STATUTORY INSTRUMENTS.

S.I. No. 272 of 2012

MEDICINAL PRODUCTS (CONTROL OF PLACING ON THE MARKET) (AMENDMENT) REGULATIONS 2012

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I, JAMES REILLY, Minister for Health, in exercise of the powers conferred on me by section 32 (as amended by section 16 of the Irish Medicines Board (Miscellaneous Provisions) Act 2006 (No. 3 of 2006)) of the Irish Medicines Board Act 1995 (No. 29 of 1995), and including for the purpose of giving effect to Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008[1], Directive 2009/53/EC of the European Parliament and of the Council of 18 June 2009[2] and Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010[3], and for the purpose of giving full effect to Regulation (EU) No. 1235/2010 of the European Parliament and of the Council of 15 December 2010[4], hereby make the following regulations:

1. These Regulations may be cited as the Medicinal Products (Control of Placing on the Market) (Amendment) Regulations 2012.

2. In these Regulations "Principal Regulations" means the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007).

3. Regulation 3(1) (as amended by the Medicinal Products (Control of Placing on the Market) Regulations 2007 (Amendment) Regulations 2010 (S.I. No. 287 of 2010)) of the Principal Regulations is amended—

(*a*) by substituting for the definition of "Act" the following:

> "'Act' means the Irish Medicines Board Act 1995 (No. 29 of 1995), as amended by s. 197 of the Finance Act 1999 (No. 2 of 1999), Regulation 3 of the European Communities (In Vitro Diagnostic Medical Devices) Regulations 2001 (S.I. No. 304 of 2001), Regulation 2 of the European Communities (Medical Devices) (Amendment) Regulations 2001 (S.I. No. 444 of 2001), Regulation 3 of the European Communities (Medical Devices) (Amendment) Regulations 2002 (S.I. No. 576 of 2002), the Irish Medicines Board (Miscellaneous Provisions) Act 2006 (No. 3 of 2006) and the European Communities (Amendment of the Irish Medicines Board Act 1995) Regulations 2007 (S.I. No. 542 of 2007);",

(*b*) by substituting for the definition of "2001 Directive" the following:

[1]OJ No. L 81, 20.3.2008, p. 51.
[2]OJ No. L 168, 30.6.2009, p. 33.
[3]OJ No. L 348, 31.12.2010, p. 74. As affected by Corrigendum to Directive 2010/84/EU, OJ No. L 21, 25.1.2011, p. 8.
[4]OJ No. L 348, 31.12.2010, p. 1.

Notice of the making of this Statutory Instrument was published in "Iris Oifigiúil" of 27*th July*, 2012.

"'2001 Directive' means Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001[5], as amended by Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003[6], Commission Directive 2003/63/EC of 25 June 2003[7], Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004[8], Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004[9], the Community Regulation on medicinal products for paediatric use, the advanced therapy regulation, Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008[1], Directive 2009/53/EC of the European Parliament and of the Council of 18 June 2009[2], Commission Directive 2009/120/EC of 14 September 2009[10] and Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010[3];",

(*c*) by inserting after the definition of "EEA State" the following definition:

"'Eudravigilance database' means the database and data-processing network referred to in Article 24 of Regulation (EC) No. 726/2004;",

(*d*) by inserting after the definition of "pharmacist" the following definition:

"'Pharmacovigilance Risk Assessment Committee' means the committee of the Agency established by Article 56(1) of Regulation (EC) No. 726/2004;",

(*e*) by substituting for the definition of "Regulation (EC) No. 726/2004" the following:

"'Regulation (EC) No. 726/2004' means Regulation (EC) No. 726/2004 of the European Parliament and of the Council of 31 March 2004[11], as amended by Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006[12], the advanced therapy regulation, Regulation (EC) No. 219/2009 of the European Parliament and of the Council of 11 March 2009[13], Regulation (EC) No. 470/2009 of the European Parliament and of the Council of

[5]OJ No. L 311, 28.11.2001, p. 67.
[6]OJ No. L 33, 8.2.2003, p. 30.
[7]OJ No. L 159, 27.6.2003, p. 46.
[8]OJ No. L 136, 30.4.2004, p. 85.
[9]OJ No. L 136, 30.4.2004, p. 34.
[10]OJ No. L 242, 15.9.2009, p. 3.
[11]OJ No. L 136, 30.4.2004, p. 1.
[12]OJ No. L 378, 27.12.2006, p. 1.
[13]OJ No. L 87, 31.3.2009, p. 109.

6 May 2009[14] and Regulation (EU) No. 1235/2010 of the European Parliament and of the Council of 15 December 2010[4].", and

(*f*) in the definition of "relevant Community provisions", by substituting for subparagraphs (*h*) and (i) the following:

"(*h*) the Community Regulation on medicinal products for paediatric use,

(i) the advanced therapy regulation, and

(*j*) Regulation (EU) No. 1235/2010 of the European Parliament and of the Council of 15 December 2010[4];".

4. Regulation 5(2) (as amended by the Medicinal Products (Control of Placing on the Market) Regulations 2007 (Amendment) Regulations 2009 (S.I. No. 3 of 2009)) of the Principal Regulations is amended by substituting for subparagraphs (*a*) to (*c*) the following:

"(*a*) Articles 10, 61(1), 61a(1)(*a*) and (3), 62(2) and 65 of Regulation (EC) No. 726/2004;

(*b*) Articles 5, 16h(2), 27(2), 33, 34(2), 69(2), 101(3), 110, 121 and 127b of the 2001 Directive;

(*c*) Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999[15], as amended by Regulation (EC) No. 596/2009 of the European Parliament and of the Council of 18 June 2009[16];".

5. Regulation 9(7) of the Principal Regulations is amended by substituting "9 months" for "6 months".

6. Regulation 10 of the Principal Regulations is amended—

(*a*) by inserting after paragraph (2) the following subparagraph:

"(2A) Where the Board grants a marketing authorisation, certificate of registration or certificate of traditional-use registration it shall also make publicly available:

(i) the package leaflet,

(ii) the summary of product characteristics,

(iii) any conditions established in accordance with Articles 21a, 22 and 22a of the 2001 Directive,

[14]OJ No. L 152, 16.6.2009, p. 11.
[15]OJ No. L 18, 22.1.2000, p. 1.
[16]OJ No. L 188, 18.7.2009, p. 14.

(iv) any deadlines for fulfilment of those conditions for each medicinal product authorised or registered, and

(v) a public assessment report prepared in accordance with Article 21(4) of the 2001 Directive, and a summary thereof,

(vi) a summary of the risk management plan for each medicinal product authorised or registered", and

(*b*) in paragraph (5), by inserting "including exposure of an insufficient number of patients to the medicinal product concerned," after "on justified grounds relating to pharmacovigilance,".

7. Regulation 14 of the Principal Regulations is amended—

(*a*) in paragraph (1), by inserting ", refuse to renew" after "suspend",

(*b*) in paragraph (5), by substituting "revokes, suspends or refuses to renew" for "revokes or suspends" in each place where it occurs,

(*c*) in paragraphs (5) and (8), by substituting "revocation, suspension or non-renewal" for "revocation or suspension" in each place where it occurs,

(*d*) in paragraph (9)(*a*), by substituting "suspend, revoke or refuse to renew" for "suspend or revoke",

(*e*) in paragraph (10)(*a*), by substituting "suspends, revokes or refuses to renew" for "suspends or revokes", and

(*f*) by inserting after paragraph (10) the following:

"(11) Where, pursuant to this Regulation, the supply of a medicinal product has been prohibited or a medicinal product has been withdrawn from the market, the Board may, 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.".

8. Regulation 15 of the Principal Regulations is amended—

(*a*) in paragraph (2), by substituting for subparagraph (*b*) the following:

"(*b*) comply with any obligations imposed upon him or her by the Board in the grant of the relevant authorisation or registration, including conditions imposed pursuant to Articles 21a, 22 and 22a of the 2001 Directive, and incorporate such conditions into his or her risk management system; and", and

(*b*) in paragraph (6)—

(i) by substituting for subparagraphs (*d*) to (*f*) the following subparagraphs—

"(*d*) provide the Board with any new information which might entail the amendment of the particulars or documents referred to in Article 8(3), 10, 10a, 10b, 11 or 32(5) of the 2001 Directive, or in Annex I to that Directive;

(*e*) inform the Board of any prohibition or restriction imposed by the competent authority 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, including both positive and negative results of clinical trials or other studies in all indications and populations, whether or not included in the authorisation or registration, as well as data on the use of the medicinal product where such use is outside the terms of the authorisation or registration;

(*f*) apply to the Board to make any changes or variations to the relevant authorisation or registration, as required by this paragraph and Article 23 of the 2001 Directive;",

(ii) in subparagraph (*j*), by substituting "concerned;" for "concerned.", and

(iii) by inserting after subparagraph (*j*) the following subparagraphs:

"(*k*) apply for any variation to the authorisation or registration that is required pursuant to Article 107g, 107k or 107q of the 2001 Directive, within the timetable for implementation determined in accordance with the applicable Article, and include in the application an updated summary of product characteristics and an updated package leaflet;

(*l*) ensure that the product information is kept up to date with the current scientific knowledge, including the conclusions of the assessments and recommendation made public by means of the European medicines web-portal established in accordance with Article 26 of Regulation (EC) No. 726/2004;

(*m*) submit any data requested by the Board pursuant to Article 23(4) or the final paragraph of Article 23a of the 2001 Directive, within the time frame specified in the said request; and

(*n*) submit a copy of the pharmacovigilance system master file to the Board, if requested by the Board, no later than 7 days after the said request.".

9. Regulation 16 (as amended by the Medicinal Products (Control of Placing on the Market) (Amendment) Regulations 2011 (S.I. No. 722 of 2011)) of the Principal Regulations is amended by inserting after paragraph (7) the following paragraph:

"(8) Notwithstanding the provisions of this Regulation, when a medicinal product is not intended to be delivered directly to the patient, or where there are severe problems in respect of the availability of a medicinal product, the Board may, subject to measures it considers necessary to safeguard human health, do either or both of the following—

(*a*) grant an exemption to the requirements of paragraph (1)(*a*) and (*b*), or

(*b*) grant a full or partial exemption to the requirements of paragraph (1)(*c*).".

10. Regulation 25 (as amended by the Medicinal Products (Control of Placing on the Market) Regulations 2007 (Amendment) Regulations 2009 (S.I. No. 3 of 2009)) of the Principal Regulations is amended by inserting after paragraph (6) the following paragraphs:

"(7) The obligation, in Regulation 31(1)(*d*), to maintain and make available on request a pharmacovigilance system master file shall not apply in respect of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration granted before 21 July 2012 until—

(*a*) the date, after 21 July 2012, on which that authorisation or registration is renewed, or

(*b*) 21 July 2015,

whichever is earlier.

(8) The procedure provided for in Regulations 36 and 37 applies only to post-authorisation safety studies which have commenced after 21 July 2012.

(9) (*a*) The obligations, in Regulation 32(1)(*c*) and (*d*), to submit information on suspected adverse reactions electronically to the Eudravigilance database shall not apply until a date, designated by the Board, not more than 6 months after the functionalities of the Eudravigilance database have been announced by the Agency.

(*b*) Until the date referred to in subparagraph (*a*), the holder of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration shall report, within 15 days of the

day on which he or she gains knowledge of the event, all serious suspected adverse reactions that occur—

(i) in the State, to the Board,

(ii) in the territory of another EEA State, to the competent authority of that state, or

(iii) in the territory of a third country, to the Agency,

and, if requested, to the competent authorities of the EEA States in which the relevant medicinal product is authorised.

(*c*) Until the date referred to in subparagraph (*a*), the holder of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration shall collect follow-up information on suspected adverse reactions and submit updates to the body to which he or she reported in accordance with subparagraph (*b*).

(*d*) Until the date referred to in subparagraph (*a*), the Board shall promptly, and in any case within 15 days of receiving notification of the serious suspected adverse reaction, make available to the Eudravigilance database any report made to it pursuant to subparagraph (*b*)(i).

(10) (*a*) The obligation, in Regulation 34(1), to submit periodic safety update reports to the Agency shall not apply until a date, designated by the Board, not more than 12 months after the functionalities of the repository of periodic safety update reports have been announced by the Agency.

(*b*) Until the date referred to in subparagraph (*a*), the holder of a Community marketing authorisation, marketing authorisation, or certificate of traditional-use registration shall submit periodic safety update reports to the Board.

11. The Principal Regulations are amended by inserting after Part 6 the following Part:

"PART 7

PHARMACOVIGILANCE

System to be operated by Board

30. The Board shall operate a pharmacovigilance system in accordance with the provisions of this Part, Title IX of the 2001 Directive and Chapter 3 of Title II of Regulation (EC) No. 726/2004, and shall, as part of that system—

(*a*) collect information on the risks of medicinal products as regards patients' or public health,

(*b*) evaluate all information scientifically, consider options for risk minimisation and prevention and take regulatory action concerning marketing authorisations, as necessary,

(*c*) encourage and facilitate the reporting of adverse reactions to medicinal products by patients, doctors, pharmacists and other healthcare professionals,

(*d*) provide information to the public regarding pharmacovigilance,

(*e*) establish and maintain a web-portal for the provision of pharmacovigilance information, in accordance with Article 106 of the 2001 Directive,

(*f*) establish and maintain a system for the collection and follow-up of adverse reactions and the identification of the medicinal product involved,

(*g*) ensure that the confidentiality of personal and commercially sensitive information is maintained when publishing safety messages, unless the public disclosure of such information is necessary for the protection of public health,

(*h*) perform a regular audit of its pharmacovigilance system and provide a copy of the outcomes of the audit to the Commission, in accordance with Article 101(2), and to the Minister.

System to be operated by holder of authorisation or registration

31. (1) The holder of a Community marketing authorisation, marketing authorisation, or certificate of traditional-use registration shall operate a pharmacovigilance system equivalent to the Board's system provided for under this Part, Title IX of the 2001 Directive and Chapter 3 of Title II of Regulation (EC) No. 726/2004, and shall, as part of that system—

(*a*) evaluate all information scientifically, consider options for risk minimisation and prevention and take appropriate measures as necessary;

(*b*) have permanently and continuously at his or her disposal an appropriately qualified person responsible for pharmacovigilance, who shall reside and operate in the European Economic Area and shall be responsible for the establishment and maintenance of the system;

(*c*) submit the name and contact details of the person referred to in paragraph (*b*) to the Board and the Agency;

(*d*) maintain and make available on request a pharmacovigilance system master file;

(*e*) perform regular audits of the system, note the main findings of such audits on the pharmacovigilance system master file and ensure that

appropriate corrective action is prepared and implemented before removing the note;

(*f*) operate a risk management system for the medicinal product;

(*g*) monitor the outcome of risk minimisation measures which are contained in the risk management plan or which are laid down as conditions of the grant of the authorisation or registration;

(*h*) 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.

(2) Notwithstanding paragraph (1)(*b*), where the person referred to in that subparagraph resides and operates outside the State, the Board may require the nomination of a contact person in the State reporting to the person referred to in that subparagraph.

(3) Notwithstanding paragraph (1)(*f*), a risk management system shall not be required for a medicinal product the subject of an authorisation or registration granted before 21 July 2012, unless required by the Board, pursuant to Article 104a of the 2001 Directive and Regulation 14.

(4) A person shall not, in operating the system referred to in paragraph (1), communicate information relating to pharmacovigilance concerns about a medicinal product to the general public without giving prior or simultaneous notification to the Board, the Agency and the Commission.

(5) In any case where information of the nature referred to in paragraph (4) is communicated by any such person, the said information shall be presented objectively and shall not be misleading.

Suspected adverse reactions — obligations of holder of authorisation or registration

32. (1) Subject to paragraphs (2) and (3), the holder of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration shall—

(*a*) make and retain a detailed record of all suspected adverse reactions to the relevant medicinal product which are brought to his or her attention, whether reported spontaneously by patients or healthcare professionals, or occurring in the context of a post-authorisation safety study, and whether received electronically or by any other means;

(*b*) make all such records accessible at a single point within the European Economic Area;

(*c*) subject to Regulation 25(9), submit to the Eudravigilance database information on all suspected adverse reactions—

(i) in the case of serious suspected adverse reactions, no later than 15 days, or

(ii) in the case of non-serious suspected adverse reactions, no later than 90 days,

following the day on which he or she gained knowledge of the event.

(*d*) subject to Regulation 25(9)(*c*), collect follow-up information on suspected adverse reactions and submit updates to the Eudravigilance Database;

(*e*) establish procedures in order to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reactions;

(*f*) collaborate with the Agency and the Board in the detection of duplicates of suspected adverse reaction reports;

(*g*) in the case of a suspected adverse reaction to a biological medicinal product prescribed, dispensed or sold in the State, record the brand name and the batch number of the biological medicinal product concerned.

(2) Any suspected adverse reaction occurring in the context of a clinical trial shall be recorded and reported in accordance with Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001[17], as amended by Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006[18] and Regulation (EC) No. 596/2009 of the European Parliament and of the Council of 18 June 2009[19].

(3) In the case of 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, the holder of the relevant authorisation or registration shall not be required to report to the Eudravigilance database the suspected adverse reactions recorded in the listed medical literature for that medicinal product, but he or she shall monitor all other medical literature and report any suspected adverse reactions.

Suspected adverse reactions — obligations of Board and other authorities

33. (1) Where a suspected adverse reaction to a medicinal product in the State is brought to the attention of the Board, the Board shall—

(*a*) make a record of the suspected adverse reaction;

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

[17]OJ No. L 121, 1.5.2001, p. 34.
[18]OJ No. L 378, 27.12.2006, p. 1.
[19]OJ No. L 188, 18.7.2009, p. 14.

(*c*) involve patients and healthcare professionals, as appropriate, in the follow-up of the suspected adverse reaction;

(2) In the case of a suspected adverse reaction report submitted by the holder of a Community marketing authorisation, marketing authorisation, certificate of registration or certificate of traditional-use registration, the Board may involve that person in the follow-up of the report.

(3) The Board shall collaborate with the Agency and holders of authorisations and registrations in the detection of duplicates of suspected adverse reaction reports.

(4) The Board shall,

(*a*) in the case of a report of a serious suspected adverse reaction, within 15 days following receipt of such report, and

(*b*) in the case of a report of a non-serious suspected adverse reaction, within 90 days following receipt of such report,

submit the report electronically to the Eudravigilance database.

(5) The Board shall ensure that reports of suspected adverse reactions arising from an error associated with the use of a medicinal product that are brought to its attention are made available to the Eudravigilance database and to any State authorities responsible for patient safety.

(6) Where any State authority receives a report of a suspected adverse reaction, it shall promptly inform the Board of same.

(7) In the case of a report submitted to the Board regarding a suspected adverse reaction to a biological medicinal product which has been prescribed, dispensed or sold in the State, the report shall identify the brand name and the batch number of the biological medicinal product concerned.

Periodic safety update reports — obligations of holder of authorisation or registration

34. (1) Subject to paragraph (2), the holder of a Community marketing authorisation, marketing authorisation, certificate of registration or certificate of traditional-use registration shall electronically submit to the Agency periodic safety update reports, presented in a format which complies with any relevant implementing measure adopted by the Commission in accordance with Article 108 of the 2001 Directive and 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 authorisation or registration;

(*b*) a scientific evaluation of the risk-benefit balance of the medicinal product, based on all available data, including data from clinical trials in unauthorised indications and populations;

(*c*) all data relating to the volume of sales of the medicinal product and any data in his or her possession relating to the volume of prescriptions, including an estimate of the population exposed to the medicinal product; and

(*d*) such other information as may be specified by the Commission in implementing measures adopted in accordance with Article 108 of the 2001 Directive.

(2) The holder of a Community marketing authorisation, marketing authorisation, certificate of registration or certificate of traditional-use registration for a medicinal product referred to in Article 10(1), 10a, 14 or 16a of the 2001 Directive, shall only be required to submit periodic safety update reports—

(*a*) where such obligation has been laid down as a condition of the authorisation or registration in accordance with Article 21a or 22 of the 2001 Directive, or

(*b*) when requested to do so by the Board in accordance with Article 107b(3)(*b*) of the 2001 Directive.

(3) Subject to paragraphs (4) to (6), the frequency with which periodic safety update reports are to be submitted pursuant to this Regulation shall be specified in the relevant authorisation or registration and the dates of submission shall be calculated from the date of the relevant authorisation or registration.

(4) In the case of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration granted before 21 July 2012, and which does not specify the frequency and dates of submission of periodic safety update reports, periodic safety update reports shall be submitted in accordance with paragraph (5) until another frequency or other submission dates are laid down in the authorisation or registration or a Union reference date is established in accordance with Article 107c(4) to (7) of the 2001 Directive.

(5) The periodic safety update reports referred to in paragraph (4) shall be submitted immediately upon request by the Agency or the Board or in accordance with the following—

(*a*) where the medicinal product has not yet been placed on the market, at least every 6 months following authorisation and until the placing on the market, and

(*b*) where the 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 three-yearly intervals thereafter.

(6) Paragraph (5) shall also apply to medicinal products which are authorised only in one EEA State and to which Article 107c(4) to (7) of the 2001 Directive does not apply.

Periodic safety update reports — obligations of Board

35. (1) The Board shall assess periodic safety update reports other than where the assessment is undertaken by the competent authority of another EEA State pursuant to the single assessment procedure set out in Article 107e of the 2001 Directive.

(2) In assessing periodic safety update reports in accordance with paragraph (1), the Board shall determine whether there are new risks or whether risks have changed or whether there are changes to the risk-benefit balance of medicinal products.

(3) Following the assessment of periodic safety update reports, the Board shall consider whether any action concerning the authorisation or registration for the medicinal product concerned is necessary and shall maintain, vary, suspend or revoke the said authorisation or registration as appropriate.

(4) Where action is to be taken pursuant to Article 107g of the 2001 Directive arising from a single assessment of periodic safety update reports, the Board shall adopt necessary measures to maintain, vary, suspend or revoke the authorisation or registration concerned in accordance with the timetable for implementation determined in accordance with that Article.

Post-authorisation safety studies generally

36. (1) This Regulation applies to non-interventional post-authorisation safety studies, involving the collection of safety data from patients or healthcare professionals and initiated, managed or financed by the holder of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration, whether voluntarily or in accordance with Article 21a or 22a of the 2001 Directive.

(2) Post-authorisation safety studies shall not be performed where the act of conducting the study promotes the use of a medicinal product.

(3) Payments to healthcare professionals for participating in post-authorisation safety studies shall be restricted to the compensation for time and expenses incurred.

(4) The Board may require the holder of an authorisation or registration to submit the protocol and progress reports of a post-authorisation safety study to—

(*a*) the Board, in the case of a study which is conducted in the State, or

(*b*) the competent authority of another EEA State, in the case of a study which is conducted in that State.

(5) The holder of an authorisation or registration shall—

(*a*) monitor the data generated during the study and consider its implications for the risk-benefit balance of the medicinal product concerned, and

(*b*) in the case of a study to which paragraph (4)(*a*) applies, send the final report of the study to the Board within 12 months of the end of data collection.

(6) The holder of the authorisation or registration shall, in accordance with Article 23 of the 2001 Directive, and without prejudice to his or her obligations under Regulation 34, communicate to the Board any new information arising from the post-authorisation safety study which might influence the evaluation of the risk-benefit balance of the medicinal product concerned.

Post-authorisation safety studies under Article 21a or 22a of the 2001 Directive

37. (1) This Regulation applies exclusively to non-interventional post-authorisation safety studies, involving the collection of safety data from patients or healthcare professionals and initiated, managed or financed by the holder of a Community marketing authorisation, marketing authorisation or certificate of traditional-use registration in accordance with Article 21a or 22a of the 2001 Directive.

(2) Subject to paragraph (3), before a post-authorisation safety study is conducted, the holder of the authorisation or registration shall submit a draft protocol for the study to the Pharmacovigilance Risk Assessment Committee.

(3) In the case of studies to be conducted exclusively in the State in accordance with a request under Article 22a, the holder of the relevant authorisation or registration shall submit a draft protocol to the Board.

(4) A post-authorisation safety study may commence only when written endorsement has been issued by the Pharmacovigilance Risk Assessment Committee, pursuant to Article 107n(2) of the 2001 Directive or the Board, pursuant to paragraph (5), as appropriate.

(5) Within 60 days of the submission of a draft protocol to the Board in accordance with paragraph (3), the Board shall issue—

(*a*) a letter endorsing the draft protocol,

(*b*) where it considers that the conduct of the study promotes the use of a medicinal product or that the design of the study does not fulfil the study objectives, a letter of objection setting out in detail the grounds for the objection, or

(*c*) a letter notifying the holder of the relevant authorisation or registration that the study is a clinical trial falling under the scope of Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001[17].

(6) Where a letter of endorsement has been issued by the Pharmacovigilance Risk Assessment Committee pursuant to Article 107n(2) of the 2001 Directive in respect of a post-authorisation safety study to be conducted in the State, the holder of the relevant authorisation or registration shall forward the protocol to

the Board and may thereafter commence the study according to the endorsed protocol.

(7) After a post-authorisation safety study has been commenced, any substantial amendments to the protocol shall be submitted, before their implementation, to the Board or to the Pharmacovigilance Risk Assessment Committee, as appropriate.

(8) The Board shall assess amendments submitted pursuant to paragraph (7) and inform the holder of the relevant authorisation or registration of its endorsement or objection.

(9) Upon completion of a post-authorisation safety study, and within 12 months of the end of data collection, the following shall be submitted to the Board or to the Pharmacovigilance Risk Assessment Committee, as appropriate—

(*a*) a final study report, and

(*b*) an abstract of the study results, submitted electronically,

unless a written waiver has been granted by the Board or the Pharmacovigilance Risk Assessment Committee, as appropriate.

(10) The holder of the relevant authorisation or registration shall evaluate whether the results of the post-authorisation safety study have an impact on the authorisation or registration and shall, if necessary, submit to the Board an application to vary the authorisation or registration.

Inspections, including pharmacovigilance inspections

38. (1) Pursuant to ss. 32A to 32F of the Act and Article 111 of the 2001 Directive, the Board shall, by means of inspections, including unannounced inspections if necessary, ensure that the legal requirements governing medicinal products are complied with.

(2) Pursuant to ss. 32A to 32F of the Act and Article 111 of the 2001 Directive, the Board shall, by means of inspections, including unannounced inspections if necessary, ensure that the pharmacovigilance requirements governing medicinal products and that the requirements laid down in Title IX of the 2001 Directive are complied with.

(3) The Board shall share information with the Agency on inspections which have been carried out, and inspections which are planned, and shall cooperate with the Agency in coordinating inspections in third countries.

(4) After every inspection referred to in paragraph (1), the Board shall report on whether the inspected entity complies with the requirements laid down in Title IX of the 2001 Directive.

(5) The Board shall communicate the content of the report referred to in paragraph (3) to the inspected entity and shall, prior to adopting the report, give that person the opportunity to submit comments on the report.

(6) If the outcome of an inspection referred to in paragraph (1) is that the inspected entity does not comply with the pharmacovigilance system, as described in the pharmacovigilance system master file, and with Title IX of the 2001 Directive, the Board shall—

(*a*) bring the deficiencies to the attention of that person and give him or her the opportunity to submit comments, and

(*b*) inform the other EEA States, the Agency and the Commission."

12. Schedule 2 to the Principal Regulations is amended in paragraph (1), in the definition of "time allowed", by substituting "30 days" for "28 days".

13. Regulations 17 and 18 of the Principal Regulations are revoked.

L.S.

GIVEN under my Official Seal,
25 July 2012.

JAMES REILLY,
Minister for Health.

EXPLANATORY NOTE

(This note is not part of the Instrument and does not purport to be a legal interpretation.)

These Regulations amend the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007).

These Regulations give effect to Directive 2010/84/EU of the European Parliament and of the Council of the 15 December 2010, which amended, as regards pharmacovigilance, Directive 2001/83/EC.

These Regulations may be cited as the Medicinal Products (Control of Placing on the Market) (Amendment) Regulations 2012.

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