I to XIV
Spiny (Deep-sea) Scorpionfish	TJX	<i>Trachyscorpia cristulata</i>	I to XIV

Appendix

Statements on Article 51

'The European Parliament, the Council and the Commission note that any of the provisions of a non-essential character of the basic legislative act, which now are listed under Article 51 of the Regulation (delegation of powers), can become at any time in the future a significant element of the existing NEAFC control scheme from a political point of view, in which case the European Parliament, the Council and the Commission recall that either of the legislators, the Council or the European Parliament, can immediately exercise either the right to object to a draft Commission delegated act or the right to revoke the delegated powers as provided under Article 48 and Article 49 of the Regulation respectively.'

'The Council and the Parliament agree that the inclusion of any provision of the NEAFC control scheme into this Regulation as a non-essential element, now listed under Article 51, does not imply per se that such provisions will automatically be considered by the legislators to be of a non-essential character in any future Regulations.'

'The European Parliament, the Council and the Commission declare that the provisions of this Regulation shall be without prejudice to any future position of the institutions as regards the implementation of Article 290 TFEU or individual legislative acts containing such provisions.'

**REGULATION (EU) No 1237/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 15 December 2010**

**amending Council Regulation (EC) No 2187/2005 as regards the prohibition of highgrading and
restrictions on fishing for flounder and turbot in the Baltic Sea, the Belts and the Sound**

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE
EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European
Union, and in particular Article 43(2) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national
parliaments,

Having regard to the opinion of the European Economic and
Social Committee ⁽¹⁾,

Acting in accordance with the ordinary legislative procedure ⁽²⁾,

Whereas:

(1) Council Regulation (EC) No 2187/2005 ⁽³⁾ lays down
specific technical measures for the conservation of
fishery resources in the Baltic Sea, the Belts and the
Sound, and in particular restrictions on fishing as
regards certain species, mesh sizes and areas.

(2) Council Regulation (EC) No 1226/2009 of 20 November
2009 fixing the fishing opportunities and associated
conditions for certain fish stocks and groups of fish
stocks applicable in the Baltic Sea for 2010 ⁽⁴⁾ provides
for the prohibition of highgrading and for restrictions on
fishing for flounder and turbot.

(3) This prohibition and these restrictions are technical
measures of a permanent nature which should no
longer be included in the regulatory framework estab-
lishing annual fishing opportunities. From January
2011, they should therefore be incorporated into Regu-
lation (EC) No 2187/2005.

(4) The term 'Community' used in the enacting terms of
Regulation (EC) No 2187/2005 should be changed
following the entry into force of the Treaty of Lisbon
on 1 December 2009.

(5) Regulation (EC) No 2187/2005 should therefore be
amended accordingly.

(6) In order to ensure the continuous application of the
measures provided for in this Regulation, it should
enter into force on the day following its publication in
the *Official Journal of the European Union*,

HAVE ADOPTED THIS REGULATION:

Article 1

Regulation (EC) No 2187/2005 is hereby amended as follows:

1. the following article is inserted:

'Article 15a

Prohibition of highgrading

Any species which is subject to a quota and which is caught
during fishing operations shall be brought aboard the vessel
and subsequently landed unless this would be contrary to
obligations laid down in Union fisheries regulations estab-
lishing technical, control and conservation measures in
particular in this Regulation, in Regulation (EC) No
2371/2002 or in Council Regulation (EC) No 1224/2009
of 20 November 2009 establishing a Community control
system for ensuring compliance with the rules of the
common fisheries policy ^(*).

^(*) OJ L 343, 22.12.2009, p. 1.;

2. the following article is inserted:

'Article 18a

Restrictions on fishing for flounder and turbot

1. The retention on board of the following species of fish
shall be prohibited where they are caught within the
geographical areas and during the periods mentioned below:

⁽¹⁾ Opinion of 15 September 2010 (not yet published in the Official
Journal).

⁽²⁾ Position of the European Parliament of 23 November 2010 (not yet
published in the Official Journal) and decision of the Council of
6 December 2010.

⁽³⁾ OJ L 349, 31.12.2005, p. 1.

⁽⁴⁾ OJ L 330, 16.12.2009, p. 1.

Species	Geographical area	Period
Flounder (<i>Platichthys flesus</i>)	Subdivisions 26, 27, 28 and 29 south of 59° 30' N	15 February to 15 May
	Subdivision 32	15 February to 31 May
Turbot (<i>Psetta maxima</i>)	Subdivisions 25, 26 and 28 south of 56° 50' N	1 June to 31 July

2. By way of derogation from paragraph 1, when fishing with trawls, Danish seines or similar gears with a mesh size equal to or greater than 105 mm or with gillnets, entangling nets or trammel nets with a mesh size equal to or greater than 100 mm, by-catches of flounder and turbot may be

retained on board and landed within a limit of 10 % by live weight of the total catch retained on board and landed during the periods of prohibition referred to in paragraph 1.;

3. in Article 26(1) and (2), the noun 'Community', or the corresponding adjective, is replaced by the noun 'Union', or the corresponding adjective, and any grammatical adjustments needed as a consequence of this replacement shall be made.

Article 2

This Regulation shall enter into force on the day following its publication in the *Official Journal of the European Union*.

It shall apply from 1 January 2011.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg, 15 December 2010.

For the European Parliament

The President

J. BUZEK

For the Council

The President

O. CHASTEL

**REGULATION (EU) No 1238/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 15 December 2010**

amending Annex I to Council Regulation (EEC) No 2658/87 as regards the provision of duty-free treatment for specified pharmaceutical active ingredients bearing an 'international non-proprietary name' (INN) from the World Health Organization and specified products used for the manufacture of finished pharmaceuticals

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 207 thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Acting in accordance with the ordinary legislative procedure ⁽¹⁾,

Whereas:

(1) In the course of the Uruguay Round negotiations, the Community and a number of countries agreed that duty-free treatment should be granted to pharmaceutical products falling within the Harmonised System (HS) Chapter 30 and HS headings 2936, 2937, 2939 and 2941 as well as to designated pharmaceutical active ingredients bearing an 'international non-proprietary name' (INN) from the World Health Organization, specified salts, esters and hydrates of such INNs, and designated pharmaceutical intermediates used for the production and manufacture of finished pharmaceuticals.

(2) The results of the discussions, as set out in the Record of Discussions, were incorporated into the tariff schedules of the participants annexed to the Marrakesh Protocol to the General Agreement on Tariffs and Trade (GATT) 1994.

(3) Participants concluded that representatives of World Trade Organization (WTO) members, party to the Record of Discussions, would meet under the auspices of the Council for Trade in Goods of the WTO, normally at least once every three years, to review the product coverage with a view to including, by consensus, additional pharmaceutical products for tariff elimination.

(4) Three such reviews have taken place with the result that a certain number of additional INNs and pharmaceutical

intermediates used for the production and manufacture of finished pharmaceuticals have been granted duty-free treatment, that some of those intermediates have been transferred to the list of INNs, and that the list of specified prefixes and suffixes for salts, esters or hydrates of INNs has been expanded.

(5) A fourth review was deemed appropriate and was launched in 2009. It concluded that a certain number of additional INNs and pharmaceutical intermediates used for the production and manufacture of finished pharmaceuticals should be granted duty-free treatment, that some of those intermediates already included in the pharmaceutical sectoral arrangement and its revisions should be transferred to the list of INNs, and that the list of specified prefixes and suffixes for salts, esters or hydrates of INNs should be expanded.

(6) Council Regulation (EEC) No 2658/87 of 23 July 1987 on the tariff and statistical nomenclature and on the Common Customs Tariff ⁽²⁾ established the Combined Nomenclature (CN) and set out the conventional duty rates of the Common Customs Tariff.

(7) Regulation (EEC) No 2658/87 should therefore be amended accordingly.

(8) In order to ensure that the measures provided for in this Regulation apply from 1 January 2011, it should enter into force on the day following that of its publication,

HAVE ADOPTED THIS REGULATION:

Article 1

Annexes 3, 4 and 6 of Section II of Part Three of Annex I to Regulation (EEC) No 2658/87 (Lists of pharmaceutical substances which qualify for duty-free treatment) are hereby amended as follows:

1. As from 1 January 2011 the Union shall extend duty-free treatment to the INNs listed in Annex I.

⁽¹⁾ Position of the European Parliament of 23 November 2010 (not yet published in the Official Journal) and decision of the Council of 10 December 2010.

⁽²⁾ OJ L 256, 7.9.1987, p. 1.

2. As from 1 January 2011 the list of prefixes and suffixes which, in combination with the INNs included in the pharmaceutical sectoral arrangement and its revisions, describe the salts, esters or hydrates of INNs which are also eligible for duty-free treatment, on condition that they are classifiable in the same six-digit HS subheading as the corresponding INN, shall be amended as set out in Annex II.
3. As from 1 January 2011 the Union shall extend duty-free treatment to the pharmaceutical intermediates used in the production and manufacture of finished pharmaceuticals, listed in Annex III.
4. As from 1 January 2011 the pharmaceutical intermediates listed in Annex IV shall be withdrawn from the list of such compounds receiving duty-free treatment.

Article 2

This Regulation 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 January 2011.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg, 15 December 2010.

For the European Parliament
The President
J. BUZEK

For the Council
The President
O. CHASTEL

ANNEX I

List of international non-proprietary names (INNs) to be added to the list of products receiving duty-free treatment included in Annex 3 to Annex I to Regulation (EEC) No 2658/87

CN code	CAS RN	Name
2842 90 80	119175-48-3	fermagate
2843 90 90	759457-82-4	padeliporfin
2844 40 30	123748-56-1	iodofiltic acid (¹²³ I)
2904 10 00	21668-77-9	eprodiate
2906 19 00	199798-84-0	elocalcitol
2909 30 90	24150-24-1	terameprocol
2916 19 95	81485-25-8	peretinoin
2916 39 00	51543-40-9	tarenflurbil
2918 19 98	174022-42-5	bevirimat
2919 90 00	258516-89-1	fospropofol
2920 90 85	163133-43-5	naproxcinod
2921 19 99	3687-18-1	tramiprosate
2922 19 85	68392-35-8	afimoxifene
2922 19 85	753449-67-1	ronacaleret
2922 29 00	433265-65-7	faxeladol
2922 50 00	121524-08-1	amibegron
2922 50 00	329773-35-5	cinaciguat
2922 50 00	643094-49-9	fasobegron
2923 10 00	856676-23-8	choline fenofibrate
2924 29 98	847353-30-4	arbaclofen placarbil
2924 29 98	194785-19-8	bedoradrine
2924 29 98	194085-75-1	carisbamate
2924 29 98	254750-02-2	emricasan
2924 29 98	355129-15-6	eprotirome
2924 29 98	402567-16-2	firategrast
2924 29 98	478296-72-9	gabapentin enacarbil
2924 29 98	15866-90-7	incyclinide
2924 29 98	202844-10-8	indantadol

CN code	CAS RN	Name
2924 29 98	96847-55-1	levomilnacipran
2924 29 98	608137-32-2	lisdexamfetamine
2924 29 98	652990-07-3	milveterol
2924 29 98	181816-48-8	ombrabulin
2924 29 98	289656-45-7	senicapoc
2925 19 95	19171-19-8	pomalidomide
2928 00 90	22033-87-0	olesoxime
2928 00 90	2675-35-6	sivifene
2928 00 90	816458-31-8	tecovirimat
2928 00 90	238750-77-1	tosedostat
2928 00 90	149647-78-9	vorinostat
2929 90 00	31645-39-3	palifosfamide
2930 90 99	608141-41-9	apremilast
2930 90 99	216167-92-9	camobucol
2930 90 99	211513-37-0	dalcetrapib
2930 90 99	69819-86-9	darinaparsin
2930 90 99	488832-69-5	elesclomol
2930 90 99	216167-95-2	elsibucol
2930 90 99	168682-53-9	ezatiostat
2930 90 99	58569-55-4	metenkefalin
2930 90 99	887148-69-8	monepantel
2930 90 99	603139-19-1	odanacatib
2930 90 99	162520-00-5	salirasib
2930 90 99	216167-82-7	succinobucol
2930 90 99	125961-82-2	tipelukast
2931 00 99	125973-56-0	amsilarotene
2932 19 00	253128-41-5	eribulin
2932 19 00	186953-56-0	pafuramidine
2932 29 85	195883-06-8	omtriptolide
2932 99 00	664338-39-0	arterolane
2932 99 00	183133-96-2	cabazitaxel

CN code	CAS RN	Name
2932 99 00	401925-43-7	celivarone
2932 99 00	461432-26-8	dapagliflozin
2932 99 00	118457-15-1	dexnebivolol
2932 99 00	156294-36-9	larotaxel
2932 99 00	118457-16-2	levonebivolol
2932 99 00	83461-56-7	mifamurtide
2932 99 00	117570-53-3	vadimezan
2933 19 90	496775-61-2	eltrombopag
2933 19 90	206884-98-2	niraxostat
2933 19 90	410528-02-8	palovarotene
2933 19 90	376592-42-6	totrombopag
2933 29 90	183659-72-5	catramilast
2933 29 90	944263-65-4	demiditraz
2933 29 90	867153-61-5	dulanermin
2933 29 90	320367-13-3	lixisenatide
2933 29 90	698389-00-3	rolipoltide
2933 29 90	697766-75-9	velafermin
2933 39 99	147084-10-4	alcaftadine
2933 39 99	54-96-6	amifampridine
2933 39 99	249921-19-5	anamorelin
2933 39 99	319460-85-0	axitinib
2933 39 99	208110-64-9	befiradol
2933 39 99	330942-05-7	betrixaban
2933 39 99	201034-75-5	daporinad
2933 39 99	209783-80-2	entinostat
2933 39 99	412950-27-7	goxalapladi
2933 39 99	218791-21-0	imisopasem manganese
2933 39 99	103129-82-4	levamlodipine
2933 39 99	154357-42-3	levonadifloxacin
2933 39 99	108147-54-2	migalastat
2933 39 99	453562-69-1	motesanib

CN code	CAS RN	Name
2933 39 99	139145-27-0	parogrelil
2933 39 99	459856-18-9	pexacerfont
2933 39 99	706779-91-1	pimavanserin
2933 39 99	362665-56-3	pitolisant
2933 39 99	861151-12-4	rosonabant
2933 39 99	701977-09-5	taranabant
2933 39 99	189950-11-6	tropantioI
2933 39 99	793655-64-8	vapitadine
2933 39 99	139290-65-6	volinaserin
2933 49 90	141388-76-3	besifloxacin
2933 49 90	697761-98-1	elvitegravir
2933 49 90	185055-67-8	ferroquine
2933 49 90	445041-75-8	intiquinate
2933 49 90	378746-64-6	nemonoxacin
2933 49 90	245765-41-7	ozenoxacin
2933 49 90	412950-08-4	rilapladib
2933 49 90	871224-64-5	almorexant
2933 49 90	863029-99-6	balamapimod
2933 49 90	698387-09-6	neratinib
2933 49 90	154652-83-2	tezampanel
2933 49 90	128253-31-6	veliflapon
2933 59 95	791828-58-5	aderbasib
2933 59 95	840486-93-3	adipiplon
2933 59 95	850649-61-5	alogliptin
2933 59 95	859212-16-1	bafetinib
2933 59 95	380843-75-4	bosutinib
2933 59 95	839712-12-8	cariprazine
2933 59 95	414910-27-3	casopitant
2933 59 95	288383-20-0	cediranib
2933 59 95	849550-05-6	cevipabulin
2933 59 95	827318-97-8	danusertib

CN code	CAS RN	Name
2933 59 95	356057-34-6	darapladib
2933 59 95	501000-36-8	dutacatib
2933 59 95	247257-48-3	fimasartan
2933 59 95	3432-99-3	folitixorin
2933 59 95	668270-12-0	linagliptin
2933 59 95	441798-33-0	macitentan
2933 59 95	641571-10-0	nilotinib
2933 59 95	763113-22-0	olaparib
2933 59 95	686344-29-6	otenabant
2933 59 95	625115-55-1	riociguat
2933 59 95	486460-32-6	sitagliptin
2933 59 95	425637-18-9	sotrastaurin
2933 59 95	309913-83-5	talmapimod
2933 59 95	113857-87-7	talotrexin
2933 59 95	274693-27-5	ticagrelor
2933 59 95	306296-47-9	vicriviroc
2933 69 80	775351-65-0	imeglimin
2933 79 00	461443-59-4	aplaviroc
2933 79 00	189691-06-3	bremelanotide
2933 79 00	813452-18-5	carmegliptin
2933 79 00	405169-16-6	dovitinib
2933 79 00	536748-46-6	eribaxaban
2933 79 00	473289-62-2	ilepatril
2933 79 00	180694-97-7	mimopezil
2933 79 00	579475-18-6	orvepitant
2933 79 00	449811-01-2	pamapimod
2933 79 00	248282-01-1	paquinimod
2933 79 00	380917-97-5	perampanel
2933 79 00	552292-08-7	rolapitant
2933 79 00	425386-60-3	semagacestat
2933 79 00	515814-01-4	voclosporin

CN code	CAS RN	Name
2933 99 80	481629-87-2	aleplasinin
2933 99 80	394730-60-0	boceprevir
2933 99 80	649735-63-7	brivanib alaninate
2933 99 80	483369-58-0	denaglipitin
2933 99 80	284019-34-7	denibulin
2933 99 80	481631-45-2	diaplasinin
2933 99 80	272105-42-7	disitertide
2933 99 80	227318-71-0	epetirimod
2933 99 80	259793-96-9	favipiravir
2933 99 80	871576-03-3	flovagatran
2933 99 80	229305-39-9	golotimod
2933 99 80	258818-34-7	larazotide
2933 99 80	571170-77-9	laropiprant
2933 99 80	616202-92-7	lorcaserin
2933 99 80	868771-57-7	meloglipitin
2933 99 80	803712-67-6	obatoclax
2933 99 80	404950-80-7	panobinostat
2933 99 80	625114-41-2	piragliatin
2933 99 80	74847-35-1	pyronaridine
2933 99 80	872178-65-9	rabeximod
2933 99 80	355151-12-1	rotigaptide
2933 99 80	497221-38-2	rusalatide
2933 99 80	187602-11-5	sofigatran
2933 99 80	227318-75-4	sotirimod
2933 99 80	402957-28-2	telaprevir
2933 99 80	848084-83-3	tigapotide
2933 99 80	393105-53-8	tiplasinin
2933 99 80	620948-93-8	vabicaserin
2933 99 80	794466-70-9	vernakalant
2934 10 00	544417-40-5	capadenoson
2934 10 00	302962-49-8	dasatinib

CN code	CAS RN	Name
2934 10 00	223132-37-4	inolitazone
2934 10 00	241479-67-4	isavuconazole
2934 10 00	338990-84-4	isavuconazonium chloride
2934 10 00	607723-33-1	lobeglitazone
2934 10 00	280782-97-0	managlinat dialanetil
2934 10 00	790299-79-5	masitinib
2934 10 00	223673-61-8	mirabegron
2934 10 00	501948-05-6	rosabulin
2934 10 00	447406-78-2	sodelglitazar
2934 10 00	760937-92-6	teneligliptin
2934 20 80	848344-36-5	bentamapimod
2934 20 80	870093-23-5	talarozole
2934 99 90	320345-99-1	aclidinium bromide
2934 99 90	222551-17-9	adoprazine
2934 99 90	207623-20-9	agatolimod
2934 99 90	475479-34-6	aleglitazar
2934 99 90	870524-46-2	amolimogene bepiplasmid
2934 99 90	875446-37-0	anacetrapib
2934 99 90	250386-15-3	apadenoson
2934 99 90	541550-19-0	apilimod
2934 99 90	160707-69-7	apricitabine
2934 99 90	147403-03-0	azilsartan
2934 99 90	863031-21-4	azilsartan medoxomil
2934 99 90	757942-43-1	bederocin
2934 99 90	627861-07-8	bepminogene perplasmid
2934 99 90	959961-96-7	bevasiranib
2934 99 90	769901-96-4	capeserod
2934 99 90	868540-17-4	carfilzomib
2934 99 90	872847-66-0	cenersen
2934 99 90	80295-38-1	conestat alfa
2934 99 90	903916-27-8	custirsen

CN code	CAS RN	Name
2934 99 90	187865-22-1	derquantel
2934 99 90	134379-77-4	dexelvucitabine
2934 99 90	247046-52-2	dilopetine
2934 99 90	480449-70-5	edoxaban
2934 99 90	188181-42-2	elacytarabine
2934 99 90	98819-76-2	esreboxetine
2934 99 90	763903-67-9	fosalvudine tidoxil
2934 99 90	172673-20-0	fosaprepitant
2934 99 90	522664-63-7	ibodutant
2934 99 90	405159-59-3	idrabiota-parinux sodium
2934 99 90	188116-07-6	imepitoin
2934 99 90	335619-18-6	inakalant
2934 99 90	1391-36-2	lancovutide
2934 99 90	189059-71-0	lapaquistat
2934 99 90	327026-93-7	lensiprazine
2934 99 90	170632-47-0	lificiguat
2934 99 90	852313-25-8	litenimod
2934 99 90	1000120-98-8	mipomersen
2934 99 90	62253-63-8	nepidermin
2934 99 90	26833-87-4	omacetaxine mepesuccinate
2934 99 90	269718-84-5	pardoprunox
2934 99 90	219923-85-0	pramiconazole
2934 99 90	377727-87-2	preladenant
2934 99 90	524684-52-4	prinaberel
2934 99 90	865311-47-3	quarfloxin
2934 99 90	869884-78-6	radezolid
2934 99 90	496054-87-6	radiprodil
2934 99 90	518048-05-0	raltegravir
2934 99 90	787548-03-2	regrelor
2934 99 90	820957-38-8	retosiban
2934 99 90	572924-54-0	ridaforolimus

CN code	CAS RN	Name
2934 99 90	128517-07-7	romidepsin
2934 99 90	93265-81-7	ropidoxuridine
2934 99 90	151823-14-2	sapacitabine
2934 99 90	379231-04-6	saracatinib
2934 99 90	791635-59-1	simotaxel
2934 99 90	119567-79-2	taribavirin
2934 99 90	332012-40-5	relatinib
2934 99 90	925681-61-4	trabedersen
2934 99 90	189003-92-7	trelanserin
2934 99 90	296251-72-4	velimogene aliplasmid
2934 99 90	904302-98-3	viquidacin
2934 99 90	872525-61-6	votucalis
2934 99 90	221877-54-9	zotarolimus
2935 00 90	197904-84-0	apricoxib
2935 00 90	769169-27-9	begacestat
2935 00 90	414864-00-9	belinostat
2935 00 90	313682-08-5	brecanavir
2935 00 90	839673-52-8	cevoglitazar
2935 00 90	358970-97-5	drinabant
2935 00 90	865200-20-0	giripladib
2935 00 90	464213-10-3	ibipinabant
2935 00 90	173424-77-6	laromustine
2935 00 90	398507-55-6	lodenafil carbonate
2935 00 90	136564-68-6	masilukast
2935 00 90	170569-88-7	mavacoxib
2935 00 90	862189-95-5	mirodenafil
2935 00 90	439687-69-1	nelivaptan
2935 00 90	691852-58-1	nesbuvir
2935 00 90	778576-62-8	oglemilast
2935 00 90	444731-52-6	pazopanib
2935 00 90	362505-84-8	relacatib

CN code	CAS RN	Name
2935 00 90	243984-11-4	resatorvid
2935 00 90	519055-62-0	tasisulam
2935 00 90	186497-07-4	zibotentan
2936 29 00	104121-92-8	eldecalcitol
2936 29 00	31690-09-2	levomefolic acid
2937 19 00	782500-75-8	albiglutide
2937 19 00	348119-84-6	obinepitide
2937 19 00	295350-45-7	ozarelix
2937 19 00	275371-94-3	taspeglutide
2937 19 00	218949-48-5	tesamorelin
2937 19 00	22006-64-0	tridecactide
2937 22 00	132245-57-9	dexamethasone cipeclate
2937 22 00	397864-44-7	fluticasone furoate
2937 29 00	211254-73-8	lonaprisan
2937 50 00	333963-42-1	cobiprostone
2937 50 00	172740-14-6	posaraprost
2937 90 00	834153-87-6	elagolix
2937 90 00	609799-22-6	tasimelteon
2937 90 00	342577-38-2	velneperit
2939 19 00	73232-52-7	methylnaltrexone bromide
2939 59 00	136199-02-5	rolofylline
2939 99 00	850607-58-8	darotropium bromide
2939 99 00	187852-63-7	delimotecan
2940 00 00	9007-72-1	ferric carboxymaltose
2940 00 00	442201-24-3	remogliflozin etabonate
2940 00 00	408504-26-7	sergliflozin etabonate
2941 90 00	467214-20-6	alvespimycin
2941 90 00	677017-23-1	berubicin
2941 90 00	229016-73-3	ceftaroline fosamil
2941 90 00	318498-76-9	flopristin
2941 90 00	145435-72-9	gamithromycin

CN code	CAS RN	Name
2941 90 00	325965-23-9	linopristin
2941 90 00	857402-23-4	retaspimycin
2941 90 00	305841-29-6	sagopilone
2941 90 00	75747-14-7	tanespimycin
2941 90 00	328898-40-4	tildipirosin
2941 90 00	222400-20-6	tomopenem
2941 90 00	63409-12-1	tylvalosin
3001 90 91	9041-08-1	semuloparin sodium
3002 10 91	792921-10-9	abagovomab
3002 10 91	910649-32-0	anrukinzumab
3002 10 91	648904-28-3	bavituximab
3002 10 91	402710-27-4 (light chain) 402710-25-2 (heavy chain)	canakinumab
3002 10 99	945228-49-9	citatumumab bogatox
3002 10 91	880486-59-9	dacetuzumab
3002 10 91	615258-40-7	denosumab
3002 10 91	762260-74-2	efungumab
3002 10 91	89957-37-9	gantenerumab
3002 10 91	680188-33-4	ibalizumab
3002 10 91	477202-00-9	ipilimumab
3002 10 91	640735-09-7	iratumumab
3002 10 91	845816-02-6	lexatumumab
3002 10 91	903512-50-5	lucatumumab
3002 10 91	899796-83-9	milatumumab
3002 10 91	677010-34-3	motavizumab
3002 10 91	676258-98-3	naptumomab estafenatox
3002 10 91	828933-51-3	nimotuzumab
3002 10 91	949142-50-1	obinutuzumab
3002 10 91	637334-45-3	ocrelizumab
3002 10 91	881191-44-2	otelixizumab

CN code	CAS RN	Name
3002 10 91	372075-37-1	sontuzumab
3002 10 91	705287-60-1	stamulumab
3002 10 91	339086-80-5	tadocizumab
3002 10 91	592557-43-2 (light chain) 592557-41-0 (heavy chain)	tenatumomab
3002 10 91	876387-05-2	teplizumab
3002 10 91	918127-53-4	tigatuzumab
3002 10 91	745013-59-6	tremelimumab
3002 10 91	339986-90-2	tucotuzumab celmoleukin
3002 10 91	728917-18-8	veltuzumab
3002 10 91	896731-82-1	conatumumab
3002 10 91	892553-42-3	etaracizumab
3002 10 91	944548-38-3	foravirumab
3002 10 91	944548-37-2	rafivirumab
3002 10 91	880266-57-9	tanezumab
3002 10 91	815610-63-0	ustekinumab
3002 10 95	862111-32-8	aflibercept
3002 10 95	845264-92-8	atacicept
3002 10 95	909110-25-4	baminercept
3002 10 95	9001-27-8	beroctocog alfa
3002 10 95	879555-13-2	epoetin kappa
3002 10 95	762263-14-9	epoetin theta
3002 10 95	501081-76-1	rilonacept
3002 10 95	267639-76-9	romiplostim
3002 10 95	869858-13-9	thrombin alfa
3002 10 95	897936-89-9	vatreptacog alfa (activated)
3002 10 95	472960-22-8	albinterferon alfa-2b
3002 10 95	869881-54-9	briobacept
3002 10 95	606138-08-3	catridecacog
3002 10 95	716840-32-3	denenicokin

CN code	CAS RN	Name
3002 10 95	931101-84-7	tropasminogen alfa
3002 10 99	934216-54-3	alacizumab pegol
3002 20 00	181477-43-0	disomotide
3002 20 00	181477-91-8	ovemotide
3002 20 00	915019-08-8	tertomotide
3002 20 00	295371-00-5	verpasep caltespen
3002 90 90	473553-86-5	alferminogene tadenovec
3002 90 90	929881-05-0	alipogene tiparvovec
3002 90 90	600735-73-7	contusugene ladenovec
3002 90 90	851199-59-2	linaclotide
3002 90 90	898830-54-1	sitimagene ceradenovec
3002 90 90	721946-42-5	transferrin aldifitox
3507 90 90	9026-00-0	bucelipase alfa
3507 90 90	885051-90-1	pegloticase
3507 90 90	884604-91-5	velagluclerace alfa
3911 90 99	892497-01-7	azoximer bromide

ANNEX II

List of prefixes and suffixes which, in combination with the INNs of Annex 3 to Annex I to Regulation (EEC) No 2658/87, describe the salts, esters or hydrates of INNs; these salts, esters and hydrates are free of duty, on condition that they are classifiable in the same six-digit HS subheading as the corresponding INN

The references to 'International Nonproprietary Names (INN) for pharmaceutical substances, names for radicals and groups, comprehensive list 2004' are replaced by 'International Nonproprietary Names (INN) for pharmaceutical substances, names for radicals, groups and others, comprehensive list 2007'.

The following prefixes or suffixes are added to the list included in Annex 4 to Annex I to Regulation (EEC) No 2658/87:

Preferred prefix or suffix	Synonym	Systematic name when different
alanetil (INNREG)		[(S)-1-ethoxy-1-oxo-propan-2-yl]amino (INNEN)
alaninate (INNREG)		L-alaninate (INNEN)
alapivoxil (INNREG)		L-alanyl, [(2,2-dimethylpropanoyl)oxy]methyl (INNEN)
aldifitox (INNREG)		(4-iminobutane-1,4-diyl)sulfanediyl[(3RS)-2,5-dioxopyrrolidine-1,3-diyl]-1,3-phenylenecarbonyl and forming an N-benzoyl derivative of a primary amine group of diphtheria [550-L-phenylalanine]toxin from <i>Corynebacterium diphtheriae</i> -(26-560)-peptide (INNEN)
besudotox (INNREG)		L-lysyl-L-alanyl-L-seryl-glycylglycine (linker) fusion protein with des-(365-380)-[Asn ³⁶⁴ ,Val ⁴⁰⁷ ,Ser ⁵¹⁵ ,Gln ⁵⁹⁰ ,Gln ⁶⁰⁶ ,Arg ⁶¹³]exotoxin A (<i>Pseudomonas aeruginosa</i>)-(251-613)-peptide (toxin with region IA and first 16 residues of region IB deleted) (INNEN)
ceribate (INNREG)		rac-2,3-dihydroxypropyl carbonate (ester) (INNEN)
cipecilate (INNREG)		cyclohexanecarboxylate (ester), cyclopropanecarboxylate (ester) (INNEN)
dalanated (INNREG)		des-B30-alanine (INNEN)
enacarbíl (INNREG)		{rac-1-[(2-methylpropanoyl)oxy]ethoxy}carbonyl (INNEN)
estafenatox (INNREG)		glycylglycyl-L-proline (linker) fusion protein with enterotoxin type A (<i>Staphylococcus aureus</i>)-(1-33)-peptidyl-L-seryl[Ser ³⁶ ,Ser ³⁷ ,Glu ³⁸ ,Lys ³⁹ ,Ala ⁴¹ ,Thr ⁴⁶ ,Thr ⁷¹ ,Ala ⁷² ,Ser ⁷⁵ ,Glu ⁷⁶ ,Glu ⁷⁸ ,Ser ⁸⁰ ,Ser ⁸¹ ,Thr ²¹⁴ ,Ser ²¹⁷ ,Thr ²¹⁹ ,Ser ²²⁰ ,Ser ²²² ,Ser ²²⁴]enterotoxin type E (<i>Staphylococcus aureus</i>)-(32-230)-peptide (synthetic superantigen SEA/E-120) (INNEN)
etexilate (INNREG)		ethyl, (hexyloxy)carbonyl
fosamil (INNREG)		phosphono (INNEN)
glucuronide (INNREG)		β-D-glucopyranosiduronic acid [oside] (INNEN)
medocaril (INNREG)		[(5-methyl-2-oxo-1,3-dioxol-4-yl)methoxy]carbonyl (INNEN)

Preferred prefix or suffix	Synonym	Systematic name when different
paptox (INN^{RG})		protein PAP (<i>Phytolacca americana</i> antiviral) (INN ^{CN})
placarbil (INN^{RG})		(R)-2-methyl-1-[(2-methylpropanoyl)oxy]propoxy}carbonyl) (INN ^{CN})

The systematic name of the following prefix or suffix is amended as follows:

Preferred prefix or suffix	Synonym	Systematic name when different
aritox (INN^{RG})		ricin A chain (INN ^{CN})

ANNEX III

List of pharmaceutical intermediates, i.e. compounds used for the manufacture of finished pharmaceutical products, to be added to the list of products receiving duty-free treatment included in Annex 6 to Annex I to Regulation (EEC) No 2658/87

CN code	CAS RN	Name
2843 29 00	22199-08-2	[4-amino-N-(pyrimidin-2(1H)-ylidene-κN1)benzenesulfonamidato-κO]silver
2905 39 95	281214-27-5	(2R,3R)-2,3-dimethylbutane-1,4-diyl bis(4-methylbenzenesulfonate)
2905 59 98	441002-17-1	4-chlorobutyl 2-nitrobenzenesulfonate
2909 30 90	92878-95-0	2-(3-chloropropoxy)-1-methoxy-4-nitrobenzene
2909 30	503070-57-3	2-({2-[(6-bromohexyl)oxy]ethoxy)methyl}-1,3-dichlorobenzene
2909 30	461432-23-5	4-(5-bromo-2-chlorobenzyl)phenyl ethyl ether
2909 49 80	185954-75-0	(3R)-3-methoxydecan-1-ol
2909 49 80	85309-91-7	2-[(2,6-dichlorobenzyl)oxy]ethanol
2909 49 80	160969-03-9	2-[2-(2,2,2-trifluoroethoxy)phenoxy]ethyl methanesulfonate
2909 50 00	167145-13-3	2-[2-(3-methoxyphenyl)ethyl]phenol
2910 20 00	15448-47-2	(2R)-2-methyloxirane
2910 90 00	62600-71-9	(2R)-2-(3-chlorophenyl)oxirane
2910 90 00	702687-42-1	(2R)-2-[(5-bromo-2,3-difluorophenoxy)methyl]oxirane
2910 90 00	683276-64-4	[(2R)-2-methyloxiran-2-yl]methyl 4-nitrobenzenesulfonate
2913 00 00	90035-34-0	4'-(trifluoromethyl)biphenyl-4-carbaldehyde
2914 40 90	17752-16-8	(3β)-3-hydroxycholest-5-en-24-one
2914 50 00	974-23-2	(3β,16α)-3-hydroxy-16,17-epoxypregn-5-en-20-one
2914 70 00	13054-81-4	4-chloro-heptane-3,5-dione
2914 70 00	10226-30-9	6-chlorohexan-2-one
2915 60 90	53064-79-2	iodomethyl pivalate
2915 90 00	22328-90-1	(3R)-3-methylhexanoic acid
2915 90 00	1069-66-5	sodium 2-propylpentanoate
2916 20 00	211515-46-7	1-(2-ethylbutyl)cyclohexanecarbonyl chloride
2916 20 00	381209-09-2	1-(2-ethylbutyl)cyclohexanecarboxylic acid
2916 20 00	7077-05-6	trans-4-(propan-2-yl)cyclohexanecarboxylic acid

CN code	CAS RN	Name
2916 39 00	21900-39-0	5-fluoro-2-methylbenzoyl chloride
2916 39 00	17625-03-5	sodium hydrogen 3-sulfonatobenzoate
2917 19 90	76-72-2	diethyl ethyl(pentan-2-yl)propanedioate
2918 29 00	376592-58-4	5'-chloro-2'-hydroxy-3'-nitrobiphenyl-3-carboxylic acid
2918 99 90	709031-28-7	(3-hydroxytricyclo[3.3.1.1(3,7)]dec-1-yl)(oxo)acetic acid
2918 99 90	35480-52-5	2,5-bis(2,2,2-trifluoroethoxy)benzoic acid
2918 99 90	4651-67-6	(3 α ,5 β)-3-hydroxy-7-oxocholan-24-oic acid
2918 99 90	52179-28-9	ethyl 2-[4-(2,2-dichlorocyclopropyl)phenoxy]-2-methylpropanoate
2918 99 90	530141-60-7	methyl 3-(5-[[4-(cyclopentyloxy)-2-hydroxyphenyl]carbonyl]-2-hydroxyphenyl)propanoate
2920 90 10	91526-18-0	4-(hydroxymethyl)-5-methyl-1,3-dioxol-2-one
2921 49 00	334477-60-0	(1R)-1-[3,5-bis(trifluoromethyl)phenyl]-N-methylethanamine
2921 49 00	376608-71-8	(1R,2S)-2-(3,4-difluorophenyl)cyclopropanaminium (2R)-hydroxy(phenyl)ethanoate
2921 49 00	1034457-07-2	2-(2,3-dihydro-1H-inden-2-yl)propan-2-amine hydrochloride
2921 49 00	945717-05-5	2-(4-chloro-3-ethylphenyl)ethanamine hydrochloride
2921 49 00	89-97-4	2-chlorobenzylamine
2921 49 00	945717-43-1	N-(4-tert-butylbenzyl)-2-(4-chloro-3-ethylphenyl)ethanamine
2921 51 90	150812-21-8	N4-[(4-fluorophenyl)methyl]-2-nitro-1,4-benzenediamine
2922 19 85	1035455-90-3	(2R)-1-(5-bromo-2,3-difluorophenoxy)-3-[[1-(2,3-dihydro-1H-inden-2-yl)-2-methylpropan-2-yl]amino]propan-2-ol hydrochloride
2922 19 85	0-00-0	[2-(chloromethyl)-4-(dibenzylamino)phenyl]methanol hydrochloride
2922 19 85	133-51-7	antimonic acid – 1-deoxy-1-(methylamino)-D-glucitol (1:1)
2922 19 85	1035455-87-8	ethyl (2E)-3-(3-[[[(2R)-3-[[1-(2,3-dihydro-1H-inden-2-yl)-2-methylpropan-2-yl]amino]-2-hydroxypropyl]oxy]-4,5-difluorophenyl]prop-2-enoate hydrochloride
2922 19 85	702686-97-3	ethyl 3-(3-[[[(2R)-3-[[1-(2,3-dihydro-1H-inden-2-yl)-2-methylpropan-2-yl]amino]-2-hydroxypropyl]oxy]-4,5-difluorophenyl]propanoate hydrochloride

CN code	CAS RN	Name
2922 29 00	20059-73-8	2-[4-(aminomethyl)phenoxy]-N,N-dimethylethanamine
2922 49 85	848133-35-7	(2E)-4-(dimethylamino)but-2-enoic acid hydrochloride
2922 49 85	610300-07-7	(3S,5R)-3-amino-5-methyloctanoic acid
2922 49 85	610300-00-0	(3S,5R)-3-amino-5-methyloctanoic acid hydrochloride
2922 49 85	143785-86-8	4-(1-aminocyclopropyl)-2,3,5-trifluorobenzoic acid
2922 49 85	848949-85-9	4-fluoro-L-leucine – ethyl hydrogen sulfate (1:1)
2922 49 85	39068-93-4	methyl 2-(dimethylamino)-2-phenylbutanoate
2922 49 85	168619-25-8	methyl 3'-aminobiphenyl-3-carboxylate
2922 49 85	82834-12-6	N-[(2S)-1-ethoxy-1-oxopentan-2-yl]-L-alanine
2922 49 85	94133-84-3	sodium 2-amino-2-phenylbutanoate
2922 50 00	503070-58-4	triphenylacetic acid – 4-[(1R)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl]-2-(hydroxymethyl)phenol (1:1)
2924 19 00	62009-47-6	2-aminomalonamide
2924 19 00	7355-58-0	N-(2-chloroethyl)acetamide
2924 29 98	361442-00-4	{2-[(tert-butoxycarbonyl)amino]-3-hydroxy-tricyclo[3.3.1.1(3,7)]dec-1-yl}acetic acid
2924 29 98	266993-72-0	2,3-diaminobenzamide dihydrochloride
2924 29 98	168080-49-7	2-chloro-4-[(5-fluoro-2-methylphenyl)carbonyl]amino}benzoic acid
2924 29 98	317374-08-6	2-methyl-4-[(2-methylphenyl)carbonyl]amino}benzoic acid
2924 29 98	143785-84-6	4-(1-carbamoylcyclopropyl)-2,3,5-trifluorobenzoic acid
2924 29 98	143785-87-9	4-[1-(acetylaminocyclopropyl)-2,3,5-trifluorobenzoic acid
2924 29 98	108166-22-9	4-[(2-methylphenyl)carbonyl]amino}benzoic acid
2924 29 98	150812-23-0	ethyl {4-[(4-fluorobenzyl)amino]-2-nitrophenyl} carbamate
2924 29 98	22316-45-6	ethyl 3-[(5-chloro-2-nitrophenyl)(phenyl)amino]-3-oxopropanoate
2924 29 98	316173-29-2	methyl (1S,2S,3S,4R)-3-[(1S)-1-amino-2-ethylbutyl]-4-[(tert-butoxycarbonyl)amino]-2-hydroxycyclopentanecarboxylate

CN code	CAS RN	Name
2924 29 98	1142-20-7	N-benzyloxycarbonyl-L-alanine
2924 29 98	84996-93-0	N-cyclohexyl-5-hydroxypentanamide
2924 29 98	579494-66-9	propyl {4-[2-(diethylamino)-2-oxoethoxy]-3-ethoxyphenyl}acetate
2925 19 95	265136-65-0	ethyl 3-amino-4-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethoxy]but-2-enoate
2926 90 95	855425-38-6	1-(2-ethylbutyl)cyclohexanecarbonitrile
2926 90 95	846023-24-3	2-cyano-N-(2,4-dichloro-5-methoxyphenyl)acetamide
2926 90 95	591769-05-0	3-cyclopentylprop-2-enenitrile
2926 90 95	20099-89-2	4-(bromoacetyl)benzonitrile
2926 90 95	474554-45-5	4,5-diethoxy-3-fluorobenzene-1,2-dicarbonitrile
2926 90 95	79370-78-8	5-hydroxybenzene-1,3-dicarbonitrile
2926 90 95	139481-28-0	methyl 2-([(2'-cyanobiphenyl-4-yl)methyl]amino)-3-nitrobenzoate
2928 00 90	860035-10-5	1-([(2,5-dioxopyrrolidin-1-yl)oxy]carbonyl)oxyethyl 2-methylpropanoate
2928 00 90	910656-45-0	2-hydroxy-2-(trifluoromethyl)butanehydrazide
2928 00 90	95759-10-7	4-chloro-2-[(2-methoxy-2-oxoethoxy)imino]-3-oxobutanoic acid
2928 00 90	473927-63-8	ethyl (2Z)-chloro[2-(4-methoxyphenyl)hydrazinylidene]ethanoate
2928 00 90	158671-29-5	N,2-dihydroxy-4-methylbenzamide
2928 00 90	84080-68-2	tert-butyl (2Z)-2-[(2-methoxy-2-oxoethoxy)imino]-3-oxobutanoate
2928 00 90	268544-50-9	tert-butyl-2-[(2-methoxy-2-oxoethoxy)imino]-3-oxobutanoate
2930 90 99	13459-62-6	{2-[(4-chlorophenyl)sulfanyl]phenyl}acetic acid
2930 90 99	211513-21-2	1-(2-ethylbutyl)-N-(2-sulfanylphenyl)cyclohexanecarboxamide
2930 90 99	860035-07-0	1-([(methylsulfanyl)carbonyl]oxy)ethyl 2-methylpropanoate
2930 90 99	893407-18-6	2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]ethanone
2930 90 99	60759-00-4	3,4-diethoxybenzenecarbothioamide

CN code	CAS RN	Name
2930 90 99	21048-05-5	N-methylbenzenecarbothiohydrazide
2931 00 99	13682-94-5	(2-bromoethenyl)(trimethyl)silane
2931 00 99	914922-89-7	(2R,4R)-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-N-methoxy-N,2-dimethyl-7-oxoheptanamide
2931 00 99	914922-88-6	(2R,4R)-4-[[tert-butyl(dimethyl)silyl]oxy]-N-methoxy-N,2-dimethyloct-7-enamide
2931 00 99	871355-80-5	(4R)-2-bromo-7-[[tert-butyl(diphenyl)silyl]oxy]hept-1-en-4-yl 4-methylbenzenesulfonate
2931 00 99	89694-48-4	(5-chloro-2-methoxyphenyl)boronic acid
2931 00 99	701278-08-2	[(1R,5S)-5-[dimethyl(phenyl)silyl]-2-[[[(2-methoxypropan-2-yl)oxy]methyl]cyclopent-2-en-1-yl]methanol
2931 00 99	701278-09-3	{(4S,5R)-5-[(benzyloxy)methyl]-4-[dimethyl(phenyl)silyl]cyclopent-1-en-1-yl}methanol
2931 00 99	796967-18-5	1-(2-fluoro-5-methylphenyl)-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]urea
2931 00 99	172732-52-4	2-(1,3,2-dioxaborinan-2-yl)benzonitrile
2931 00 99	185411-12-5	methyl 3-(trimethylsilyl)pent-4-enoate
2932 19 00	253128-10-8	(1S)-1,5:7,10-dianhydro-1,2,13-bis-O-[tert-butyl(dimethyl)silyl]-2,3,4,6,8,11-hexadeoxy-1-{2-[(2S,5S)-5-(3-hydroxypropyl)-3-methylidenetetrahydrofuran-2-yl]ethyl}-3-methyl-9-O-methyl-4-methylidene-8-[(phenylsulfonyl)methyl]-D-arabino-D-altro-tridecitol
2932 19 00	441045-17-6	(1S,3S,6S,9S,12S,14R,16R,18S,20R,21R,22S,26R,29S,31R,32S,33R,35R,36S)-20-[(2S)-3-amino-2-hydroxypropyl]-21-methoxy-14-methyl-8,15-bis(methylene)-2,19,30,34,37,39,40,41-octaoxononacyclo[24.9.2.13,32.13,33.16,9.112,16.018,22.029,36.031,35]hentetracontan-24-one methanesulfonate
2932 29 85	916069-80-2	(4S)-4-(fluoromethyl)dihydrofuran-2(3H)-one
2932 29 85	63106-93-4	1-phenyl-3-oxabicyclo[3.1.0]hexan-2-one
2932 29 85	7734-80-7	2-oxo-2H-chromene-6-carboxylic acid
2932 29 85	0-00-0	4-(4-fluorophenyl)-7-(isothiocyanatomethyl)-2H-chromen-2-one
2932 29 85	947408-91-5	6-[(2,4-dihydroxyphenyl)carbonyl]-2H-chromen-2-one
2932 29 85	947408-90-4	6-[(2,4-dimethoxyphenyl)carbonyl]-2H-chromen-2-one
2932 99 00	452342-08-4	(1R)-2-(benzylamino)-1-(2,2-dimethyl-4H-1,3-benzodioxin-6-yl)ethanol

CN code	CAS RN	Name
2932 99 00	99541-23-8	(1R,2S,3R,4R,5R)-4-azido-2-[[[(4aR,6S,7R,8S,8aR)-7,8-bis(benzyloxy)-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-6-yl]oxy]-6,8-dioxabicyclo[3.2.1]oct-3-yl acetate
2932 99 00	461432-25-7	(1S)-2,3,4,6-tetra-O-acetyl-1,5-anhydro-1-[4-chloro-3-(4-ethoxybenzyl)phenyl]-D-glucitol
2932 99 00	196597-79-2	(2E)-1,2,6,7-tetrahydro-8H-indeno[5,4-b]furan-8-ylideneethanenitrile
2932 99 00	3308-94-9	2-(3-chloropropyl)-2-(4-fluorophenyl)-1,3-dioxolane
2932 99 00	274693-53-7	[(3aS,4R,6S,6aR)-6-hydroxy-2,2-dimethyltetrahydro-3aH-cyclopenta[d][1,3]dioxol-4-yl]carbamate
2932 99 00	185954-98-7	[6(2Z,3R)]-3-O-decyl-2-deoxy-6-O-[2-deoxy-3-O-(3-methoxydecyl)-6-methyl-2-[(1-oxo-11-octadecenyl)amino]-4-O-phosphono-β-D-glucopyranosyl]-2-[(1,3-dioxotetradecyl)amino]-α-D-glucopyranose 1-(dihydrogen phosphate) tetrasodium salt
2932 99 00	136172-58-2	1,6-di-O-acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-D-glucopyranose
2932 99 00	196597-80-5	2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl]ethanamine hydrochloride
2932 99 00	666860-59-9	2-amino-2-oxoethyl{3-[trans-5-(6-methoxynaphthalen-1-yl)-1,3-dioxan-2-yl]propyl}carbamate
2932 99 00	117661-72-0	5-(chloromethyl)-6-methyl-1,3-benzodioxole
2932 99 00	959624-24-9	6-(hydroxymethyl)-4-phenyl-3,4-dihydro-2H-chromen-2-ol
2932 99 00	960404-59-5	but-2-yne-1,4-diol – methyl 1-C-[4-chloro-3-(4-ethoxybenzyl)phenyl]-α-D-glucopyranoside (1:1)
2932 99 00	15826-37-6	disodium 5,5'-[(2-hydroxypropane-1,3-diyl)bis(oxy)]bis(4-oxo-4H-chromene-2-carboxylate)
2932 99 00	204254-84-2	ethyl (3aR,7R,7aR)-2,2-dimethyl-7-[(methylsulfonyl)oxy]-3a,6,7,7a-tetrahydro-1,3-benzodioxole-5-carboxylate
2932 99 00	99541-26-1	methyl (2S,3S,4S,5S,6S)-6-[[[(1S,2S,3S,4R,5R)-3-(acetyloxy)-4-azido-6,8-dioxabicyclo[3.2.1]oct-2-yl]methyl]-4,5-bis(benzyloxy)-3-hydroxytetrahydro-2H-pyran-2-carboxylate
2932 99 00	114869-97-5	methyl 6-O-acetyl-4-O-(2-O-acetyl-3-O-benzyl-6-methyl-α-L-idopyranuronosyl)-3-O-benzyl-2-[[[(benzyloxy)carbonyl]amino]-2-deoxy-α-D-glucopyranoside
2933 19 90	1035677-60-1	(4S)-3-(4-chlorophenyl)-N-methyl-4-phenyl-4,5-dihydro-1H-pyrazole-1-carboximidamide 2,3-dihydroxybutanedioate

CN code	CAS RN	Name
2933 19 90	18048-64-1	2-(3,4-dimethylphenyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one
2933 19 90	1035675-24-1	3-(4-chlorophenyl)-N-methyl-4-phenyl-4,5-dihydro-1H-pyrazole-1-carboximidamide
2933 19 90	1028026-83-6	5-methyl-1-(propan-2-yl)-4-[4-(propan-2-yloxy)benzyl]-1,2-dihydro-3H-pyrazol-3-one
2933 19 90	473921-12-9	5-[[3,5-diethyl-1-(2-hydroxyethyl)-1H-pyrazol-4-yl]oxy]benzene-1,3-dicarbonitrile
2933 29 90	65902-59-2	2-bromo-4-nitro-1H-imidazole
2933 29 90	57531-37-0	2-chloro-4-nitro-1H-imidazole
2933 29 90	1000164-35-1	3-(1,1-dimethylethyl)-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-1-(triphenylmethyl)-L-histidyl-2-methylalanyl-L- α -glutamylglycine
2933 29 90	152074-97-0	L- α -aspartyl-L- α -glutamyl-L-asparaginy-L-prolyl-L-valyl-L-valyl-L-histidyl-L-phenylalanyl-L-phenylalanyl-L-lysyl-L-asparaginy-L-isoleucyl-L-valyl-L-threonyl-L-prolyl-L-arginyl-L-threonine
2933 29 90	781666-30-6	L- α -aspartyl-L- α -glutamyl-L-asparaginy-L-prolyl-L-valyl-L-valyl-L-histidyl-L-phenylalanyl-L-phenylalanyl-L-lysyl-L-asparaginy-L-isoleucyl-L-valyl-L-threonyl-L-prolyl-L-arginyl-L-threonine tetraacetate
2933 29 90	451470-33-0	methyl 3'-(2-methyl-4,5-dihydro-1H-imidazol-1-yl)biphenyl-3-carboxylate
2933 39 99	925978-49-0	(+)-5-[6-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl]-1-azabicyclo[3.2.1]octane
2933 39 99	876170-44-4	(1S,5S)-3-(5,6-dichloropyridin-3-yl)-3,6-diazabicyclo[3.2.0]heptane benzenesulfonate
2933 39 99	741705-70-4	(2R)-phenyl[(2R)-piperidin-2-yl]ethanoic acid hydrochloride
2933 39 99	414910-13-7	(2S)-hydroxy(phenyl)ethanoic acid – (2R)-2-(4-fluoro-2-methylphenyl)piperidin-4-one (1:1)
2933 39 99	0-00-0	(3aR,6aR)-1-(pyridin-3-yl)octahydropyrrolo[3,4-b]pyrrole 4-methylbenzenesulfonate
2933 39 99	370882-57-8	(3aR,6aR)-1-(pyridin-3-yl)octahydropyrrolo[3,4-b]pyrrole dihydrochloride
2933 39 99	334618-23-4	(3R)-piperidin-3-amine dihydrochloride
2933 39 99	1062580-52-2	(3R,4R)-1-benzyl-N,4-dimethylpiperidin-3-amine dihydrochloride

CN code	CAS RN	Name
2933 39 99	27262-47-1	(S)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide
2933 39 99	105812-81-5	[(3S,4R)-4-(4-fluorophenyl)-1-methylpiperidin-3-yl]methanol
2933 39 99	876068-51-8	[(3S,4S)-4-amino-1-(5,6-dichloropyridin-3-yl)pyrrolidin-3-yl]methanol
2933 39 99	871022-14-9	1-({4-[[[2-oxo-3-(propan-2-yl)-2,3-dihydro-1H-benzimidazol-1-yl]carbonyl]amino)methyl]piperidin-1-yl)methyl)cyclobutanecarboxylic acid
2933 39 99	5421-92-1	1-(pyridin-4-yl)pyridinium chloride hydrochloride
2933 39 99	272776-12-2	1,1'-binaphthalene-2,2'-diol -5-methoxy-2-[(S)-[4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfinyl]-1H-benzimidazole (1:1)
2933 39 99	871022-19-4	1-[(4-[[[tert-butoxycarbonyl]amino)methyl]piperidin-1-yl)methyl]cyclobutanecarboxylic acid
2933 39 99	3613-73-8	2,8-dimethyl-5-[2-(6-methylpyridin-3-yl)ethyl]-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole
2933 39 99	179687-79-7	2-[(2-chloro-4-nitrophenoxy)methyl]pyridine
2933 39 99	122321-04-4	2-[methyl(pyridin-2-yl)amino]ethanol
2933 39 99	945405-37-8	2-methyl-3-[(2S)-pyrrolidin-2-ylmethoxy]pyridine 2,3-dihydroxybutanedioate
2933 39 99	936637-40-0	3,3'-piperidine-1,4-diyl dipropan-1-ol 4-methylbenzenesulfonate
2933 39 99	88150-62-3	3-ethyl-5-methyl-4-(2-chlorophenyl)-2-[[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethoxy)methyl]-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate
2933 39 99	84100-54-9	4-(ethylamino)piperidine-4-carboxamide
2933 39 99	873546-30-6	4,4'-[piperidine-1,4-diylbis(propane-3,1-diylloxy)]bis[N'-hydroxybenzenecarboximidamide]
2933 39 99	873546-74-8	4,4'-[piperidine-1,4-diylbis(propane-3,1-diylloxy)]bis[N'-(acetyloxy)benzenecarboximidamide]
2933 39 99	873546-38-4	4,4'-[piperidine-1,4-diylbis(propane-3,1-diylloxy)]dibenzenecarboximidamide trihydrochloride pentahydrate
2933 39 99	873546-80-6	4,4'-[piperidine-1,4-diylbis(propane-3,1-diylloxy)]dibenzonitrile
2933 39 99	78750-61-5	4-[(3-nitropyridin-2-yl)amino]phenol
2933 39 99	866109-93-5	4-{4-[4-(trifluoromethoxy)phenoxy]piperidin-1-yl}phenol 4-methylbenzenesulfonate

CN code	CAS RN	Name
2933 39 99	927889-51-8	4-bromo-2,6-diethylpyridine 4-methylbenzenesulfonate
2933 39 99	691882-47-0	4-hydroxybenzoic acid – (2S,4E)-N-methyl-5-[5-(propan-2-yloxy)pyridin-3-yl]pent-4-en-2-amine (1:1)
2933 39 99	876068-46-1	5,6-dichloro-N-(2,2-dimethoxyethyl)pyridin-3-amine
2933 39 99	1072-98-6	5-chloropyridin-2-amine
2933 39 99	298692-34-9	6-(chloroacetyl)pyridine-2-carboxylic acid
2933 39 99	550349-58-1	7-chloro-3-(6-methoxypyridin-3-yl)-N,N,5-trimethyl-4-oxo-4,5-dihydro-3H-pyridazino[4,5-b]indole-1-carboxamide
2933 39 99	414909-98-1	benzyl 2-(4-fluoro-2-methylphenyl)-4-oxo-3,4-dihydropyridine-1(2H)-carboxylate
2933 39 99	56880-11-6	ethyl [(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl) acetate
2933 39 99	548797-97-3	N-(2-[[[(2S)-3-[[1-(4-chlorobenzyl)piperidin-4-yl]amino]-2-hydroxy-2-methylpropyl]oxy]-4-hydroxyphenyl]acetamide
2933 39 99	0-00-0	N-[(S)-1-azabicyclo[2.2.2]oct-2-yl(phenyl)methyl]-2,6-dichloro-3-(trifluoromethyl)benzamide hydrochloride
2933 39 99	329003-65-8	sodium hydrogen [1-hydroxy-1-phosphono-2-(pyridin-3-yl)ethyl]phosphonate hemipentahydrate
2933 49 10	417716-92-8	4-{3-chloro-4-[(cyclopropylcarbamoyl)amino]phenoxy}-7-methoxyquinoline-6-carboxamide methanesulfonate
2933 49 90	503291-53-0	2-ethylbutyl (3S,4aS,6S,8aR)-6-[3-chloro-2-(1H-tetrazol-5-yl)phenoxy]decahydro-3-isoquinolinecarboxylate 4-methylbenzenesulfonate
2933 49 90	103733-32-0	benzyl (3S)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylate hydrochloride
2933 49 90	503293-98-9	(3S,4aS,6S,8aR)-6-hydroxy-2-(methoxycarbonyl)decahydroisoquinoline-3-carboxylic acid
2933 49 90	503290-66-2	(3S,4aS,6S,8aR)-6-[3-chloro-2-(2H-tetrazol-5-yl)phenoxy]decahydro-3-isoquinolinecarboxylic acid hydrochloride
2933 49 90	134388-95-7	(3S,4aS,8aR)-2-(methoxycarbonyl)-6-oxodecahydroisoquinoline-3-carboxylic acid – (1R)-1-phenylethanamine (1:1)
2933 49 90	868210-14-4	4-(4-[[[(2S,4R)-4-[acetyl(4-chlorophenyl)amino]-2-methyl-3,4-dihydroquinolin-1(2H)-yl]carbonyl]phenoxy]-2,2-dimethylbutanoic acid

CN code	CAS RN	Name
2933 49 90	00-00-0	methyl 2-[(3R)-3-{3-[(E)-2-(7-chloroquinolin-2-yl)ethenyl]phenyl}-3-({[1-(hydroxymethyl)cyclopropyl]methyl}sulfanyl)propyl]benzoate hydrochloride
2933 49 90	848133-76-6	N-(4-chloro-3-cyano-7-ethoxyquinolin-6-yl)acetamide
2933 59 95	869490-23-3	(3,3-difluoropyrrolidin-1-yl){(2S,4S)-4-[4-(pyrimidin-2-yl)piperazin-1-yl]pyrrolidin-2-yl}methanone
2933 59 95	941685-40-1	(3R)-3-cyclopentyl-3-[4-(7-{[2-(trimethylsilyl)ethoxy]methyl}-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile
2933 59 95	941678-49-5	(3R)-3-cyclopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile
2933 59 95	941685-41-2	(3S)-3-cyclopentyl-3-[4-(7-{[2-(trimethylsilyl)ethoxy]methyl}-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile
2933 59 95	957187-34-7	[(8R)-8-(3,5-difluorophenyl)-10-oxo-6,9-diaz-aspiro[4.5]dec-9-yl]acetic acid
2933 59 95	356058-42-9	{2-[(4-fluorobenzyl)sulfanyl]-4-oxo-4,5,6,7-tetrahydro-1H-cyclopenta[d]pyrimidin-1-yl}acetic acid
2933 59 95	0-00-0	2,3-dihydroxy-2,3-bis(phenylcarbonyl)butanedioic acid – ethyl [(8R)-8-(3,5-difluorophenyl)-10-oxo-6,9-diaz-aspiro[4.5]dec-9-yl]acetate (1:1)
2933 59 95	90213-66-4	2,4-dichloro-7H-pyrrolo[2,3-d]pyrimidine
2933 59 95	3934-20-1	2,4-dichloropyrimidine
2933 59 95	451487-18-6	2-[(4-fluorobenzyl)sulfanyl]-1,5,6,7-tetrahydro-4H-cyclopenta[d]pyrimidin-4-one
2933 59 95	865758-96-9	2-[(6-chloro-3-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl]benzonitrile
2933 59 95	934815-71-1	2-[3-(6-{[2-(2,4-dichlorophenyl)ethyl]amino}-2-methoxy-pyrimidin-4-yl)phenyl]-2-methylpropanoic acid phosphate
2933 59 95	722543-31-9	2-{ethyl[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]quinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate
2933 59 95	1032066-96-8	2-amino-9-[(1S,3R,4S)-3-[(benzyloxy)methyl]-4-[dimethyl(phenyl)silyl]-2-methylidenecyclopentyl]-1,9-dihydro-6H-purin-6-one – methanesulfonate (2:1)
2933 59 95	540737-29-9	3-[(3R,4R)-4-methyl-3-[methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]piperidin-1-yl]-3-oxopropanenitrile 2-hydroxypropane-1,2,3-tricarboxylate

CN code	CAS RN	Name
2933 59 95	1137917-12-4	3-[[6-(ethylsulfonyl)pyridin-3-yl]oxy]-5-[[{(2S)-1-hydroxypropan-2-yl]oxy}benzoic acid – 1,4-diazabicyclo[2.2.2]octane (2:1)
2933 59 95	941685-39-8	3-cyclopentyl-3-[4-(7-[[2-(trimethylsilyl)ethoxy]methyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile
2933 59 95	941685-27-4	4-(1H-pyrazol-4-yl)-7-[[2-(trimethylsilyl)ethoxy]methyl]-7H-pyrrolo[2,3-d]pyrimidine
2933 59 95	1780-26-3	4,6-dichloro-2-methylpyrimidine
2933 59 95	145783-14-8	4,6-dichloro-5-nitro-2-(propylsulfanyl)pyrimidine
2933 59 95	3680-69-1	4-chloro-7H-pyrrolo[2,3-d]pyrimidine
2933 59 95	61379-64-4	4-cyclopentylpiperazin-1-amine
2933 59 95	55112-42-0	4-methylpiperazine-1-carbonyl chloride hydrochloride
2933 59 95	0-00-0	5-(benzylamino)-2-(3-methoxyphenyl)-7-(4-methylpiperazin-1-yl)[1,2,4]triazolo[1,5-a]quinoline-4-carbonitrile – (2E)-but-2-enedioate (2:1) hydrate
2933 59 95	55293-96-4	5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidine-2-carbaldehyde
2933 59 95	179688-01-8	7-(benzyloxy)-6-methoxyquinazolin-4(3H)-one
2933 59 95	444731-74-2	N-(2-chloropyrimidin-4-yl)-2,3-dimethyl-2H-indazol-6-amine
2933 59 95	0-00-0	N-(5-fluoro-3-methyl-1H-indol-1-yl)-4-methyl-2-(pyridin-2-yl)pyrimidine-5-carboxamide
2933 79 00	586414-48-4	(-)-3-[3-bromo-4-[(2,4-difluorobenzyl)oxy]-6-methyl-2-oxopyridin-1(2H)-yl]-N,4-dimethylbenzamide
2933 79 00	425663-71-4	(1S)-1-amino-3-methyl-1,3,4,5-tetrahydro-2H-3-benzazepin-2-one hydrochloride
2933 79 00	813452-14-1	(4S)-1-[(2S,3S,11bS)-2-amino-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-3-yl]-4-(fluoromethyl)pyrrolidin-2-one dihydrochloride
2933 79 00	5162-90-3	3-(2-oxo-1,2-dihydroquinolin-4-yl)alanine
2933 79 00	536760-29-9	3-chloro-1-(4-nitrophenyl)-5,6-dihydropyridin-2(1H)-one
2933 79 00	4876-10-2	4-(bromomethyl)quinolin-2(1H)-one
2933 79 00	5057-12-5	4,6,7,8-tetrahydroquinoline-2,5(1H,3H)-dione
2933 79 00	54197-66-9	6-hydroxy-3,4-dihydroquinolin-2(1H)-one

CN code	CAS RN	Name
2933 79 00	22246-18-0	7-hydroxy-3,4-dihydroquinolin-2(1H)-one
2933 79 00	536759-91-8	ethyl 1-(4-methoxyphenyl)-6-(4-nitrophenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxylate
2933 79 00	503614-91-3	ethyl 1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxopiperidin-1-yl)phenyl]-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxylate
2933 79 00	586379-61-5	methyl 3-(4-hydroxy-6-methyl-2-oxopyridin-1(2H)-yl)-4-methylbenzoate
2933 99 80	709031-45-8	(1S,3S,5S)-2-azabicyclo[3.1.0]hexane-3-carboxamide methanesulfonate
2933 99 80	649735-46-6	(2R)-1-({4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yl)oxy}propan-2-ol
2933 99 80	51077-14-6	(2S)-1-(tert-butoxycarbonyl)azetidine-2-carboxylic acid
2933 99 80	631916-97-7	(2S)-N-{4-[(Z)-amino(methoxyimino)methyl]benzyl}-1-((2R)-2-[3-chloro-5-(difluoromethoxy)phenyl]-2-hydroxyethanoyl)azetidine-2-carboxamide – benzenesulphonic acid (1:1)
2933 99 80	80875-98-5	(2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid
2933 99 80	948846-40-0	(2S,3S)-2,3-bis[(phenylcarbonyl)oxy]butanedioic acid – ethyl (3aR,6aR)-hexahydropyrrolo[3,4-b]pyrrole-5(1H)-carboxylate (1:1)
2933 99 80	1000164-36-2	(5S,8S,11S,14S,17S,20S,23S,26S,29S,32S,35S,38S)-5-(3-amino-3-oxopropyl)-20-benzyl-23-[(2S)-butan-2-yl]-14,38-bis{4-[(tert-butoxycarbonyl)amino]butyl}-29-[[1-(tert-butoxycarbonyl)-1H-indol-3-yl]methyl]-17-(3-tert-butoxy-3-oxopropyl)-1-(1H-fluoren-9-yl)-8,11,26,41,41-pentamethyl-32-(2-methylpropyl)-3,6,9,12,15,18,21,24,27,30,33,36,39-tridecaoxo-35-(propan-2-yl)-2-oxa-4,7,10,13,16,19,22,25,28,31,34,37,40-tridecaazadotetran-42-oic acid
2933 99 80	22162-51-2	1-(2-nitrobenzyl)-1H-pyrrole-2-carbaldehyde
2933 99 80	35681-40-4	1-(propan-2-yl)-1,3-dihydro-2H-benzimidazol-2-one
2933 99 80	166170-15-6	1-(tert-butoxycarbonyl)-2-methyl-D-proline
2933 99 80	796967-16-3	1-[4-(3-amino-1H-indazol-4-yl)phenyl]-3-(2-fluoro-5-methylphenyl)urea
2933 99 80	0-00-0	1-[4-(3-amino-1H-indazol-4-yl)phenyl]-3-(2-fluoro-5-methylphenyl)urea hydrochloride
2933 99 80	444731-72-0	2,3-dimethyl-2H-indazol-6-amine
2933 99 80	19686-05-6	2,8-dimethyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole

CN code	CAS RN	Name
2933 99 80	912444-00-9	2-[(2R)-2-methylpyrrolidin-2-yl]-1H-benzimidazole-4-carboxamide
2933 99 80	912445-36-4	2-[(2S)-2-methylpyrrolidin-2-yl]-1H-benzimidazole-4-carboxamide dihydrochloride
2933 99 80	163457-23-6	3,3-difluoropyrrolidine hydrochloride
2933 99 80	239463-85-5	3-{5-[(2R)-2-aminopropyl]-7-cyano-2,3-dihydro-1H-indol-1-yl}propyl benzoate (2R,3R)-2,3-dihydroxybutanedioate
2933 99 80	55321-99-8	3-oxo-3,4-dihydropyrazine-2-carboxamide
2933 99 80	952490-01-6	4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yl 2,2-dimethylpropanoate
2933 99 80	942436-93-3	4-amino-8-(2,5-dimethoxyphenyl)-N-propylcinnoline-3-carboxamide
2933 99 80	942437-37-8	4-amino-8-(2-fluoro-6-methoxyphenyl)-N-propylcinnoline-3-carboxamide
2933 99 80	288385-88-6	4-fluoro-2-methyl-1H-indol-5-ol
2933 99 80	503293-47-8	5-(2-chloro-6-fluorophenyl)-2H-tetrazole
2933 99 80	73963-42-5	5-(4-chlorobutyl)-1-cyclohexyl-1H-tetrazole
2933 99 80	606143-52-6	5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-N-(2-hydroxyethoxy)-1-methyl-1H-benzimidazole-6-carboxamide
2933 99 80	0-00-0	5-fluoro-1-(3-fluorobenzyl)-N-(1H-indol-5-yl)-1H-indole-2-carboxamide
2933 99 80	872206-47-8	5-methyl-4-oxo-1,4-dihydropyrrolo[2,1-f][1,2,4]triazin-6-yl 2,2-dimethylpropanoate
2933 99 80	259793-88-9	6-bromo-3-oxo-3,4-dihydropyrazine-2-carboxamide
2933 99 80	1137606-74-6	6-fluoro-3-oxo-3,4-dihydropyrazine-2-carbonitrile – N-cyclohexylcyclohexanamine (1:1)
2933 99 80	261953-36-0	6-iodo-1H-indazole
2933 99 80	80076-47-7	8,9-difluoro-5-methyl-1-oxo-6,7-dihydro-1H,5H-pyrido[3,2,1-ij]quinoline-2-carboxylic acid
2933 99 80	52602-39-8	9H-carbazol-4-ol
2933 99 80	145641-35-6	benzyl (2S,3aR,7aS)-octahydro-1H-indole-2-carboxylate hydrochloride
2933 99 80	87269-87-2	benzyl (2S,3aS,6aS)-octahydrocyclopenta[b]pyrrole-2-carboxylate hydrochloride

CN code	CAS RN	Name
2933 99 80	1012065-72-3	ethyl 2-amino-9,10-dimethoxy-1,6,7,11b-tetrahydro-4H-pyrido[2,1-a]isoquinoline-3-carboxylate
2933 99 80	131707-24-9	ethyl 6-bromo-5-hydroxy-1-methyl-2-[(phenylsulfanyl)methyl]-1H-indole-3-carboxylate
2933 99 80	105152-95-2	ethyl 7-(3-aminopyrrolidin-1-yl)-1-(2,4-difluorophenyl)-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylate
2933 99 80	139481-44-0	methyl 1-[(2'-cyanobiphenyl-4-yl)methyl]-2-ethoxy-1H-benzimidazole-7-carboxylate
2933 99 80	0-00-0	methyl 1-tert-butyl-2-hydroxy-1H-pyrrolo[2,3-b]pyridine-3-carboxylate
2933 99 80	21688-11-9	N2-[(benzyloxy)carbonyl]-L-glutaminy-L-asparaginy-L-S-benzyl-L-cysteinyl-L-prolyl-L-leucylglycinamide
2933 99 80	361440-67-7	tert-butyl (1S,3S,5S)-3-carbamoyl-2-azabicyclo[3.1.0]hexane-2-carboxylate
2933 99 80	709031-38-9	tert-butyl (2S)-2-carbamoyl-2,3-dihydro-1H-pyrrole-1-carboxylate
2933 99 80	709031-43-6	tert-butyl [(1S)-2-[(1S,3S,5S)-3-cyano-2-azabicyclo[3.1.0]hex-2-yl]-1-(3-hydroxy-tricyclo[3.3.1.1(3,7)]dec-1-yl)-2-oxoethyl]carbamate
2933 49 90	936359-25-0	methyl 2-((R)-3-(3-((E)-2-(7-chloroquinolin-2-yl)vinyl)phenyl)-3-(((1-(hydroxymethyl)cyclopropyl)methyl)sulfanyl)propyl)benzoate
2934 10 00	110130-88-6	(2Z)-[(acetyloxy)imino](2-amino-1,3-thiazol-4-yl)ethanoic acid
2934 10 00	68672-66-2	(2Z)-{[(1-tert-butoxy-2-methyl-1-oxopropan-2-yl)oxy]imino}[2-(tritylamino)-1,3-thiazol-4-yl]ethanoic acid
2934 10 00	291536-35-1	(5Z)-5-(4-fluorobenzylidene)-1,3-thiazolidine-2,4-dione
2934 10 00	302964-24-5	2-amino-N-(2-chloro-6-methylphenyl)-1,3-thiazole-5-carboxamide
2934 10 00	866920-24-3	3-[2-chloro-4-((4-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-thiazol-5-yl)methoxy)phenyl]-1,2,4-oxadiazol-5(4H)-one
2934 10 00	752253-39-7	4-(2-chloro-4-methoxy-5-methylphenyl)-N-[(1S)-2-cyclopropyl-1-(3-fluoro-4-methylphenyl)ethyl]-5-methyl-N-(prop-2-yn-1-yl)-1,3-thiazol-2-amine
2934 10 00	914361-45-8	L-lysine – {[(2R,3R)-3-[4-(4-cyanophenyl)-1,3-thiazol-2-yl]-2-(2,4-difluorophenyl)-1-(1H-1,2,4-triazol-1-yl)butan-2-yl]oxy}methyl dihydrogen phosphate – ethanol (1:1:1)

CN code	CAS RN	Name
2934 10 00	302964-08-5	N-(2-chloro-6-methylphenyl)-2-[(6-chloro-2-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carboxamide
2934 10 00	127660-04-2	sodium (2Z)-(2-amino-1,3-thiazol-4-yl)(hydroxyimino)ethanoate
2934 99 90	17381-54-3	(1-benzothiophen-5-yl)acetic acid
2934 99 90	630100-90-2	(1R)-1,2-anhydro-4-C-[(1E,3E)-4-[(1S,2S,3E,5R,6R,9R)-5-(1-carboxylato-4-cycloheptylpiperazin-2-yl)-6,9-dihydroxy-2,6-dimethyl-11-oxooxacyclododec-3-en-1-yl]penta-1,3-dien-1-yl]-3,5-dideoxy-1-[(2R,3S)-3-hydroxypentan-2-yl]-D-erythropentitol
2934 99 90	220099-91-2	(2R)-3'H-spiro[4-azabicyclo[2.2.2]octane-2,2'-furo[2,3-b]pyridine]
2934 99 90	220100-81-2	(2R)-3'H-spiro[4-azabicyclo[2.2.2]octane-2,2'-furo[2,3-b]pyridine] (S,S)-2,3-dihydroxybutanedioate
2934 99 90	161599-46-8	(2R,3R,4R,5R)-2-(4-amino-5-fluoro-2-oxopyrimidin-1(2H)-yl)-2-fluoro-5-methyltetrahydrofuran-3,4-diyl diacetate
2934 99 90	690270-65-6	(2R,3S,4R)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)-2-azido-2-[(2-methylpropanoyl)oxy]methyl]tetrahydrofuran-3,4-diyl bis(2-methylpropanoate) hydrochloride
2934 99 90	265121-04-8	(3-[[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(2-fluorophenyl)morpholin-4-yl]methyl]-5-oxo-2,5-dihydro-1H-1,2,4-triazol-1-yl]phosphonic acid - 1-deoxy-1-(methylamino)-D-glucitol (1:2)
2934 99 90	163680-80-6	(3S)-10-[1-(acetylamino)cyclopropyl]-9-fluoro-3-methyl-7-oxo-2,3-dihydro-7H-[1,4]oxazino[2,3,4-ij]quinoline-6-carboxylic acid
2934 99 90	132335-46-7	(3S)-N,N-dimethyl-3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propan-1-amine
2934 99 90	133413-70-4	(3S,6R,9S,12R,15S,18R,21S,24R)-6,18-dibenzyl-4,10,12,16,22,24-hexamethyl-3,9,15,21-tetrakis(2-methylpropyl)-1,7,13,19-tetraoxa-4,10,16,22-tetraazacyclotetracosane-2,5,8,11,14,17,20,23-octone
2934 99 90	503068-36-8	(5R)-3-(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)-5-(2,2-dimethyl-4H-1,3-benzodioxin-6-yl)-1,3-oxazolidin-2-one
2934 99 90	452339-73-0	(5R)-5-(2,2-dimethyl-4H-1,3-benzodioxin-6-yl)-1,3-oxazolidin-2-one
2934 99 90	877130-28-4	(6R)-6-cyclopentyl-6-[2-(2,6-diethylpyridin-4-yl)ethyl]-3-[(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)methyl]-4-hydroxy-5,6-dihydro-2H-pyran-2-one

CN code	CAS RN	Name
2934 99 90	132335-44-5	(S)-3-(dimethylamino)-1-(thiophen-2-yl)propan-1-ol
2934 99 90	812647-80-6	{{(2R,3S,4R,5R)-2-azido-5-(2,4-dioxo-3,4-dihydro-pyrimidin-1(2H)-yl)-3,4-bis[(phenylcarbonyl)oxy]tetrahydrofuran-2-yl)methyl 3-chlorobenzoate
2934 99 90	00-00-0	1-(1-{4-[2-(4-fluorophenyl)-1,3-dioxolan-2-yl]butyl}-1,2,3,6-tetrahydropyridin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one
2934 99 90	1029716-44-6	1-(1-ethoxyethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole
2934 99 90	165172-60-1	1-[(2R,5S)-5-(hydroxymethyl)-2,5-dihydrofuran-2-yl]-5-methylpyrimidine-2,4(1H,3H)-dione – 1-methylpyrrolidin-2-one (1:1)
2934 99 90	519187-97-4	1-[3-(2-benzo[b]thien-5-ylethoxy)propyl]-3-azetidinol – (2Z)-2-butenedioate (1:1)
2934 99 90	127000-90-2	1-[[{(2R,3S)-2-(2,4-difluorophenyl)-3-methyloxiran-2-yl)methyl]-1H-1,2,4-triazole
2934 99 90	710281-33-7	2-(((1R,3S)-3-[[2-(3-methoxyphenyl)-5-methyl-1,3-oxazol-4-yl]methoxy]cyclohexyl)oxy)methyl)-6-methylbenzoic acid
2934 99 90	96803-30-4	2-(1-benzothiophen-5-yl)ethanol
2934 99 90	913695-00-8	2-[[{(4-[(2,2-dimethyl-1,3-dioxan-5-yl)methoxy]-3,5-dimethylpyridin-2-yl)methyl)sulfinyl]-1Hbenzimidazole, sodium salt (1:1)
2934 99 90	376608-74-1	2-[[{(3aR,4S,6R,6aS)-6-[[5-amino-6-chloro-2-(propylsulfanyl)pyrimidin-4-yl]amino]-2,2-dimethyltetrahydro-3aH-cyclopenta[d][1,3]dioxol-4-yl]oxy]ethanol
2934 99 90	474554-48-8	2-bromo-1-[3-tert-butyl-4-methoxy-5-(morpholin-4-yl)phenyl]ethanone
2934 99 90	530141-72-1	3-(5-[[4-(cyclopentyloxy)-2-hydroxyphenyl]carbonyl]-2-[(3-hydroxy-1,2-benzoxazol-6-yl)methoxy]phenyl)propanoic acid
2934 99 90	519188-55-7	3-[2-(1-benzothiophen-5-yl)ethoxy]-1-(3-hydroxyazetidin-1-yl)propan-1-one
2934 99 90	519188-42-2	3-[2-(1-benzothiophen-5-yl)ethoxy]propionic acid
2934 99 90	753015-42-8	3-((E)-2-[(3R)-pyrrolidin-3-yl]ethenyl)-5-(tetrahydro-2H-pyran-4-yloxy)pyridine
2934 99 90	26638-53-9	3-chloro-6-methyldibenzo[c,f][1,2]thiazepin-11(6H)-one 5,5-dioxide

CN code	CAS RN	Name
2934 99 90	499785-81-8	3-oxo-4-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-3,4-dihydropyrazine-2-carboxamide
2934 99 90	356782-84-8	3-oxo-4-(β-D-ribofuranosyl)-3,4-dihydropyrazine-2-carboxamide
2934 99 90	6504-57-0	4-[3-hydroxy-3-phenyl-3-(thiophen-2-yl)propyl]-4-methylmorpholin-4-ium methyl sulfate
2934 99 90	871484-32-1	4-[4-({3-[(4-deoxy-4-fluoro-β-D-glucopyranosyl)oxy]-5-(propan-2-yl)-1H-pyrazol-4-yl)methyl}phenyl]-N-[1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl]butanamide
2934 99 90	166964-09-6	4-chloro-3-methyl-1,2-oxazol-5-amine
2934 99 90	655233-39-3	4-nitrobenzyl(6R,7R)-7-amino-8-oxo-3-[(2S)-tetrahydrofuran-2-yl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate hydrochloride
2920 90 85	89729-09-9	5,7-dioxa-6-thiaspiro[2.5]octane-6-oxide
2934 99 90	388082-75-5	5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furancarboxaldehyde – 4-methylbenzenesulfonate (1:1)
2934 99 90	4923-87-9	5-bromo-1-benzothiophene
2934 99 90	947408-95-9	6-(bromomethyl)-2-triphenylmethyl-1,2-benzisoxazol-3(2H)-one
2934 99 90	947408-94-8	6-methyl-2-trityl-1,2-benzoxazol-3(2H)-one
2934 99 90	67978-05-6	diphenylmethyl(2R)-3-methyl-2-[(1R,5S)-3-(4-methylphenyl)-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl]but-3-enoate
2934 99 90	1001859-46-6	DNA (synthetic plasmid vector pCOR human interferon beta signal peptide fusion protein with 21-154-human acidic fibroblast growth factor-specifying)
2934 99 90	665058-78-6	DNA, d(T-sp-C-G-sp-T-sp-C-G-sp-T-sp-T-sp-T-sp-G-sp-A-sp-C-G-sp-T-sp-T-sp-T-sp-T-sp-Gsp-T-sp-C-G-sp-T-sp-T)
2934 99 90	923591-06-4	methyl (5R,7S,10S)-10-tert-butyl-15,15-dimethyl-3,9,12-trioxo-6,7,9,10,11,12,14,15,16,17,18,19-dodecahydro-1H,5H-2,23:5,8-dimethano-4,13,2,8,11-benzodioxatria-zacyclohenicosine-7(3H)-carboxylate
2934 99 90	59337-92-7	methyl 3-(chlorosulfonyl)thiophene-2-carboxylate
2934 99 90	947409-01-0	methyl 3-[5-[4-(cyclopentyloxy)-2-hydroxybenzoyl]-2-[(2-triphenylmethyl-1,2-benzisoxazol-3(2H)-on-6-yl)methoxy]phenyl]propionate
2934 99 90	85006-31-1	methyl 3-amino-4-methylthiophene-2-carboxylate

CN code	CAS RN	Name
2934 99 90	893428-72-3	N-(5-chloro-1,3-benzodioxol-4-yl)-7-[2-(4-methyl-1-piperazinyl)ethoxy]-5-[(tetrahydro-2H-pyran-4-yl)oxy]-4-quinazolinamine – (2E)-2-butenedioate (1:2)
2934 99 90	390800-88-1	N,N',N''-(boroxin-2,4,6-triyltris{[(1S)-3-methylbutane-1,1-diyl]imino[(2S)-1-oxo-3-phenylpropane-1,2-diyl]})tripyrazine-2-carboxamide
2934 99 90	112913-94-7	N-[[4-(4-fluorobenzyl)morpholin-2-yl]methyl]acetamide
2934 99 90	120788-03-6	S-[(1R,3S)-1-oxidotetrahydrothiophen-3-yl] ethanethioate
2935 00 90	1198178-65-2	(1R,2R)-1-[(cyclopropylsulfonyl)carbamoyl]-2-ethylcyclopropanaminium 4-methylbenzenesulfonate
2935 00 90	39570-96-2	(2R)-3-(benzylsulfanyl)-N-[(2S)-1-[(2S,3S)-1-hydrazinyl-3-methyl-1-oxopentan-2-yl]amino]-3-(4-hydroxyphenyl)-1-oxopropan-2-yl]-2-[[4-methylphenyl)sulfonyl]amino}propanamide
2935 00 90	24310-36-9	1-[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydro-5H-1-benzazepin-5-one
2935 00 90	0-00-0	2-(cyclohexylmethyl)-N-{2-[(2S)-1-methylpyrrolidin-2-yl]ethyl}-1,2,3,4-tetrahydroisoquinoline-7-sulfonamide di[(2E)-but-2-enedioate] hydrate
2935 00 90	941690-55-7	3-[(methylsulfonyl)amino]-2-phenyl-N-[(1S)-1-phenylpropyl]quinoline-4-carboxamide
2935 00 90	6973-09-7	5-amino-2-methylbenzenesulfonamide
2935 00 90	193686-76-9	7-chloro-1-[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydro-5H-1-benzazepin-5-one
2935 00 90	123664-84-6	N-(5-methoxy-2-phenoxyphenyl)methanesulfonamide
2935 00 90	149457-03-4	N-[4-(N-formylglycyl)-5-hydroxy-2-phenoxyphenyl]methanesulfonamide
2935 00 90	149456-98-4	N-[4-(N-formylglycyl)-5-methoxy-2-phenoxyphenyl]methanesulfonamide
2935 00 90	141450-48-8	N-{2-[(4-hydroxyphenyl)amino]pyridin-3-yl}-4-methoxybenzenesulfonamide hydrochloride
2935 00 90	289042-10-0	N-{5-[(diphenylphosphoryl)methyl]-4-(4-fluorophenyl)-6-(propan-2-yl)pyrimidin-2-yl}-N-methylmethanesulfonamide
2939 99 00	7689-03-4	(4S)-4-ethyl-4-hydroxy-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione

CN code	CAS RN	Name
2939 99 00	477-29-2	colchicoside
2940 00 00	604-69-3	1,2,3,4,6-penta-O-acetyl- β -D-glucopyranose
2940 00 00	647834-15-9	2-(4-methoxybenzyl)thiophen-3-yl β -D-glucopyranoside
2941 90 00	76610-92-9	(6R,7R)-7-({N-[(4-ethyl-2,3-dioxopiperazin-1-yl)carbonyl]-D-threonyl}amino)-3-[[[(1-methyl-1H-tetrazol-5-yl)sulfanyl]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid
3907 20 99	913976-27-9	poly(oxy-1,2-ethanediyl), α -hydro- ω -methoxy, diester with 21N6, 21'N6-[[[(N2, N6-dicarboxy-L-lysyl- β -alanyl)imino]bis(1-oxo-2, 1-ethanediyl)]bis[N-acetyl-glycyl-L-leucyl-L-tyrosyl-L-alanyl-L-cysteinyl-L-histidyl-L-methionylglycyl-L-prolyl-L-isoleucyl-L-threonyl-3-(1-naphthalenyl)-L-alanyl-L-valyl-L-cysteinyl-L-glutaminyl-L-prolyl-L-leucyl-L-arginyl-N-methylglycyl-L-lysineamide] cyclic (6 $\rightarrow$ 15), (6' $\rightarrow$ 15') bis(disulfide)

ANNEX IV

List of pharmaceutical intermediates, i.e. compounds used for the manufacture of finished pharmaceutical products, to be withdrawn from the list of products receiving duty-free treatment included in Annex 6 to Annex I to Regulation (EEC) No 2658/87 due to their transfer to the list of products receiving duty-free treatment included in Annex 3 to Annex I to Regulation (EEC) No 2658/87

CN code	CAS RN	Name
2915 39 00	7753-60-8	17- α -hydroxy-3,20-dioxopregna-4,9(11)-diene-21-yl acetate
2937 29 00		see anecortave (INN)
2920 90 85	163133-43-5	4-(nitrooxy)butyl (2S)-2-(6-methoxy-2-naphthyl) propanoate see naproxcinod (INN)
2924 29 98	194085-75-1	2-(2-chlorophenyl)-2-hydroxyethyl carbamate see carisbamate (INN)
2933 39 99	103129-82-4	3-ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate see levamlodipine (INN)
2933 39 99	319460-85-0	N-methyl-2-[[3-((E)-2-pyridin-2-ylvinyl)-1H-indazol-6-yl]sulfanyl]benzamide see axitinib (INN)
2934 10 00	302962-49-8	N-(2-chloro-6-methylphenyl)-2-((6-[4-(2-hydroxyethyl)piperazin-1-yl]-2-methylpyrimidin-4-yl)amino)thiazole-5-carboxamide see dasatinib (INN)
2934 99 90	143491-57-0	(2R,5S)-4-amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl]pyrimidin-2(1H)-one see emtricitabine (INN)
2934 99 90	98819-76-2	(2S)-2-[(S)-(2-ethoxyphenoxy)phenylmethyl]morpholine see esreboxetine (INN)
2934 99 90	475479-34-6	(2S)-2-methoxy-3-{4-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]-1-benzothiophen-7-yl}propanoic acid see aleglitazar (INN)
2934 99 90	377727-87-2	2-(2-furyl)-7-(2-{4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl}ethyl)-7H-pyrazolo[4,3-e][1,2,4]triazolo[2,3-c]pyrimidin-5-amine see preladenant (INN)
2934 99 90	189003-92-7	2-{7-fluoro-2-oxo-4-[2-(4-thieno[3,2-c]pyridin-4-yl)piperazin-1-yl]ethyl}quinolin-1(2H)-yl}acetamide see trelanserine (INN)
2934 99 90	134379-77-4	4-amino-5-fluoro-1-[(2R,5S)-5-(hydroxymethyl)-2,5-dihydrofuran-2-yl]pyrimidin-2(1H)-one see dexelvucitabine (INN)

CN code	CAS RN	Name
2934 99 90	518048-05-0	potassium 4-[N-(2-fluorobenzyl)carbamoyl]-1-methyl-2-[1-methyl-1-(5-methyl-1,3,4-oxadiazole-2-carboxamido)ethyl]-6-oxo-1,6-dihydropyrimidine-5-olate see raltegravir (INN)
2935 00 90	170569-88-7	4-[5-(4-fluorophenyl)-3-(trifluoromethyl)pyrazol-1-yl]benzene-1-sulfonamide see mavacoxib (INN)
2935 00 90	186497-07-4	N-(3-methoxy-5-methylpyrazin-2-yl)-2-[4-(1,3,4-oxadiazol-2-yl)phenyl]pyridine-3-sulfonamide see zibotentan (INN)

DIRECTIVES

DIRECTIVE 2010/84/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 15 December 2010

amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee ⁽¹⁾,

Having regard to the opinion of the Committee of the Regions ⁽²⁾,

Having regard to the opinion of the European Data Protection Supervisor ⁽³⁾,

Acting in accordance with the ordinary legislative procedure ⁽⁴⁾,

Whereas:

(1) 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 ⁽⁵⁾ lays down harmonised rules for the authorisation, supervision and pharmacovigilance of medicinal products for human use within the Union.

(2) Pharmacovigilance rules are necessary for the protection of public health in order to prevent, detect and assess

adverse reactions to medicinal products placed on the Union market, as the full safety profile of medicinal products can only be known after they have been placed on the market.

(3) In the light of the experience acquired and following an assessment by the Commission of the Union system of pharmacovigilance, it has become clear that it is necessary to take measures in order to improve the operation of Union law on the pharmacovigilance of medicinal products.

(4) While the fundamental objective of the regulation of medicinal products is to safeguard public health, this aim should nevertheless be achieved by means that do not impede the free movement of safe medicinal products within the Union. It has emerged from the assessment of the Union system of pharmacovigilance that divergent actions by Member States in relation to safety issues pertaining to medicinal products are creating obstacles to the free movement of medicinal products. In order to prevent or eliminate those obstacles the existing pharmacovigilance provisions at Union level should be strengthened and rationalised.

(5) For the sake of clarity, the definition of the term 'adverse reaction' should be amended to ensure that it covers noxious and unintended effects resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse of the medicinal product. The suspicion of an adverse drug reaction, meaning that there is at least a reasonable possibility of there being a causal relationship between a medicinal product and an adverse event, should be sufficient reason for reporting. Therefore, the term 'suspected adverse reaction' should be used when referring to reporting obligations. Without prejudice to the existing Union and national provisions and practices on medical confidentiality, Member States should ensure that reporting and processing of personal data related to suspected adverse reactions, including those associated with medication errors is carried out on a confidential basis. This should not affect Member States' obligations regarding the mutual exchange of

⁽¹⁾ OJ C 306, 16.12.2009, p. 28.

⁽²⁾ OJ C 79, 27.3.2010, p. 50.

⁽³⁾ OJ C 229, 23.9.2009, p. 19.

⁽⁴⁾ Position of the European Parliament of 22 September 2010 [not yet published in the Official Journal] and Council Decision of 29 November 2010.

⁽⁵⁾ OJ L 311, 28.11.2001, p. 67.

- information on pharmacovigilance issues or their obligation to make available to the public important information on pharmacovigilance concerns. Furthermore, the principle of confidentiality should not affect the obligations of the persons concerned to provide information under criminal law.
- (6) The pollution of waters and soils with pharmaceutical residues is an emerging environmental problem. Member States should consider measures to monitor and evaluate the risk of environmental effects of such medicinal products, including those which may have an impact on public health. The Commission should, based, *inter alia*, on data received from the European Medicines Agency, the European Environment Agency and Member States, produce a report on the scale of the problem, along with an assessment on whether amendments to Union legislation on medicinal products or other relevant Union legislation are required.
- (7) The marketing authorisation holder should establish a pharmacovigilance system to ensure the monitoring and supervision of one or more of its authorised medicinal products, recorded in a pharmacovigilance system master file which should be permanently available for inspection. The competent authorities should undertake to supervise those pharmacovigilance systems. Applications for marketing authorisations should therefore be accompanied by a brief description of the corresponding pharmacovigilance system, which should include a reference to the location where the pharmacovigilance system master file for the medicinal product concerned is kept and available for inspection by the competent authorities.
- (8) Marketing authorisation holders should plan pharmacovigilance measures for each individual medicinal product in the context of a risk management system. The measures should be proportionate to the identified risks, the potential risks, and the need for additional information on the medicinal product. It should also be ensured that any key measures included in a risk management system are made conditions of the marketing authorisation.
- (9) It is necessary from a public health perspective to complement the data available at the time of authorisation with additional data about the safety and, in certain cases, the efficacy of authorised medicinal products. Competent authorities should therefore be empowered to impose on the marketing authorisation holder the obligation to conduct post-authorisation studies on safety and on efficacy. It should be possible to impose that obligation at the time of the granting of the marketing authorisation or later, and it should be a condition of the marketing authorisation. Such studies may be aimed at collecting data to enable the assessment of the safety or efficacy of medicinal products in everyday medical practice.
- (10) It is essential that a strengthened system of pharmacovigilance not lead to the premature granting of marketing authorisations. However, some medicinal products are authorised subject to additional monitoring. This includes all medicinal products with a new active substance and biological medicinal products, including biosimilars, which are priorities for pharmacovigilance. Competent authorities may also require additional monitoring for specific medicinal products that are subject to the obligation to conduct a post-authorisation safety study or to conditions or restrictions with regard to the safe and effective use of the medicinal product. Medicinal products subject to additional monitoring should be identified as such by a black symbol and an appropriate standardised explanatory sentence in the summary of product characteristics and in the package leaflet. A publicly available list of medicinal products subject to additional monitoring should be kept up to date by the European Medicines Agency established by 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⁽¹⁾ (hereinafter referred to as the 'Agency').
- (11) The Commission should, in collaboration with the Agency and national competent authorities and following consultations with organisations representing patients, consumers, doctors and pharmacists, social health insurers, and other interested parties, present to the European Parliament and the Council an assessment report regarding the readability of the summaries of product characteristics and the package leaflets and their value to the healthcare professionals and the general public. Following an analysis of that data, the Commission should, if appropriate, make proposals to improve the layout and content of the summaries of product characteristics and of the package leaflets to ensure that they represent a valuable source of information for healthcare professionals and the general public respectively.
- (12) Experience has shown that the responsibilities of marketing authorisation holders with regard to pharmacovigilance of authorised medicinal products should be clarified. The marketing authorisation holder should be responsible for continuously monitoring the safety of its medicinal products, for informing the authorities of any changes that might impact on the marketing authorisation, and for ensuring that the product information is kept up to date. As medicinal products could be used outside the terms of the marketing authorisation, the marketing authorisation holder's responsibilities should include providing all available information, including the results of clinical trials or other studies, as well as reporting any use of the medicinal product which is outside the terms of the marketing authorisation. It is also appropriate to ensure that all relevant information

⁽¹⁾ OJ L 136, 30.4.2004, p. 1.

collected on the safety of the medicinal product is taken into account when the marketing authorisation is being renewed.

- (13) In order to ensure close cooperation between the Member States in the area of pharmacovigilance, the mandate of the coordination group set up by Article 27 of Directive 2001/83/EC should be enlarged to include the examination of questions related to the pharmacovigilance of all medicinal products authorised by the Member States. In order to fulfil its new tasks, the coordination group should be further strengthened through the adoption of clear rules as regards the expertise required, the procedures for reaching agreements or positions, transparency, independence and professional secrecy of its members, and the need for cooperation between Union and national bodies.
- (14) With a view to ensuring the same level of scientific expertise in the area of pharmacovigilance decision-making at both Union and national levels, the coordination group should rely on the recommendations of the Pharmacovigilance Risk Assessment Committee when fulfilling its pharmacovigilance tasks.
- (15) In order to avoid duplication of work, the coordination group should agree on a single position for pharmacovigilance assessments concerning medicinal products authorised in more than one Member State. Agreement within the coordination group should suffice for pharmacovigilance measures to be implemented throughout the Union. Where no agreement is reached within the coordination group, the Commission should be authorised to adopt a decision concerning the necessary regulatory action in respect of the marketing authorisation, addressed to the Member States.
- (16) A single assessment should also be conducted in the case of pharmacovigilance issues which concern medicinal products authorised by the Member States and medicinal products authorised in accordance with Regulation (EC) No 726/2004. In such cases, the Commission should adopt harmonised measures for all medicinal products concerned on the basis of an assessment at Union level.
- (17) Member States should operate a pharmacovigilance system to collect information that is useful for the monitoring of medicinal products, including information on suspected adverse reactions arising from use of a medicinal product within the terms of the marketing authorisation as well as from use outside the terms of the marketing authorisation, including overdose, misuse, abuse and medication errors, and suspected adverse reactions associated with occupational exposure. Member States should ensure the quality of the pharmacovigilance system through the follow-up of cases of suspected adverse reactions. For those tasks, Member States should establish a permanent pharmacovigilance system, supported by the appropriate expertise, so that the obligations under this Directive can be fully met.
- (18) In order to further increase the coordination of resources between the Member States, Member State should be authorised to delegate certain pharmacovigilance tasks to another Member State.
- (19) In order to simplify the reporting of suspected adverse reactions, the marketing authorisation holders and the Member States should report those reactions only to the Union pharmacovigilance database and data-processing network referred to in Article 57(1)(d) of Regulation (EC) No 726/2004 (the 'Eudravigilance database'). The Eudravigilance database should be equipped to immediately forward reports on suspected adverse reactions received from marketing authorisation holders to the Member States on whose territory the reaction occurred.
- (20) In order to increase the level of transparency of the pharmacovigilance processes, the Member States should create and maintain medicines web-portals. To the same end, the marketing authorisation holders should provide the competent authorities with prior or simultaneous warnings about safety announcements and the competent authorities should also provide each other with advance notice of safety announcements.
- (21) Union rules in relation to pharmacovigilance should continue to rely on the crucial role of healthcare professionals in monitoring the safety of medicinal products, and should take account of the fact that patients are also well placed to report suspected adverse reactions to medicinal products. It is therefore appropriate to facilitate the reporting of suspected adverse reactions to medicinal products by both healthcare professionals and patients, and to make methods for such reporting available to them.
- (22) As a result of the submission of all suspected adverse reaction data directly to the Eudravigilance database, it is appropriate to amend the scope of periodic safety update reports so that they present an analysis of the risk-benefit balance of a medicinal product rather than a detailed listing of individual case reports already submitted to the Eudravigilance database.

- (23) Obligations imposed in respect of periodic safety update reports should be proportionate to the risks posed by medicinal products. Periodic safety update reporting should therefore be linked to the risk management system for newly authorised medicinal products and routine reporting should not be required for generic medicinal products, for medicinal products containing an active substance for which well-established medicinal use has been demonstrated, for homeopathic medicinal products or for traditional-use registered herbal medicinal products. However, in the interests of public health, the competent authorities should require periodic safety update reports for such medicinal products when concerns arise relating to pharmacovigilance data or as a result of the lack of available safety data when the use of the active substance concerned is concentrated in medicinal products for which periodic safety update reporting is not routinely required.
- (24) It is necessary to increase the shared use of resources between competent authorities for the assessment of periodic safety update reports. A single assessment of periodic safety update reports for medicinal products authorised in more than one Member State should be provided for. Moreover, procedures should be established to set single frequency and submission dates of periodic safety update reports for all medicinal products containing the same active substance or the same combination of active substances.
- (25) Following a single assessment of periodic safety update reports, any resulting measures as regards the maintenance, variation, suspension or revocation of the marketing authorisations concerned should be adopted through a Union procedure leading to a harmonised result.
- (26) The Member States should automatically submit certain safety issues related to medicinal products to the Agency thereby triggering a Union-wide assessment of the issue. Therefore it is appropriate to establish rules for an assessment procedure by the Pharmacovigilance Risk Assessment Committee, and for the subsequent follow-up as regards the marketing authorisations concerned with a view to the adoption of harmonised measures across the Union.
- (27) In connection with the clarification and strengthening of the provisions relating to pharmacovigilance activities in Directive 2001/83/EC, it is also appropriate to further clarify the procedures for all Union-wide post-authorisation assessments of safety issues concerning medicinal products. To that end, the number of procedures for Union-wide assessment should be limited to two, one of which allows for a swift assessment and should be applied when urgent action is considered necessary. Regardless of whether the urgent procedure or the normal procedure is applied, and whether the medicinal product was authorised through the centralised or non-centralised procedure, the Pharmacovigilance Risk Assessment Committee should always give its recommendation when the reason for taking action is based on pharmacovigilance data. It is appropriate that the coordination group and the Committee for Medicinal Products for Human Use should rely on this recommendation when performing their assessment of the issue.
- (28) It is necessary to introduce harmonised guiding principles for, and regulatory supervision of, post-authorisation safety studies that are requested by competent authorities and that are non-interventional, that are initiated, managed or financed by the marketing authorisation holder, and that involve the collection of data from patients or healthcare professionals and that therefore fall outside of the scope of Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use⁽¹⁾. The supervision of such studies should be the responsibility of the Pharmacovigilance Risk Assessment Committee. Studies requested after the marketing authorisation of a medicinal product by only one competent authority to be conducted in only one Member State should be supervised by the national competent authority of the Member State in which the study is to be conducted. Provision should also be made for the subsequent follow-up, if appropriate, as regards the marketing authorisations concerned with a view to the adoption of harmonised measures across the Union.
- (29) In order to enforce the provisions relating to pharmacovigilance, the Member States should ensure that effective, proportionate and dissuasive penalties are applied to marketing authorisation holders for non-compliance with pharmacovigilance obligations. If the conditions included in the marketing authorisation are not fulfilled within the given deadline, the national competent authorities should have the power to review the marketing authorisation.

⁽¹⁾ OJ L 121, 1.5.2001, p. 34.

- (30) In order to protect public health, the pharmacovigilance activities of national competent authorities should be adequately funded. It should be ensured that adequate funding is possible for pharmacovigilance activities by empowering the national competent authorities to charge fees to marketing authorisation holders. However, the management of those collected funds should be under the permanent control of the national competent authorities in order to guarantee their independence in the performance of those pharmacovigilance activities.
- (31) It should be possible for Member States to allow the relevant actors, under certain conditions, to deviate from certain provisions of Directive 2001/83/EC related to the requirements for labelling and packaging in order to address severe availability problems related to the potential lack of authorised medicinal products or of medicinal products placed on the market or shortages thereof.
- (32) Since the objective of this Directive, namely to improve the safety of medicinal products placed on the market in the Union in a harmonised way across the Member States, cannot be sufficiently achieved by the Member States and can, by reason of the scale of the measures, be better achieved at Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union (TEU). In accordance with the principle of proportionality, as set out in that Article, this Directive does not go beyond what is necessary in order to achieve this objective.
- (33) This Directive shall apply without prejudice to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data ⁽¹⁾ and Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data ⁽²⁾. In order to detect, assess, understand and prevent adverse reactions, and to identify and take actions to reduce the risks of, and increase the benefits from, medicinal products for the purpose of safeguarding public health, it should be possible to process personal data within the Eudravigilance system while respecting Union legislation relating to data protection. The purpose of safeguarding public health constitutes a substantial public interest and consequently the processing of personal data can be justified if identifiable health data are processed only when necessary and only when the parties involved assess this necessity at every stage of the pharmacovigilance process.
- (34) The provisions on the monitoring of medicinal products in Directive 2001/83/EC constitute specific provisions within the meaning of Article 15(2) of Regulation (EC) No 765/2008 of the European Parliament and of the Council of 9 July 2008 setting out the requirements for accreditation and market surveillance relating to the marketing of products ⁽³⁾.
- (35) The pharmacovigilance activities provided for in this Directive require that uniform conditions be established as concerns the contents and maintenance of the pharmacovigilance system master file, as well as the minimum requirements for the quality system for the performance of pharmacovigilance activities by the national competent authorities and marketing authorisation holders, the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities, and the minimum requirements for the monitoring of the data contained in the Eudravigilance database to determine whether there are new risks or whether risks have changed. The format and content of the electronic transmission of suspected adverse reactions by Member States and marketing authorisation holders, the format and content of electronic periodic safety update reports and risk management plans as well as the format of protocols, abstracts and final study reports for the post-authorisation safety studies should also be established. In accordance with Article 291 of the Treaty on the Functioning of the European Union (TFEU), rules and general principles concerning mechanisms for the control by Member States of the Commission's exercise of implementing powers are to be laid down in advance by a regulation adopted in accordance with the ordinary legislative procedure. Pending the adoption of that new regulation, Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission ⁽⁴⁾ continues to apply, with the exception of the regulatory procedure with scrutiny, which is not applicable.
- (36) The Commission should be empowered to adopt delegated acts in accordance with Article 290 TFEU in order to supplement the provisions in Articles 21a and 22a of Directive 2001/83/EC. The Commission should be empowered to adopt supplementary measures laying down the situations in which post-authorisation efficacy studies may be required. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level.
- (37) In accordance with point 34 of the Interinstitutional Agreement on better law-making ⁽⁵⁾, Member States are encouraged to draw up, for themselves and in the interests of the Union, their own tables illustrating, as far as possible, the correlation between this Directive and the transposition measures, and to make them public.
- (38) Directive 2001/83/EC should be amended accordingly,

⁽¹⁾ OJ L 281, 23.11.1995, p. 31.

⁽²⁾ OJ L 8, 12.1.2001, p. 1.

⁽³⁾ OJ L 218, 13.8.2008, p. 30.

⁽⁴⁾ OJ L 184, 17.7.1999, p. 23.

⁽⁵⁾ OJ C 321, 31.12.2003, p. 1.

HAVE ADOPTED THIS DIRECTIVE:

Article 1

Amendments to Directive 2001/83/EC

Directive 2001/83/EC is hereby amended as follows:

1. Article 1 is amended as follows:

(a) point 11 is replaced by the following:

‘11. Adverse reaction: A response to a medicinal product which is noxious and unintended.’;

(b) point 14 is deleted;

(c) point 15 is replaced by the following:

‘15. Post-authorisation safety study: Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures.’;

(d) the following points are inserted:

‘28b. Risk management system: a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those activities and interventions.

28c. Risk management plan: a detailed description of the risk management system.

28d. Pharmacovigilance system: a system used by the marketing authorisation holder and by Member States to fulfil the tasks and responsibilities listed in Title IX and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance.

28e. Pharmacovigilance system master file: A detailed description of the pharmacovigilance system used by the marketing authorisation holder with respect to one or more authorised medicinal products.’.

2. Article 8(3) is amended as follows:

(a) point (ia) is replaced by the following:

‘(ia) A summary of the applicant’s pharmacovigilance system which shall include the following elements:

— proof that the applicant has at his disposal a qualified person responsible for pharmacovigilance,

— the Member States in which the qualified person resides and carries out his/her tasks,

— the contact details of the qualified person,

— a statement signed by the applicant to the effect that the applicant has the necessary means to fulfil the tasks and responsibilities listed in Title IX,

— a reference to the location where the pharmacovigilance system master file for the medicinal product is kept.’,

(b) the following point is inserted after point (ia):

‘(iaa) The risk management plan describing the risk management system which the applicant will introduce for the medicinal product concerned, together with a summary thereof.’;

(c) point (l) is replaced by the following:

‘(l) Copies of the following:

— any authorisation, obtained in another Member State or in a third country, to place the medicinal product on the market, a summary of the safety data including the data contained in the periodic safety update reports, where available, and suspected adverse reactions reports, together with a list of those Member States in which an application for authorisation submitted in accordance with this Directive is under examination;

— the summary of the product characteristics proposed by the applicant in accordance with Article 11 or approved by the competent authorities of the Member State in accordance with Article 21 and the package leaflet proposed in accordance with Article 59 or approved by the competent authorities of the Member State in accordance with Article 61;

— details of any decision to refuse authorisation, whether in the Union or in a third country, and the reasons for such a decision.’,

(d) point (n) is deleted;

(e) the following subparagraphs are added after the second subparagraph:

‘The risk management system referred to in point (iaa) of the first subparagraph shall be proportionate to the identified risks and the potential risks of the medicinal product, and the need for post-authorisation safety data.

The information referred to in the first subparagraph shall be updated where and when appropriate.’.

3. In Article 11 the following subparagraphs are added:

‘For medicinal products included on the list referred to in Article 23 of Regulation (EC) No 726/2004, the summary of product characteristics shall include the statement: “This medicinal product is subject to additional monitoring”. This

statement shall be preceded by the black symbol referred to in Article 23 of Regulation (EC) No 726/2004 and followed by an appropriate standardised explanatory sentence.

For all medicinal products, a standard text shall be included expressly asking healthcare professionals to report any suspected adverse reaction in accordance with the national spontaneous reporting system referred to in Article 107a(1). Different ways of reporting, including electronic reporting, shall be available in compliance with the second subparagraph of Article 107a(1).'

4. Article 16g(1) is replaced by the following:

'1. Article 3(1) and (2), Article 4(4), Article 6(1), Article 12, Article 17(1), Articles 19, 20, 23, 24, 25, 40 to 52, 70 to 85, 101 to 108b, Article 111(1) and (3), Articles 112, 116, 117, 118, 122, 123, 125, the second paragraph of Article 126, and Article 127 of this Directive as well as Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use (*) shall apply, by analogy, to traditional-use registration granted under this Chapter.

(*) OJ L 262, 14.10.2003, p. 22.'

5. Article 17 is amended as follows:

- (a) in the second subparagraph of paragraph 1, the words 'Articles 27' are replaced by the words 'Articles 28';
- (b) in paragraph 2, the words 'Articles 27' are replaced by the words 'Articles 28';

6. In Article 18, the words 'Articles 27' are replaced by the words 'Articles 28'.

7. In Article 21, paragraphs 3 and 4 are replaced by the following:

'3. The national competent authorities shall, without delay, make publicly available the marketing authorisation together with the package leaflet, the summary of the product characteristics and any conditions established in accordance with Articles 21a, 22 and 22a, together with any deadlines for the fulfilment of those conditions for each medicinal product which they have authorised.

4. The national competent authorities shall draw up an assessment report and make comments on the file as

regards the results of the pharmaceutical and pre-clinical tests, the clinical trials, the risk management system and the pharmacovigilance system of the medicinal product concerned. The assessment report shall be updated whenever new information becomes available which is important for the evaluation of the quality, safety or efficacy of the medicinal product concerned.

The national competent authorities shall make the assessment report publicly accessible without 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 indication applied for.

The public assessment report 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 following Article is inserted:

'Article 21a

In addition to the provisions laid down in Article 19, 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 which are stricter than those referred to in Title 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. Such an obligation to conduct such studies shall be based on the delegated acts adopted pursuant to Article 22b while taking into account the scientific guidance referred to in Article 108a.

The marketing authorisation shall lay down deadlines for the fulfilment of these conditions where necessary.'

9. Article 22 is replaced by the following:

'Article 22

In exceptional circumstances and following consultation with the applicant, the marketing authorisation may be granted subject to certain conditions, in particular relating to the safety of the medicinal product, notification to the national competent authorities of any incident relating to its use, and action to be taken.

The marketing authorisation may be granted only when the applicant can show that he is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use, for objective, verifiable reasons and must be based on one of the grounds set out in Annex I.

Continuation of the marketing authorisation shall be linked to the annual reassessment of these conditions.'

10. The following Articles are inserted:

'Article 22a

1. After the granting of a marketing authorisation, the national competent authority may impose an obligation on the marketing authorisation holder:

(a) to conduct a post-authorisation safety study if there are concerns about the risks of an authorised medicinal product. If the same concerns apply to more than one medicinal product, the national competent authority shall, following consultation with the Pharmacovigilance Risk Assessment Committee, encourage the marketing authorisation holders concerned to conduct a joint post-authorisation safety study;

(b) to conduct a post-authorisation efficacy study when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly. The obligation to conduct the post-authorisation efficacy study shall be based on the delegated acts adopted pursuant to Article 22b while taking into account the scientific guidance referred to in Article 108a.

The imposition of such an obligation shall be duly justified, notified in writing, and shall include the objectives and timeframe for submission and conduct of the study.

2. The national competent authority shall provide the marketing authorisation holder with an opportunity to present written observations in response to the imposition of the obligation within a time limit which it shall specify,

if the marketing authorisation holder so requests within 30 days of receipt of the written notification of the obligation.

3. On the basis of the written observations submitted by the marketing authorisation holder, the national competent authority shall withdraw or confirm the obligation. Where the national competent authority confirms the obligation, the marketing authorisation shall be varied to include the obligation as a condition of the marketing authorisation and the risk management system shall be updated accordingly.

Article 22b

1. In order to determine the situations in which post-authorisation efficacy studies may be required under Articles 21a and 22a of this Directive, the Commission may adopt, by means of delegated acts in accordance with Article 121a, and subject to the conditions of Articles 121b and 121c, measures supplementing the provisions in Articles 21a and 22a.

2. When adopting such delegated acts, the Commission shall act in accordance with the provisions of this Directive.

Article 22c

1. The marketing authorisation holder shall incorporate any conditions referred to in Articles 21a, 22 or 22a in his risk management system.

2. The Member States shall inform the Agency of the marketing authorisations that they have granted subject to conditions pursuant to Articles 21a, 22 or 22a.'

11. Article 23 is replaced by the following:

'Article 23

1. After a marketing authorisation has been granted, the marketing authorisation holder shall, in respect of the methods of manufacture and control provided for in Article 8(3)(d) and (h), take account of scientific and technical progress and introduce any changes that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods.

Those changes shall be subject to the approval of the competent authority of the Member State concerned.

2. The marketing authorisation holder shall forthwith provide the national competent authority with any new information which might entail the amendment of the particulars or documents referred to in Article 8(3), Articles 10, 10a, 10b and 11, or Article 32(5), or Annex I.

In particular, the marketing authorisation holder shall forthwith inform the national competent authority of any prohibition or restriction imposed by the competent authorities of any country in which the medicinal product is marketed and of any other new information which might influence the evaluation of the benefits and risks of the medicinal product concerned. The information shall include both positive and negative results of clinical trials or other studies in all indications and populations, whether or not included in the marketing authorisation, as well as data on the use of the medicinal product where such use is outside the terms of the marketing authorisation.

3. The marketing authorisation holder shall ensure that the product information is kept up to date with the current scientific knowledge, including the conclusions of the assessment and recommendations made public by means of the European medicines web-portal established in accordance with Article 26 of Regulation (EC) No 726/2004.

4. In order to be able to continuously assess the risk-benefit balance, the national competent authority may at any time ask the marketing authorisation holder to forward data demonstrating that the risk-benefit balance remains favourable. The marketing authorisation holder shall answer fully and promptly any such request.

The national competent authority may at any time ask the marketing authorisation holder to submit a copy of the pharmacovigilance system master file. The marketing authorisation holder shall submit the copy at the latest 7 days after receipt of the request.’

12. Article 24 is amended as follows:

- (a) in paragraph 2, the second subparagraph is replaced by the following:

‘To this end, the marketing authorisation holder shall provide the national competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including the evaluation of data contained in suspected adverse reactions reports and periodic safety update reports submitted in accordance with Title IX, and information on all variations introduced since the marketing authorisation was granted, at least 9 months before the marketing authorisation ceases to be valid in accordance with paragraph 1.’;

- (b) paragraph 3 is replaced by the following:

‘3. Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the national

competent authority decides, on justified grounds relating to pharmacovigilance, including exposure of an insufficient number of patients to the medicinal product concerned, to proceed with one additional five-year renewal in accordance with paragraph 2.’

13. The title ‘Chapter 4 Mutual recognition and decentralised procedure’ is deleted.

14. Article 27 is amended as follows:

- (a) paragraphs 1 and 2 are replaced by the following:

‘1. A coordination group shall be set up for the following purposes:

- (a) the examination of any question relating to a marketing authorisation of a medicinal product in two or more Member States in accordance with the procedures laid down in Chapter 4;
- (b) the examination of questions related to the pharmacovigilance of medicinal products authorised by the Member States, in accordance with Articles 107c, 107e, 107k and 107q;
- (c) the examination of questions relating to variations of marketing authorisations granted by the Member States, in accordance with Article 35(1).

The Agency shall provide the secretariat of this coordination group.

For the fulfilment of its pharmacovigilance tasks, including approving risk management systems and monitoring their effectiveness, the coordination group shall rely on the scientific assessment and the recommendations of the Pharmacovigilance Risk Assessment Committee provided for in Article 56(1)(aa) of Regulation (EC) No 726/2004.

2. The coordination group shall be composed of one representative per Member State appointed for a renewable period of 3 years. Member States may appoint an alternate for a renewable period of 3 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 national competent authorities. Each national competent authority shall monitor the level of expertise of the evaluations carried out and facilitate the activities of nominated coordination group members and experts.

Article 63 of Regulation (EC) No 726/2004 shall apply to the coordination group as regards transparency and the independence of its members.’;

(b) the following paragraphs are added:

‘4. The Executive Director of the Agency or his representative 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 national competent authorities, including the consultative bodies concerned with the marketing authorisation.

6. Save where otherwise provided for in this Directive, the Member States represented within the coordination group 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.’.

15. After Article 27 the following heading is inserted:

‘CHAPTER 4

Mutual recognition and decentralised procedure.

16. Article 31(1) is amended as follows:

(a) the first subparagraph is replaced by the following:

‘The Member States, the Commission, the applicant or the marketing authorisation holder shall, in specific cases where the interests of the Union are involved, refer the matter to the Committee for application of the procedure laid down in Articles 32, 33 and 34 before any decision is reached on an application for a marketing authorisation or on the suspension or revocation of a marketing authorisation, or on any other variation of the marketing authorisation which appears necessary.’;

(b) the following subparagraphs are inserted after the first subparagraph:

‘Where the referral results from the evaluation of data relating to pharmacovigilance of an authorised medicinal product, the matter shall be referred to the Pharmacovigilance Risk Assessment Committee and Article 107j(2) may be applied. The Pharmacovigilance Risk Assessment Committee shall issue a recommendation according to the procedure laid down in Article 32. The final recommendation shall be forwarded to the Committee for Medicinal Products for Human Use or to the coordination group, as appropriate, and the procedure laid down in Article 107k shall apply.

However, where urgent action is considered necessary, the procedure laid down in Articles 107i to 107k shall apply.’.

17. Article 36 is deleted.

18. Article 59 is amended as follows:

(a) paragraph 1 is amended as follows:

(i) point (e) is replaced by:

‘(e) a description of the adverse reactions which may occur under normal use of the medicinal product and, if necessary, the action to be taken in such a case.’;

(ii) the following subparagraphs are added:

‘For medicinal products included in the list referred to in Article 23 of Regulation (EC) No 726/2004, the following additional statement shall be included “This medicinal product is subject to additional monitoring”. This statement shall be preceded by the black symbol referred to in Article 23 of Regulation (EC) No 726/2004 and followed by an appropriate standardised explanatory sentence.

For all medicinal products, a standardised text shall be included, expressly asking patients to communicate any suspected adverse reaction to his/her doctor, pharmacist, healthcare professional or directly to the national spontaneous reporting system referred to in Article 107a(1), and specifying the different ways of reporting available (electronic reporting, postal address and/or others) in compliance with the second subparagraph of Article 107a(1).’;

(b) the following paragraph is added:

‘4. By 1 January 2013, the Commission shall present to the European Parliament and the Council an assessment report on current shortcomings in the summary of product characteristics and the package leaflet and how they could be improved in order to better meet the needs of patients and healthcare professionals. The Commission shall, if appropriate, and on the basis of the report, and consultation with appropriate stakeholders, present proposals in order to improve the readability, layout and content of these documents.’

19. Article 63(3) is replaced by the following:

‘3. When the medicinal product is not intended to be delivered directly to the patient, or where there are severe problems in respect of the availability of the medicinal product, the competent authorities may, subject to measures they consider necessary to safeguard human health, grant an exemption to the obligation that certain particulars should appear on the labelling and in the package leaflet. They may also grant a full or partial exemption to the obligation that the labelling and the package leaflet must be in the official language or languages of the Member State in which the medicinal product is placed on the market.’

20. Title IX is replaced by the following:

TITLE IX

PHARMACOVIGILANCE

CHAPTER 1

General provisions

Article 101

1. Member States shall operate a pharmacovigilance system for the fulfilment of their pharmacovigilance tasks and their participation in Union pharmacovigilance activities.

The pharmacovigilance system shall be used to collect information on the risks of medicinal products as regards patients' or public health. That information shall in particular refer to adverse reactions in human beings, arising from use of the medicinal product within the terms of the marketing authorisation as well as from use outside the terms of the marketing authorisation, and to adverse reactions associated with occupational exposure.

2. Member States shall, by means of the pharmacovigilance system referred to in paragraph 1, evaluate all information scientifically, consider options for risk minimisation and prevention and take regulatory action

concerning the marketing authorisation as necessary. They shall perform a regular audit of their pharmacovigilance system and report the results to the Commission on 21 September 2013 at the latest and then every 2 years thereafter.

3. Each Member State shall designate a competent authority for the performance of pharmacovigilance tasks.

4. The Commission may request Member States to participate, under the coordination of the Agency, in international harmonisation and standardisation of technical measures in relation to pharmacovigilance.

Article 102

The Member States shall:

(a) take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority; for these tasks, organisations representing consumers, patients and healthcare professionals may be involved as appropriate;

(b) facilitate patient reporting through the provision of alternative reporting formats in addition to web-based formats;

(c) take all appropriate measures to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports;

(d) ensure that the public is given important information on pharmacovigilance concerns relating to the use of a medicinal product in a timely manner through publication on the web-portal and through other means of publicly available information as necessary;

(e) ensure, through the methods for collecting information and where necessary through the follow-up of suspected adverse reaction reports, that all appropriate measures are taken to identify clearly any biological medicinal product prescribed, dispensed, or sold in their territory which is the subject of a suspected adverse reaction report, with due regard to the name of the medicinal product, in accordance with Article 1(20), and the batch number;

(f) take the necessary measures to ensure that a marketing authorisation holder who fails to discharge the obligations laid down in this Title is subject to effective, proportionate and dissuasive penalties.

For the purposes of point (a) and (e) of the first paragraph the Member States may impose specific obligations on doctors, pharmacists and other health-care professionals.

Article 103

A Member State may delegate any of the tasks entrusted to it under this Title to another Member State subject to a written agreement of the latter. Each Member State may represent no more than one other Member State.

The delegating Member State shall inform the Commission, the Agency and all other Member States of the delegation in writing. The delegating Member State and the Agency shall make that information public.

Article 104

1. The marketing authorisation holder shall operate a pharmacovigilance system for the fulfilment of his pharmacovigilance tasks equivalent to the relevant Member State's pharmacovigilance system provided for under Article 101(1).

2. The marketing authorisation holder shall by means of the pharmacovigilance system referred to in paragraph 1 evaluate all information scientifically, consider options for risk minimisation and prevention and take appropriate measures as necessary.

The marketing authorisation holder shall perform a regular audit of his pharmacovigilance system. He shall place a note concerning the main findings of the audit on the pharmacovigilance system master file and, based on the audit findings, ensure that an appropriate corrective action plan is prepared and implemented. Once the corrective actions have been fully implemented, the note may be removed.

3. As part of the pharmacovigilance system, the marketing authorisation holder shall:

- (a) have permanently and continuously at his disposal an appropriately qualified person responsible for pharmacovigilance;
- (b) maintain and make available on request a pharmacovigilance system master file;
- (c) operate a risk management system for each medicinal product;
- (d) monitor the outcome of risk minimisation measures which are contained in the risk management plan or which are laid down as conditions of the marketing authorisation pursuant to Articles 21a, 22 or 22a;
- (e) update the risk management system and monitor pharmacovigilance data to determine whether there are new risks or whether risks have changed or whether there are changes to the benefit-risk balance of medicinal products.

The qualified person referred to in point (a) of the first subparagraph shall reside and operate in the Union and shall be responsible for the establishment and maintenance of the pharmacovigilance system. The marketing authorisation holder shall submit the name and contact details of the qualified person to the competent authority and the Agency.

4. Notwithstanding the provisions of paragraph 3, national competent authorities may request the nomination of a contact person for pharmacovigilance issues at national level reporting to the qualified person responsible for pharmacovigilance activities.

Article 104a

1. Without prejudice to paragraphs 2, 3 and 4 of this Article, holders of marketing authorisations granted before 21 July 2012 shall, by way of derogation from Article 104(3)(c), not be required to operate a risk management system for each medicinal product.

2. The national competent authority may impose an obligation on a marketing authorisation holder to operate a risk management system, as referred to in Article 104(3)(c), if there are concerns about the risks affecting the risk-benefit balance of an authorised medicinal product. In that context, the national competent authority shall also oblige the marketing authorisation holder to submit a detailed description of the risk-management system which he intends to introduce for the medicinal product concerned.

The imposition of such obligations shall be duly justified, notified in writing and shall include the timeframe for submission of the detailed description of the risk-management system.

3. The national competent authority shall provide the marketing authorisation holder with an opportunity to present written observations in response to the imposition of the obligation within a time limit which it shall specify, if the marketing authorisation holder so requests within 30 days of receipt of the written notification of the obligation.

4. On the basis of the written observations submitted by the marketing authorisation holder, the national competent authority shall withdraw or confirm the obligation. Where the national competent authority confirms the obligation, the marketing authorisation shall be varied accordingly to include the measures to be taken as part of the risk management system as conditions of the marketing authorisation referred to in point (a) of Article 21a.

Article 105

The management of funds intended for activities connected with pharmacovigilance, the operation of communication networks and market surveillance shall be under the permanent control of the national competent authorities in order to guarantee their independence in the performance of those pharmacovigilance activities.

The first paragraph shall not preclude the national competent authorities from charging fees to marketing authorisation holders for performing those activities by the national competent authorities on the condition that their independence in the performance of those pharmacovigilance activities is strictly guaranteed.

*CHAPTER 2****Transparency and communications****Article 106*

Each Member State shall set up and maintain a national medicines web-portal which shall be linked to the European medicines web-portal established in accordance with Article 26 of Regulation (EC) No 726/2004. By means of the national medicines web-portals, the Member States shall make publicly available at least the following:

- (a) public assessment reports, together with a summary thereof;
- (b) summaries of product characteristics and package leaflets;
- (c) summaries of risk management plans for medicinal products authorised in accordance with this Directive;
- (d) the list of medicinal products referred to in Article 23 of Regulation (EC) No 726/2004;
- (e) information on the different ways of reporting suspected adverse reactions to medicinal products to national competent authorities by healthcare professionals and patients, including the web-based structured forms referred to in Article 25 of Regulation (EC) No 726/2004.

Article 106a

1. As soon as the marketing authorisation holder intends to make a public announcement relating to information on pharmacovigilance concerns in relation to the use of a medicinal product, and in any event at the same time or before the public announcement is made, he shall be required to inform the national competent authorities, the Agency and the Commission.

The marketing authorisation holder shall ensure that information to the public is presented objectively and is not misleading.

2. Unless urgent public announcements are required for the protection of public health, the Member States, the Agency and the Commission shall inform each other not less than 24 hours prior to a public announcement relating to information on pharmacovigilance concerns.

3. For active substances contained in medicinal products authorised in more than one Member State, the Agency shall be responsible for the coordination between national competent authorities of safety announcements and shall provide timetables for the information being made public.

Under the coordination of the Agency, the Member States shall make all reasonable efforts to agree on a common message in relation to the safety of the medicinal product concerned and the timetables for their distribution. The Pharmacovigilance Risk Assessment Committee shall, at the request of the Agency, provide advice on those safety announcements.

4. When the Agency or national competent authorities make public information referred to in paragraphs 2 and 3, any information of a personal or commercially confidential nature shall be deleted unless its public disclosure is necessary for the protection of public health.

*CHAPTER 3****Recording, reporting and assessment of pharmacovigilance data****Section 1****Recording and reporting of suspected adverse reactions****Article 107*

1. Marketing authorisation holders shall record all suspected adverse reactions in the Union or in third countries which are brought to their attention, whether reported spontaneously by patients or healthcare professionals, or occurring in the context of a post-authorisation study.

Marketing authorisation holders shall ensure that those reports are accessible at a single point within the Union.

By way of derogation from the first subparagraph, suspected adverse reactions occurring in the context of a clinical trial shall be recorded and reported in accordance with Directive 2001/20/EC.

2. Marketing authorisation holders shall not refuse to consider reports of suspected adverse reactions received electronically or by any other appropriate means from patients and healthcare professionals.

3. Marketing authorisation holders shall submit electronically to the database and data-processing network referred to in Article 24 of Regulation (EC) No 726/2004 (hereinafter referred to as the "Eudravigilance database") information on all serious suspected adverse reactions that occur in the Union and in third countries within 15 days following the day on which the marketing authorisation holder concerned gained knowledge of the event.

Marketing authorisation holders shall submit electronically to the Eudravigilance database information on all non-serious suspected adverse reactions that occur in the Union, within 90 days following the day on which the marketing authorisation holder concerned gained knowledge of the event.

For medicinal products containing the active substances referred to in the list of publications monitored by the Agency pursuant to Article 27 of Regulation (EC) No 726/2004, marketing authorisation holders shall not be required to report to the Eudravigilance database the suspected adverse reactions recorded in the listed medical literature, but they shall monitor all other medical literature and report any suspected adverse reactions.

4. Marketing authorisation holders shall establish procedures in order to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports. They shall also collect follow-up information on these reports and submit the updates to the Eudravigilance database.

5. Marketing authorisation holders shall collaborate with the Agency and the Member States in the detection of duplicates of suspected adverse reaction reports.

Article 107a

1. Each Member State shall record all suspected adverse reactions that occur in its territory which are brought to its attention from healthcare professionals and patients. Member States shall involve patients and healthcare professionals, as appropriate, in the follow-up of any reports they receive in order to comply with Article 102(c) and (e).

Member States shall ensure that reports of such reactions may be submitted by means of the national medicines web-portals or by other means.

2. For reports submitted by a marketing authorisation holder, Member States on whose territory the suspected adverse reaction occurred may involve the marketing authorisation holder in the follow-up of the reports.

3. Member States shall collaborate with the Agency and the marketing authorisation holders in the detection of duplicates of suspected adverse reaction reports.

4. Member States shall, within 15 days following the receipt of the reports of serious suspected adverse reactions referred to in paragraph 1, submit the reports electronically to the Eudravigilance database.

They shall, within 90 days from the receipt of reports referred to in paragraph 1, submit reports of non-serious suspected adverse reactions electronically to the Eudravigilance database.

Marketing authorisation holders shall access those reports through the Eudravigilance database.

5. Member States shall ensure that reports of suspected adverse reactions arising from an error associated with the use of a medicinal product that are brought to their attention are made available to the Eudravigilance database and to any authorities, bodies, organisations and/or institutions, responsible for patient safety within that Member State. They shall also ensure that the authorities responsible for medicinal products within that Member State are informed of any suspected adverse reactions brought to the attention of any other authority within that Member State. These reports shall be appropriately identified in the forms referred to in Article 25 of Regulation (EC) No 726/2004.

6. Unless there are justifiable grounds resulting from pharmacovigilance activities, individual Member States shall not impose any additional obligations on marketing authorisation holders for the reporting of suspected adverse reactions.

Section 2

Periodic safety update reports

Article 107b

1. Marketing authorisation holders shall submit to the Agency periodic safety update reports containing:

- (a) summaries of data relevant to the benefits and risks of the medicinal product, including results of all studies with a consideration of their potential impact on the marketing authorisation;
- (b) a scientific evaluation of the risk-benefit balance of the medicinal product;
- (c) all data relating to the volume of sales of the medicinal product and any data in possession of the marketing authorisation holder relating to the volume of prescriptions, including an estimate of the population exposed to the medicinal product.

The evaluation referred to in point (b) shall be based on all available data, including data from clinical trials in unauthorised indications and populations.

The periodic safety update reports shall be submitted electronically.

2. The Agency shall make available the reports referred to in paragraph 1 to the national competent authorities, the members of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use and the coordination group by means of the repository referred to in Article 25a of Regulation (EC) No 726/2004.

3. By way of derogation from paragraph 1 of this Article, the holders of marketing authorisations for medicinal products referred to in Article 10(1), or Article 10a, and the holders of registrations for medicinal products referred to in Articles 14 or 16a, shall submit periodic safety update reports for such medicinal products in the following cases:

- (a) where such obligation has been laid down as a condition in the marketing authorisation in accordance with Article 21a or Article 22; or
- (b) when requested by a competent authority on the basis of concerns relating to pharmacovigilance data or due to the lack of periodic safety update reports relating to an active substance after the marketing authorisation has been granted. The assessment reports of the requested periodic safety update reports shall be communicated to the Pharmacovigilance Risk Assessment Committee, which shall consider whether there is a need for a single assessment report for all marketing authorisations for medicinal products containing the same active substance and inform the coordination group or the Committee for Medicinal Products for Human Use accordingly, in order to apply the procedures laid down in Article 107c(4) and Article 107e.

Article 107c

1. The frequency with which the periodic safety update reports are to be submitted shall be specified in the marketing authorisation.

The dates of submission according to the specified frequency shall be calculated from the date of the authorisation.

2. Holders of marketing authorisations which were granted before 21 July 2012, and for which the

frequency and dates of submission of the periodic safety update reports are not laid down as a condition to the marketing authorisation, shall submit the periodic safety update reports in accordance with the second subparagraph of this paragraph until another frequency or other dates of submission of the reports are laid down in the marketing authorisation or determined in accordance with paragraphs 4, 5 or 6.

Periodic safety update reports shall be submitted to the competent authorities immediately upon request or in accordance with the following:

- (a) where a medicinal product has not yet been placed on the market, at least every 6 months following authorisation and until the placing on the market;
- (b) where a medicinal product has been placed on the market, at least every 6 months during the first 2 years following the initial placing on the market, once a year for the following 2 years and at three-yearly intervals thereafter.

3. Paragraph 2 shall also apply to medicinal products which are authorised only in one Member State and for which paragraph 4 does not apply.

4. Where medicinal products that are subject to different marketing authorisations contain the same active substance or the same combination of active substances, the frequency and dates of submission of the periodic safety update reports resulting from the application of paragraphs 1 and 2 may be amended and harmonised to enable a single assessment to be made in the context of a periodic safety update report work-sharing procedure and to set a Union reference date from which the submission dates are calculated.

This harmonised frequency for the submission of the reports and the Union reference date may be determined, after consultation of the Pharmacovigilance Risk Assessment Committee, by one of the following:

- (a) the Committee for Medicinal Products for Human Use, where at least one of the marketing authorisations for the medicinal products containing the active substance concerned has been granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004;
- (b) the coordination group, in other cases than those referred to in point (a).

The harmonised frequency for the submission of the reports determined pursuant to the first and second subparagraphs shall be made public by the Agency. Marketing authorisation holders shall submit an application for a variation of the marketing authorisation accordingly.

5. For the purposes of paragraph 4, the Union reference date for medicinal products containing the same active substance or the same combination of active substances shall be one of the following:

- (a) the date of the first marketing authorisation in the Union of a medicinal product containing that active substance or that combination active substances;
- (b) if the date referred to in point (a) cannot be ascertained, the earliest of the known dates of the marketing authorisations for a medicinal product containing that active substance or that combination of active substances.

6. Marketing authorisation holders shall be allowed to submit requests to the Committee for Medicinal Products for Human Use or the coordination group, as appropriate, to determine Union reference dates or to change the frequency of submission periodic safety update reports on one of the following grounds:

- (a) for reasons relating to public health;
- (b) in order to avoid a duplication of the assessment;
- (c) in order to achieve international harmonisation.

Such requests shall be submitted in writing and shall be duly justified. The Committee for Medicinal Products for Human Use or the coordination group shall, following the consultation with the Pharmacovigilance Risk Assessment Committee, shall either approve or deny such requests. Any change in the dates or the frequency of submission of periodic safety update reports shall be made public by the Agency. The marketing authorisation holders shall accordingly submit an application for a variation of the marketing authorisation.

7. The Agency shall make public a list of Union reference dates and frequency of submission of periodic safety update reports by means of the European medicines web-portal.

Any change to the dates of submission and frequency of periodic safety update reports specified in the marketing

authorisation as a result of the application of paragraphs 4, 5 and 6 shall take effect 6 months after the date of such publication.

Article 107d

The national competent authorities shall assess periodic safety update reports to determine whether there are new risks or whether risks have changed or whether there are changes to the risk-benefit balance of medicinal products.

Article 107e

1. A single assessment of periodic safety update reports shall be performed for medicinal products authorised in more than one Member State and, in the cases of paragraphs 4 to 6 of Article 107c, for all medicinal products containing the same active substance or the same combination of active substances and for which a Union reference date and frequency of periodic safety update reports has been established.

The single assessment shall be conducted by either of the following:

- (a) a Member State appointed by the coordination group where none of the marketing authorisations concerned has been granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004; or
- (b) a rapporteur appointed by the Pharmacovigilance Risk Assessment Committee, where at least one of the marketing authorisations concerned has been granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004.

When selecting the Member State in accordance with point (a) of the second subparagraph, the coordination group shall take into account whether any Member State is acting as a reference Member State, in accordance with Article 28(1).

2. The Member State or rapporteur, as appropriate, shall prepare an assessment report within 60 days of receipt of the periodic safety update report and send it to the Agency and to the Member States concerned. The Agency shall send the report to the marketing authorisation holder.

Within 30 days of receipt of the assessment report, the Member States and the marketing authorisation holder may submit comments to the Agency and to the rapporteur or Member State.

3. Following the receipt of the comments referred to in paragraph 2, the rapporteur or Member State shall within 15 days update the assessment report taking into account any comments submitted, and forward it to the Pharmacovigilance Risk Assessment Committee. The Pharmacovigilance Risk Assessment Committee shall adopt the assessment report with or without further changes at its next meeting and issue a recommendation. The recommendation shall mention the divergent positions with the grounds on which they are based. The Agency shall include the adopted assessment report and the recommendation in the repository set up under Article 25a of Regulation (EC) No 726/2004 and forward both to the marketing authorisation holder.

Article 107f

Following the assessment of periodic safety update reports, the national competent authorities shall consider whether any action concerning the marketing authorisation for the medicinal product concerned is necessary.

They shall maintain, vary, suspend or revoke the marketing authorisation as appropriate.

Article 107g

1. In the case of a single assessment of periodic safety update reports that recommends any action concerning more than one marketing authorisation in accordance with Article 107e(1) which does not include any marketing authorisation granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004, the coordination group shall, within 30 days of receipt of the report of the Pharmacovigilance Risk Assessment Committee, consider the report and reach a position on the maintenance, variation, suspension or revocation of the marketing authorisations concerned, including a timetable for the implementation of the agreed position.

2. If, within the coordination group, the Member States represented reach agreement on the action to be taken by consensus, the chairman shall record the agreement and send it to the marketing authorisation holder and the Member States. The Member States shall adopt necessary measures to maintain, vary, suspend or revoke the marketing authorisations concerned in accordance with the timetable for implementation determined in the agreement.

In the event of a variation, the marketing authorisation holder shall submit to the national competent authorities an appropriate application for a modification, including an updated summary of product characteristics and package leaflet within the determined timetable for implementation.

If an agreement by consensus cannot be reached, the position of the majority of the Member States represented

within the coordination group shall be forwarded to the Commission which shall apply the procedure laid down in Articles 33 and 34.

Where the agreement reached by the Member States represented within the coordination group or the position of the majority of Member States differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the coordination group shall attach to the agreement or the majority position a detailed explanation of the scientific grounds for the differences together with the recommendation.

3. In the case of a single assessment of periodic safety update reports that recommends any action concerning more than one marketing authorisation in accordance with Article 107e(1) which includes at least one marketing authorisation granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004, the Committee for Medicinal Products for Human Use shall, within 30 days of receipt of the report of the Pharmacovigilance Risk Assessment Committee, consider the report and adopt an opinion on the maintenance, variation, suspension or revocation of the marketing authorisations concerned, including a timetable for the implementation of the opinion.

Where this opinion of the Committee for Medicinal Products for Human Use differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences together with the recommendation.

4. On the basis of the opinion of the Committee for Medicinal Products for Human Use referred to in paragraph 3, the Commission shall:

- (a) adopt a decision addressed to the Member States concerning the measures to be taken in respect of marketing authorisations granted by the Member States and concerned by the procedure provided for in this section; and
- (b) where the opinion states that regulatory action concerning the marketing authorisation is necessary, adopt a decision to vary, suspend or revoke the marketing authorisations granted in accordance with the centralised procedure provided for in Regulation (EC) No 726/2004 and concerned by the procedure provided for in this section.

Articles 33 and 34 of this Directive shall apply to the adoption of the decision referred to in point (a) of the first subparagraph of this paragraph and to its implementation by the Member States.

Article 10 of Regulation (EC) No 726/2004 shall apply to the decision referred to in point (b) of the first subparagraph of this paragraph. Where the Commission adopts such decision, it may also adopt a decision addressed to the Member States pursuant to Article 127a of this Directive.

Section 3

Signal detection

Article 107h

1. Regarding medicinal products authorised in accordance with this Directive, national competent authorities in collaboration with the Agency, shall take the following measures:

- (a) monitor the outcome of risk minimisation measures contained in risk management plans and of the conditions referred to in Articles 21a, 22 or 22a;
- (b) assess updates to the risk management system;
- (c) monitor the data in the Eudravigilance database to determine whether there are new risks or whether risks have changed and whether those risks impact on the risk-benefit balance.

2. The Pharmacovigilance Risk Assessment Committee shall perform the initial analysis and prioritisation of signals of new risks or risks that have changed or changes to the risk-benefit balance. Where it considers that follow-up action may be necessary, the assessment of those signals and agreement on any subsequent action concerning the marketing authorisation shall be conducted in a timescale commensurate with the extent and seriousness of the issue.

3. The Agency and national competent authorities and the marketing authorisation holder shall inform each other in the event of new risks or risks that have changed or changes to the risk-benefit balance being detected.

Member States shall ensure that marketing authorisation holders inform the Agency and national competent authorities in the event of new risks or risks that have changed or when changes to the risk-benefit balance have been detected.

Section 4

Urgent Union procedure

Article 107i

1. A Member State or the Commission, as appropriate, shall initiate the procedure provided for in this section, by

informing the other Member States, the Agency and the Commission when urgent action is considered necessary, as a result of the evaluation of data resulting from pharmacovigilance activities, in any of the following cases:

- (a) it considers suspending or revoking a marketing authorisation;
- (b) it considers prohibiting the supply of a medicinal product;
- (c) it considers refusing the renewal of a marketing authorisation;
- (d) it is informed by the marketing authorisation holder that, on the basis of safety concerns, he has interrupted the placing on the market of a medicinal product or has taken action to have a marketing authorisation withdrawn, or that he intends to do so;
- (e) it considers that a new contraindication, a reduction in the recommended dose, or a restriction to the indications is necessary.

The Agency shall verify whether the safety concern relates to medicinal products other than the one covered by the information, or whether it is common to all products belonging to the same range or therapeutic class.

Where the medicinal product involved is authorised in more than one Member State, the Agency shall without undue delay inform the initiator of the procedure of the outcome of this verification, and the procedures laid down in Articles 107j and 107k shall apply. Otherwise, the safety concern shall be addressed by the Member State concerned. The Agency or the Member State, as applicable, shall make information that the procedure has been initiated available to marketing authorisation holders.

2. Without prejudice to the provisions of paragraph 1 of this Article, and Articles 107j and 107k, a Member State may, where urgent action is necessary to protect public health, suspend the marketing authorisation and prohibit the use of the medicinal product concerned on its territory until a definitive decision is adopted. It shall inform the Commission, the Agency and the other Member States no later than the following working day of the reasons for its action.

3. At any stage of the procedure laid down in Articles 107j to 107k, the Commission may request Member States in which the medicinal product is authorised to take temporary measures immediately.

Where the scope of the procedure, as determined in accordance with paragraph 1, includes medicinal products authorised in accordance with Regulation (EC) No 726/2004, the Commission may, at any stage of the procedure initiated under this section, take temporary measures immediately in relation to those marketing authorisations.

4. The information referred to in this Article may relate to individual medicinal products or to a range of medicinal products or a therapeutic class.

If the Agency identifies that the safety concern relates to more medicinal products than those which are covered by the information or that it is common to all medicinal products belonging to the same range or therapeutic class, it shall extend the scope of the procedure accordingly.

Where the scope of the procedure initiated under this Article concerns a range of medicinal products or therapeutic class, medicinal products authorised in accordance with Regulation (EC) No 726/2004 which belong to that range or class shall also be included in the procedure.

5. At the time of the information referred to in paragraph 1, the Member State shall make available to the Agency all relevant scientific information that it has at its disposal and any assessment by the Member State.

Article 107j

1. Following receipt of the information referred to in Article 107i(1), the Agency shall publicly announce the initiation of the procedure by means of the European medicines web-portal. In parallel, Member States may publicly announce the initiation on their national medicines web-portals.

The announcement shall specify the matter submitted to the Agency in accordance with Article 107i, and the medicinal products and, where applicable, the active substances concerned. It shall contain information on the right of the marketing authorisation holders, healthcare professionals and the public to submit to the Agency information relevant to the procedure and it shall state how such information may be submitted.

2. The Pharmacovigilance Risk Assessment Committee shall assess the matter which has been submitted to the Agency in accordance with Article 107i. The rapporteur shall closely collaborate with the rapporteur appointed by the Committee for Medicinal Products for Human Use and the Reference Member State for the medicinal products concerned.

For the purposes of that assessment, the marketing authorisation holder may submit comments in writing.

Where the urgency of the matter permits, the Pharmacovigilance Risk Assessment Committee may hold public hearings, where it considers that this is appropriate on justified grounds particularly with regard to the extent and seriousness of the safety concern. The hearings shall be held in accordance with the modalities specified by the Agency and shall be announced by means of the European medicines web-portal. The announcement shall specify the modalities of participation.

In the public hearing, due regard shall be given to the therapeutic effect of the medicinal product.

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 78 of Regulation (EC) No 726/2004.

Where a marketing authorisation holder or another person intending to submit information has confidential data relevant to the subject matter of the procedure, he may request permission to present that data to the Pharmacovigilance Risk Assessment Committee in a non-public hearing.

3. Within 60 days of the information being submitted, the Pharmacovigilance Risk Assessment Committee shall make a recommendation, stating the reasons on which it is based, having due regard to the therapeutic effect of the medicinal product. The recommendation shall mention the divergent positions and the grounds on which they are based. In the case of urgency, and on the basis of a proposal by its chairman, the Pharmacovigilance Risk Assessment Committee may agree to a shorter deadline. The recommendation shall include any or a combination of the following conclusions:

- (a) no further evaluation or action is required at Union level;
- (b) the marketing authorisation holder should conduct further evaluation of data together with the follow-up of the results of that evaluation;
- (c) the marketing authorisation holder should sponsor a post-authorisation safety study together with the follow up evaluation of the results of that study;
- (d) the Member States or marketing authorisation holder should implement risk minimisation measures;

(e) the marketing authorisation should be suspended, revoked or not renewed;

(f) the marketing authorisation should be varied.

For the purposes of point (d) of the first subparagraph, the recommendation shall specify the risk minimisation measures recommended and any conditions or restrictions to which the marketing authorisation should be made subject.

Where, in the cases referred to in point (f) of the first subparagraph, it is recommended to change or add information in the summary of product characteristics or the labelling or package leaflet, the recommendation shall suggest the wording of such changed or added information and where in the summary of the product characteristics, labelling or package leaflet such wording should be placed.

Article 107k

1. Where the scope of the procedure, as determined in accordance with Article 107i(4), does not include any marketing authorisation granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004, the coordination group shall, within 30 days of receipt of the recommendation of the Pharmacovigilance Risk Assessment Committee, consider the recommendation and reach a position on the maintenance, variation, suspension, revocation or refusal of the renewal of the marketing authorisation concerned, including a timetable for the implementation of the agreed position. Where an urgent adoption of the position is necessary, and on the basis of a proposal by its chairman, the coordination group may agree to a shorter deadline.

2. If, within the coordination group, the Member States represented reach agreement on the action to be taken by consensus, the chairman shall record the agreement and send it to the marketing authorisation holder and the Member States. The Member States shall adopt necessary measures to maintain, vary, suspend, revoke or refuse renewal of the marketing authorisation concerned in accordance with the implementation timetable determined in the agreement.

In the event that a variation is agreed upon, the marketing authorisation holder shall submit to the national competent authorities an appropriate application for a variation, including an updated summary of product characteristics and package leaflet within the determined timetable for implementation.

If an agreement by consensus cannot be reached, the position of the majority of the Member States represented within the coordination group shall be forwarded to the Commission which shall apply the procedure laid down in

Articles 33 and 34. However, by way of derogation from Article 34(1), the procedure referred to in Article 121(2) shall apply.

Where the agreement reached by the Member States represented within the coordination group or the position of the majority of the Member States represented within the coordination group differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the coordination group shall attach to the agreement or majority position a detailed explanation of the scientific grounds for the differences together with the recommendation.

3. Where the scope of the procedure, as determined in accordance with Article 107i(4), includes at least one marketing authorisation granted in accordance with the centralised procedure provided for in Chapter 1 of Title II of Regulation (EC) No 726/2004, the Committee for Medicinal Products for Human Use shall, within 30 days of receipt of the recommendation of the Pharmacovigilance Risk Assessment Committee, consider the recommendation and adopt an opinion on the maintenance, variation, suspension, revocation or refusal of the renewal of the marketing authorisations concerned. Where an urgent adoption of the opinion is necessary, and on the basis of a proposal by its chairman, the Committee for Medicinal Products for Human Use may agree to a shorter deadline.

Where the opinion of the Committee for Medicinal Products for Human Use differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the Committee for Medicinal Products for Human Use shall attach to its opinion a detailed explanation of the scientific grounds for the differences together with the recommendation.

4. On the basis of the opinion of the Committee for Medicinal Products for Human Use referred to in paragraph 3, the Commission shall:

- (a) adopt a decision addressed to the Member States concerning the measures to be taken in respect of marketing authorisations that are granted by the Member States and that are subject to the procedure provided for in this section; and
- (b) where the opinion is that regulatory action is necessary, adopt a decision to vary, suspend, revoke or refuse renewal of the marketing authorisations granted in accordance with Regulation (EC) No 726/2004 and subject to the procedure provided for in this section.

Articles 33 and 34 of this Directive shall apply to the adoption of the decision referred to in point (a) of the first subparagraph of this paragraph and to its implementation by the Member States. However, by way of derogation from Article 34(1) of this Directive, the procedure referred to in Article 121(2) thereof shall apply.

Article 10 of Regulation (EC) No 726/2004 shall apply to the decision referred to in point (b) of the first subparagraph of this paragraph. However, by way of derogation from Article 10(2) of that Regulation, the procedure referred to in Article 87(2) thereof shall apply. Where the Commission adopts such decision, it may also adopt a decision addressed to the Member States pursuant to Article 127a of this Directive.

Section 5

Publication of assessments

Article 107l

The Agency shall make public the final assessment conclusions, recommendations, opinions and decisions referred to in Articles 107b to 107k by means of the European medicines web-portal.

CHAPTER 4

Supervision of post-authorisation safety studies

Article 107m

1. This Chapter applies to non-interventional post-authorisation safety studies which are initiated, managed or financed by the marketing authorisation holder voluntarily or pursuant to obligations imposed in accordance with Articles 21a or 22a, and which involve the collection of safety data from patients or healthcare professionals.

2. This Chapter is without prejudice to national and Union requirements for ensuring the well-being and rights of participants in non-interventional post-authorisation safety studies.

3. The studies shall not be performed where the act of conducting the study promotes the use of a medicinal product.

4. Payments to healthcare professionals for participating in non-interventional post-authorisation safety studies shall be restricted to the compensation for time and expenses incurred.

5. The national competent authority may require the marketing authorisation holder to submit the protocol and the progress reports to the competent authorities of the Member States in which the study is conducted.

6. The marketing authorisation holder shall send the final report to the competent authorities of the Member States in which the study was conducted within 12 months of the end of data collection.

7. While a study is being conducted, the marketing authorisation holder shall monitor the data generated and consider its implications for the risk-benefit balance of the medicinal product concerned.

Any new information which might influence the evaluation of the risk-benefit balance of the medicinal product shall be communicated to the competent authorities of the Member State in which the medicinal product has been authorised in accordance with Article 23.

The obligation laid down in the second subparagraph is without prejudice to the information on the results of studies that the marketing authorisation holder shall make available by means of the periodic safety update reports as laid down in Article 107b.

8. Articles 107n to 107q shall apply exclusively to studies referred to in paragraph 1 which are conducted pursuant to an obligation imposed in accordance with Articles 21a or 22a.

Article 107n

1. Before a study is conducted, the marketing authorisation holder shall submit a draft protocol to the Pharmacovigilance Risk Assessment Committee, except for studies to be conducted in only one Member State that requests the study according to Article 22a. For such studies, the marketing authorisation holder shall submit a draft protocol to the national competent authority of the Member State in which the study is conducted.

2. Within 60 days of the submission of the draft protocol the national competent authority or the Pharmacovigilance Risk Assessment Committee, as appropriate, shall issue:

- (a) a letter endorsing the draft protocol;
- (b) a letter of objection, which shall set out in detail the grounds for the objection, in any of the following cases:
 - (i) it considers that the conduct of the study promotes the use of a medicinal product;
 - (ii) it considers that the design of the study does not fulfil the study objectives; or
- (c) a letter notifying the marketing authorisation holder that the study is a clinical trial falling under the scope of Directive 2001/20/EC.

3. The study may commence only when the written endorsement from the national competent authority or the Pharmacovigilance Risk Assessment Committee, as appropriate, has been issued.

Where a letter of endorsement as referred to in paragraph 2(a) has been issued, the marketing authorisation holder shall forward the protocol to the competent authorities of the Member States in which the study is to be conducted and may thereafter commence the study according to the endorsed protocol.

Article 107o

After a study has been commenced, any substantial amendments to the protocol shall be submitted, before their implementation, to the national competent authority or to the Pharmacovigilance Risk Assessment Committee, as appropriate. The national competent authority or the Pharmacovigilance Risk Assessment Committee, as appropriate, shall assess the amendments and inform the marketing authorisation holder of its endorsement or objection. Where applicable, the marketing authorisation holder shall inform Member States in which the study is conducted.

Article 107p

1. Upon completion of the study, a final study report shall be submitted to the national competent authority or the Pharmacovigilance Risk Assessment Committee within 12 months of the end of data collection unless a written waiver has been granted by the national competent authority or the Pharmacovigilance Risk Assessment Committee, as appropriate.

2. The marketing authorisation holder shall evaluate whether the results of the study have an impact on the marketing authorisation and shall, if necessary, submit to the national competent authorities an application to vary the marketing authorisation.

3. Together with the final study report, the marketing authorisation holder shall electronically submit an abstract of the study results to the national competent authority or the Pharmacovigilance Risk Assessment Committee.

Article 107q

1. Based on the results of the study and after consultation of the marketing authorisation holder, the Pharmacovigilance Risk Assessment Committee may make recommendations concerning the marketing authorisation, stating the reasons on which they are based. The recommendations shall mention the divergent positions and the grounds on which they are based.

2. When recommendations for the variation, suspension or revocation of the marketing authorisation are made for a medicinal product authorised by the Member States pursuant to this Directive, the Member States represented within the coordination group shall agree a position on the matter taking into account the recommendation referred to

in paragraph 1 and including a timetable for the implementation of the agreed position.

If, within the coordination group, the Member States represented reach agreement on the action to be taken by consensus, the chairman shall record the agreement and send it to the marketing authorisation holder and the Member States. The Member States shall adopt necessary measures to vary, suspend or revoke the marketing authorisation concerned in accordance with the implementation timetable determined in the agreement.

In the event that a variation is agreed upon, the marketing authorisation holder shall submit to the national competent authorities an appropriate application for a variation, including an updated summary of product characteristics and package leaflet within the determined timetable for implementation.

The agreement shall be made public on the European medicines web-portal established in accordance with Article 26 of Regulation (EC) No 726/2004.

If an agreement by consensus cannot be reached, the position of the majority of the Member States represented within the coordination group shall be forwarded to the Commission, which shall apply the procedure laid down in Articles 33 and 34.

Where the agreement reached by the Member States represented within the coordination group or the position of the majority of Member States differs from the recommendation of the Pharmacovigilance Risk Assessment Committee, the coordination group shall attach to the agreement or majority position a detailed explanation of the scientific grounds for the differences together with the recommendation.

CHAPTER 5

Implementation, Delegation and Guidance

Article 108

In order to harmonise the performance of the pharmacovigilance activities provided for in this Directive, the Commission shall adopt implementing measures in the following areas for which pharmacovigilance activities are provided for in Article 8(3), and in Articles 101, 104, 104a, 107, 107a, 107b, 107h, 107n and 107p:

- (a) the content and maintenance of the pharmacovigilance system master file kept by the marketing authorisation holder;
- (b) the minimum requirements for the quality system for the performance of pharmacovigilance activities by the national competent authorities and the marketing authorisation holder;

- (c) the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities;
- (d) the minimum requirements for the monitoring of data in the Eudravigilance database to determine whether there are new risks or whether risks have changed;
- (e) the format and content of the electronic transmission of suspected adverse reactions by Member States and the marketing authorisation holder;
- (f) the format and content of electronic periodic safety update reports and risk management plans;
- (g) the format of protocols, abstracts and final study reports for the post-authorisation safety studies.

Those measures shall take account of the work on international harmonisation carried out in the area of pharmacovigilance and shall, where necessary, be revised to take account of technical and scientific progress. Those measures shall be adopted in accordance with the regulatory procedure referred to in Article 121(2).

Article 108a

In order to facilitate the performance of pharmacovigilance activities within the Union, the Agency shall, in cooperation with competent authorities and other interested parties, draw up:

- (a) guidance on good pharmacovigilance practices for both competent authorities and marketing authorisation holders;
- (b) scientific guidance on post-authorisation efficacy studies.

Article 108b

The Commission shall make public a report on the performance of pharmacovigilance tasks by the Member States on 21 July 2015 at the latest and then every 3 years thereafter.

21. Article 111 is amended as follows:

- (a) paragraph 1 is amended as follows:

- (i) the first subparagraph is replaced by the following:

The competent authority of the Member State concerned shall, in cooperation with the Agency, ensure that the legal requirements governing

medicinal products are complied with, by means of inspections, if necessary unannounced, and, where appropriate, by asking an Official Medicines Control Laboratory or a laboratory designated for that purpose to carry out tests on samples. This cooperation shall consist in sharing information with the Agency on both inspections that are planned and that have been conducted. Member States and the Agency shall cooperate in the coordination of inspections in third countries;

- (ii) in the fifth subparagraph, point (d) is replaced by the following:

‘(d) inspect the premises, records, documents and pharmacovigilance system master file of the marketing authorisation holder or any firms employed by the marketing authorisation holder to perform the activities described in Title IX.’;

- (b) paragraph 3 is replaced by the following:

‘3. After every inspection referred to in paragraph 1, the competent authority shall report on whether the inspected entity complies with the principles and guidelines of good manufacturing practice and good distribution practices referred to in Articles 47 and 84, or whether the marketing authorisation holder complies with the requirements laid down in Title IX.

The competent authority which carried out the inspection shall communicate the content of those reports to the inspected entity.

Before adopting the report, the competent authority shall give the inspected entity concerned the opportunity to submit comments.’;

- (c) paragraph 7 is replaced by the following:

‘7. If the outcome of the inspection as referred to in points (a), (b) and (c) of paragraph 1 or the outcome of an inspection of a distributor of medicinal products or active substances or a manufacturer of excipients used as starting materials is that the inspected entity does not comply with the legal requirements and/or the principles and guidelines of good manufacturing practice or good distribution practices as provided for by Union law, the information shall be entered in the Union database as provided for in paragraph 6.’;

(d) the following paragraph is added:

‘8. If the outcome of the inspection referred to in paragraph 1(d) is that the marketing authorisation holder does not comply with the pharmacovigilance system as described in the pharmacovigilance system master file and with Title IX, the competent authority of the Member State concerned shall bring the deficiencies to the attention of the marketing authorisation holder and give him the opportunity to submit comments.

In such case the Member State concerned shall inform the other Member States, the Agency and the Commission.

Where appropriate, the Member State concerned shall take the necessary measures to ensure that a marketing authorisation holder is subject to effective, proportionate and dissuasive penalties.’

22. Article 116 is replaced by the following:

‘Article 116

The competent authorities shall suspend, revoke or vary a marketing authorisation if the view is taken that the medicinal product is harmful or that it lacks therapeutic efficacy, or that the risk-benefit balance is not favourable, or that its qualitative and quantitative composition is not as declared. Therapeutic efficacy shall be considered to be lacking when it is concluded that therapeutic results cannot be obtained from the medicinal product.

A marketing authorisation may also be suspended, revoked or varied where the particulars supporting the application as provided for in Articles 8, 10 or 11 are incorrect or have not been amended in accordance with Article 23, or where any conditions referred to in Articles 21a, 22 or 22a have not been fulfilled or where the controls referred to in Article 112 have not been carried out.’

23. Article 117 is amended as follows:

(a) paragraph 1 is amended as follows:

(i) point (a) is replaced by the following:

‘(a) the medicinal product is harmful; or’;

(ii) point (c) is replaced by the following:

‘(c) the risk-benefit balance is not favourable; or’;

(b) the following paragraph is added:

‘3. The competent authority may, for a medicinal product for which the supply has been prohibited or which has been withdrawn from the market in accordance with paragraphs 1 and 2, in exceptional circumstances during a transitional period allow the supply of the medicinal product to patients who are already being treated with the medicinal product.’

24. The following Articles are inserted:

‘Article 121a

1. The power to adopt the delegated acts referred to in Article 22b shall be conferred on the Commission for a period of 5 years from 20 January 2011. The Commission shall draw up a report in respect of the delegated powers not later than 6 months before the end of the 5 year period. The delegation of powers shall be automatically extended for periods of an identical duration, unless the European Parliament or the Council revokes it in accordance with Article 121b.

2. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.

3. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in Articles 121b and 121c.

Article 121b

1. The delegation of powers referred to in Article 22b may be revoked at any time by the European Parliament or by the Council.

2. The institution which has commenced an internal procedure for deciding whether to revoke the delegation of powers shall endeavour to inform the other institution and the Commission within a reasonable time before the final decision is taken, indicating the delegated powers which could be subject to revocation and possible reasons for a revocation.

3. The decision of revocation shall put an end to the delegation of the powers specified in that decision. It shall take effect immediately or at a later date specified therein. It shall not affect the validity of the delegated acts already in force. It shall be published in the *Official Journal of the European Union*.

Article 121c

1. The European Parliament or the Council may object to a delegated act within a period of 2 months from the date of notification.

At the initiative of the European Parliament or the Council that period shall be extended by 2 months.

2. If, on expiry of the period referred to in paragraph 1, neither the European Parliament nor the Council has objected to the delegated act, it shall be published in the *Official Journal of the European Union* and shall enter into force on the date stated therein.

The delegated act may be published in the *Official Journal of the European Union* and enter into force before the expiry of that period if the European Parliament and the Council have both informed the Commission of their intention not to raise objections.

3. If either the European Parliament or the Council objects to the delegated act within the period referred to in paragraph 1, it shall not enter into force. The institution which objects shall state the reasons for objecting to the delegated act.’

25. Article 122(2) is replaced by the following:

‘2. Upon reasoned request, Member States shall send electronically the reports referred to in Article 111(3) to the competent authorities of another Member State or to the Agency.’

26. Article 123(4) is replaced by the following:

‘4. The Agency shall make public annually a list of the medicinal products for which marketing authorisations have been refused, revoked or suspended, whose supply has been prohibited or which have been withdrawn from the market.’

27. In Article 126a, paragraphs 2 and 3 are replaced by the following:

‘2. When a Member State avails itself of this possibility, it shall adopt the necessary measures in order to ensure that the requirements of this Directive are complied with, in particular those referred to in Titles V, VI, VIII, IX and XI. Member States may decide that Article 63(1) and (2) shall not apply to medicinal products authorised under paragraph 1.

3. Before granting such a marketing authorisation, a Member State:

- (a) shall notify the marketing authorisation holder, in the Member State in which the medicinal product concerned is authorised, of the proposal to grant a marketing authorisation under this Article in respect of the medicinal product concerned.
- (b) may request the competent authority in that Member State to submit copies of the assessment report referred

to in Article 21(4) and of the marketing authorisation in force in respect of the medicinal product concerned. If so requested, the competent authority in that Member State shall supply, within 30 days of receipt of the request, a copy of the assessment report and the marketing authorisation in respect of the medicinal product concerned.’

28. Article 127a is replaced by the following:

‘Article 127a

When a medicinal product is to be authorised in accordance with Regulation (EC) No 726/2004, and the Committee for Medicinal Products for Human Use in its opinion refers to recommended conditions or restrictions as provided for in points (c), (ca), (cb) or (cc) of Article 9(4) thereof, the Commission may adopt a decision addressed to the Member States, in accordance with Articles 33 and 34 of this Directive, for the implementation of those conditions or restrictions.’

Article 2

Transitional provisions

1. With regard to the obligation on the part of the marketing authorisation holder to maintain and make available on request a pharmacovigilance system master file in respect of one or more medicinal products provided for in Article 104(3)(b) of Directive 2001/83/EC as amended by this Directive, the Member States shall ensure that that obligation applies to marketing authorisations granted before 21 July 2011 as from either:

a) the date on which those marketing authorisations are renewed; or

b) the expiry of a period of 3 years starting from 21 July 2011,

whichever is earlier.

2. The Member States shall ensure that the procedure provided for in Articles 107m to 107q of Directive 2001/83/EC as amended by this Directive applies only to studies which have commenced after 21 July 2011.

3. With regard to the obligation on the part of the marketing authorisation holder to submit information on suspected adverse reactions electronically to the Eudravigilance database, provided for in Article 107(3) of Directive 2001/83/EC as amended by this Directive, the Member States shall ensure that this obligation applies as from 6 months after the functionalities of the database are established and have been announced by the Agency.

4. Until the Agency can ensure the functionalities of the Eudravigilance database as specified in Article 24 of Regulation (EC) No 726/2004 as amended by Regulation (EU) No 1235/2010 ⁽¹⁾ of the European Parliament and of the Council, marketing authorisation holders shall report, within 15 days of the day on which the holder concerned gained knowledge of the event, all serious suspected adverse reactions that occur in the Union, to the competent authority of the Member State on whose territory the incident occurred and shall report all serious suspected adverse reactions that occur on the territory of a third country to the Agency and, if requested, to the competent authorities of the Member States in which the medicinal product is authorised.

5. Until the Agency can ensure the functionalities of the Eudravigilance database as specified in Article 24 of Regulation (EC) No 726/2004 as amended by Regulation (EU) No 1235/2010, the competent authority of a Member State may require marketing authorisation holders to report to it all non-serious suspected adverse reactions that occur on the territory of that Member State, within 90 days of the day on which the marketing authorisation holder concerned gained knowledge of the event.

6. During this period, Member States shall ensure that the reports referred to in paragraph 4 that relate to events that occurred in their territory are promptly made available to the Eudravigilance database, and in any case within 15 days of the notification of suspected serious adverse reactions.

7. With regard to the obligation on the part of the marketing authorisation holder to submit periodic safety update reports to the Agency as provided for in Article 107b(1) of Directive 2001/83/EC as amended by this Directive, the national competent authorities shall ensure that this obligation applies as from 12 months after the functionalities of the repository have been established and have been announced by the Agency.

Until the Agency can ensure the functionalities agreed for the repository of the periodic safety update reports, the marketing authorisation holders shall submit the periodic safety reports to all Member States in which the medicinal product has been authorised.

Article 3

Transposition

1. Member States shall adopt and publish, by 21 July 2012 at the latest, the laws, regulations and administrative provisions necessary to comply with this Directive. They shall forthwith communicate to the Commission the text of those provisions.

They shall apply those provisions from 21 July 2012.

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

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

Article 4

Entry into force

This Directive shall enter into force on the 20th day following its publication in the *Official Journal of the European Union*.

Article 5

Addressees

This Directive is addressed to the Member States.

Done at Strasbourg, 15 December 2010.

For the European Parliament
The President
J. BUZEK

For the Council
The President
O. CHASTEL

⁽¹⁾ See page 1 of this Official Journal.

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