
STATUTORY INSTRUMENTS

2019 No. 775

**EXITING THE EUROPEAN UNION
MEDICINES**

**The Human Medicines (Amendment
etc.) (EU Exit) Regulations 2019**

Made - - - - 1st April 2019

Coming into force in accordance with regulation 1

The Secretary of State makes these Regulations in exercise of the powers conferred by section 8(1) of, and paragraphs 1(1) and 7(2) of Schedule 4 and paragraph 21 of Schedule 7 to, the European Union (Withdrawal) Act 2018⁽¹⁾.

The Treasury has consented to the making of these Regulations as required by paragraphs 3(1) and 10 of Schedule 4 to the European Union (Withdrawal) Act 2018.

In accordance with paragraphs 1(1) and 12(1) of Schedule 7 to the European Union (Withdrawal) Act 2018, a draft of these Regulations has been laid before and approved by a resolution of each House of Parliament.

PART 1

General

Citation and commencement

1. These Regulations may be cited as the Human Medicines (Amendment etc.) (EU Exit) Regulations 2019 and come into force on exit day.

Amendment of the Human Medicines Regulations 2012

2. The Human Medicines Regulations 2012⁽²⁾ are amended in accordance with Parts 2 to 19.

(1) 2018 c. 16.
(2) S.I. 2012/1916.

Amendment of the Medicines (Products for Human Use) (Fees) Regulations 2016

3. Schedule 1 amends the Medicines (Products for Human Use) (Fees) Regulations 2016(3) and makes saving provision.

PART 2**Amendment of Part 1 (General)****Definitions in relation to advanced therapy medicinal products**

4. After regulation 2, insert—

“Definition of advanced therapy medicinal product etc.

2A.—(1) In these Regulations, “advanced therapy medicinal product” means any of the following products—

- (a) a gene therapy medicinal product;
- (b) a somatic cell therapy medicinal product; or
- (c) a tissue engineered product.

(2) A “gene therapy medicinal product” is a biological medicinal product which has the following characteristics—

- (a) it contains an active substance which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence; and
- (b) its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.

(3) A vaccine against infectious diseases is not to be treated as a gene therapy medicinal product.

(4) A “somatic cell medicinal product” is a medicinal product which has the following characteristics—

- (a) it contains or consists of cells or tissues that—
 - (i) have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or
 - (ii) are not intended to be used for the same essential function in the recipient as in the donor; and
- (b) it is presented as having properties for, or is used in or administered to human beings with a view to, treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues.

(5) A “tissue engineered product” is a medicinal product which—

- (a) contains or consists of engineered cells or tissues; and
- (b) is presented as having properties for, or is used in or administered to human beings with a view to, regenerating, repairing or replacing a human tissue.

- (6) A tissue engineered product may contain—
 - (a) cells or tissues of human or animal origin;
 - (b) viable or non-viable cells or tissues; and
 - (c) additional substances, including cellular products, bio-molecules, biomaterials, chemical substances, scaffolds or matrices.
- (7) A product is not a tissue engineered product if it—
 - (a) contains or consists exclusively of non-viable human or animal cells or tissues;
 - (b) does not contain any viable cells or tissues; and
 - (c) does not act principally by pharmacological, immunological or metabolic action.
- (8) Cells or tissues are engineered if they—
 - (a) have been subject to substantial manipulation, so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved; or
 - (b) are not intended to be used for the same essential function in the recipient as in the donor.
- (9) The following manipulations are not substantial manipulations for the purposes of paragraphs (4)(a) and (8)(a)—
 - (a) cutting;
 - (b) grinding;
 - (c) shaping;
 - (d) centrifugation;
 - (e) soaking in antibiotic or antimicrobial solutions;
 - (f) sterilisation;
 - (g) irradiation;
 - (h) cell separation, concentration or purification;
 - (i) filtering;
 - (j) lyophilisation;
 - (k) freezing;
 - (l) cryopreservation; and
 - (m) vitrification.
- (10) In these Regulations, “combined advanced therapy medicinal product” means an advanced therapy medicinal product—
 - (a) which incorporates, as an integral part of the product, one or more medical devices or one or more active implantable medical devices; and
 - (b) the cellular part of which—
 - (i) contains viable cells or tissues; or
 - (ii) contains non-viable cells or tissues which are liable to act upon the human body with action that can be considered as primary to that of the medical devices.
- (11) Where an advanced therapy medicinal product contains viable cells or tissues, the pharmacological, immunological or metabolic action of those cells or tissues is to be treated as the principal mode of action of the product.

(12) An advanced therapy medicinal product containing both autologous and allogeneic cells or tissues is to be treated as being for allogeneic use.

(13) A product which falls within the definition of a tissue engineered product and within the definition of a somatic cell therapy medicinal product is to be treated as a tissue engineered product.

(14) A product which falls within the definition of—

- (a) a somatic cell therapy medicinal product or a tissue engineered product; and
- (b) a gene therapy medicinal product,

is to be treated as a gene therapy medicinal product.”.

Amendment of regulation 3 (scope of Regulations: special provisions)

5.—(1) Regulation 3 is amended as follows.

(2) In paragraph (12)(d)—

- (a) in paragraph (i) insert “UK” before “marketing authorisation”;
- (b) at the end of paragraph (ii) insert “or”; and
- (c) omit paragraph (iv) (and “or” immediately preceding it).

(3) In paragraph (15)—

- (a) in sub-paragraph (a) insert “UK” before “marketing authorisation”; and
- (b) at the end of sub-paragraph (b) insert “or”; and
- (c) omit sub-paragraph (d) (and “or” immediately preceding it).

Amendment of regulation 4 (special provision for pharmacies etc)

6. In regulation 4(4)(d)—

- (a) in paragraph (i) insert “UK” before “marketing authorisation”;
- (b) at the end of paragraph (ii) insert “or”; and
- (c) omit paragraph (iv) (and “or” immediately preceding it).

Amendment of regulation 5 (classification of medicinal products)

7.—(1) Regulation 5 is amended as follows.

(2) Omit paragraph (1)(b) (and “or” immediately preceding it).

(3) In paragraph (2)—

- (a) at the end of sub-paragraph (b), insert “or”; and
- (b) omit sub-paragraph (d) (and “or” immediately preceding it).

(4) In paragraph (3)—

- (a) omit sub-paragraph (b); and
- (b) in paragraph (d), omit “or (b)”.

(5) In paragraph (4), omit sub-paragraph (b) (and “or” immediately preceding it).

(6) In paragraph (5)—

- (a) omit sub-paragraph (b); and
- (b) in paragraph (d), omit “or (b)”.

Amendment of Schedule 1 (further provisions for classification of medicinal products)

8. In Schedule 1(4), in each place where it occurs, insert “UK” before “marketing authorisation”.

Amendment of regulation 6 (the licensing authority and the Ministers)

9. In regulation 6—
- (a) in paragraph (3) omit sub-paragraph (b) (and “or” immediately preceding it); and
 - (b) omit paragraphs (4) and (5).

Amendment of regulation 8 (general interpretation)

- 10.—(1) Regulation 8(5) is amended as follows.
- (2) In paragraph (1), at the appropriate places, insert—
- ““active implantable medical device”—
 - (a) has the meaning given in regulation 2 of the Medical Devices Regulations 2002(6); or
 - (b) to the extent necessary for the practical application of that definition, also or instead has the meaning given in regulation 137 of those Regulations(7);”;
 - ““agreed paediatric investigation plan” means a paediatric investigation plan which the licensing authority has agreed in accordance with regulation 50B;”;
 - ““Annex I to the 2001 Directive” means Annex I to the 2001 Directive, as modified in accordance with Schedule 8B;”;
 - ““approved country for batch testing list” means the list published by the licensing authority under paragraph 14(3) of Schedule 7 (obligations of qualified persons) and “approved country for batch testing” means a country included in that list;”;
 - ““approved country for import list” means the list published by the licensing authority under regulation 18A (approved country for import) and “approved country for import” means a country included in that list;”;
 - ““the Committee for Medicinal Products for Human Use” means the committee established under Article 5(1) of Regulation (EC) No 726/2004;”;
 - ““conditional marketing authorisation” means a UK marketing authorisation granted under regulation 49(1)(a) in accordance with regulation 58F;”;
 - ““country” means a country or territory;”;
 - ““Directive 2001/18/EC” means Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC – Commission Declaration(8);”;
 - ““EU Exit Regulations” means the Human Medicines (Amendment etc.) (EU Exit) Regulations 2019;”;
 - ““medical device”—
 - (a) has the meaning given in regulation 2 of the Medical Devices Regulations 2002; or

(4) Schedule 1 was amended by [S.I. 2014/490](#).

(5) Regulation 8 was amended by [S.I. 2013/1855](#) and [2593](#), [2015/1503](#), [2016/186](#), [190](#) and [696](#), [2017/715](#), [2018/199](#) and [2019/62](#).

(6) [S.I. 2002/618](#). It was amended by [S.I. 2008/2936](#).

(7) Regulation 137 is inserted by the Medical Devices (Amendment etc.) (EU Exit) Regulations 2019.

(8) OJ No. L 106, 17.4.2001, p. 1, as last amended by Commission Directive (EU) 2018/350.

- (b) to the extent necessary for the practical application of that definition, also or instead has the meaning given in regulation 69 of those Regulations⁽⁹⁾”;
- ““orphan criteria” means the criteria listed in regulation 50G(2);”;
- ““orphan marketing authorisation” means a UK marketing authorisation granted under regulation 49(1)(a) in accordance with regulation 58C;”;
- ““Orphan Regulation” means Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products⁽¹⁰⁾ as it has effect in EU law;”;
- ““paediatric indication” means a term of a UK marketing authorisation enabling the medicinal product to which the authorisation relates to be used by or administered to persons under the age of 18 years;”;
- ““paediatric population” means that part of the population consisting of persons under the age of 18 years;”;
- ““supplementary protection certificate” has the meaning given in section 128B(2) of the Patents Act 1977⁽¹¹⁾”; and
- ““variation to the terms of a UK marketing authorisation” means any change to—
- (a) the information provided in accordance with regulations 50 to 57 and Schedule 8; or
 - (b) the terms of the decision granting the UK marketing authorisation, including the summary of the product characteristics and any conditions, obligations, or restrictions affecting that UK marketing authorisation, or changes to the labelling or the package leaflet connected with changes to the summary of the product characteristics,
- and “vary” and “variation” in relation to a UK marketing authorisation are to be construed accordingly;”.
- (3) In paragraph (1), amend or substitute (as the case may be) the following definitions—
- (a) in the definition of “the Good Manufacturing Practice Directive” insert at the end “as modified in accordance with Schedule 2A”;
 - (b) in the definition of “homoeopathic medicinal product”, in paragraph (b), for “in any pharmacopoeia used officially in an EEA State” substitute “the British Pharmacopoeia, or in any pharmacopoeia used officially in a country that is included in a list published by the licensing authority for this purpose”;
 - (c) in the definition of “import”⁽¹²⁾, insert at the end “and “imported” is to be construed accordingly”;
 - (d) in the definition of “name”, omit paragraphs (b) and (c);
 - (e) in the definition of “pharmacovigilance system”, “pharmacovigilance system master file” and “post-authorisation safety study”, for “marketing authorisation, traditional herbal registration or Article 126a authorisation” substitute “UK marketing authorisation or traditional herbal registration”;
 - (f) in the definition of “post-authorisation efficacy study”, insert “UK” before “marketing authorisation”;
 - (g) at the end of the definition of “Regulation (EC) No 726/2004”, insert “, as it has effect in EU law”;

⁽⁹⁾ Regulation 69 is inserted by the Medical Devices (Amendment etc.) (EU Exit) Regulations 2019.

⁽¹⁰⁾ OJ No. L 018, 22.01.2000, p. 1.

⁽¹¹⁾ 1977 c. 37. Section 128B was inserted by S.I. 2007/3293 and subsection (2) was amended by S.I.2014/2411.

⁽¹²⁾ The definition of “import” was inserted by S.I. 2013/1855.

- (h) at the end of the definition of “Regulation (EC) No 1234/2008”, insert “, as it has effect in EU law”;
 - (i) in the definition of “special medicinal product” for “an EEA State” substitute “a country”;
 - (j) in the definition of “the summary of the product characteristics”, omit paragraph (b) (and “or” immediately preceding it); and
 - (k) in the definition of “UK marketing authorisation”, omit paragraph (b) (and “or” immediately preceding it).
- (4) In paragraph (1), omit the following definitions—
- (i) “advanced therapy medicinal product”,
 - (ii) “Article 126a authorisation”,
 - (iii) “care home”(13),
 - (iv) “Commission Regulation 2016/161”(14),
 - (v) “Directive 2002/98/EC”,
 - (vi) “Directive 2004/23/EC”,
 - (vii) “healthcare institution”(15),
 - (viii) “hospice”(16),
 - (ix) “marketing authorisation”,
 - (x) “Paediatric Regulation”,
 - (xi) “the Pharmacovigilance Risk Assessment Committee”,
 - (xii) “Regulation (EC) No 1394/2007”, and
 - (xiii) “third country”.
- (5) In paragraph (5)(a) insert “UK” before “marketing authorisation”.
- (6) In paragraph (6)(a)—
- (a) insert “UK” before “marketing authorisation”; and
 - (b) for “or 60(1)” substitute “, 60(1) or 60A”.
- (7) In paragraph (8)(17), for “References” substitute “Subject to regulation C17(6), references”.

Insertion of Schedule 8B (modifications of Annex I to the 2001 Directive)

11. Schedule 2 inserts a new Schedule 8B after Schedule 8A.

Insertion of Schedule 2A (modifications of Commission Directive 2003/94/EC)

12. Schedule 3 inserts a new Schedule 2A after Schedule 2.

(13) The definition of “care home” was inserted by [S.I. 2019/62](#).

(14) The definition of “Commission Regulation 2016/161” was inserted by [S.I. 2019/62](#).

(15) The definition of “healthcare institution” was inserted by [S.I. 2019/62](#).

(16) The definition of “hospice” was inserted by [S.I. 2019/62](#).

(17) Paragraph (8) was inserted by [S.I. 2013/1855](#).

PART 3

Amendment of Part 3 (manufacture and distribution of medicinal products and active substances)

New regulation B17 and C17 (good manufacturing practice and good distribution practice)

13. After regulation A17(18) insert—

“Chapter 1A

Good manufacturing practice and good distribution practice

Regulations on good manufacturing practice

B17.—(1) The Ministers may by regulations set out principles and guidelines of good manufacturing practice in respect of medicinal products and investigational medicinal products.

(2) Regulations under paragraph (1) may in particular make provisions as to—

- (a) inspections;
- (b) compliance with good manufacturing practice and, where relevant, the UK marketing authorisation;
- (c) quality assurance systems;
- (d) personnel;
- (e) premises and equipment;
- (f) documentation;
- (g) production;
- (h) quality control;
- (i) the contracting out of work;
- (j) complaints and product recall;
- (k) self-inspection.

(3) Subject to any provision made in regulations under paragraph (1), the principles and guidelines set out in the Good Manufacturing Practice Directive have effect on and after exit day as they had effect immediately before exit day, but subject to the modifications specified in Schedule 2A.

(4) The Ministers may by regulations amend or revoke Schedule 2A.

Guidelines on good manufacturing practice and good distribution practice

C17.—(1) The licensing authority may publish—

- (a) detailed guidelines of good manufacturing practice in respect of medicinal products, and investigational medicinal products, referred to in Article 46(f) of the 2001 Directive, including guidelines as to the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients;
- (b) principles and guidelines of good manufacturing practice for active substances, referred to in the first paragraph of point (f) of Article 46 and in Article 46b of that Directive;

(c) principles and guidelines of good distribution practice referred to in the first paragraph of point (f) of Article 46, and Article 84, of that Directive.

(2) Guidelines or principles under paragraph (1) may replace, amend or otherwise modify any guidelines or principles published or adopted by the European Commission under the second, third, fourth or fifth paragraph of Article 47, or Article 84, of the 2001 Directive.

(3) Unless replaced by principles or guidelines published under paragraph (1), principles and guidelines published or adopted by the European Commission under the second, third, fourth or fifth paragraph of Article 47, or Article 84, of the 2001 Directive, as they applied immediately before exit day⁽¹⁹⁾, continue to apply on and after exit day (subject to any amendments or modifications published under paragraph (1)).

(4) Before exercising the power under paragraph (1), the licensing authority must consult such persons as it considers appropriate.

(5) The licensing authority may only exercise its power under paragraph (1) if it considers that it is necessary in order to take account of technical or scientific progress.

(6) If the licensing authority publishes principles and guidelines under paragraph (1), any reference in these Regulations to any principle or guideline adopted under the provisions of the 2001 Directive specified in those paragraphs is instead to be read as a reference to the principle or guideline published under paragraph (1), or that principle or guideline as amended or modified (as the case may be).”.

Amendment of regulation 17 (manufacturing of medicinal products)

14.—(1) Regulation 17 is amended as follows.

(2) In paragraph (1)(a), for “state other than an EEA State” substitute “country other than an approved country for import”.

(3) In paragraph (3)(a), for “a marketing authorisation, Article 126a authorisation” substitute “a UK marketing authorisation”.

(4) Omit paragraph (4).

(5) In paragraph (5), for “state other than EEA State” substitute “country other than an approved country for import”.

Amendment of regulation 18 (wholesale dealing in medicinal products)

15.—(1) Regulation 18⁽²⁰⁾ is amended as follows.

(2) In paragraph (1)—

(a) in sub-paragraph (a), omit “or”;

(b) in sub-paragraph (b) for “distribution.” substitute “distribution; or”;

(c) insert at the end—

“(c) import a medicinal product from an approved country for import for either purpose.”.

(3) In paragraph (6), for “a marketing authorisation, Article 126a authorisation” substitute “a UK marketing authorisation”.

(4) Omit paragraph (7).

⁽¹⁹⁾ The principles and guidelines are available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

⁽²⁰⁾ Regulation 18 was substituted by S.I. 2013/1855 and further amended by S.I. 2016/186.

Insertion of new regulation 18A (approved country for import)

16. After regulation 18, insert—

“Approved country for import

18A.—(1) The licensing authority must—

- (a) publish a list of countries from which medicinal products may be imported under a wholesale dealing licence (“approved country for import list”); and
- (b) only include in that list a country which is included in the approved country for batch testing list.

(2) In order to determine whether a country should be included in the approved country for import list, the licensing authority may, in particular, take into account—

- (a) the country’s system for ensuring that each batch of a medicinal product has been manufactured and checked in accordance with the requirements of its legislation and any authorisation in respect of that product;
- (b) the country’s rules for good distribution practice;
- (c) the regularity of inspections to verify compliance with good distribution practice;
- (d) the effectiveness of enforcement of good distribution practice;
- (e) the regularity and rapidity of information provided by that country relating to non-compliant manufacturers and distributors of medicinal products;
- (f) any on-site review of that country’s regulatory system undertaken by the licensing authority;
- (g) any on-site inspection of a manufacturing site in that country observed by the licensing authority; and
- (h) any other relevant documentation available to the licensing authority.

(3) The licensing authority must—

- (a) remove a country from the approved country for import list if that country is removed from the approved country for batch testing list;
- (b) in any event review the countries it has included in the approved country for import list to determine if it is still satisfied that the country should remain on that list, and if it is not so satisfied, remove that country from the list; and
- (c) undertake that review at least every three years beginning with the date on which that country is included in that list.”

Amendment of regulation 19 (exemptions from requirement for wholesale dealer’s licence)

17.—(1) Regulation 19(21) is amended as follows.

(2) In paragraph (1)(a), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(3) In paragraph (1)(b), after “or assembled the product” insert “in the United Kingdom”.

Amendment of Schedule 3 (applications for licences under Part 3)

18.—(1) Schedule 3 is amended as follows.

(21) Regulation 19 was amended by [S.I. 2013/1855](#).

(2) In paragraph 1(2)(g), for “marketing authorisation, Article 126a authorisation,” substitute “UK marketing authorisation”.

(3) In paragraph 2(1), for “state other than an EEA state” substitute “country other than an approved country for import”.

(4) In paragraph 3—

(a) in sub-paragraph (2)(d) at the end insert “or the responsible person (import)”.

(b) in sub-paragraph (3)(b)—

(i) in paragraph (i), insert “UK” before “marketing authorisation”,

(ii) omit paragraph (iv), and

(iii) after paragraph (iii) insert—

“(v) an authorisation granted by an authority in a country other than the United Kingdom to sell or supply the medicinal product in that other country;”;

(c) in sub-paragraph (3)(d)—

(i) in paragraph (i) omit “or”,

(ii) in paragraph (ii) for “etc;” substitute “etc, or”,

(iii) at the end insert—

“(iii) to be distributed by means of export to an approved country for import;”;
and

(d) for sub-paragraph (4) substitute—

“(4) In sub-paragraph (2)(d)—

“the responsible person” means the person who has the functions described in regulation 45(2);

“the responsible person (import)” means the person who has the functions described in regulation 45AA(4).”.

Amendment of regulation 23 (grant or refusal of licence)

19. In regulation 23(1)(b), omit “and any European Union obligation”.

Amendment of Schedule 4 (standard provisions of licences under Part 3)

20.—(1) Schedule 4 is amended as follows.

(2) In paragraph 13(b), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(3) In the heading of Part 2, for “State Other Than an EEA State” substitute “Country other than an Approved Country for Import”.

(4) In paragraphs 15, 22(1) and 23, for “state other than an EEA State” substitute “country other than an approved country for import”.

(5) In paragraph 25(m), for the words “referred to in Article 8(2) of [Directive 2004/23/EC](#)”, substitute—

“assigned by a tissue establishment pursuant to—

(a) paragraph 1 of Schedule 3A to the Human Fertilisation and Embryology Act 1990⁽²²⁾, as regards human gametes and embryos; and

⁽²²⁾ 1990 c. 37. Schedule 3A was inserted by the Human Fertilisation and Embryology (Quality and Safety) Regulations 2007/1522, regulation 30.

- (b) paragraph 1 of Schedule 2 to the Human Tissue (Quality and Safety for Human Application) Regulations 2007⁽²³⁾, as regards other human tissues and cells.”.
- (6) In paragraph 33, for “another EEA State” substitute “an approved country for import”.

Amendment of regulation 26 (general power to suspend, revoke or vary licences)

21. In regulation 26(5)(a), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of Schedule 5 (review upon oral representations)

- 22.**—(1) Schedule 5⁽²⁴⁾ is amended as follows.
- (2) In paragraph 1(2)(e), 3(11)(b) and 5(2)(d) after—
- (a) “UK marketing authorisation,” in each place it appears, insert “parallel import licence,”; and
 - (b) “an authorisation,” or “the authorisation,” in each place it appears, insert “licence.”.
- (3) In paragraph 3 omit sub-paragraph (11)(b)(iii).
- (4) In paragraph 5 omit sub-paragraph (2)(c).

Amendment of regulation 29 (variation of licence on the application of the holder)

- 23.** In regulation 29(5)—
- (a) in sub-paragraph (b) omit “or”;
 - (b) in sub-paragraph (c) for “granted.” substitute “granted; or”;
 - (c) at the end insert—
 - “(d) the responsible person (import) under regulation 45AA.”.

Amendment of regulation 31 (certification of manufacturer’s licence)

- 24.**—(1) Regulation 31 is amended as follows.
- (2) In paragraph (1)(c), for “an EEA State” substitute “the United Kingdom”.
 - (3) In paragraphs (3)(b), (5)(a) and (5)(b) insert “UK” before “marketing authorisation”.

Amendment of regulation 33 (offence concerning data for advanced therapy medicinal products)

- 25.**—(1) Regulation 33 is amended as follows.
- (2) In paragraph (1)(a)—
 - (a) for “Article 15(1) of Regulation 1394/2007” substitute “paragraph 8 of Schedule 6”; and
 - (b) for “Article 15(4) of that Regulation” substitute “paragraph 9 of that Schedule”.
 - (3) In paragraph (1)(b), for “Article 15(1)” substitute “paragraph 8”.
 - (4) In paragraph (2) for “Article 15(4)” substitute “paragraph 9”.

⁽²³⁾ S.I. 2007/1523.

⁽²⁴⁾ Schedule 5 was amended by S.I. 2013/1855.

Amendment of Schedule 6 (manufacturer's and wholesale dealer's licences for exempt advanced therapy medicinal products)

26.—(1) Schedule 6 is amended as follows.

(2) In paragraph 3, for “[Directive 2004/23/EC](#)”, substitute—

“requirements imposed pursuant to—

- (a) paragraphs 6 to 9 of Schedule 3A to the Human Fertilisation and Embryology Act 1990, as regards gametes and embryos; and
- (b) paragraphs 9 to 12 of Schedule 2 to the Human Tissue (Quality and Safety for Human Application) Regulations 2007, as regards other tissues and cells.”.

(3) In paragraph 4, for the words “laid down in” to the end, substitute—

“imposed pursuant to—

- (a) Schedule 3A to the Human Fertilisation and Embryology Act 1990, as regards gametes and embryos; and
- (b) Schedule 2 to the Human Tissue (Quality and Safety for Human Application) Regulations 2007, as regards other tissues and cells.”.

(4) In paragraph 5, for the words from “Commission” to the end substitute “the Blood Quality and Safety Regulations 2005(25)”.

(5) In paragraph 11, for the words from “laid down in” to the end, substitute—

“imposed pursuant to—

- (a) as regards gametes and embryos, sections 12(3), and 33A to 33D of, and paragraph 1 of Schedule 3A to, the Human Fertilisation and Embryology Act 1990(26);
- (b) as regards blood cells, regulations 8, 9(e) and 14 of the Blood Safety and Quality Regulations 2005; and
- (c) as regards other cells and tissues, regulations 13 and 16 of, and paragraph 1 of Schedule 2 to, the Human Tissue (Quality and Safety for Human Application) Regulations 2007;”.

Amendment of regulation 36 (conditions for manufacturer's licence)

27. In regulation 36(27), omit paragraphs (4) to (7).

Amendment of regulation 37 (manufacturing and assembly)

28.—(1) Regulation 37(28) is amended as follows.

(2) In paragraph (4)(b)—

- (a) for “third country” substitute “country other than an approved country for import”; and
- (b) for “competent authority of a member State” substitute “appropriate authority for the registration of such persons in the approved country for import”.

(3) In paragraph (5)(b), for “paragraph 5 of Article 47 of the 2001 Directive” substitute “the guidelines which apply under or by virtue of regulation C17”.

(4) In paragraph (6)(b), for “marketing authorisations, Article 126a authorisations” substitute “UK marketing authorisations”.

(25) [S.I. 2005/50](#). It was amended by [S.I. 2005/1098](#) and [2898, 2006/2013, 2007/604, 2008/525](#) and [941, 2009/372](#) and [3307, 2010/554, 2016/604, 2017/1320](#) and [2018/231](#).

(26) Sections 33A to 33D were inserted by the Human Fertilisation and Embryology Act 2008, c. 22.

(27) Regulation 36 was amended by [S.I. 2013/1855](#) and [2019/62](#).

(28) Regulation 37 was substituted by [S.I. 2013/1855](#).

(5) In paragraph (9)(a), from “Commission” to the end substitute “the Blood Quality and Safety Regulations 2005⁽²⁹⁾; or”.

(6) In paragraph (11)—

- (a) for “competent authority of a member State” substitute “licensing authority”; and
- (b) insert “UK” before “marketing authorisation”.

Amendment of regulation 38 (imports)

29.—(1) Regulation 38⁽³⁰⁾ is amended as follows.

(2) In the heading, for “states other than EEA states” substitute “countries other than approved countries for import”.

(3) In paragraphs (2) and (3)(b), for “state other than an EEA State” substitute “country other than an approved country for import”.

Amendment of regulation 39 (further requirements for manufacturer’s licence)

30. In regulation 39(8)⁽³¹⁾, omit “, 43A”.

Amendment of regulation 42 (conditions for wholesale dealer’s licence)

31.—(1) Regulation 42⁽³²⁾ is amended as follows.

- (2) In paragraph (1), for “45” substitute “45AA”.
- (3) Omit paragraphs (4) and (5).

Amendment of Schedule 7 (qualified persons)

32.—(1) Schedule 7⁽³³⁾ is amended as follows.

(2) In Part 1—

- (a) in paragraph 3, for “the member State in which it is studied” substitute “the licensing authority”;
- (b) in paragraph 6, for “the member State in which the courses take place” substitute “the licensing authority”.

(3) In Part 3 (obligations of qualified person)—

- (a) in paragraph 12—
 - (i) the existing text becomes sub-paragraph (1),
 - (ii) in paragraph (a) of that sub-paragraph—
 - (aa) for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”,
 - (bb) after “herbal registration” insert “, or an equivalent authorisation,”, and
 - (cc) insert “and” at the end,
 - (iii) in paragraph (b) of that sub-paragraph—

⁽²⁹⁾ S.I. 2005/50. It has been amended by S.I. 2005/1098 and 2898, 2006/2013, 2007/604, 2008/525 and 941, 2009/372 and 3307, 2010/554, 2016/604, 2017/1320 and 2018/231.

⁽³⁰⁾ Regulation 38 was amended by S.I. 2015/1503.

⁽³¹⁾ Regulation 39 was amended by S.I. 2013/1855, 2015/354 and 2019/62.

⁽³²⁾ Regulation 42 was amended by S.I. 2013/1855 and 2019/62.

⁽³³⁾ Schedule 7 was amended by S.I. 2019/62.

- (aa) for “medicinal products imported from a non-EEA State, irrespective of whether the products have been manufactured in an EEA State” substitute “medicinal products imported from a country other than approved country for import, irrespective of whether the products have been manufactured in the United Kingdom or an approved country for import”, and
 - (bb) in paragraph (iii), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”, and
 - (cc) after “herbal registration” insert “, or an equivalent authorisation,”,
- (iv) omit paragraph (c) of that sub-paragraph, and
- (v) after that sub-paragraph insert—
- “(2) In this paragraph “equivalent authorisation” means, in respect of a medicinal product that does not have a UK marketing authorisation, certificate of registration or traditional herbal registration, such equivalent authorisation or registration granted by an appropriate authority for the licensing of medicinal products in an approved country for import.”.
- (b) omit paragraph 13;
- (c) in paragraph 14—
- (i) in sub-paragraph (1)(a) for “country other than an EEA State” substitute “country other than approved country for import”,
 - (ii) in sub-paragraph (1)(b)—
 - (aa) for “European Union” substitute “licensing authority”,
 - (bb) for “that country” substitute “the country from which those products are imported”, and
 - (cc) in sub-paragraph (i), for “laid down by the European Union” substitute “in the Good Manufacturing Practice Directive, as supplemented by the guidelines and principles which apply under, or by virtue of, regulation C17”,
 - (iii) at the end insert—
 - (3) The licensing authority must publish a list of the countries with whom it has made appropriate arrangements under sub-paragraph (1)(b) (“approved country for batch testing list”).
 - (4) A country may be included in the approved country for batch testing list subject to any condition or restriction that the licensing authority considers appropriate, including as to categories of medicinal product, and any such condition or restriction must be included in the list.
 - (5) In order to satisfy itself of the matters specified in sub-paragraph (1)(b)(i) and (ii), the licensing authority may, in particular, take into account—
 - (a) the country’s rules for good manufacturing practice;
 - (b) the regularity of inspections to verify compliance with good manufacturing practice;
 - (c) the effectiveness of enforcement of good manufacturing practice;
 - (d) the regularity and rapidity of information provided by that country relating to non-compliant manufacturers;
 - (e) any on-site review of that country’s regulatory system undertaken by the licensing authority;

- (f) any on-site inspection of a manufacturing site in that country observed by the licensing authority;
- (g) any other relevant documentation available to the licensing authority.
- (6) The licensing authority must—
 - (a) review any appropriate arrangements it has made under sub-paragraph (1)(b) to determine if that country still satisfies the requirements of sub-paragraph (1)(b)(i) and (ii), and whether any condition or restriction in those arrangements remains appropriate;
 - (b) if it is not so satisfied, remove that country from the approved country for batch testing list or, as the case may be, amend or remove that condition or restriction; and
 - (c) undertake such a review at least every three years beginning with the date on which the country is included in that list.”.

Amendment of regulation 43 (obligations of licence holder)

33.—(1) Regulation 43(34) is amended as follows.

(2) In paragraph (1), for “by the European Commission in accordance with Article 84 of the 2001 Directive” substitute “under, or that apply by virtue of, regulation C17”.

(3) In paragraph (5)(a) and 7(b)(ii), for “marketing authorisation, Article 126a authorisation”, substitute “UK marketing authorisation”.

(4) In paragraph (6)—

- (a) in sub-paragraph (a), insert at the end “in the United Kingdom”; and
- (b) for sub-paragraph (b), substitute—

“(b) the export to an approved country for import, or supply for the purposes of such export, of a medicinal product which may be placed on the market in that country without—

- (i) a marketing authorisation, certificate of registration or traditional herbal registration within the meaning of the 2001 Directive, by virtue of legislation adopted by that country under Article 5(1) of that Directive, where the approved country for import is an EEA State, or
- (ii) such equivalent authorisation, certificate or registration in the approved country for import, under legislation in that country that makes provision that is equivalent to Article 5(1) of the 2001 Directive, where the approved country for import is not an EEA State.”.

(5) In paragraph (7)—

(a) in sub-paragraph (b)—

- (i) in sub-paragraph (i), for “the competent authority of any EEA State” substitute “an appropriate authority for the licensing of medicinal products in an approved country for import”, and
- (ii) in sub-paragraph (ii), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”; and

(b) omit sub-paragraph (c)(vii).

(6) For paragraph (8) substitute—

- “(8) Paragraph (8A) applies to a person (“P”) who—
- (a) imports a medicinal product, other than for the sole purpose of wholesale distribution of that product to a person in a country other than the United Kingdom; but
 - (b) is not the holder of a UK marketing authorisation, certificate of registration or traditional herbal registration in respect of that product.
- (8A) Where this paragraph applies, P must—
- (a) notify—
 - (i) the holder of any authorisation, certificate or registration, granted by an authority in the country from which the product is exported, to sell or supply that product in that country, and
 - (ii) the licensing authority,of the intention to import that product; and
 - (b) pay a fee to the licensing authority in accordance with the Fees Regulations.”
- (7) Omit paragraphs (10) and (11).
- (8) In paragraph (13), insert “UK” before “marketing authorisation holder”.
- (9) Omit paragraph (15).

Omission of regulation 43A (requirement for wholesale dealer to decommission the unique identifier)

34. Omit regulation 43A(35).

Amendment of regulation 44 (requirement for wholesale dealers to deal only with specified persons)

- 35.—(1) Regulation 44(36) is amended as follows.
- (2) In paragraph (2)—
- (a) in sub-paragraph (b), for “another EEA State” substitute “an approved country for import”; and
 - (b) in sub-paragraph (c), for “from a third country (“A”) for export to a third country (“B”)”, substitute “from a country that is not an approved country for import (“A”), for export to a country that is not an approved country for import (“B”)”.
- (3) In paragraph (5)(b), for “competent authority of another EEA State” substitute “appropriate authority of an approved country for import that is responsible for”.
- (4) In paragraph (5)(e)—
- (a) for “third countries” substitute “countries other than approved countries for import”; and
 - (b) for “third country concerned” substitute “country to which the product is supplied”.
- (5) In paragraph (6)—
- (a) insert “and” at the end of sub-paragraph (c); and
 - (b) omit sub-paragraph (e) (and “and” immediately preceding it).

(35) Regulation 43A was inserted by [S.I. 2019/62](#).

(36) Regulation 44 was amended by [S.I. 2013/1855](#), [2015/1503](#) and [2016/186](#).

Amendment of regulation 45 (requirement as to responsible persons)

36.—(1) Regulation 45 is amended as follows.

(2) In paragraph (1), for “The licence holder” insert substitute “Subject to regulation 45AA, the licence holder”.

(3) In paragraph (2)(b) for “marketing authorisations, Article 126a authorisations” substitute “UK marketing authorisations”.

Insertion of new regulations 45AA and 45AB (responsible persons: import)

37. After regulation 45, insert—

“Requirement as to responsible persons where licence holder imports from an approved country for import

45AA.—(1) Subject to paragraph (2), this regulation applies where the licence holder imports a medicinal product from an approved country for import under a wholesale dealer’s licence.

(2) The requirements of this regulation do not apply where an unlicensed medicinal product falling under paragraph (1) is imported—

- (a) from an approved country for import for the sole purpose of distribution by way of wholesale dealing as a special medicinal product; or
- (b) for the sole purpose of wholesale distribution of that product to a person in a country other than an approved country for import.

(3) The licence holder must ensure that there is available at all times at least one person (referred to in this regulation as the “responsible person (import)”) whose name is included in the register established under regulation 45AB.

(4) A responsible person (import) must—

- (a) carry out the functions under regulation 45(2), unless a responsible person under regulation 45 is performing those functions in respect of the licence; and
- (b) ensure that there is appropriate evidence to confirm that each production batch of a medicine imported from an approved country for import under the licence has been certified as provided for in Article 51 of the 2001 Directive, or such equivalent certification procedure as applies in the approved country for import.

(5) The licensing authority must publish guidance on the documentation that it considers to be appropriate evidence for the purposes of paragraph (4)(b).

(6) Guidance published under paragraph (5) may be taken into account by the licensing authority in determining whether it considers there has been a failure to comply with this regulation.

(7) The licence holder must apply to vary the licence if a change is proposed to the responsible person (import).

(8) The licence holder must not permit any person to act as a responsible person (import) other than the person named in the licence.

(9) Paragraph (10) applies if—

- (a) the person acting as responsible person (import) in respect of the licence is no longer included in the register under 45AB;
- (b) the licensing authority thinks, after giving the licence holder and a person acting as a responsible person (import) the opportunity to make representations (orally or

in writing), that the responsible person (import) is failing to carry out the functions referred to in paragraph (4) adequately or at all.

- (10) Where this paragraph applies the licensing authority—
 - (a) must notify the licence holder in writing that the person is not permitted to act as a responsible person (import) in respect of that licence; and
 - (b) may, subject to regulation 45AB(3)(b), remove that person's name from the register under regulation 45AB.
- (11) In this regulation, “unlicensed medicinal product” means a medicinal product in respect of which—
 - (a) there is no marketing authorisation, within the meaning of the 2001 Directive, in any EEA State in respect of that product, where the product is imported from an approved country for import that is an EEA State; or
 - (b) there is no licence or authorisation in respect of that product as regards its sale or supply in the approved country for import, where the product is imported from an approved country for import that is not an EEA State.

Register for responsible persons (import)

45AB.—(1) The licensing authority must maintain a register of persons (“the responsible person (import) register”) who may carry out the role of responsible person (import) under regulation 45AA.

(2) The licensing authority may only include a person's name in the responsible person (import) register if that person—

- (a) holds—
 - (i) a diploma, certificate or other evidence of formal qualifications awarded on completion of a university or other higher education course of study in pharmacy, chemistry, medicine, biology or a related life science, or
 - (ii) such other qualification as the licensing authority is satisfied is equivalent;
 - (b) is a member of—
 - (i) the Royal Society of Biology,
 - (ii) the Royal Pharmaceutical Society,
 - (iii) the Pharmaceutical Society of Northern Ireland,
 - (iv) the Royal Society of Chemistry, or
 - (v) such other body as may be specified by the licensing authority for the purpose of this paragraph; and
 - (c) has a minimum of 2 years' experience in performing the functions of a responsible person under regulation 45, or in performing such other functions that appear to the licensing authority to be equivalent.
- (3) The licensing authority—
- (a) may remove a person's name from the responsible person (import) register if it no longer considers that the person satisfies the requirements of paragraph (2); but
 - (b) it may not exercise that power unless it has given that person the opportunity to make representations to it (orally or in writing).”.

Amendment of regulation 45A (brokering in medicinal products)

38.—(1) Regulation 45A(37) is amended as follows.

(2) In paragraph (1)—

(a) in sub-paragraph (a) for paragraphs (i) and (ii) substitute—

“(i) by the licensing authority, or

(ii) by an appropriate authority responsible for the licensing of medicinal products in an approved country for import;”;

(b) in sub-paragraph (b)—

(i) in paragraph (i), for “a competent authority of a member State” substitute “the licensing authority”,

(ii) in paragraph (ii), omit “except where the person is validly registered with the competent authority of another EEA State”, and

(iii) in paragraph (iii), for “published by the European Commission in accordance with Article 84 of the 2001 Directive” substitute “which apply under, or by virtue of, regulation C17”.

(3) In paragraph (2)—

(a) in sub-paragraph (a), for “a competent authority of a member State” substitute “the licensing authority”;

(b) in sub-paragraph (c), for “competent authority of a member State” substitute “licensing authority”.

(4) Omit paragraph (3).

Amendment of regulation 45D (grant or refusal of a broker’s registration)

39. In regulation 45D(1)(b)(38) omit sub-paragraph (ii) (and “and” immediately preceding it).

Amendment of regulation 45E (criteria of broker’s registration)

40. In regulation 45E(3)(39)—

(a) in sub-paragraph (b)(i), for “the competent authority of any EEA State” substitute “an appropriate authority responsible for the licensing of medicinal products in an approved country for import”; and

(b) omit sub-paragraph (d)(iii).

Amendment of regulation 45F (provision of information)

41. In regulation 45F(1)(40) for sub-paragraph (b) substitute—

“(b) either—

(i) the UK marketing authorisation holder; or

(ii) where applicable, the holder of the licence or authorisation granted by an appropriate authority responsible for the licensing of medicinal products in an approved country for import;”.

(37) Regulation 45A was inserted by [S.I. 2013/1855](#).

(38) Regulation 45D was inserted by [S.I. 2013/1855](#).

(39) Regulation 45E was inserted by [S.I. 2013/1855](#).

(40) Regulation 45F was inserted by [S.I. 2013/1855](#).

Amendment of regulation 45M (criteria for importation, manufacture or distribution of an active substance)

42.—(1) Regulation 45M(41) is amended as follows.

(2) In paragraph (2)(a), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(3) In paragraph (3), omit “from a state other than an EEA State”.

Amendment of Schedule 7A (information to be provided for registration as an importer, manufacturer or distributor of active substances)

43.—(1) Schedule 7A(42) is amended as follows.

(2) In paragraph 13(b), omit “from third countries”.

(3) In paragraph 15(c), omit “to a third country”.

Amendment of regulation 45O (requirements for registration as an importer, manufacturer or distributor of an active substance)

44.—(1) Regulation 45O(43) is amended as follows.

(2) In paragraph (1), for “the Commission has adopted principles and guidelines of good manufacturing practice under the third paragraph of Article 47 of the 2001 Directive which applies” substitute “principles and guidelines of good manufacturing practice have been published under, or apply by virtue of, regulation C17, which apply”.

(3) In paragraph (2), for “the Commission has adopted principles and guidelines of good distribution practice under the fourth paragraph of Article 47 of the 2001 Directive which applies” substitute “principles and guidelines of good distribution practice have been published under, or apply by virtue of, regulation C17, which apply”.

(4) In paragraph (3)—

(a) for “the Commission has adopted principles and guidelines of good manufacturing practice under the third paragraph of Article 47 of the 2001 Directive which applies” substitute “principles and guidelines of good manufacturing practice have been published under, or apply by virtue of, regulation C17, which apply”;

(b) for “imported from a third country” substitute “so imported”;

(c) in sub-paragraph (c)—

(i) omit “third” in both places it appears,

(ii) in paragraph (ii), for “Union” substitute “United Kingdom”, and

(iii) in paragraph (iii), for “Union” substitute “licensing authority”.

(5) In paragraph (4)—

(a) in sub-paragraph (a), for “Article 111b of the 2001 Directive” substitute “paragraph (6)”; and

(b) in sub-paragraph (b)(i), for “competent authority of a member State” substitute “licensing authority or an appropriate authority responsible for the licensing of medicinal products in a country included in a list under paragraph (6)”.

(6) At the end insert—

(41) Regulation 45M was inserted by [S.I. 2013/1855](#).

(42) Schedule 7A was inserted by [S.I. 2013/1855](#).

(43) Regulation 45O was inserted by [S.I. 2013/1855](#).

“(6) The licensing authority may publish a list of countries which it is satisfied have a regulatory framework applicable to active substances exported to the United Kingdom that is equivalent to the regulatory framework in the United Kingdom, in that the respective control and enforcement activities in those countries ensures an equivalent level of protection of public health.

(7) Before including a country in the list under paragraph (6), the licensing authority must assess the equivalence referred to in that paragraph by—

- (a) reviewing relevant documentation; and
- (b) unless the country is included in the approved country for batch testing list, carrying out—
 - (i) an on-site review of the country’s regulatory system, and
 - (ii) if the licensing authority considers it necessary, an inspection of one or more of that country’s manufacturing sites for active substances.

(8) In carrying out an assessment under paragraph (7) the licensing authority must in particular take account of the—

- (a) country’s rules for good manufacturing practice;
- (b) regularity of inspections to verify compliance with good manufacturing practice;
- (c) effectiveness of enforcement of good manufacturing practice; and
- (d) regularity and rapidity of information provided by that country relating to non-compliant producers of active substances.

(9) The licensing authority must—

- (a) review the list under paragraph (6) to determine if a country included in it still satisfies the requirements for inclusion in the list, and if it is not so satisfied, remove that country; and
- (b) undertake such a review at least every three years, beginning with the date on which a country is included in the list.”.

PART 4

Amendment of Part 4 (requirement for authorisation)

Amendment of regulation 46 (requirement for authorisation)

45.—(1) Regulation 46 is amended as follows.

(2) In paragraph (2)—

- (a) in sub-paragraph (a), before “marketing authorisation”, insert “UK”;
- (b) at the end of sub-paragraph (b), insert “or”; and
- (c) omit sub-paragraph (d) (and “or” immediately preceding it).

(3) In paragraph (3), before “European Economic Area” insert “United Kingdom or the”.

(4) In paragraph (6)—

- (a) in sub-paragraph (a), before “marketing authorisation”, insert “UK”;
- (b) at the end of sub-paragraph (b), insert “or”; and
- (c) omit sub-paragraph (d) (and “or” immediately preceding it).

(5) In paragraph (7), omit sub-paragraph (b) (and “and” immediately preceding it).

- (6) In paragraph (9), before “European Economic Area” insert “United Kingdom or the”.
- (7) In paragraph (11)(a), before “European Economic Area” insert “United Kingdom or the”.

Amendment of regulation 47 (breach of requirement)

46.—(1) Regulation 47 is amended as follows.

(2) In paragraphs (3) and (4), before “European Economic Area”, insert “United Kingdom or the”.

(3) In paragraph (6), for “marketing authorisation, certificate of registration, traditional herbal registration or Article 126a authorisation”, substitute “UK marketing authorisation, certificate of registration or traditional herbal registration”.

PART 5

Amendment of Part 5 (marketing authorisations)

Amendment of regulation 48 (application of Part 5)

47.—(1) Regulation 48(**44**) is amended as follows.

(2) In paragraph (2)—

(a) at the appropriate place insert—

““EU reference medicinal product” means a medicinal product which falls within paragraph (b) of the definition of “reference medicinal product”;”;

(b) for the definition of “generic medicinal product”, substitute—

““generic medicinal product”, in relation to a reference medicinal product, means a medicinal product—

- (a) that has the same qualitative and quantitative composition in active substances as the reference medicinal product;
- (b) that has the same pharmaceutical form as the reference medicinal product; and
- (c) whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies;”;

(c) for the definition of “parallel import licence” substitute—

““parallel import licence” means a licence that is granted by the licensing authority under this Part authorising the holder to place on the market a medicinal product imported in to the United Kingdom from an EEA State where that product—

- (a) has been granted an EU marketing authorisation or a marketing authorisation in an EEA State under the 2001 Directive; and
- (b) is essentially similar to a product that has been granted a UK marketing authorisation;”;

(d) for the definition of “reference medicinal product”, substitute—

““reference medicinal product” means a medicinal product—

- (a) authorised under regulation 49(1)(a), in accordance with the provisions of regulation 50; or
- (b) in relation to which an EU marketing authorisation was in force on exit day, but in relation to which no UK marketing authorisation is in force because the

(44) Regulation 48 was amended by [S.I. 2014/1878](#).

holder of the EU marketing authorisation notified the licensing authority in accordance with paragraph 6(3) of Schedule 33A that it did not wish to be the holder of a converted EU marketing authorisation.”.

(3) After paragraph (2) insert—

“(3) In this Part, references to a medicinal product to be imported that is “essentially similar to a product that has been granted a UK marketing authorisation” are to be read as references to a medicinal product to be imported that—

- (a) has been manufactured to the same formulation as a product that has been granted a UK marketing authorisation (“the UK product”);
- (b) contains the same active ingredients as the UK product;
- (c) has the same therapeutic effect as the UK product,

and for the purposes of sub-paragraph (a), any differences in a product’s formulation are to be ignored in so far as they are considered to be immaterial by the licensing authority.

(4) For the purposes of the definition of generic medicinal product—

- (a) the different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance are considered to be the same active substance, unless they differ significantly in properties with regard to safety or efficacy; and
- (b) the various immediate-release oral pharmaceutical forms are considered to be the same pharmaceutical form.

(5) When a medicinal product has been granted a UK marketing authorisation under regulation 49(1)(a) in accordance with the provisions of regulation 50 (“initial marketing authorisation”), any additional strengths, pharmaceutical forms, administration routes, presentations, variations and extensions in relation to which a UK marketing authorisation is granted under regulation 49(1)(a), or which are included in the initial UK marketing authorisation, belong to the same “global marketing authorisation”.

(6) Paragraph (7) applies if a medicinal product—

- (a) belongs to a global marketing authorisation but is not the initial marketing authorisation; and
- (b) is used as a reference medicinal product in accordance with regulations 51 to 53.

(7) Where this paragraph applies, the medicinal product is treated for the purposes of the application of regulation 51(1) and (8) as if it had been authorised on the date of authorisation of the medicinal product to which the initial marketing authorisation relates.

(8) Paragraph (9) applies in relation to a medicinal product if—

- (a) it is an EU reference medicinal product;
- (b) it is used as a reference medicinal product in accordance with regulations 51 to 53; and
- (c) it belongs to a global marketing authorisation, as described in the second paragraph of Article 6(1) of the 2001 Directive; but
- (d) it is not the initial marketing authorisation for the purposes of that global marketing authorisation.

(9) Where this paragraph applies, the medicinal product is treated for the purposes of the application of regulation 51(1) and (8) as if it had been authorised on the date of authorisation of the initial marketing authorisation for the purposes of the global marketing authorisation to which the product belongs.”.

Amendment of regulation 49 (application for grant of UK marketing authorisation or parallel import licence)

- 48.**—(1) Regulation 49(45) is amended as follows.
- (2) In paragraph (1), after “regulation 58,” insert “58C, 58E, 58F and 58G,”.
- (3) After paragraph (1) insert—
- “(1A) The licensing authority may only grant a parallel import licence if it is able to obtain the information necessary, whether from a competent authority of an EEA State or otherwise, to satisfy itself that the medicinal product to be imported—
- (a) has been granted an EU marketing authorisation or a marketing authorisation under the 2001 Directive; and
- (b) is essentially similar to a product that has already been granted a UK marketing authorisation.”.
- (4) In paragraph (3), for “European Union” substitute “United Kingdom.”
- (5) After paragraph (3) insert—
- “(3A) An application for a parallel import licence may not be made by—
- (a) the holder of the marketing authorisation, within the meaning of the 2001 Directive, or the EU marketing authorisation, in respect of the relevant medicinal product to be imported; or
- (b) a company which is in the same group as the holder of that marketing authorisation.”.
- (6) At the end insert—
- “(9) In this regulation “group” has the same meaning as in Part 15 of the Companies Act 2006(46) (see section 474(1) of that Act).”.

Amendment of regulation 50 (accompanying material)

- 49.**—(1) Regulation 50(47) is amended as follows.
- (2) In paragraph (4), omit “from a country other than an EEA State”.
- (3) After paragraph (5) insert—
- “(5A) The Ministers may by regulations amend Schedule 8B (modifications of Annex I) for the purpose of further modifying Annex I to the 2001 Directive in order to take account of scientific and technical progress.
- (5B) The licensing authority may publish, for the purposes of applications made pursuant to this regulation—
- (a) guidance on the presentation and content of the material specified in Schedule 8;
- (b) scientific guidelines relating to the quality, safety and efficacy of medicinal products; and
- (c) guidelines describing the active substance manufacturing process and process controls.
- (5C) Unless replaced by guidance or guidelines published under the power conferred by paragraph (5B), the following guidance and guidelines continue to apply as they applied

(45) Regulation 49 was amended by [S.I. 2014/1878](#).

(46) [2006 c.46](#).

(47) Regulation 50 was amended by [S.I. 2014/1878](#).

immediately before exit day (subject to any amendments or variations published under that paragraph)—

- (a) the guidance published by the European Commission in the rules governing medicinal products in the European Community, Volume 2B, Notice to Applicants, Medicinal Products for human use, Presentation and content of the dossier, Common Technical Document(48);
- (b) the scientific guidelines relating to the quality, safety and efficacy of medicinal products as adopted by the Committee for Medicinal Products for Human Use and published by the EMA and the other pharmaceutical Community guidelines published by the European Commission in the different volumes of the rules governing medicinal products in the European Community(49); and
- (c) guidelines published by the EMA for the purposes of paragraph 3.2.1.2 of Part I of Annex I to the 2001 Directive(50).”.

(4) In paragraph (6), before sub-paragraph (a), insert—

- “(za) regulation 50A (requirement for certain applications to include results of paediatric investigation plan);
- (zb) regulation 50E (application for paediatric use marketing authorisation);
- (zc) regulation 50F (other applications including paediatric indications);
- (zd) regulation 50G (applications relating to orphan medicinal products);
- (ze) regulation 50H (applications relating to advanced therapy medicinal products);
- (zf) regulation 50I (applications relating to conditional marketing authorisations);
- (zg) regulation 50J (applications relating to medicinal products containing or consisting of genetically modified organisms);”.

(5) After paragraph (6), insert—

“(7) The licensing authority may make appropriate arrangements with any EEA State or the EMA in order to obtain the information it considers necessary to satisfy itself that a product to be imported under a parallel import licence is essentially similar to a product that has been granted a UK marketing authorisation.

(8) If the licensing authority makes arrangements under paragraph (7), it must publish a list of the EEA States or the organisation with which it has made such arrangements.”.

Amendment of Schedule 8 (material to accompany an application for a UK marketing authorisation)

50.—(1) Schedule 8(51) is amended as follows.

(2) In paragraph 12—

- (a) in sub-paragraph (a), after “pharmacovigilance” insert “who is ordinarily resident, and operates, in the United Kingdom”;
- (b) omit sub-paragraph (b); and

(48) The guidance is available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

(49) The guidelines are available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

(50) The guidance is available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

(51) Schedule 8 was amended by S.I. 2013/1855.

- (c) in paragraph (e) at the end insert “or, if kept in electronic form, from which it can be accessed, which in either case, must be in the United Kingdom”.
- (3) For paragraph 18 substitute—
 - “**18.** Where an application for authorisation for the medicinal product to be placed on the market is under consideration in a country other than the United Kingdom, or by the EMA, notification of that fact.”.
- (4) In paragraph 19, for “a member state or by a third country”, substitute “a country other than the United Kingdom or by the European Commission”.
- (5) Omit paragraph 20.
- (6) In paragraph 21, for “a member state or by a third country”, substitute “a country other than the United Kingdom”.
- (7) Omit paragraph 22.
- (8) In paragraph 23—
 - (a) for “Article 23 of Regulation (EC) No 726/2004” substitute “regulation 202A”;
 - (b) before “statement”, insert “symbol and”; and
 - (c) before “This”, insert “▼”.
- (9) After paragraph 25, insert—
 - “**25A.** In the case of an advanced therapy medicinal product which contains cells or tissues, a detailed description of those cells or tissues and of their specific origin, including the species of animal in cases of non-human origin.”.
- (10) After paragraph 35, insert—
 - “**36.** In the case of an advanced therapy medicinal product—
 - (a) references in this Part of this Schedule to administration of a product include references to the advanced therapy medicinal product’s use, application or implantation; and
 - (b) descriptions, instructions and warnings must include explanatory drawings and pictures where necessary.”.

Amendment of Schedule 8A (material to accompany an application for a parallel import licence)

- 51.** Paragraph 6 of Schedule 8A(**52**) is amended as follows—
 - (a) in sub-paragraph (a), after “pharmacovigilance” insert “who resides and operates in the United Kingdom”;
 - (b) omit sub-paragraph (b); and
 - (c) in paragraph (e) at the end inset “or, if kept in electronic form, from which it can be accessed, which in either case, must be in the United Kingdom”.

Amendment of Schedule 9 (undertakings by non-United Kingdom manufacturers)

- 52.**—(1) Schedule 9 is amended as follows.
- (2) In the heading, for “EEA” substitute “United Kingdom”.
- (3) In each place where it occurs, insert “UK” before “marketing authorisation”.

(52) Schedule 8A was inserted by [S.I. 2014/1878](#).

New regulation 50A to 50J (applications in relation to particular medicinal products)

53. After regulation 50, insert—

“Requirement for certain applications to include results of paediatric investigation plan

50A.—(1) This regulation applies in relation to an application—

- (a) under regulation 49 for a UK marketing authorisation for a relevant medicinal product which is an initial marketing authorisation for the purposes of a global marketing authorisation, as described in regulation 48(5), or
- (b) under regulation 49 or 65C for a new indication (including a paediatric indication), a new pharmaceutical form or a new route of administration in relation to a relevant medicinal product which is already the subject of a UK marketing authorisation.

(2) Paragraph (1)(b) only applies if the medicinal product in relation to which the new indication, new pharmaceutical form or new route of administration is sought is protected in the United Kingdom by a supplementary protection certificate or a patent which qualifies for the granting in the United Kingdom of a supplementary protection certificate.

(3) An applicant making an application to which this regulation applies must, in addition to the material specified in regulation 50, or in Schedule 10A, provide to the licensing authority the results of all studies performed, and details of all information collected, in compliance with an agreed paediatric investigation plan.

(4) Where paragraph (1)(b) applies, the material provided pursuant to paragraph (3) must cover both the existing and new indication, pharmaceutical form or route of administration.

(5) Paragraph (3) does not apply—

- (a) to the extent that the licensing authority has, in relation to all or part of the paediatric population, granted—
 - (i) a deferral under regulation 50C of the initiation or completion of some or all of the measures set out in a paediatric investigation plan, or
 - (ii) a waiver under regulation 50D of the obligation to produce the information referred to in paragraph (3); or
- (b) if one of regulations 51 to 54 applies to the application.

(6) The applicant making an application to which this regulation applies must include in the application details of the measures intended to ensure the follow up of efficacy and of possible adverse reactions to the paediatric use of the medicinal product.

Agreement and modification of paediatric investigation plan

50B.—(1) Any person may prepare a paediatric investigation plan and submit it to the licensing authority with a request for agreement.

(2) A paediatric investigation plan must—

- (a) specify the timing and measures proposed to assess the safety, quality and efficacy of a medicinal product in the paediatric population; and
- (b) describe any measures to adapt the formulation of the medicinal product so as to make its use more acceptable, easier, safer or more effective for different subsets of the paediatric population.

(3) A person who requests the agreement of a paediatric investigation plan must submit it to the licensing authority not later than upon completion of the human pharmaco-kinetic

studies in adults in relation to the medicinal product to which the plan relates, as specified in section 5.2.3 of Part I of Annex I to the 2001 Directive, unless the licensing authority agrees to accept a later request.

(4) The licensing authority may request the person applying for agreement of a paediatric investigation plan to supply further information in relation to the plan or to submit proposed modifications to it.

(5) The licensing authority must decide whether or not—

- (a) the proposed studies will ensure the generation of the necessary data determining the conditions in which the medicinal product may be used to treat the paediatric population or subsets of it; and
- (b) the expected therapeutic benefits of the medicinal product justify the studies proposed; and

in doing so must consider whether or not the measures proposed to adapt the formulation of the medicinal product for use in different subsets of the paediatric population are appropriate.

(6) If, following a decision by the licensing authority to agree a paediatric investigation plan, the person carrying out the plan encounters such difficulties with its implementation as to render the plan unworkable or no longer appropriate, that person may propose changes or request a deferral or a waiver, by submitting a request to the licensing authority, explaining the grounds for the request.

(7) Schedule 11 makes provision about advice and representations in relation to proposals to agree, or to refuse to agree, a paediatric investigation plan under paragraph (5) or to grant, or to refuse to grant, a deferral or waiver requested under paragraph (6).

Deferral of initiation or completion of measures in paediatric investigation plan

50C.—(1) At the same time as the paediatric investigation plan is submitted under regulation 50B(1), the person requesting agreement of it may request the agreement of the licensing authority to a deferral of the initiation or completion of some or all of the measures set out in the plan.

(2) If the licensing authority is satisfied that a deferral of the initiation or completion of some or all of the measures set out in a paediatric investigation plan can be justified on scientific and technical grounds, or on grounds related to public health, it may—

- (a) agree to a request by the applicant to grant a deferral; or
- (b) decide of its own motion to grant a deferral.

(3) If the licensing authority is satisfied as set out in paragraph (2), it must decide to grant a deferral where it is satisfied that—

- (a) it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population; or
- (b) studies in the paediatric population will take longer to conduct than studies in adults.

(4) If the licensing authority grants an application to which regulation 50A applies, it must, if it also grants a deferral in accordance with this regulation—

- (a) record that fact in the product's summary of product characteristics, and, if it considers that it would be appropriate to do so, in the package leaflet; and
- (b) specify in the document notifying the applicant of the grant of the deferral the time limits for the initiation or completion of the measures to which the deferral relates.

(5) Schedule 11 makes provision about advice and representations in relation to proposals to grant, or to refuse to grant, a deferral under paragraph (2) or (3).

Waiver of production of information in a paediatric investigation plan

50D.—(1) The applicant making an application to which regulation 50A applies is exempt from the obligation to provide to the licensing authority the results of all studies performed, and details of all information collected, in compliance with an agreed paediatric investigation plan, if a waiver is granted in accordance with this regulation.

(2) The licensing authority may grant a waiver in accordance with this regulation if it is satisfied that there is evidence showing that—

- (a) the medicinal product or class of medicinal products is likely to be ineffective or unsafe in all or part of the paediatric population;
- (b) the disease or condition for which the medicinal product or class of medicinal products is intended occurs only in adult populations; or
- (c) the medicinal product does not represent a significant therapeutic benefit over existing treatments for patients in the paediatric population.

(3) The licensing authority may grant a waiver in accordance with this regulation—

- (a) in respect of the entire paediatric population, or a subset of it;
- (b) in respect of all of the therapeutic indications for the medicinal product concerned, or only some of them;
- (c) of its own motion, or at the request of the applicant; or
- (d) in respect of a specific product or a class of medicinal products.

(4) A person who requests a waiver in accordance with this regulation must submit the request to the licensing authority not later than upon completion of the human pharmacokinetic studies in adults in relation to the medicinal product concerned, as specified in section 5.2.3 of Part I of Annex I to the 2001 Directive, unless the licensing authority agrees to accept a later application.

(5) The licensing authority must maintain and publish a list of waivers which are granted under this regulation in respect of a class of medicinal products.

(6) The licensing authority may review a waiver which it has granted under this regulation and may revoke it if it considers it appropriate, having regard to the matters specified in paragraph (2).

(7) If the licensing authority revokes a waiver granted under this regulation, the holder of the UK marketing authorisation to which the waiver relates must, at the end of the period of 36 months beginning with the date of publication of the decision to revoke the waiver, submit the information referred to in regulation 50A(3) to the licensing authority.

(8) If the licensing authority grants an application to which regulation 50A applies, it must, if it also grants a waiver in accordance with this regulation, record that fact in the product's summary of product characteristics, and, if it considers that it would be appropriate to do so, in the package leaflet.

(9) Schedule 11 makes provision about advice and representations in relation to proposals to grant, or to refuse to grant, a waiver in response to a request made in accordance with paragraph (4) and to revoke a waiver under paragraph (6).

Application for paediatric use marketing authorisation

50E.—(1) This regulation applies in relation to an application for a UK marketing authorisation—

- (a) for a relevant medicinal product which is not protected in the United Kingdom by a supplementary protection certificate or by a patent which qualifies for the granting of a supplementary protection certificate; and
- (b) which covers exclusively therapeutic indications which are relevant for use in the paediatric population, or subsets of it, including the appropriate strength, pharmaceutical form or route of administration for that product.

(2) The applicant for a UK marketing authorisation to which this regulation applies must, in addition to the material specified in regulation 50, provide to the licensing authority material necessary to establish the quality, safety and efficacy of the product in the paediatric population, including any specific data needed to support an appropriate strength, pharmaceutical form or route of administration for the product, in accordance with an agreed paediatric investigation plan.

(3) An application to which this regulation applies may, in accordance with regulations 51 to 55, refer to material supplied by the holder of a UK marketing authorisation.

(4) The applicant for a UK marketing authorisation to which this regulation applies must include in the application details of the measures intended to ensure the follow up of efficacy and of possible adverse reactions to the paediatric use of the medicinal product.

Other applications including paediatric indications

50F.—(1) This regulation applies in relation to an application to which neither regulation 50A nor 50E applies and which is—

- (a) an application for a UK marketing authorisation for a relevant medicinal product which includes a paediatric indication; or
- (b) an application to include a paediatric indication in an existing UK marketing authorisation.

(2) The applicant making an application to which this regulation applies must include in the application details of the measures intended to ensure the follow up of efficacy and of possible adverse reactions to the paediatric use of the medicinal product.

Applications relating to orphan medicinal products

50G.—(1) This regulation applies in relation to an application for a UK marketing authorisation for a relevant medicinal product in relation to which the applicant intends to demonstrate that the orphan criteria are met.

(2) The orphan criteria are that—

- (a) the medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition;
- (b) either—
 - (i) the condition referred to in sub-paragraph (a) affects not more than five in 10,000 persons in the United Kingdom; or
 - (ii) the medicinal product is unlikely, when marketed, to generate sufficient financial return to justify the necessary investment; and

- (c) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the United Kingdom, or if such method exists, the medicinal product will be of significant benefit to those affected by the condition.
- (3) The applicant for a UK marketing authorisation to which this regulation applies must, in addition to the material specified in regulation 50, provide to the licensing authority material that demonstrates that the orphan criteria are met.
- (4) Schedule 9A makes further provision about the orphan criteria and terms used in regulation 58D.
- (5) The Ministers may by regulations amend Schedule 9A.

Applications relating to advanced therapy medicinal products

50H.—(1) This regulation applies in relation to an application for a UK marketing authorisation for a relevant medicinal product which is an advanced therapy medicinal product.

(2) The applicant for a UK marketing authorisation to which this regulation applies must, in addition to the material specified in regulation 50, provide to the licensing authority information about the measures the applicant envisages putting in place to ensure the follow up of the efficacy of the product and of any adverse reactions to it.

(3) In relation to an application for a UK marketing authorisation for a combined advanced therapy medicinal product, the applicant must, in addition to the material specified in regulation 50 and paragraph (2), provide to the licensing authority evidence of conformity with the requirements of the Medical Devices Regulations 2002⁽⁵³⁾, including, where available, the results of the assessment of a notified body in accordance with those Regulations.

Applications relating to conditional marketing authorisations

50I.—(1) This regulation applies in relation to an application for a UK marketing authorisation for a relevant medicinal product which falls within paragraph (2).

- (2) A relevant medicinal product falls within this paragraph if it is—
 - (a) aimed at the treatment, prevention or diagnosis of seriously debilitating or life-threatening diseases; or
 - (b) to be used in emergency situations, in response to public health threats.
- (3) The applicant for a UK marketing authorisation to which this regulation applies may request that the licensing authority grant a conditional marketing authorisation if—
 - (a) comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied; and
 - (b) the applicant can demonstrate that—
 - (i) the positive therapeutic effects of the product outweigh the risks to the health of patients or of the public associated with the product,
 - (ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data,
 - (iii) unmet medical needs will be fulfilled, and

⁽⁵³⁾ S.I. 2002/618, as amended by the Medical Devices (Amendment etc.) (EU Exit) Regulations 2019.

- (iv) the benefit to the public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required.

(4) In this regulation, “unmet medical needs” means medical needs in relation to a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the United Kingdom, or, even if such method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected.

(5) The applicant for a UK marketing authorisation to which this regulation applies must include in the application material which demonstrates that the criteria in paragraph (3)(b) are met.

Applications in relation to medicinal products containing or consisting of genetically modified organisms

50J.—(1) This regulation applies in relation to an application for a UK marketing authorisation for a relevant medicinal product which contains or consists of genetically modified organisms.

(2) The applicant for a UK marketing authorisation to which this regulation applies must, in addition to the material specified in regulation 50, provide to the licensing authority—

- (a) a copy of the consent to the deliberate release into the environment of the genetically modified organisms for research and development purposes given pursuant to—
 - (i) regulation 21 of the Genetically Modified Organisms (Deliberate Release) Regulations 2002(**54**),
 - (ii) regulation 22 of the Genetically Modified Organisms (Deliberate Release) (Wales) Regulations 2002(**55**),
 - (iii) regulation 21 of the Genetically Modified Organisms (Deliberate Release) (Scotland) Regulations 2002(**56**), or
 - (iv) regulation 21 of the Genetically Modified Organisms (Deliberate Release) Regulations (Northern Ireland) 2003(**57**);
- (b) a complete technical dossier supplying the information specified in Annexes III and IV to [Directive 2001/18/EC](#);
- (c) an environmental risk assessment in accordance with the principles set out in Annex II to [Directive 2001/18/EC](#); and
- (d) the results of any investigations performed for the purposes of research or development.

(3) In this regulation, “genetically modified organism” has the meaning given in Article 2(2) of [Directive 2001/18/EC](#).”.

Insertion of new Schedule in relation to orphan provisions

54. Schedule 4 inserts a new Schedule 9A after Schedule 9.

(54) S.I. 2002/2443, as amended by S.I. 2004/2411.

(55) S.I. 2002/3188, as amended by S.I. 2005/1913.

(56) S.S.I. 2002/541, as amended by S.S.I. 2004/439.

(57) S.R. 2003/167, as amended by S.R. 2005/272.

Amendment of Schedule 10 (national homoeopathic products)

55. In paragraph 4(4)(a) of Schedule 10 (exceptions to requirement to submit safety data) insert “UK” before “marketing authorisation”.

Substitution of regulation 51 (applications relating to generic medicinal products)

56. For regulation 51 substitute—

“(1) An applicant for a UK marketing authorisation for a generic medicinal product may, by way of derogation from paragraph 10 of Schedule 8, omit from the application the results of pre-clinical tests and of clinical trials if the applicant can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised for not less than eight years—

- (a) under regulation 49(1)(a) (subject to paragraphs (2) and (3)); or
- (b) if the product is an EU reference medicinal product, under Regulation (EC) No 726/2004.

(2) If, after exit day but before the date of grant of the UK marketing authorisation in relation to the reference medicinal product, an EU marketing authorisation took effect in relation to that product, the period of not less than eight years referred to in paragraph (1) is treated as having started on the date on which the EU marketing authorisation took effect.

(3) If, after exit day but before the date of grant of the UK marketing authorisation in relation to the reference medicinal product, the competent authority of an EEA state granted a marketing authorisation in relation to that product, the period of not less than eight years referred to in paragraph (1) is treated as having started on the date on which the marketing authorisation in the first EEA state in which the product was authorised took effect.

(4) In the case of an application under this regulation in relation to a salt, ester, ether, isomer, mixture of isomers, complex or derivative of an authorised active substance which differs significantly in properties with regard to safety or efficacy from the active substance in the reference medicinal product, the applicant must supply additional information providing proof of the safety or efficacy of the salt, ester, ether, isomer, mixture of isomers, complex or derivative.

(5) The applicant may omit bioavailability studies from an application under this regulation if the applicant can demonstrate that the generic medicinal product meets the relevant criteria as specified in the guidelines referred to in paragraph (6).

(6) The licensing authority may publish guidelines specifying the criteria to be met by generic medicinal products for the purpose of omitting bioavailability studies from an application in accordance with paragraph (5).

(7) Until replaced by guidelines published under paragraph (6), the guidelines published by the EMA under Article 10(2)(b) of the 2001 Directive⁽⁵⁸⁾ continue to apply on and after exit day as they applied immediately before exit day (subject to any amendments or variations published under paragraph (6)).

(8) If the licensing authority grants a UK marketing authorisation in relation to the generic medicinal product in accordance with paragraph (1), it is a term of the authorisation that the product must not be sold or supplied, or offered for sale or supply, in the United Kingdom before the expiry of ten years beginning with—

(58) The guidelines are available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

- (a) the date on which the reference medicinal product was granted a UK marketing authorisation;
- (b) the date referred to in paragraph (2) or (3), if earlier than the date in subparagraph (a); or
- (c) if the reference medicinal product is an EU reference medicinal product, the date on which the EU marketing authorisation for the reference medicinal product took effect.

(9) Paragraph (10) applies where an EU reference medicinal product is used as a reference medicinal product for the purposes of this regulation.

(10) Where this paragraph applies, the terms of the marketing authorisation of the EU reference medicinal product are treated as being the terms of the product's EU marketing authorisation as they stood immediately before exit day.

(11) Paragraph (12) applies if—

- (a) during the first eight of the ten years referred to in paragraph (8) the marketing authorisation holder for the reference medicinal product obtained a UK marketing authorisation for one or more new therapeutic indications; and
- (b) during the scientific evaluation prior to their authorisation, the licensing authority considers the new indications bring a significant clinical benefit in comparison with existing therapies.

(12) Where this paragraph applies, the period of ten years referred to in paragraph (8) is extended to eleven years, subject to the provisions of paragraphs (13) and (14).

(13) Where the European Commission, or an EEA state, has granted or varied a marketing authorisation in relation to the new therapeutic indication before the licensing authority does so, the one year extension of the period of ten years referred to in paragraph (8) is reduced by the period of time—

- (a) beginning on the date on which the EU or EEA state marketing authorisation took effect or was varied; and
- (b) ending immediately before the date on which the licensing authority granted or varied the UK marketing authorisation.

(14) If the period of time by which the one year extension is to be reduced in accordance with paragraph (13) is one year or longer, paragraph (12) does not apply.

(15) Paragraph (16) applies where—

- (a) an application is made in relation to a new indication for a well-established substance; and
- (b) significant pre-clinical or clinical studies were carried out in relation to the new indication.

(16) Where this paragraph applies, the applicant for a UK marketing authorisation under paragraph (1) or regulation 52 or 53 may not refer in its application to the studies mentioned in paragraph (15)(b) for the period of one year beginning on the date on which the licensing authority grants or varies a UK marketing authorisation in relation to the new indication (subject to paragraphs (17) and (18)).

(17) Where the European Commission, or an EEA state, has granted or varied a marketing authorisation in relation to the new indication before the licensing authority does so, the period of one year referred to in paragraph (10) is reduced by the period of time—

- (a) beginning on the date on which the EU or EEA state marketing authorisation took effect or was varied; and

(b) ending immediately before the date on which the licensing authority granted or varied the UK marketing authorisation.

(18) If the period of time by which the one year period in paragraph (16) is to be reduced in accordance with paragraph (17) is one year or longer, paragraph (16) does not apply.”.

Amendment of regulation 52 (applications relating to certain medicinal products that do not qualify as generic etc)

57.—(1) Regulation 52 is amended as follows.

(2) In paragraph (1)(a), for “as reference medicinal product” substitute—

“which is or has been authorised for not less than eight years—

- (i) under regulation 49(1)(a) (subject to paragraphs (2) and (3) of regulation 51), or
- (ii) if the reference medicinal product is an EU reference medicinal product, under Regulation (EC) No 726/2004”.

(3) For paragraph (1)(b) substitute—

- “(b) one or more of the following circumstances applies in respect of the application—
- (i) the medicinal product to which the application relates does not fall within the definition of generic medicinal product,
 - (ii) bioequivalence with the reference medicinal product cannot be demonstrated through bioavailability studies, or
 - (iii) the medicinal product to which the application relates differs from the reference medicinal product in terms of changes in the active substance, therapeutic indications, strength, pharmaceutical form or route of administration.”.

(4) For paragraph (2), substitute—

- “(2) The applicant—
- (a) may, by way of derogation from paragraph 10 of Schedule 8, omit from the application the results of pre-clinical tests and of clinical trials relating to the reference medicinal product; but
 - (b) must provide the results of the appropriate pre-clinical tests or clinical trials relating to the applicable circumstance in paragraph (1)(b).”.

(5) In paragraph (3)—

- (a) for “Regulation 51(2)” substitute “Paragraphs (2) to (14) of regulation 51”; and
- (b) for “it applies” substitute “they apply”.

Amendment of regulation 53 (applications relating to similar biological medicinal products)

58.—(1) Regulation 53 is amended as follows.

(2) In paragraph (1), for the words from “any of the reasons” to the end, substitute “differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference medicinal product.”

(3) For paragraph (2), substitute—

- “(2) The applicant—
- (a) may, by way of derogation from paragraph 10 of Schedule 8, omit from the application the results of pre-clinical tests and of clinical trials relating to the reference medicinal product; but

(b) must provide the results of appropriate pre-clinical tests or clinical trials relating to the differences referred to in paragraph (1).

(2A) The type and quantity of supplementary data to be provided by the applicant under paragraph (2)(b) must comply with the relevant criteria in Annex I to the 2001 Directive and in the related detailed guidelines published by the licensing authority under paragraph (2B), or (as the case may be) as mentioned in paragraph (2C).

(2B) The licensing authority may publish guidelines concerning the type and quantity of supplementary data to be provided by an applicant under paragraph (2)(b).

(2C) Unless replaced by guidelines published under paragraph (2B), the guidelines published by the EMA under Article 10(4) of the 2001 Directive⁽⁵⁹⁾ continue to apply on and after exit day as they applied immediately before exit day (subject to any amendments or variations published under that paragraph).”

(4) In paragraph (3) —

(a) for “Regulation 51(2)” substitute “Paragraphs (2) to (8) of regulation 51”; and

(b) for “it applies” substitute “they apply”.

Amendment of regulation 54 (applications relating to products in well-established medicinal use)

59.—(1) Regulation 54 is amended as follows.

(2) In paragraph (1) before “European Union”, insert “United Kingdom or the”.

(3) For paragraph (2), substitute—

“(2) The applicant may, by way of derogation from paragraph 10 of Schedule 8, replace the results of pre-clinical tests or clinical trials with appropriate scientific literature.”.

Amendment of regulation 55 (applications relating to new combinations of active substances)

60.—(1) Regulation 55 is amended as follows.

(2) In paragraph (1)(a), omit “, the 2001 Directive or Regulation (EC) No 726/2004”.

(3) For paragraph (2), substitute—

“(2) The applicant must provide the results of new pre-clinical tests or new clinical trials relating to that combination in accordance with paragraph 10 of Schedule 8, but does not need to provide scientific references relating to each individual active substance.”.

Amendment of regulation 56 (applications containing information supplied in relation to another product with consent)

61. In regulation 56(2), omit “in accordance with Article 10c of the 2001 Directive”.

Amendment of regulation 58 (consideration of application)

62.—(1) Regulation 58 is amended as follows.

(2) After paragraph (4), insert—

“(4A) When considering an application for a UK marketing authorisation, the licensing authority may, if it considers it appropriate, have regard to—

⁽⁵⁹⁾ The guidelines are available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

- (a) an opinion of the Committee for Medicinal Products for Human Use; or
- (b) the results of an assessment of an application for a marketing authorisation by the appropriate authority for the licensing of medicinal products of a country other than the United Kingdom ,

in respect of the medicinal product to which the application relates.

(4B) The licensing authority may under paragraph (4A)—

- (a) decide to have regard to the opinions and assessments described in sub-paragraphs (a) and (b) in relation to certain types of medicinal products only; and
- (b) determine and publish a list of the countries other than the United Kingdom whose assessments of applications for a marketing authorisation are relevant for the purposes of paragraph (4A)(b).”.

(3) Omit paragraphs (6) and (7).

Amendment of Schedule 11 (advice and representations)

63.—(1) Schedule 11 is amended as follows.

(2) In paragraph 1 (application of Part 1)—

(a) in sub-paragraph (1)—

- (i) in sub-paragraph (b) omit “and”, and
- (ii) at the end insert—

“(d) a proposal to agree, or to refuse to agree, a paediatric investigation plan;

(e) a proposal to grant, or to refuse to grant, or to revoke, a waiver or deferral of the initiation or completion of some or all of the measures set out in a paediatric investigation plan; and

(f) a proposal to decide that the orphan criteria are not met in relation to a medicinal product which is the subject of an application for the grant of a UK marketing authorisation.”;

(b) after sub-paragraph (1) insert—

“(1A) Paragraphs 12 and 13 of this Part also apply to—

- (a) an application for the grant of a parallel import licence;
- (b) an application to renew a parallel import licence;
- (c) a proposal to revoke, vary or suspend a parallel import licence (including variation by the variation or removal of a condition to which a parallel import licence is subject) other than a proposal to vary the licence on the application of or by agreement with its holder; and
- (d) a refusal to vary a parallel import licence following an application for a variation by the holder.”; and

(c) omit sub-paragraph (2).

(3) In paragraph 12 (licensing authority decision in other cases), in sub-paragraphs (1), (2) and (5)—

(a) insert “, parallel import licence” after “UK marketing authorisation” in each place it appears; and

(b) insert “, licence” after “the authorisation” in each place it appears.

- (4) In paragraph 14(a) (application of Part 2), for the words from “Article 2(3)” to the end, substitute “paragraph 1 of Schedule 10A; and”.
- (5) In paragraph 15(2) and (3)(b), insert “UK” before “marketing authorisation”.
- (6) In paragraph 16—
 - (a) in sub-paragraph (2)(b), insert “UK” before “marketing authorisation”; and
 - (b) in sub-paragraph (5), omit the words from “or in any Directive” to the end.
- (7) Omit paragraph 17.
- (8) In Part 3 (referral to the Committee for Herbal Medicinal Products)—
 - (a) in the heading to Part 3, for “Committee for Herbal Medicinal Products” substitute “appropriate committee for traditional herbal registrations”;
 - (b) in paragraph 24—
 - (i) in sub-paragraph (1), for the words from “Committee” to the end substitute “appropriate committee in accordance with regulation 130A(1)”; and
 - (ii) omit sub-paragraph (2); and
 - (c) in paragraph 29(1), for “proceed with its proposal” substitute “grant or refuse the application”.
- (9) Omit Part 4 (exceptions to Schedule).

Insertion of provisions concerning consideration of certain applications for UK marketing authorisations

64. After regulation 58, insert—

“Paediatric rewards

58A.—(1) Paragraph (2) applies if—

- (a) an application to which regulation 50A (requirement for certain applications to include the results of a paediatric investigation plan) applies, and in relation to which there is an agreed paediatric investigation plan, is granted by the licensing authority; and
- (b) the licensing authority is satisfied that the material provided by the applicant pursuant to regulation 50A(3) demonstrates compliance with the agreed paediatric investigation plan.

(2) Where this paragraph applies, the licensing authority must—

- (a) include in the UK marketing authorisation a statement to the effect that it is satisfied as set out in paragraph (1)(b); and
- (b) ensure that the results of all studies referred to in the paediatric investigation plan are included in the summary of product characteristics and, if the licensing authority considers that the information would be useful to patients, in the package leaflet.

(3) Where paragraph (2) applies, the holder of a patent or supplementary protection certificate covering the medicinal product to which the application relates is entitled to a six month extension of the period referred to in Articles 13(1) and 13(3) of Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products (subject to paragraphs (4) and (5)).

- (4) Paragraph (3) does not apply if the grant of the application referred to in paragraph (1) (a)—
- (a) relates to a new paediatric indication; and
 - (b) the holder of the UK marketing authorisation—
 - (i) is entitled to a one year extension of the ten year period referred to in regulation 51(8), under regulation 51(12),
 - (ii) is entitled to an extension of that ten year period of less than one year by virtue of the application of regulation 51(13), or
 - (iii) would have been entitled to a one year extension of that ten year period but for the application of regulation 51(14).

(5) If the UK marketing authorisation to which this regulation applies is an orphan marketing authorisation, paragraph (3) does not apply and regulation 58D(5) (orphan rewards) applies.

(6) Paragraphs (7) and (8) apply if the licensing authority grants a UK marketing authorisation in response to an application to which regulation 50E (paediatric use marketing authorisation) applies.

(7) Where this paragraph applies, the medicinal product to which the paediatric use marketing authorisation relates may retain the name of any medicinal product which contains the same active substance and in respect of which the holder of the paediatric use marketing authorisation has been granted a UK marketing authorisation for use in adults.

(8) Where this paragraph applies, the holder of the paediatric use marketing authorisation is entitled to benefit from the periods of data and marketing exclusivity referred to in regulation 51(1) and (8) in relation to the material supplied pursuant to regulation 50E(2).

Publication of information relating to paediatric marketing authorisations

58B.—(1) The licensing authority must publish a register of UK marketing authorisations—

- (a) which include a paediatric indication following completion of an agreed investigation paediatric plan; and
- (b) in relation to which the medicinal product was placed on the market for other indications before the holder obtained that paediatric indication.

(2) The register referred to in paragraph (1) must include the date by which the product must be placed on the market taking account of the paediatric indication in accordance with regulation 78A(4) (post-authorisation requirements in relation to UK marketing authorisations to which paediatric specific provisions apply).

(3) The licensing authority must publish a list of the marketing authorisation holders which have—

- (a) benefitted from any of the rewards in regulation 58A; or
- (b) failed to comply with any of the obligations in regulation 78A.

(4) The licensing authority must publish decisions made under—

- (a) regulation 50B(5) or (7) (agreement and modification of paediatric investigation plan);
- (b) regulation 50C(2) (deferral of the initiation or completion of measures in a paediatric investigation plan); and
- (c) regulation 50D(2) (waiver of production of information in a paediatric investigation plan) in relation to a specific medicinal product.

(5) The decisions referred to in paragraph (4) must be published, with the omission of information of a commercially confidential nature, as soon as reasonably practicable after the decision has been made.

Consideration of applications relating to orphan medicinal products

58C.—(1) If the licensing authority is satisfied in relation to an application for a UK marketing authorisation—

- (a) the orphan criteria are met in relation to all of the therapeutic indications to which the application relates; and
- (b) it is otherwise appropriate to grant a UK marketing authorisation in respect of the application under regulation 49(1)(a),

it may grant a UK marketing authorisation which is known as an orphan marketing authorisation.

(2) The licensing authority must publish and keep up to date a list of orphan marketing authorisations.

(3) Schedule 11 makes provision about advice and representations in relation to proposals to grant a UK marketing authorisation in respect of which the applicant intended to demonstrate that the orphan criteria were met, in cases where the licensing authority considers that those criteria are not met.

Orphan rewards

58D.—(1) Subject to the following provisions of this regulation, for the period of ten years beginning with the date on which the licensing authority grants an orphan marketing authorisation, the licensing authority must not—

- (a) grant an application for a UK marketing authorisation; or
- (b) grant an application to vary a UK marketing authorisation;

in relation to a medicinal product which is similar to the medicinal product to which the orphan marketing authorisation relates and in respect of the therapeutic indications which are covered by the orphan marketing authorisation.

(2) Paragraph (3) applies if—

- (a) an EU marketing authorisation took effect in relation to the medicinal product to which an orphan marketing authorisation relates on or after exit day but before the licensing authority granted the orphan marketing authorisation; and
- (b) the EU marketing authorisation was granted on the basis that the product was an orphan medicinal product within the meaning of the Orphan Regulation.

(3) Where this paragraph applies, the period of ten years referred to in paragraph (1) is reduced by the period of time—

- (a) beginning on the date on which the EU marketing authorisation took effect; and
- (b) ending immediately before the date on which the licensing authority granted the orphan marketing authorisation.

(4) The period of ten years referred to in paragraph (1) may be reduced to six years if, at the end of the fifth year beginning on the date referred to in paragraph (1), the licensing authority is satisfied that the orphan criteria are no longer met in relation to the medicinal product.

(5) The period of ten years referred to in paragraph (1) is extended to twelve years if regulation 58A(2) (paediatric rewards) applies to the orphan marketing authorisation.

- (6) Paragraph (1) does not apply if—
- (a) the holder of the orphan marketing authorisation consents to the grant or variation of a UK marketing authorisation in relation to a similar medicinal product;
 - (b) the licensing authority is satisfied that the holder of the orphan marketing authorisation is unable to supply sufficient quantities of the medicinal product to which the orphan marketing authorisation relates; or
 - (c) a subsequent applicant can establish to the satisfaction of the licensing authority that the medicinal product to which the application relates, although similar to the medicinal product to which the orphan marketing authorisation relates, is safer or more effective than, or clinically superior to, that product.

Consideration of applications relating to combined advanced therapy medicinal products

58E.—(1) When determining an application to which regulation 50H(3) (applications relating to combined advanced therapy medicinal products) applies, the licensing authority must—

- (a) assess the entire combined advanced therapy medicinal product in accordance with these Regulations; and
- (b) recognise the results of the assessment of the notified body, if supplied.

(2) The licensing authority may request the notified body, if relevant, to provide it with information related to the results of the assessment.

(3) Paragraph (4) applies if an application to which regulation 50H(3) applies does not include the results of the assessment of a notified body, or if the notified body fails to supply information related to the results of the assessment when requested by the licensing authority.

(4) Where this paragraph applies, the licensing authority must seek an opinion on the conformity of the device part in accordance with the Medical Devices Regulations 2002(60) from a notified body identified in conjunction with the applicant, unless the licensing authority decides that the involvement of a notified body is not required.

Consideration of applications relating to conditional marketing authorisations

58F.—(1) If the licensing authority is satisfied in relation to an application to which regulation 50I (applications relating to conditional marketing authorisations) applies that—

- (a) the criteria in regulation 50I(3)(b) are met; and
- (b) it is otherwise appropriate to grant a UK marketing authorisation in respect of the application in accordance with regulation 49(1)(a),

it may grant a UK marketing authorisation which is known as a conditional marketing authorisation.

(2) Where regulation 50I(2)(b) (applications relating to conditional marketing authorisations) applies, the licensing authority may grant a conditional marketing authorisation if, in addition to comprehensive clinical data, comprehensive pre-clinical or pharmaceutical data have not been supplied.

(3) The licensing authority may, of its own motion, propose that a conditional marketing authorisation be granted if, having consulted the applicant for a UK marketing authorisation, it considers that the criteria in regulation 50I(3)(b) are met.

(4) If the licensing authority grants a conditional marketing authorisation in relation to a medicinal product, it may at any time decide that it is appropriate to grant a UK marketing authorisation in relation to that product which is not a conditional marketing authorisation.

(5) If the licensing authority grants a conditional marketing authorisation, the product's summary of product characteristics and package leaflet must include a statement to that effect, and the summary of product characteristics must include the date on which the conditional marketing authorisation is due for renewal.

Consideration of applications in relation to medicinal products containing or consisting of genetically modified organisms

58G.—(1) When determining an application for a UK marketing authorisation in relation to which regulation 50J (applications relating to medicinal products containing or consisting of genetically modified organisms) applies, the licensing authority must be satisfied that the application respects the environmental safety requirements laid down by [Directive 2001/18/EC](#).

(2) In reaching its view under paragraph (1), the licensing authority must consult the bodies responsible for the giving of consent pursuant to the legislation referred to in regulation 50J(2)(a).”.

Amendment of regulation 59 (conditions of UK marketing authorisation or parallel import licence: general)

65.—(1) Regulation 59(**61**) is amended as follows.

(2) For paragraph (3) substitute—

“(3) An obligation to conduct such studies as are referred to in paragraph (2)(f) must—

- (a) be based on the delegated acts adopted pursuant to Article 22b of the 2001 Directive; and
- (b) take into account the scientific guidance that applies under regulation 205B in relation to post-authorisation efficacy studies.”.

(3) After paragraph (3), insert—

“(3A) The Ministers may by regulations make provision specifying the situations in which post-authorisation efficacy studies may be required by virtue of the condition referred to in paragraph (2)(f).

(3B) Paragraph (3)(a) ceases to apply on the coming into force of regulations made under paragraph (3A).”.

(4) In paragraph (4), insert “UK” before “marketing authorisation”.

(5) After paragraph (4), insert—

“(4A) Where the application is one to which regulation 50A, 50E or 50F (applications to which paediatric-specific provisions apply) applies, the licensing authority must, if it considers that there is a particular cause for concern, grant the UK marketing authorisation subject to a condition that—

- (a) a risk management system be set up comprising a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of those interventions; or
- (b) specific post-marketing studies be performed and submitted for review.

(61) Regulation 59 was amended by [S.I. 2014/1878](#).

(4B) The licensing authority may request the holder to submit, in addition to the assessment required to be submitted pursuant to Part 9 of Schedule 12A (post-authorisation safety studies), a report assessing the effectiveness of any risk management system, and the results of any studies performed, in compliance with a condition imposed under paragraph (4A).

(4C) If the licensing authority grants a conditional marketing authorisation—

- (a) it must impose, as a condition of the conditional marketing authorisation, an obligation on the holder of the authorisation to complete ongoing studies, or to conduct new studies, with a view to confirming that the positive therapeutic effects of the product outweigh the risks to the health of patients or the public associated with the product, and to provide the additional data referred to in regulation 50I(3)(a);
- (b) it may impose, as a condition of the conditional marketing authorisation, an obligation on the holder of that authorisation in relation to collection of pharmacovigilance data.

(4D) If the licensing authority grants a UK marketing authorisation in relation to an advanced therapy medicinal product, it must, if it considers that there is a particular cause for concern, grant the UK marketing authorisation subject to a condition that—

- (a) a risk management system be set up which is designed to identify, characterise, prevent or minimise risks related to advanced therapy medicinal products, including an evaluation of the effectiveness of that system; or
- (b) that specific post-marketing studies be carried out and submitted for review by the licensing authority.

(4E) The licensing authority may request the holder to submit, in addition to the assessment required to be submitted pursuant to Part 9 of Schedule 12A, a report assessing the effectiveness of any risk management system, and the results of any studies performed, in compliance with a condition imposed under paragraph (4D).”.

(6) Omit paragraph (5).

Amendment of regulation 60 (conditions of UK marketing authorisation: exceptional circumstances)

66. In regulation 60, omit paragraph (9).

Insertion of new regulations 60A (condition as to the submitting of samples and other information to the appropriate authority)

67. After regulation 60, insert—

“Condition as to the submitting of samples and other information to the appropriate authority

60A.—(1) In this regulation—

“the appropriate authority” is to be construed in accordance with section 57(7) of the Health and Social Care Act 2012(62);

“appropriate documentation”, in relation to a sample of a batch submitted to the appropriate authority in accordance with the batch testing condition or pursuant to a notification under paragraph (12), means—

- (a) any certificate issued by a laboratory in an approved country for batch testing and certification of biological medicinal products that relates to the sample of the batch submitted to the appropriate authority with that certificate; and
- (b) such other documentation as the appropriate authority notifies the holder of the UK marketing authorisation to which the sample relates that it requires;

“approved country list for batch testing and certification of biological medicinal products” means the list described in paragraph (5), and “approved country for batch testing and certification of biological medicinal products” means a country included in that list;

“the batch testing condition”, in respect of a UK marketing authorisation, is a condition to the effect that, unless the batch testing exemption applies, the holder of the UK marketing authorisation—

- (a) must submit a sample from each batch of the medicinal product that is the subject of that authorisation to the appropriate authority, together with appropriate documentation; and
- (b) must not sell or supply, or offer to sell or supply, a medicinal product that forms part of that batch in the United Kingdom until the appropriate authority has examined—
 - (i) the sample from that batch,
 - (ii) the appropriate documentation, or
 - (iii) both that sample and that documentation,

and confirmed that it is satisfied that the batch is in conformity with the approved specifications in the UK marketing authorisation; and

“the batch testing exemption” means that—

- (a) a certificate has been issued by a laboratory in a country other than the United Kingdom;
- (b) an agreement has been made between that country and the United Kingdom (whether or not the agreement is solely with that country, a group of countries or an organisation of which that country is a part); and
- (c) that agreement is to the effect that the appropriate authority will recognise that certificate in respect of the batch of the medicinal product, in place of the appropriate authority’s own examination of a sample from the batch, the appropriate documentation or both.

(2) The licensing authority may impose the batch testing condition in respect of a UK marketing authorisation for a medicinal product that is—

- (a) a live vaccine;
- (b) an immunological medicinal product used in the primary immunisation of infants or other groups at risk;
- (c) an immunological product used in public health immunisation programmes;
- (d) subject to paragraph (3), a new immunological product manufactured using new or altered kinds of technology or new for a particular manufacturer; or
- (e) derived from human blood or human plasma.

(3) If the licensing authority imposes a condition in respect of a UK marketing authorisation for a medicinal product of a kind mentioned in paragraph (2)(d), it must, in imposing that condition, specify a period of time for the duration of the condition.

(4) The appropriate authority must complete its examination of the sample for testing, the appropriate documentation or both (as the case may be) within the period of 60 days, beginning with the date on which the appropriate authority is in receipt of both the sample for testing, and the appropriate documentation.

(5) The appropriate authority must publish a list, to be known as the approved country list for batch testing and certification of biological medicinal products, specifying the countries that are approved for the purposes of the appropriate authority's assessment under paragraph (6).

(6) Where a holder of a UK marketing authorisation, in order to comply with the batch testing condition, submits appropriate documentation that includes a certificate issued by a laboratory in an approved country for batch testing and certification of biological medicinal products in respect of the batch, the appropriate authority must, in addition to any other factors it considers relevant, take that into account in determining whether the appropriate authority needs to undertake any further testing of the medicinal product submitted to it.

(7) In order to determine whether a country should be included in the approved country list for batch testing and certification of biological medicinal products, the appropriate authority may, in particular, take into account whether the relevant certification process in that country is based on testing performed under a quality assurance system that undergoes regular external assessment to ensure it meets an appropriate standard of competence for testing biological medicines.

(8) The appropriate authority must—

- (a) review the countries it has included in the approved country list for batch testing and certification of biological medicinal products to determine if it is still satisfied that the country should remain on that list, and if it is not so satisfied, remove that country from the list; and
- (b) undertake that review at least every three years beginning with the date on which that country is included in the list.

(9) The appropriate authority must—

- (a) publish a list of countries, or organisations, with whom the United Kingdom has an agreement for the purposes of the application of the batch testing exemption;
- (b) include in that list any conditions or restrictions in that agreement that affect the applicability of the batch testing exemption; and
- (c) update that list as soon as reasonably practicable if—
 - (i) the United Kingdom no longer has an agreement with a country or organisation included in the list,
 - (ii) any such agreement is amended, or
 - (iii) the United Kingdom enters in to a new agreement with a country or organisation.

(10) Where a holder of a UK marketing authorisation relies on the batch testing exemption in relation to a batch of a medicinal product, that holder must submit the certificate in respect of that batch to the licensing authority and the appropriate authority, and such other documentation as those authorities may notify that holder they require, before it sells or supplies, or offers to sell or supply, a medicinal product that forms part of that batch in the United Kingdom.

(11) Paragraph (12) applies where the appropriate authority considers that there are public health concerns in respect of a batch of a medicinal product (“the relevant batch”) in relation to which the batch testing exemption would otherwise apply.

(12) Where this paragraph applies, the appropriate authority must, subject to paragraph (13), notify the holder of the UK marketing authorisation in respect of the relevant batch that it nevertheless requires that holder—

- (a) to submit a sample from the relevant batch to the appropriate authority, together with appropriate documentation; and
- (b) not to sell or supply, or to offer to sell or supply, a medicinal product that forms part of that batch in the United Kingdom until the appropriate authority has examined—
 - (i) the sample from that batch,
 - (ii) the appropriate documentation, or
 - (iii) both that sample and that documentation,

and confirmed that it is satisfied that the relevant batch is in conformity with the approved specifications in the UK marketing authorisation.

(13) The appropriate authority may only exercise its powers under paragraph (12) if the agreement made between the country in which the certificate was issued, and the United Kingdom (whether the agreement is solely with that country, a group of countries or an organisation of which that country is a part) provides for the relevant batch to be re-examined by the appropriate authority in the circumstances described in paragraph (11).”.

Amendment of regulation 61 (conditions of UK marketing authorisation)

68.—(1) Regulation 61 is amended as follows.

(2) For paragraph (4), substitute—

“(4) The obligation in this paragraph is—

- (a) to conduct a post-authorisation safety study; or
- (b) to comply with such other conditions or restrictions as the licensing authority considers essential for the safe and effective use of the medicinal product.”.

(3) For paragraph (6) substitute—

“(6) If concerns as described in paragraph (2) apply to more than one medicinal product, the licensing authority—

- (a) must, where the obligation is to conduct a post-authorisation safety study, encourage the UK marketing authorisation holders concerned to conduct a joint study; and
- (b) may, where the obligation is to comply with any other conditions or restrictions, encourage the UK marketing authorisation holders concerned to take co-ordinated action to comply with the conditions or restrictions.”.

(4) For paragraph (7) substitute—

“(7) The obligation under paragraph (5) must—

- (a) be based on the delegated acts adopted pursuant to Article 22b of the 2001 Directive; and
- (b) take into account the scientific guidance that applies under regulation 205B in relation to post-authorisation efficacy studies

(7A) The Ministers may by regulations make provision specifying the situations in which post-authorisation efficacy studies may be required by virtue of the obligation under paragraph (5).

(7B) Paragraph (7)(a) ceases to apply on the coming into force of regulations made under paragraph (7A).”.

(5) Omit paragraph (13).

Amendment of regulation 64 (duties of licensing authority in connection with determination)

69. In regulation 64(4)(d), for “established in accordance with Articles 21a, 22 and 22a of the 2001 Directive” substitute “imposed under regulations 59 to 61”.

Obligation of licensing authority in case of change of classification

70. After regulation 64, insert—

“Obligation of licensing authority in case of change of classification

64A.—(1) In this regulation, “classification”, in relation to a medicinal product, means the term of the product’s UK marketing authorisation which determines the way in which the product is to be made available, as described in regulation 62(1).

(2) This regulation applies where—

- (a) the licensing authority grants or varies a UK marketing authorisation;
- (b) the grant or variation of the UK marketing authorisation involves a change of the classification of the medicinal product to which the authorisation relates; and
- (c) the application for the UK marketing authorisation or variation was supported by the results of significant pre-clinical tests or clinical trials relating to the proposed classification.

(3) Where this regulation applies, the licensing authority may not, for the period of one year beginning with the date on which the UK marketing authorisation was granted or varied, refer to the results of the tests or trials referred to in paragraph (2)(c) when examining an application by another applicant or UK marketing authorisation holder for a change of classification of the same kind as that to which the tests or trials relate.”.

Amendment of regulation 65 (validity of UK marketing authorisation)

71. In regulation 65(5) before sub-paragraph (a) insert—

“(za) regulation 65B;”.

Validity of conditional marketing authorisation and variation of a UK marketing authorisation

72. After regulation 65A(63), insert—

“Validity of conditional marketing authorisation

65B.—(1) A conditional marketing authorisation remains in force—

- (a) for an initial period of one year beginning with the date on which it is granted; and
- (b) if it is renewed in accordance with regulation 66B, for further periods of one year beginning with the date on which the renewal is granted.

(63) Regulation 65A was inserted by [S.I. 2014/1878](#).

(2) If an application for the renewal or further renewal of a conditional marketing authorisation is made in accordance with regulation 66B the authorisation remains in force until the licensing authority notifies the applicant of its decision on the application.

Variation of a UK marketing authorisation

65C.—(1) A UK marketing authorisation holder may apply to vary the authorisation.

(2) Any such application must be made in accordance with Schedule 10A.

(3) Schedule 10A does not apply to the transfer of a UK marketing authorisation from one person to another.

(4) The licensing authority may publish guidance on the details of the various categories of variations, on the operation of the procedures laid down in Schedule 10A, and on the documentation to be submitted pursuant to those procedures.

(5) Any guidance referred to in paragraph (4) must be regularly reviewed and, when necessary, updated.

(6) Unless replaced by guidelines published under paragraph (4), the guidelines published by the Commission under Article 4 of Regulation (EC) No 1234/2008⁽⁶⁴⁾ which applied immediately before exit day, insofar only as they concern applications under Chapter IIa of that Regulation, continue to apply to—

(a) applications made under regulation 65C on or after exit day; or

(b) applications made before exit day to which regulation 65C and Schedule 10A apply by virtue of Parts 3 and 5 of Schedule 33A.

(7) The Ministers may by regulations amend Schedule 10A.”.

Insertion of new Schedule 10A (variations to a UK marketing authorisation)

73. Schedule 5 inserts a new Schedule 10A after Schedule 10.

Amendment of regulation 66 (application for renewal of authorisation)

74. In regulation 66(2), for “European Union” substitute “United Kingdom”.

Amendment of regulation 66A (application for renewal of a parallel import licence)

75. In regulation 66A(2)⁽⁶⁵⁾, for “European Union” substitute “United Kingdom”.

Renewal of conditional marketing authorisation

76. After regulation 66A, insert—

“Renewal of conditional marketing authorisation

66B.—(1) The licensing authority may renew a conditional marketing authorisation in relation to an application made to it by the holder of the authorisation.

(2) The application must be made at least six months before the date on which the conditional marketing authorisation is due to expire.

⁽⁶⁴⁾ The guidelines are available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

⁽⁶⁵⁾ Regulation 66A was inserted by [S.I. 2014/1878](#).

- (3) The application must include an interim report on the fulfilment of the obligations to which the conditional marketing authorisation is subject.
- (4) When considering an application under paragraph (1), the licensing authority must consider whether—
 - (a) the positive therapeutic effects of the product continue to outweigh the risks to the health of patients and the public associated with the product; and
 - (b) the obligations referred to in regulation 59(4C) and any time limits for their fulfilment remain appropriate, modifying or removing them if necessary.
- (5) The provisions of regulation 66(2), (3), (4), (6) and (8) apply to an application for renewal of a conditional marketing authorisation.”.

Amendment of regulation 68 (revocation, variation and suspension of UK marketing authorisation or parallel import licence)

- 77.—(1) Regulation 68(66) is amended as follows.
- (2) In paragraph (5), after “exceptional circumstances)”, insert “, regulation 60A (conditions as to testing of samples by the appropriate authority)”.
 - (3) In paragraph (7)—
 - (a) after “authorisation” insert “or licence”; and
 - (b) for “European Union” substitute “United Kingdom”.
 - (4) In paragraph (8)(b), for “states other than EEA states” substitute “countries other than approved countries for import”.
 - (5) Omit paragraph (9).
 - (6) In paragraph (10)—
 - (a) in sub-paragraph (a) for “authorisation; or” substitute “authorisation or licence.”; and
 - (b) omit sub-paragraph (b).
 - (7) In paragraph (11)(a), after authorisation insert “or licence”.
 - (8) After paragraph (11A), insert—
 - (11B) Condition L is that the licensing authority thinks that the term of the authorisation which specifies the way in which the product is to be made available, as described in regulation 62(1), is incorrect.
 - (11C) Condition M is that, in respect of a parallel import licence, the UK marketing authorisation in respect of the medicinal product that was specified in the application for that licence under paragraph 4 of Schedule 8A, has been varied, suspended or revoked by the licensing authority under this regulation.
 - (11D) Condition N is that, in respect of a parallel import licence, the licensing authority is no longer satisfied that the product is essentially similar to a product that has been granted a UK marketing authorisation.
 - (11E) The licensing authority may not exercise its powers under paragraph (1) by virtue of the condition in paragraph (11D)—
 - (a) before the end of the period of one year beginning with exit day; and
 - (b) in any event, in a way that prevents the import of any medicinal product in respect of which a qualified person undertook the certification referred to in Article 51(3) of the 2001 Directive before exit day.

(11F) Condition O is that the licensing authority thinks that a variation of a UK marketing authorisation is necessary as a result of the submission of the results of a study by the holder of that authorisation under regulation 78A(14).”.

(9) In paragraph (12)—

- (a) after “UK marketing authorisation”, insert “or parallel import licence”; and
- (b) after “an authorisation” insert “or licence”.

(10) Omit paragraph (13).

Amendment of regulation 69 (suspension of use etc of relevant medicinal product)

78. In regulation 69(67), omit paragraph (10).

Omission of regulation 70 (authorisations granted under Chapter 4 of Title III of the 2001 Directive)

79. Omit regulation 70.

Amendment of regulation 71 (withdrawal of medicinal product from the market)

80.—(1) Regulation 71(68) is amended as follows.

(2) In paragraph (1)—

(a) for sub-paragraph (a) substitute—

“(a) under regulation 68 the licensing authority revokes or suspends a UK marketing authorisation or parallel import licence; or”; and

(b) in sub-paragraph (b)—

- (i) omit “or Article 20(4) of Regulation (EC) No 726/2004”; and
- (ii) insert “UK” before “marketing authorisation”.

Amendment of regulation 72 (sale etc of suspended medicinal product)

81. In regulation 72(1) omit “or 70(2) or Article 29(4) of Regulation (EC) No 726/2004”.

Amendment of regulation 73 (obligation to notify placing on the market etc)

82.—(1) Regulation 73(69) is amended as follows.

(2) In paragraph (5A)(c), for “third country” substitute “country other than the United Kingdom”.

(3) Omit paragraph (5C).

Amendment of regulation 75 (obligation to provide information relating to safety etc)

83. In regulation 75(5)(70)—

(a) for sub-paragraph (a) substitute—

“(a) in a country other than the United Kingdom;” and

(b) in sub-paragraph (b), insert “UK” before “marketing authorisation”.

(67) Regulation 69 was amended by [S.I. 2014/1878](#).

(68) Regulation 71 was amended by [S.I. 2014/1878](#).

(69) Regulation 73 was amended by [S.I. 2013/2593](#): regulation 3 inserted sub-paragraphs (5A) to (5C).

(70) Regulation 75 was amended by [S.I. 2014/1878](#).

Amendment of regulation 76 (obligation in relation to product information)

84. In regulation 76(2)(71) for the words from “European medicines web-portal” to the end, substitute “the UK web-portal established in accordance with regulation 203(1).”

Amendment of regulation 77 (record-keeping obligations)

85. In regulation 77, insert “UK” before “marketing authorisation”.

Amendment of regulation 78 (obligation to ensure appropriate and continued supplies)

86. In regulation 78, insert “UK” before “marketing authorisation”.

Post authorisation requirements in relation to UK marketing authorisations with paediatric aspects and advanced therapy medicinal products

87. After regulation 78, insert—

“Post authorisation requirements in relation to UK marketing authorisations to which paediatric specific provisions apply

78A.—(1) Paragraph (2) applies where—

- (a) a holder of a UK marketing authorisation intends to discontinue supply of the product to which that authorisation relates;
- (b) the holder of the authorisation benefited from a reward or incentive under regulation 58A(3) or (8) or 58D(5) in relation to the product; and
- (c) the period of protection provided pursuant to those regulations has expired.

(2) Where this paragraph applies, the holder of the UK marketing authorisation must—

- (a) either—
 - (i) transfer the UK marketing authorisation to another person who has declared an intention to continue to supply the product; or
 - (ii) allow such a person to use the pharmaceutical, pre-clinical and clinical documentation contained in the file on that product in accordance with regulation 56; and
- (b) notify the licensing authority of its intention to cease to supply the product before the beginning of the period of six months ending immediately before the day on which the holder does so.

(3) Paragraph (4) applies to the holder of a UK marketing authorisation if—

- (a) that authorisation includes a paediatric indication following completion of an agreed paediatric investigation plan; and
- (b) the product was placed on the market for other indications before that holder obtained that paediatric indication.

(4) Where this paragraph applies, the holder of the UK marketing authorisation must place the product on the market taking account of the paediatric indication before the end of the period of two years beginning immediately after the day on which the paediatric indication is authorised.

(5) Paragraph (6) applies if—

(71) Regulation 76 was amended by [S.I. 2014/1878](#).

- (a) a decision by the licensing authority in respect of a paediatric investigation plan is addressed to a person (“PIP sponsor”); and
 - (b) the plan refers to clinical trials carried out in a country other than the United Kingdom (“non-UK clinical trials”).
- (6) Where this paragraph applies, the PIP sponsor must send to the licensing authority the details set out in Article 11 of the Clinical Trials Directive in relation to the non-UK clinical trials within whichever is the later of—
- (a) the period of one month beginning after the day on which the decision was received; or
 - (b) the period of one month beginning after the day on which the necessary permission to conduct the clinical trial was received from the competent authorities in the country where the clinical trial is to take place.
- (7) Where paragraph (6) applies, the PIP sponsor must submit the results of those clinical trials to the licensing authority within the period of twelve months beginning with the day on which the last of those trials ended, subject to paragraph (8).
- (8) Paragraph (7) does not apply in the case of a clinical trial which forms part of a paediatric study to which paragraph (12) applies.
- (9) Paragraph (10) applies in relation to the sponsor of a paediatric clinical trial in the United Kingdom in respect of a medicinal product if—
- (a) the product has a UK marketing authorisation but the sponsor is not the holder of the authorisation; or
 - (b) the product does not have a UK marketing authorisation.
- (10) Where this paragraph applies, the sponsor of the clinical trial must submit the results of the trial to the licensing authority within the period of twelve months beginning with the day on which the trial ended.
- (11) Paragraph (12) applies in relation to the holder of a UK marketing authorisation who sponsors a paediatric clinical trial in respect of the medicinal product to which that authorisation relates.
- (12) Where this paragraph applies, the holder of the UK marketing authorisation must submit the results of the trial to the licensing authority within the period of six months beginning with the day on which the trial ended.
- (13) Paragraph (14) applies in relation to the holder of a UK marketing authorisation who sponsors a study which involves the use in the paediatric population of a medicinal product to which that UK marketing authorisation relates, irrespective of whether or not—
- (a) the studies are conducted in accordance with an agreed paediatric investigation plan; or
 - (b) the marketing authorisation holder intends to apply for a marketing authorisation for a paediatric indication in relation to the product.
- (14) Where this paragraph applies, the holder of the UK marketing authorisation must submit the results of the study to the licensing authority within the period of six months beginning with the day on which the study ended.
- (15) Where the licensing authority has granted a deferral of the initiation or completion of some or all of the measures set out in a paediatric investigation plan, in accordance with regulation 50C, the person to whom that decision was addressed must submit to the licensing authority an annual report providing an update on progress with the paediatric studies to which the deferral relates.

(16) The first report referred to in paragraph (15) must be submitted within the period of twelve months beginning with the date on which the licensing authority granted the deferral.

Post authorisation requirements in relation to UK marketing authorisations for advanced therapy medicinal products

78B.—(1) The holder of a UK marketing authorisation in respect of an advanced therapy medicinal product must—

- (a) establish and maintain a system ensuring that the individual product and its starting raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the hospital, institution or private practice where the product is used;
- (b) where the product contains human tissues or cells, ensure that the traceability system is complementary to and compatible with requirements imposed pursuant to—
 - (i) as regards gametes and embryos, sections 12(3), and 33A to 33D of, and paragraph 1 of Schedule 3A to, the Human Fertilisation and Embryology Act 1990⁽⁷²⁾,
 - (ii) as regards blood cells, regulations 8, 9(e) and 14 of the Blood Safety and Quality Regulations 2005⁽⁷³⁾, and
 - (iii) as regards other cells and tissues, regulations 13 and 16 of, and paragraph 1 of Schedule 2 to, the Human Tissue (Quality and Safety for Human Application) Regulations 2007⁽⁷⁴⁾;
- (c) keep the data referred to in paragraph (a) for a minimum of 30 years after the expiry of the date of the product, or longer if required by the licensing authority as a term of the UK marketing authorisation; and
- (d) in the event of the UK marketing authorisation holder’s bankruptcy or liquidation occurring within the period of time for which that holder is required to keep the data referred to in paragraph (a), transfer that data to another person or the licensing authority.

(2) The holder of a UK marketing authorisation who is subject to the obligations in paragraph (1) remains subject to them even if the UK marketing authorisation is suspended or revoked.”.

Omission of regulation 79 (failure to provide information on marketing authorisations to EMA)

88. Omit regulation 79.

Amendment of regulation 80 (urgent safety restrictions)

89.—(1) Regulation 80 is amended as follows.

(2) In the introductory words, insert “UK” before “marketing authorisation”.

(3) In sub-paragraph (a) for “or the European Commission in accordance with Article 22(1) of Regulation (EC) No 1234/2008” substitute “in accordance with paragraph 14(1) of Schedule 10A”.

⁽⁷²⁾ 1990 c. 37. Sections 33A to 33D were inserted by the Human Fertilisation and Embryology Act 2008, c. 22.

⁽⁷³⁾ S.I. 2005/50. It was amended by S.I. 2005/1098 and 2898, 2006/2013, 2007/604, 2008/525 and 941, 2009/372 and 3307, 2010/554, 2016/604, 2017/1320 and 2018/231.

⁽⁷⁴⁾ S.I. 2007/1523.

(4) In sub-paragraph (b) from “or the European Commission” to the end substitute “in accordance with paragraph 14(3) of Schedule 10A; or”.

(5) For sub-paragraph (c) substitute—

“(c) fails to submit an application for variation of the UK marketing authorisation to the licensing authority in accordance with paragraph 14(4) of Schedule 10A before the end of the period of fifteen days beginning with the day after—

(i) the taking under paragraph 14(1) of Schedule 10A or, as the case may be,

(ii) the imposition under paragraph 14(3) of that Schedule,

of an urgent safety restriction.”.

Omission of regulations 81 to 94 (offences relation to EU marketing authorisations)

90. Omit regulations 81 to 94(75).

Omission of regulation 94A (offences relating to Commission Regulation 2016/161)

91. Omit regulation 94A(76).

Amendment of regulation 95 (offences in connection with application)

92.—(1) Regulation 95 is amended as follows.

(2) In the introductory words, insert “UK” before “marketing authorisation”.

(3) Omit sub-paragraphs (c) and (d).

Amendment of regulation 96 (provision of misleading information)

93.—(1) Regulation 96(77) is amended as follows.

(2) In paragraph (1)—

(a) insert “UK” before “marketing authorisation”; and

(b) omit sub-paragraphs (b) and (c).

(3) In paragraph (2), for “these Regulations; or” to the end substitute “these Regulations.”.

Amendment of regulation 97 (breach of pharmacovigilance condition)

94.—(1) Regulation 97(78), is amended as follows.

(2) In each place where it occurs—

(a) for “a marketing authorisation” substitute “a UK marketing authorisation”; and

(b) for “the marketing authorisation” substitute “the UK marketing authorisation”.

(3) In paragraph (2), after “exceptional circumstances)” insert “, regulation 60A (condition as to the testing of samples by the appropriate authority)”.

Amendment of regulation 98 (general offence of breach of Part 5)

95. In regulation 98(2)(a), insert “UK” before “marketing authorisation”.

(75) Regulation 82 was previously amended by [S.I. 2013/2593](#) and regulation 84 was amended by [S.I. 2013/1855](#).

(76) Regulation 94A was inserted by [S.I. 2019/62](#).

(77) Regulation 96 was amended by [S.I. 2014/1878](#).

(78) Regulation 97 was substituted by [S.I. 2014/1878](#).

Amendment of regulation 99 (penalties)

96.—(1) Regulation 99 is amended as follows.

(2) In paragraph (1), omit “other than a breach of regulation 79 (failure to provide information on marketing authorisation to EMA)”.

(3) Omit paragraph (2).

Amendment of regulation 101 (defences)

97.—(1) Regulation 101(79) is amended as follows.

(2) In paragraph (1), insert “UK” before “marketing authorisation”.

(3) In paragraph (3), for “any of regulations 88 to 93,” substitute “either of regulations”.

PART 6

Amendment of Part 6 (certification of homoeopathic products)

Amendment of regulation 102 (regulation-making power to amend regulation 102(4) to (6))

98. In regulation 102 (application of Part 6), at the end insert—

“(7) The Ministers may by regulations amend paragraphs (4) to (6).

(8) The Ministers may only exercise the power in paragraph (7) if they consider that it is necessary to do so because of new scientific evidence.”.

Amendment of regulation 103 (application for certificate of registration)

99.—(1) Regulation 103 is amended as follows.

(2) In paragraph (4), for “European Union” substitute “United Kingdom”.

(3) In paragraph (8)—

(a) in sub-paragraph (e)—

(i) omit “or another EEA State”, and

(ii) for “that EEA State” substitute “a country other than the United Kingdom”; and

(b) in sub-paragraph (f), for “another member state” substitute “a country other than the United Kingdom”.

Amendment of regulation 104 (consideration of application)

100. Omit regulation 104(5) and (6).

Amendment of regulation 108 (application for renewal of certificate)

101. In regulation 108(2), for “European Union” substitute “United Kingdom”.

Amendment of regulation 110 (revocation, variation and suspension of certificate of registration)

102.—(1) Regulation 110(80) is amended as follows.

(79) Regulation 101 was amended by [S.I. 2014/1878](#).

(80) Regulation 110 was amended by [S.I.2013/1855](#).

- (2) In paragraph (7), for “European Union” substitute “United Kingdom”.
- (3) Omit paragraph (10).

Omission of regulation 111 (certificates granted under Chapter 4 of Title III of the 2001 Directive)

- 103.** Omit regulation 111.

Amendment of regulation 112 (withdrawal of homoeopathic medicinal product from the market)

- 104.** In regulation 112(1), omit “or regulation 111(2)”.

Amendment of regulation 113 (obligation to notify placing on the market etc)

- 105.** In regulation 113(3A)(**81**), omit “in accordance with article 123(2) of the 2001 Directive”.

Amendment of regulation 115 (obligation to provide information relating to safety etc)

- 106.** In regulation 115(5)(a) for “which is not an EEA State” substitute “other than the United Kingdom”.

Amendment of regulation 116 (obligation in relation to product information)

- 107.** In regulation 116(2) for “European” to the end substitute “UK web-portal established in accordance with regulation 203(1).”

PART 7

Amendment of Part 7 (Traditional Herbal Registrations)

Amendment of italic heading above regulation 125 (traditional herbal medicinal products)

- 108.** For the italic heading “Application of Part”, substitute “Interpretation and application of Part”.

Insertion of regulation 124A (interpretation)

- 109.** Before regulation 125 (traditional herbal medicinal products), insert—

“Interpretation of this Part

124A. In this Part, “relevant list” means—

- (a) the list referred to in Article 16f(1) of the 2001 Directive, as that list may be amended from time to time; or
- (b) if the licensing authority publishes a list under regulation 126A(1), that list.”.

(81) Paragraph (3A) was inserted by [S.I. 2013/2593](#).

Amendment of regulation 125 (traditional herbal medicinal products)

110. In regulation 125(5)(b), for “European Union” substitute “United Kingdom or a country included in the list published under regulation 125A(1)”.

Insertion of regulation 125A (list of approved countries for herbal medicinal products)

111. After regulation 125 insert—

“List of approved countries for traditional use of a herbal medicinal product

125A.—(1) The licensing authority may publish a list of countries for the purposes of regulation 125(5)(b) (condition D).

(2) In establishing the list under paragraph (1), the licensing authority may only include a country in that list if it is satisfied that—

- (a) continuous use evidence in respect of that country can be sufficiently validated by the licensing authority; and
- (b) the country has a level of pharmacovigilance that is equivalent to that in the United Kingdom to ensure that any safety issues in respect of the herbal medicinal product have been properly identified.

(3) The licensing authority must—

- (a) review any list it publishes under paragraph (1) to determine if a country still satisfies the criteria for inclusion in the list specified in paragraph (2), and if it is not so satisfied, remove that country from the list; and
- (b) undertake such a review at least every three years beginning with the date on which the country is included in that list.”.

Insertion of new italic heading and regulation 126A (list of herbal substances, preparations and combinations for use in traditional herbal medicinal products)

112. After regulation 126 (addition of vitamins or minerals) insert—

“List of herbal substances, preparations and combinations for use in traditional herbal medicinal products

Licensing authority list as to herbal substances, preparations and combinations for use in traditional herbal medicinal products

126A.—(1) The licensing authority may establish, and publish a list of, herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products.

(2) A list established under paragraph (1) must contain, with regard to each herbal substance—

- (a) the indication;
- (b) the specified strength and posology;
- (c) the route of administration; and
- (d) any other information necessary for the safe use of the herbal substance as a traditional medicinal product.

(3) The licensing authority may review and amend any list it publishes under paragraph (1) at such intervals as it considers appropriate.”.

Amendment of regulation 127 (application for grant of traditional herbal registration)

113. In regulation 127(3), for “European Union” substitute “United Kingdom”.

Amendment of regulation 128 (accompanying material)

114. In regulation 128(3), for “list referred to in Article 16f(1) of the 2001 Directive” substitute “relevant list”.

Amendment of Schedule 12 (material to accompany an application for a traditional herbal registration)

115.—(1) Schedule 12 is amended as follows.

(2) In paragraphs 16 and 17, for “another member State or a third country” substitute “a country other than the United Kingdom”.

(3) In paragraph 21—

- (a) for “Article 23 of Regulation (EC) No 726/2004” substitute “regulation 202A”;
- (b) before “statement”, insert “symbol and”; and
- (c) before “This”, insert “▼”.

Amendment of regulation 130 (consideration of application)

116.—(1) Regulation 130 is amended as follows.

(2) In paragraph (6), insert “UK” before “marketing authorisation”.

(3) In paragraph (7), for “Article” to the end substitute “regulation 130A.”.

(4) In paragraph (8), for “list referred to in Article 16f(1) of the 2001 Directive” substitute “relevant list”.

(5) Omit paragraph (9).

(6) In paragraph (10)(a) for “Article 16h(3) of the 2001 Directive” substitute “regulation 143A”.

(7) Omit paragraphs (12) and (13).

Insertion of regulation 130A (procedure where less than 15 years use of traditional herbal medicinal product)

117. After regulation 130 (consideration of application) insert—

“Procedure where less than 15 years use of traditional herbal medicinal product

130A.—(1) Where an application for a traditional herbal registration has been made and the licensing authority considers that—

- (a) the traditional herbal medicinal product does not satisfy regulation 125(5)(b) (Condition D); but
- (b) otherwise satisfies the conditions in regulation 125,

the licensing authority may refer the matter to the appropriate committee for relevant advice, and the procedure in Part 3 of Schedule 11 applies (referral to the appropriate committee for traditional herbal registrations).

(2) In this regulation—

“appropriate committee” has the same meaning as in paragraph 2(4) of Schedule 11;

“relevant advice” means advice as to whether—

- (a) the conditions in regulation 125, other than condition D, are met in relation to the application; and
- (b) the licensing authority should exercise its powers under regulation 143A to establish a herbal monograph.”.

Amendment of regulation 133 (application for renewal of registration)

118. In regulation 133(2), for “European Union” substitute “United Kingdom”.

Amendment of regulation 135 (revocation, variation and suspension of traditional herbal registration)

119.—(1) Regulation 135(**82**) is amended as follows.

(2) In paragraph (7)(b), for “from states other than EEA States” substitute “countries other than approved countries for import”.

(3) Omit paragraph (8).

(4) In paragraph (9), omit sub-paragraph (b) (and the “and” immediately preceding it).

(5) Omit paragraph (11).

Amendment of regulation 136 (revocation by licensing authority: further provisions)

120.—(1) Regulation 136 is amended as follows.

(2) In paragraph (1)(a), for “list referred to in article 16f(1) of the 2001 Directive” substitute “relevant list”.

(3) Omit paragraph (3).

Amendment of regulation 138 (suspension of use etc of traditional herbal medicinal product)

121. Omit regulation 138(10).

Omission of regulation 139 (registrations granted under Chapter 4 of Title III of the 2001 Directive)

122. Omit regulation 139.

Amendment of regulation 140 (withdrawal of traditional herbal medicinal product from the market)

123. In regulation 140(1)(a), for “regulation 135, 136, 139(2) or Article 34(3) of the 2001 Directive” substitute “regulation 135 or 136”.

Amendment of regulation 141 (sale etc of suspended traditional herbal medicinal product)

124. In regulation 141(1), omit “or 139(2)”.

Amendment of regulation 142 (obligation to notify placing on the market etc)

125. Omit regulation 142(5C)(**83**).

(82) Regulation 135 was amended by [S.I. 2013/1855](#).

(83) Regulation 142 was amended by [S.I. 2013/2593](#).

Insertion of new regulation 143A (establishment of herbal monographs)

126. After regulation 143 (obligation to take account of scientific or technical progress) insert—

“Establishment of herbal monographs

143A.—(1) The licensing authority may establish herbal monographs for herbal medicinal products and traditional herbal medicinal products.

(2) Subject to paragraph (3), the licensing authority must—

- (a) consult the appropriate committee, within the meaning of paragraph 2(4) of Schedule 11, on a proposal to establish herbal monographs under paragraph (1); and
- (b) take the advice of the appropriate committee into account in determining whether to proceed with that proposal.

(3) Where an application for a traditional herbal registration has been referred to the appropriate committee by the licensing authority under regulation 130A, the licensing authority must consider whether to exercise its powers under paragraph (1), taking into account any relevant advice of the appropriate committee given under Part 3 of Schedule 11 in relation to that application.

(4) The licensing authority must publish a list of any herbal monographs established under this regulation.

(5) Until the licensing authority exercises the power under paragraph (1), the Community herbal monographs published from time to time under Article 16h(3) of the 2001 Directive continue to apply, and holders of a traditional herbal registration and the licensing authority must continue to take them into account in exercising any function or in relation to any obligation to which they are relevant under this Part.”.

Amendment of regulation 144 (obligation following new herbal monograph)

127. In regulation 144, for “Article 16h(3) of the 2001 Directive” substitute “regulation 143A”.

Amendment of regulation 145 (obligation to provide information relating to safety etc)

128. In regulation 145(5)(a), for “which is not an EEA State” substitute “other than the United Kingdom”.

Amendment of regulation 146 (obligation in relation to product information)

129. In regulation 146(2), for “European” to the end substitute “the UK web-portal established in accordance with regulation 203(1).”

Insertion of regulation 148A (urgent safety restrictions)

130. After regulation 148 (obligation to ensure appropriate and continued supplies) insert—

“Urgent safety restrictions

148A.—(1) Where, in the event of a risk to public health, the holder of a traditional herbal registration takes urgent safety restrictions on its own initiative, it must inform the licensing authority immediately.

(2) If the licensing authority has not raised objections within 24 hours following receipt of that information, the urgent safety restrictions are deemed to be accepted by the licensing authority.

(3) In the event of a risk to public health, the licensing authority may impose urgent safety restrictions.

(4) Where an urgent safety restriction is taken by the holder of a traditional herbal registration, or imposed by the licensing authority, the holder must submit an application for variation of that registration in relation to that restriction within 15 days beginning with the date of the initiation of that restriction.”

Amendment of regulation 149 (urgent safety restrictions)

131.—(1) Regulation 149 is amended as follows.

(2) In the heading to regulation 149, at the end insert “: offences”.

(3) In sub-paragraph (a), for “or the European Commission in accordance with Article 22(1) of Regulation (EC) No 1234/2008” substitute “in accordance with regulation 148A(1)”.

(4) In sub-paragraph (b), for “or the European Commission under Article 22(2) of that Regulation” substitute “in accordance with regulation 148A(2)”.

(5) For sub-paragraph (c), substitute—

- “(c) fails to submit an application for variation of the traditional herbal registration to the licensing authority in accordance with regulation 148A(4) before the end of the period of 15 days beginning with the day after—
- (i) the taking under regulation 148A(1), or
 - (ii) the imposition under regulation 148A(2),
- of an urgent safety restriction.”

PART 8

Omission of Part 8 (Article 126a authorisations)

Omission of Part 8

132. Omit Part 8.

PART 9

Amendment of Part 9 (borderline products)

Amendment of regulation 159 (provisional determination)

133. In regulation 159(1)—

- (a) insert “UK” before “marketing authorisation”; and
- (b) for “, certificate of registration or Article 126a authorisation” substitute “or certificate of registration”.

Amendment of regulation 164 (effect of determination)

134. In regulation 164(2)(a) and (b)—

- (a) insert “UK” before “marketing authorisation”; and
- (b) for “, certificate of registration or Article 126a authorisation” substitute “or certificate of registration”.

PART 10

Amendment of Part 10 (exceptions to requirement for marketing authorisations etc)

Amendment of regulation 168 (use of non-prescription medicines in the course of a business)

135. In regulation 168, in paragraph (8)—

- (a) in sub-paragraph (a), for “EEA State” substitute “approved country for import”; and
- (b) for sub-paragraph (b) substitute—
 - “(b) imported from an approved country for import—
 - (i) it is manufactured or assembled in that country by a person who is the holder of an authorisation in that country in relation to its manufacture or assembly, and
 - (ii) it is imported by the holder of a wholesale dealer’s licence under Part 3 that includes the import of a medicinal product from such a country.”.

Amendment of regulation 169 (mixing of general sale medicinal products)

136. In regulation 169(9)(a), insert “UK” before “marketing authorisation”.

Amendment of regulation 171 (exempt advanced therapy medicinal products)

137. In regulation 171(2)(c) for “Regulation (EC) No 726/2004” substitute “regulation 49(1)”.

Amendment of regulation 173 (exemption for certain radiopharmaceuticals)

138. In regulation 173(c), insert “UK” before “marketing authorisation”.

PART 11

Amendment of Part 11 (Pharmacovigilance)

Amendment of regulation 177 (application of Part and interpretation)

139.—(1) Regulation 177(84) is amended as follows.

(2) In paragraph (1)—

- (a) for “Schedule 33”, substitute “Schedules 12A and 33”;
- (b) omit “, except to the extent set out in paragraph (4)(b),”;
- (c) in sub-paragraph (a), at the end insert “or”;

(84) Regulation 177 was amended by [S.I. 2013/1855](#) and [2014/1878](#).

- (d) omit sub-paragraph (c) (and “or” immediately preceding it).
- (3) In paragraph (2)—
 - (a) after “this Part” insert “and Schedule 12A”;
 - (b) in sub-paragraph (a), insert “or” at the end;
 - (c) omit sub-paragraph (c) (and “or” immediately preceding it).
- (4) In paragraph (3)—
 - (a) for “Schedule 33” substitute “Schedules 12A and 33”;
 - (b) in sub-paragraph (a), at the end insert “or”;
 - (c) omit sub-paragraph (c) (and “or” immediately preceding it).
- (5) Omit paragraph (4).
- (6) In paragraph (5), omit the definitions of “co-ordination group”, “Eudravigilance database”, “Implementing Regulation” and “relevant competent authorities”.

Amendment of regulation 180 (obligation on licensing authority to audit pharmacovigilance system)

- 140.—(1) Regulation 180 is amended as follows.
- (2) In paragraph (1), omit “and report the results of that audit to the European Commission”.
- (3) In paragraph (2)—
 - (a) omit “results of the”; and
 - (b) for “reported to the European Commission” substitute “performed”.

Omission of regulation 181 (delegation of obligations under Part 11)

- 141. Omit regulation 181.

Amendment of regulation 182 (obligation on holder to operate a pharmacovigilance system)

- 142.—(1) Regulation 182(85) is amended as follows.
- (2) In paragraph (2)(a), for “resides and operates in the EU” substitute “is ordinarily resident, and operates, in the United Kingdom”.
- (3) In paragraph (3), insert at the beginning “Without prejudice to the requirements set out in regulation 65C and Schedule 10A (variations to a UK marketing authorisation)”.
- (4) Omit paragraph (6).

Amendment of regulation 184 (obligation on holder to audit pharmacovigilance system)

- 143. In regulation 184, after paragraph (2) insert—
 - “(3) The holder must also comply with the requirements of paragraph 13 of Schedule 12A in relation to auditing the pharmacovigilance system.”.

Amendment of regulation 185 (recording obligations on the licensing authority)

- 144. In regulation 185(b), after “by” insert “a holder,”.

(85) Regulation 182 was amended by [S.I. 2013/1855](#).

Amendment of regulation 186 (reporting obligations on the licensing authority)

145. In regulation 186(1)—

- (a) at the end of sub-paragraph (a) insert “and”; and
- (b) omit sub-paragraphs (c) to (e).

Insertion of new regulation 187A (collaboration with the World Health Organisation)

146. After regulation 186 insert—

“**186A.** The licensing authority must collaborate with the World Health Organisation in matters of pharmacovigilance, and must in particular—

- (a) take the necessary steps to promptly submit to the World Health Organisation appropriate and adequate information regarding the measures taken in the United Kingdom which may have a bearing on public health protection in other countries; and
- (b) make available promptly all suspected adverse reaction reports occurring in the United Kingdom to the World Health Organisation.”.

Amendment of regulation 187 (recording obligations on holders)

147.—(1) Regulation 187 is amended as follows.

(2) In paragraph (1), for “in the EEA or in third countries” substitute “in the United Kingdom or another country”.

(3) In paragraph (4), for “EEA” substitute “United Kingdom”.

Amendment of regulation 188 (reporting obligations on holders)

148.—(1) Regulation 188 is amended as follows.

(2) In each place where it occurs, for “Eudravigilance database” substitute “licensing authority”.

(3) In paragraph (1)—

(a) in sub-paragraph (a)—

- (i) for “EEA” substitute “United Kingdom”, and
- (ii) for “third countries” substitute “countries other than the United Kingdom”;

(b) in sub-paragraph (b), for “EEA” substitute “United Kingdom”;

(c) in sub-paragraph (e), for “EMA and the competent authorities of the EEA States” substitute “licensing authority”.

(4) Omit paragraphs (2) and (3).

(5) In paragraph (4)(a), omit “other than monitored publications”.

(6) In paragraph (5), omit the definitions of “monitored active substance” and “monitored publication”.

(7) Omit paragraph (6).

Amendment of regulation 189 (signal detection: licensing authority obligations)

149.—(1) Regulation 189 is amended as follows.

(2) In paragraph (1)—

- (a) in sub-paragraph (a), for “in the Eudravigilance database” substitute “that it collects by virtue of operating its pharmacovigilance system under this Part”; and
 - (b) in sub-paragraph (d), for “regulations 59 to 61” substitute “regulations 59, 60 and 61”.
- (3) Omit paragraphs (2) to (4).

Amendment of regulation 190 (signal detection: holder obligation)

150. In regulation 190(1), omit “the EMA and”.

Amendment of regulation 191 (obligation on holder to submit periodic safety update reports: general requirements)

- 151.—(1) Regulation 191 is amended as follows.
- (2) In paragraphs (1) and (7), for “EMA” substitute “licensing authority”.
 - (3) In paragraph (2), insert “UK” before “marketing authorisation”.
 - (4) In paragraph (3), omit—
 - (a) “or an Article 126a authorisation” in both places it appears; and
 - (b) “or Article 126a authorisation”.
 - (5) After paragraph (4) insert—

“(4A) A PSUR must also include the content, and be submitted in the format, specified in Part 8 of Schedule 12A.”.
 - (6) After paragraph (8), insert—

“(8A) In the case of a conditional marketing authorisation, the holder must submit PSURs immediately upon the request of the licensing authority and at least every six months beginning with the date on which the authorisation for the medicinal product is granted or renewed by the licensing authority.”.
 - (7) In paragraph (10), for “within the EEA” in each place it appears substitute “in the United Kingdom”.
 - (8) Omit paragraph (11).

Amendment of regulation 192 (obligation to submit periodic safety reports: derogation from general requirements)

- 152.—(1) Regulation 192 is amended as follows.
- (2) In paragraph (1)(a), insert “UK” before “marketing authorisation”.
 - (3) In paragraph (3), for “EMA” substitute “licensing authority”.
 - (4) Omit paragraphs (9) to (11).

Amendment of regulation 193 (harmonisation of PSUR frequency or date of submission)

- 153.—(1) Regulation 193 is amended as follows.
- (2) Omit paragraph (1)(a).
 - (3) For paragraph (2) substitute—

“(2) Where one or more of the grounds in paragraph (3) is met, the holder may submit a request in writing to the licensing authority, or the licensing authority may in any event decide, to—

- (a) determine a UK reference date from which submission dates are calculated in respect of products that fall under paragraph (1); or
 - (b) change the frequency and date of submission of the PSUR.”.
- (4) For paragraph (4) substitute—

“(4) Where the licensing authority makes a decision under paragraph (2) following a written request from a holder, it must notify that holder in writing of its decision to approve or refuse the request.”.
- (5) In paragraph (5)—
 - (a) for “Article 107c(4) or Article 107c(6) of the 2001 Directive” substitute “paragraph (2)”; and
 - (b) for “EMA” substitute “licensing authority”.
- (6) For paragraph (6) substitute—

“(6) Subject to paragraph (6A), in this regulation, “UK reference date” means a date determined by the licensing authority under paragraph (2)(a) in respect of medicinal products containing the same active substance or the same combination of active substances.

(6A) Until the licensing authority makes a decision under paragraph (2), any—

 - (a) Union reference date in respect of medicinal products containing the same active substance or the same combination of active substances; or
 - (b) date of submission and frequency of periodic safety reports in respect of such products,

published by the EMA under Article 107c(7) of the 2001 Directive, is deemed to be the UK reference date or, as the case may be, the required date or frequency of PSUR submission, in respect of those medicinal products.”.
- (7) After paragraph (6A) insert—

“(7) The licensing authority must publish a list of—

 - (a) UK reference dates it determines under paragraph (2); and
 - (b) the required date of submission and frequency for PSURs in respect of medicinal products containing the same active substance or the same combination of active substances.

(8) Any change to the date of submission and frequency of PSURs as a result of the application of this regulation is to take effect after a 6 month period, such period beginning with the day after the licensing authority publishes that change under paragraph (7).”.

Omission of regulation 194 (responding to a single assessment of PSUR under Article 107e of the 2001 Directive)

154. Omit regulation 194.

Amendment of regulation 195 (obligation on licensing authority to assess PSURs)

- 155.—(1) Regulation 195(86) is amended as follows.
- (2) In the heading, omit “where EU single assessment procedure does not apply”.
 - (3) For paragraph (1) substitute—

“(1) This regulation applies where PSURs relating to a medicinal product have been submitted to the licensing authority under regulations 191 to 192.”.

(86) Regulation 195 was amended by [S.I. 2014/1878](#).

(4) After paragraph (3) insert—

“(3A) If the licensing authority considers under paragraph (3)(b) that an authorisation or registration needs to be varied, it may require the holder to submit to the licensing authority, within a time period that the licensing authority specifies, an application for a variation, including—

- (a) an updated summary of the product characteristics; and
- (b) an updated package leaflet.”.

(5) In paragraph (4), omit the definitions of “EU reference date” and “EU single assessment procedure”.

Substitution of regulation 196 (urgent action)

156. For regulation 196(87) and the italic heading immediately preceding it substitute—

“Major safety review

Major safety review by the licensing authority

196.—(1) The licensing authority may conduct a major safety review where—

- (a) on the basis of concerns resulting from the evaluation of data from pharmacovigilance activities it considers—
 - (i) suspending or revoking a UK marketing authorisation or traditional herbal registration of a medicinal product or in respect of a class of medicinal products,
 - (ii) prohibiting the supply of a medicinal product or a class of medicinal products,
 - (iii) refusing the renewal of a UK marketing authorisation or traditional herbal registration, or
 - (iv) action is necessary to vary a UK marketing authorisation or traditional herbal registration or a class of such authorisations or registrations, including to impose new conditions; or
- (b) it is informed by a holder that, on the basis of safety concerns, the holder has—
 - (i) interrupted the sale or supply, or offer of sale or supply, of the product to which a UK marketing authorisation or traditional herbal registration relates,
 - (ii) taken action to have that product’s authorisation or registration cancelled or intends to do so, or
 - (iii) not applied for the renewal of that product’s authorisation or registration.

(2) If the licensing authority conducts a review under paragraph (1), it must—

- (a) announce the initiation of that review on the UK web-portal as soon as reasonably practicable;
- (b) include in that announcement—
 - (i) an outline of its reasons for conducting a major safety review, the medicinal products concerned and, where applicable, the active substances concerned, and

- (ii) the proposed structure and time-scale of the review;
 - (c) notify a holder if the product to which that holder's authorisation or registration relates is within the scope of the review; and
 - (d) publish the outcome of that review, including any recommendations it is making, or action it is proposing to take, as soon as reasonably practicable after the conclusion of that review.
- (3) A holder who is notified under paragraph (2)(c)—
 - (a) must provide to the licensing authority such information as the licensing authority notifies that holder it requires, within such time period as the licensing authority specifies; and
 - (b) may, where such information contains confidential data relevant to the subject matter of the review, because the data relates to a manufacturing process or trade secret, notify the licensing authority that that data is provided in confidence.
- (4) Where the licensing authority proposes that action should be taken in respect of any UK marketing authorisation or traditional herbal registration—
 - (a) during the conduct of the major safety review, because urgent action is necessary to protect public health; or
 - (b) upon the conclusion of such a review,it may exercise its powers under Part 5 or 7 (as the case may be) in relation to that authorisation or registration.”.

Omission of regulation 197 (EU urgent action procedure)

157. Omit regulation 197.

Amendment of regulation 198 (post-authorisation safety studies: general provisions)

158.—(1) Regulation 198 is amended as follows.

- (2) In paragraph (2), for “competent authorities of the EEA States in which the study is conducted” substitute “licensing authority”.
- (3) In paragraph (3)—
 - (a) in sub-paragraph (c), for “relevant competent authorities” substitute “licensing authority”;
 - (b) in sub-paragraph (d), for “competent authorities of the EEA States in which the study was conducted” substitute “the licensing authority if the study is conducted in the United Kingdom”.

Amendment of regulation 199 (submission of draft study protocols for required studies)

159.—(1) Regulation 199 is amended as follows.

- (2) In paragraph (2), for “body specified in paragraph (3)” substitute “licensing authority”.
- (3) Omit paragraphs (3) and (4).
- (4) In paragraph (5), omit “Where this paragraph applies”.
- (5) In paragraph (6), omit sub-paragraph (b) (and “or” immediately preceding it).
- (6) Omit paragraphs (7) and (8).

Amendment of regulation 200 (amendment to study protocols for required studies)

- 160.**—(1) Regulation 200 is amended as follows.
- (2) In paragraph (2), for “body specified in paragraph (3)” substitute “licensing authority”.
 - (3) Omit paragraphs (3) and (4).
 - (4) In paragraph (5), omit “Where this paragraph applies”.
 - (5) Omit paragraphs (6) and (7).

Amendment of regulation 201 (submission and evaluation of final study reports for required studies)

- 161.**—(1) Regulation 201 is amended as follows.
- (2) In paragraph (2), for “body specified in paragraph (3)” substitute “licensing authority”.
 - (3) Omit paragraph (3).
 - (4) In paragraph (4), omit from “for reports” where it first appears to the end.

Omission of regulation 202 (follow up of final study reports)

- 162.** Omit regulation 202.

Insertion of new regulation 202A (medicinal products subject to additional monitoring)

- 163.** After regulation 202 insert—
“Medicinal products subject to additional monitoring

Licensing authority power in relation to medicinal products subject to additional monitoring

- 202A.**—(1) The licensing authority may establish a list of medicinal products that are subject to additional monitoring.
- (2) The list referred to in paragraph (1) is to include the names and active substances of—
 - (a) medicinal products authorised in the United Kingdom that contain a new active substance which, on 1st January 2011, was not contained in any medicinal product authorised in the United Kingdom;
 - (b) any biological medicinal product not covered by sub-paragraph (a) that was authorised in the United Kingdom after 1st January 2011;
 - (c) medicinal products that are authorised pursuant to these Regulations, subject to the conditions referred to in regulation 50I, 59(2)(b) or (c), 60 or 61(4).
 - (3) If the licensing authority considers it appropriate, medicinal products that are authorised pursuant to these Regulations, subject to the conditions referred to in regulation 59(2)(a), (d), (e) or (f), 61(5) or 183(2), may also be included in the list referred to in paragraph (1).
 - (4) For medicinal products included in the list referred to in paragraph (1)—
 - (a) the summary of product characteristics and the package leaflet must include a symbol and statement as follows: “▼ This medicinal product is subject to additional monitoring”; and
 - (b) that symbol must be proportional to the font of the subsequent standardised text, and each side of the triangle must have a minimum length of 5 millimetres.

(5) In the cases referred to in paragraph (2)(a) and (b), the licensing authority must, unless paragraph (6) applies, remove a medicinal product from the list after five years, beginning with the day after the UK reference date referred to in regulation 193.

(6) In the cases referred to in paragraph (2)(c) and (3), the licensing authority must remove a medicinal product from the list once the condition or obligation under a provision specified in those paragraphs has been fulfilled.

(7) Until the licensing authority publishes a list of medicinal products under paragraph (1), the reference to that list is instead to be read as a reference to the list referred to in Article 23 of Regulation (EC) No 726/2004, as that list may be amended from time to time.”.

Amendment of regulation 203 (obligations on licensing authority in relation to national medicines web-portal)

164.—(1) Regulation 203 is amended as follows.

(2) In paragraph (1), omit from “linked” to the end.

(3) In paragraph (2)—

(a) in sub-paragraph (e) for “Article 23 of Regulation (EC) No 726/2004” substitute “the list published by the licensing authority under, or which applies by virtue of, regulation 202A”; and

(b) in sub-paragraph (f), omit “(including by way of the web-based forms referred to in Article 25 of Regulation (EC) No 725/2004”.

Omission of regulation 204 (obligation on licensing authority in relation to public announcements)

165. Omit regulation 204.

Amendment of regulation 205 (obligations on holders in relation to public announcements)

166.—(1) Regulation 205 is amended as follows.

(2) In paragraph (2), for “bodies listed in paragraph (3)” substitute “licensing authority”.

(3) Omit paragraph (3).

Insertion of regulation 205A (further obligations in respect of pharmacovigilance activities)

167. After regulation 205 insert—

“Further obligations in respect of pharmacovigilance activities

Further obligations in respect of pharmacovigilance activities

205A.—(1) Schedule 12A makes further provision as to the obligations of a holder and the licensing authority in respect of the performance of pharmacovigilance activities under this Part.

(2) The Ministers may by regulations amend Schedule 12A.

(3) Regulations under paragraph (2) may make provision regarding the performance of pharmacovigilance activities under this Part as to—

(a) the content and maintenance of the pharmacovigilance system master file kept by the holder;

- (b) the minimum requirements for the quality system for the performance of pharmacovigilance activities by the holder and the licensing authority;
- (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 recorded by the licensing authority pursuant to regulation 185 (recording obligations on the licensing authority) 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 a holder;
- (f) the format and content of electronic periodic safety reports and risk management plans; and
- (g) the format of protocols, abstracts and final study reports for the post-authorisation safety studies.”.

Insertion of new Schedule 12A (further provision as to performance of pharmacovigilance activities)

168. Schedule 6 inserts a new Schedule 12A after Schedule 12 to the 2012 Regulations.

Insertion of regulation 205B (guidance in respect of good pharmacovigilance practice and post authorisation efficacy studies)

169. After new regulation 205A insert—
“Guidance in respect of pharmacovigilance

Guidance in respect of good pharmacovigilance practice and post authorisation efficacy studies

205B.—(1) The licensing authority may publish—

- (a) guidance on good pharmacovigilance practices for both the licensing authority and UK marketing authorisation holders;
- (b) scientific guidance on post authorisation efficacy studies.

(2) Subject to paragraph (3), the guidance issued by the Commission under Article 108a of the 2001 Directive on the matters specified in paragraph (1)(a) and (b) continues to apply until the date on which the licensing authority publishes guidance under paragraph (1).

(3) The licensing authority—

- (a) may determine that provisions of the guidance specified in paragraph (2) no longer apply, or apply subject to specified modifications, from a date that it specifies; and
- (b) must, if it so determines, publish its determination.

(4) Guidance published under paragraph (1), or which applies by virtue of paragraph (2) (as modified by any determination under paragraph (3), as the case may be), is to be taken into account in consideration of whether there has been any failure to comply with a provision in this Part, or Schedule 12A, to which the guidance is relevant.”.

Amendment of regulation 206 (infringement notices)

- 170.—(1) Regulation 206(88) is amended as follows.
- (2) In paragraph (1)—
- (a) omit “relevant”; and
 - (b) after “provision” insert “of this Part or Schedule 12A (“relevant provision”).
- (3) Omit paragraphs (3) and (4).

Amendment of regulation 207 (offences)

171. In regulation 207(1), after “other than” insert “Schedule 12A (further requirements in respect of pharmacovigilance activities) and”.

Amendment of regulation 208 (false and misleading information)

172. In regulation 208, omit “or the EMA”.

Amendment of regulation 209 (penalties)

173. In regulation 209(3), omit sub-paragraphs (h) and (i).

Omission of regulation 210 (offences relating to pharmacovigilance obligations under Regulation (EC) No 726/2004)

174. Omit regulation 210(89).

Amendment of regulation 210A (offences in relation to pharmacovigilance obligations under the Implementing Regulation)

- 175.—(1) Regulation 210A(90) is amended as follows.
- (2) In the heading, for “the Implementing Regulation” substitute “Schedule 12A”.
- (3) In paragraph (1)—
- (a) in sub-paragraph (a) for “the Implementing Regulation” substitute “Schedule 12A”; and
 - (b) in sub-paragraph (b)—
 - (i) for “the Implementing Regulation” substitute “Schedule 12A”, and
 - (ii) omit “or the EMA”.
- (4) For paragraph (2) substitute—
- “(2) The provisions of Schedule 12A mentioned in paragraph (1)(a) are—
- (a) Part 1 (pharmacovigilance system master file);
 - (b) Parts 2 and 3 (minimum requirements for the quality systems in the performance of pharmacovigilance activities);
 - (c) Part 6 (transmission of reports of suspected adverse reactions);
 - (d) paragraph 24 (update of risk management plans);
 - (e) Part 8 (periodic safety update reports); and
 - (f) Part 9 (post-authorisation safety studies).

(88) Regulation 206 was amended by [S.I. 2013/1855](#).

(89) Regulation 210 was amended by [S.I. 2013/1855](#).

(90) Regulation 210A was inserted by [S.I. 2013/1855](#).

- (3) Subject to paragraph (4), a person guilty of an offence under this regulation is liable—
- (a) on summary conviction to a fine not exceeding the statutory maximum; or
 - (b) on conviction on indictment to a fine.
- (4) A person guilty of an offence under this regulation which relates to a breach of paragraph 26(8) or 29(1) of Schedule 12A is liable—
- (a) on summary conviction to a fine not exceeding the statutory maximum; or
 - (b) on conviction on indictment to a fine, to imprisonment for a term not exceeding two years or to both.”.

Amendment of regulation 211 (persons liable)

176. In regulation 211, omit from first “or” to “No 726/2004”.

Amendment of regulation 212 (transitional arrangements)

177. In regulation 212, for “182, 186, 188, 191, 192, 198, 199, 200, 201, 202 and 210” substitute “198, 199, 200, 201 and 202”.

Amendment of Schedule 33 (transitional arrangements: pharmacovigilance)

178. In Schedule 33, omit paragraphs 1, 2 and 4 to 10.

PART 12**Amendment of Part 12 (dealings with medicinal products)****Amendment of regulation 213 (interpretation of Part 12)**

179. In regulation 213(1)(91)—

- (a) insert at the appropriate place—

““approved country health professional” means a person who is practising in a profession included in the list published under regulation 214(6A) in a country that is included in that list in relation to that profession;”;

- (b) omit the definition of “EEA health professional”(92); and
- (c) in the definition of “relevant prescriber”, for “EEA health professional” substitute “approved country health professional”.

Amendment of regulation 214 (sale or supply of prescription only medicines)

180.—(1) Regulation 214(93) is amended as follows.

(2) In paragraph (2)(a), for “EEA health professional” substitute “approved country health professional”.

(3) In paragraph (6), for “EEA health professional” substitute “approved country health professional”.

- (4) After paragraph (6) insert—

(91) Regulation 213 was amended by [S.I. 2013/235](#) and [2014/490](#) and [1878](#).

(92) The definition was substituted by [S.I. 2014/1878](#).

(93) Regulation 214 was amended [S.I. 2013/1855](#), [2014/490](#), [2016/186](#) and [2018/199](#).

“(6A) The licensing authority must publish a list of approved countries and professions for the purposes of the definition of “approved country health professional”.

(6B) In order to determine whether a country or profession should be included in the list published under paragraph (6A), the licensing authority may, in particular, take into account—

- (a) the country’s standards of professional qualification;
- (b) the country’s system for ensuring that qualified professionals have undergone training which meets the requirements that apply in that country;
- (c) the effectiveness of enforcement of professional standards;
- (d) the mechanisms the country has in place to assist members of the public in obtaining information in respect of a qualified professional who is established there; and
- (e) the regularity and rapidity of information provided by that country relating to non-compliant professionals.

(6C) The licensing authority must—

- (a) review a country or profession it has included in the list published under paragraph (6A) to determine if it is still satisfied that they should remain on the list, and if it is not so satisfied, remove it from that list; and
- (b) undertake such a review at least every 3 years beginning with the date on which that country or profession was included in that list.”.

Amendment of regulation 216 (exceptions to regulation 215)

181. In regulation 216(2), for “EEA health professional” substitute “approved country health professional”.

Amendment of regulation 217 (requirements for prescriptions: general)

182. In regulation 217(8)(a)(**94**), for “EEA health professional” substitute “approved country health professional”.

Amendment of regulation 217A (requirements for prescriptions to be dispensed in an EEA State)

183.—(1) Regulation 217A(**95**) is amended as follows.

- (2) In the heading, omit “other than the UK”.
- (3) In paragraph (2)(a), omit “other than the UK”.

Amendment of regulation 218 (requirements for prescriptions: EEA health professionals)

184.—(1) Regulation 218(**96**) is amended as follows.

(2) In the heading, and each place where it subsequently occurs, for “EEA health professional” substitute “approved country health professional”.

(3) In paragraph (5)(c) and (d)(ii)(bb), for “EEA health professional’s” substitute “approved country health professional’s”.

(94) Regulation 217 was amended by [S.I. 2014/490](#).

(95) Regulation 217A was inserted by [S.I. 2014/490](#).

(96) Regulation 218 was amended by [S.I. 2014/490](#) and [1878](#) and [2015/903](#).

(4) In paragraph (2)(a), for “relevant European State except the United Kingdom” substitute “country included in the list published under regulation 214(6A)”.

Amendment of regulation 219 (electronic prescriptions)

185. In regulation 219(2)(97), for “EEA health professional” substitute “approved country health professional”.

Amendment of regulation 219A (electronic prescriptions: EEA health professionals)

186.—(1) Regulation 219A(98) is amended as follows.

(2) In the heading, for “EEA health professionals” substitute “approved country health professionals”.

(3) In paragraph (2), for “EEA health professional” substitute “approved country health professional”.

Amendment of regulation 229 (exemption for supply by national health services bodies and local authorities)

187. In regulation 229(3)(f)(99), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of regulation 230 (exemption for supply etc under a PGD to assist doctors or dentists)

188. In regulation 230(8)(100), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of regulation 231 (exemption for supply etc under a PGD by independent hospitals etc.)

189. In regulation 231(8), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of regulation 232 (exemption for supply etc under a PGD by dental practices and clinics: England and Wales)

190. In regulation 232(8), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of regulation 233 (exemption for supply etc under a PGD by a person conducting a retail pharmacy business)

191. In regulation 233(7)(101), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(97) Regulation 219 was amended by S.I. 2015/903 and 2016/696.

(98) Regulation 219A was amended by S.I. 2015/903.

(99) Regulation 229 was amended by S.I. 2013/325, 2015/323, 2016/186 and 2018/199.

(100) Regulation 230 was amended by S.I. 2013/325.

(101) Regulation 233 was amended by S.I. 2013/235 and 2015/1503.

Amendment of regulation 234 (exemption for supply etc of products under a PGD to assist the police etc)

192. In regulation 234(9)(**102**), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of Schedule 17 (exemptions for sale, supply or administration by certain persons)

193.—(1) Schedule 17(**103**) is amended as follows.

(2) In the table in Part 1, in column 1 in entry 10, insert “UK” before “marketing authorisations”.

(3) In the table in Part 4, in columns 1 and 2 in entry 9, insert “UK” before “marketing authorisation”.

Amendment of regulation 249 (restrictions on persons to be supplied with medicinal products)

194. In regulation 249(2)—

- (a) in sub-paragraph (a), insert “UK” before “marketing authorisation”;
- (b) in sub-paragraph (b), insert “and” at the end; and
- (c) omit sub-paragraph (d) (and “and” immediately preceding it).

Amendment of regulation 254 (prohibitions concerning traceability of treatment with advanced therapy medicinal products)

195. In regulation 254(2)(a), for the words from “laid down in” to the end, substitute—
“imposed pursuant to—

- (a) as regards gametes and embryos, sections 12(3), and 33A to 33D of, and paragraph 1 of Schedule 3A to, the Human Fertilisation and Embryology Act 1990(**104**);
- (b) as regards blood cells, regulations 8, 9(e) and 14 of the Blood Safety and Quality Regulations 2005(**105**); and
- (c) as regards other cells and tissues, regulations 13 and 16 of, and paragraph 1 of Schedule 2 to, the Human Tissue (Quality and Safety for Human Application) Regulations 2007(**106**);”.

Omission of regulation 255A to 255C (enforcement and offences relating to Commission Regulation 2016/161)

196. Omit regulations 255A to 255C(**107**).

(**102**) Regulation 234 was amended by [S.I. 2015/323](#).

(**103**) Schedule 17 was amended by [S.I. 2014/1878](#), [2015/1503](#), [2016/186](#) and [2017/715](#),

(**104**) [1990 c. 37](#). Sections 33A to 33D were inserted by the Human Fertilisation and Embryology Act 2008, [c. 22](#).

(**105**) [S.I. 2005/50](#). It has been amended by [S.I. 2005/1098](#) and [2898](#), [2006/2013](#), [2007/604](#), [2008/525](#) and [941](#), [2009/372](#) and [3307](#), [2010/604](#), [2017/1320](#) and [2018/231](#).

(**106**) [S.I. 2007/1523](#).

(**107**) Regulations 255A to 255C were inserted by [S.I. 2019/62](#).

PART 13

Omission of Part 12A (sale of medicines to the public at a distance)

Omission of Part 12A

197. Part 12A(108) is omitted.

PART 14

Amendment of Part 13 (packaging and leaflets)

Amendment of regulation 257 (packaging requirements: general)

198.—(1) Regulation 257 is amended as follows.

(2) In paragraph (6), after “this regulation,” insert “regulation 257C,”.

(3) After paragraph (7) insert—

“(8) Nothing in this regulation applies to the outer or immediate packaging of an advanced therapy medicinal product.”.

Omission of regulations 257A and 257B (packaging requirements: medicinal products required to bear safety features and associated transitionals)

199. Omit regulations 257A and 257B(109).

Insertion of regulations 257C (packaging requirements: advanced therapy medicinal products) and 257D and 257E (guidance and regulations in relation to packing, leaflets and labelling)

200. After regulation 257, insert—

“Packaging requirements: advanced therapy medicinal products

257C.—(1) The information specified in Part 4 of Schedule 24 must appear—

- (a) on the outer packaging of an advanced therapy medicinal product (other than an exempt advanced therapy medicinal product); and
- (b) on the immediate packaging of the product, unless paragraph (2) or (3) applies to the packaging.

(2) This paragraph applies to the immediate packaging if the packaging is in the form of a blister pack and is placed in outer packaging which complies with the requirements of Part 4 of Schedule 24.

(3) This paragraph applies to immediate packaging if the packaging is too small to display the information required by Part 4 of Schedule 24.

(4) The information specified in Part 5 of Schedule 24 must appear on immediate packaging to which paragraph (2) or (3) applies.

(108) Part 12A was inserted by [S.I. 2013/1855](#).

(109) Regulations 257A and 257B were inserted by [S.I. 2019/62](#).

Guidance as to packaging and package leaflets

257D.—(1) The licensing authority may publish guidance on packaging and package leaflets which may, in particular, include—

- (a) the wording of certain special warnings for certain categories of medicinal products;
- (b) the particular information needs relating to products that are a pharmacy medicine;
- (c) the legibility of particulars on the labelling and package leaflet;
- (d) the methods of identification and authentication of medicinal products;
- (e) the list of excipients which must feature on the labelling of medicinal products and the way in which these excipients must be indicated.

(2) Until such time as the licensing authority publishes guidance under paragraph (1), any guidance published by the Commission under Article 65 of the 2001 Directive, insofar as that guidance was in force immediately before exit day(**110**), continues to apply as if it had been published by the licensing authority under paragraph (1).

Regulation-making power as to certain forms of labelling

257E. The Ministers may by regulations require the use of certain forms of labelling of a medicinal product in order to make it possible to ascertain—

- (a) the price of the medicinal product;
- (b) any reimbursement conditions of the National Health Service;
- (c) the legal status for supply to the patient in accordance with regulation 5 (classification), insofar as not already provided for in Schedule 25;
- (d) authenticity and identification of the medicinal product in accordance with Article 54a(5) of the 2001 Directive.”.

Amendment of Schedule 24 (packaging information requirements)

201.—(1) Schedule 24 is amended as follows.

(2) In paragraph 7(b), for “published pursuant to Article 65 of the 2001 Directive” substitute “published under regulation 257D”.

(3) In paragraphs 15, 16 and 23, for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(4) Omit paragraph 18A(**111**).

(5) After Part 3 insert—

“PART 4

Outer and immediate packaging: advanced therapy medicinal products

34. The name of the advanced therapy medicinal product which is the international non-proprietary name, or if none, the common name.

(110) The guidance is available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

(111) Paragraph (18A) was inserted by [S.I. 2019/62](#).

35. Where appropriate, whether the product is intended for babies, children or adults.
36. The expiry date in clear terms including the year and month and, if applicable, day.
37. A description of the active substance, expressed qualitatively and quantitatively.
38. Where the product contains tissues and cells of human or animal origin—
 - (a) a statement that the product contains such cells or tissues; and
 - (b) a short description of the cells or tissues and of their specific origin, including the species of animal in cases on non-human origin.
39. The pharmaceutical form and the contents by weight, volume or number of doses of the product.
40. A list of excipients, including preservative systems.
41. The method of use, application, administration or implantation and, if appropriate, the route of administration, with space provided for the prescribed dose to be indicated.
42. A special warning that the product is to be stored out of the sight and reach of children.
43. Any special warning necessary for the particular product.
44. Any special storage precautions.
45. Specific precautions relating to the disposal of the unused product or of waste derived from the product and, where appropriate, reference to any appropriate collection system.
46. The name and address of the holder of the UK marketing authorisation and, where applicable, the name of the representative appointed by the holder to represent him.
47. The UK marketing authorisation number.
48. The manufacturer's batch number.
49. The unique donation code assigned by a tissue establishment pursuant to—
 - (a) paragraph 1 of Schedule 3A to the Human Fertilisation and Embryology Act 1990⁽¹¹²⁾, as regards human gametes and embryos; and
 - (b) paragraph 1 of Schedule 2 to the Human Tissue (Quality and Safety for Human Application) Regulations 2007⁽¹¹³⁾, as regards other human tissues and cells.
50. Where the exempt advanced therapy medicinal product is for autologous use, the unique patient identifier and the words “for autologous use only”.

PART 5

Immediate packaging: blister packs and small packaging (advanced therapy medicinal products)

51. The information specified in Part 2.
52. The unique donation code assigned by a tissue establishment pursuant to—
 - (a) paragraph 1 of Schedule 3A to the Human Fertilisation and Embryology Act 1990, as regards human gametes and embryos; and

⁽¹¹²⁾1990 c. 37. Schedule 3A was inserted by the Human Fertilisation and Embryology (Quality and Safety) Regulations 2007/1522, regulation 30.

⁽¹¹³⁾S.I. 2007/1523.

(b) paragraph 1 of Schedule 2 to the Human Tissue (Quality and Safety for Human Application) Regulations 2007, as regards other human tissues and cells.

53. Where the exempt advanced therapy medicinal product is for autologous use, the unique patient identifier and the words “for autologous use only”.

Amendment of regulation 259 (packaging requirements: information for blind and partially sighted patients)

202. In regulation 259(2), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of regulation 260 (package leaflets)

203.—(1) Regulation 260 is amended as follows.

(2) After paragraph (1) insert—

“(1A) If the medicinal product is an advanced therapy medicinal product (other than an exempt advanced therapy medicinal product), the package leaflet must contain the information specified in Part 3 of Schedule 27 in the order specified in that Part.”.

(3) In paragraph (2), after “Part 2 of that Schedule)” insert “, or where the product is an advanced therapy medicinal product, the information specified in Part 3 of that Schedule,”.

(4) In paragraph (3), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of Schedule 27 (package leaflets)

204.—(1) Schedule 27(114) is amended as follows.

(2) In paragraph 8(c)(ii), for “Article 65 of the 2001 Directive”, substitute “published under regulation 257D”.

(3) In paragraph 11(f), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(4) Omit paragraph 12.

(5) In paragraph 13—

(a) for “Article 23 of Regulation (EC) No 726/2004” substitute “regulation 202A”;

(b) before “statement”, insert “symbol and”;

(c) before “This”, insert “▼”.

(6) At the end insert—

“Part 3

Advanced therapy medicinal products

18. The name of the advanced therapy medicinal product.

19. Where appropriate, whether the product is intended for babies, children or adults.

20. The common name of the advanced therapy medicinal product.

- 21.** The therapeutic group, or type of activity, of the product, in terms easily comprehensible for the patient.
- 22.** Where the product contains cells or tissues, a description of those cells or tissues and of their specific origin, including the species of animal in cases of non-human origin.
- 23.** Where the product contains medical devices or active implantable medical devices, a description of those devices and their specific origin.
- 24.** The product's therapeutic indications.
- 25.** A list of information which is necessary before the medicinal product is taken or used, including—
- (a) contra-indications;
 - (b) appropriate precautions for use;
 - (c) interactions with other medicinal products which may affect the action of the product;
 - (d) interactions with other substances, including alcohol, tobacco and foodstuffs which may affect the action of the product;
 - (e) special warnings; if any, relating to the product.
- 26.** The list mentioned in paragraph 25 must—
- (a) take into account the special requirements of particular categories of users (including, in particular, children, pregnant or breastfeeding women, the elderly and persons with specific pathological conditions);
 - (b) mention, if appropriate, possible effects on the ability to drive vehicles or operate machinery; and
 - (c) list any excipients—
 - (i) if knowledge of the excipients is important for the safe and effective use of the product; and
 - (ii) the excipients are included in the guidance published under regulation 257D.
- 27.** Instructions for proper use of the product including in particular—
- (a) the dosage;
 - (b) the method of use, application, administration or implantation and, if necessary, the route of administration;
 - (c) the frequency of administration (including, if necessary, specifying the times at which the product may or must be administered);
 - (d) the duration of treatment if this is to be time limited;
 - (e) symptoms of an overdose and the action, if any, to be taken in the case of an overdose;
 - (f) what to do if one or more doses have not been taken;
 - (g) a specific recommendation to consult a doctor or pharmacist, as appropriate, for further explanation of the use of the product.
- 28.** A description of the adverse reactions which may occur in normal use of the medicinal product and, if necessary, the action to be taken in such a case.
- 29.** A reference to the expiry date printed on the packaging of the product with—
- (a) a warning against using the product after that date;
 - (b) if appropriate, details of special storage precautions to be taken;

- (c) if necessary, a warning concerning visible signs of deterioration;
- (d) the full qualitative and quantitative composition;
- (e) the name and address of the UK marketing authorisation holder and, if applicable, the name of the holder's appointed representative; and
- (f) the name and address of the manufacturer.

30. The date on which the package leaflet was last revised.”.

Amendment of regulation 266 (language requirements etc)

205.—(1) Regulation 266 is amended as follows.

- (2) In paragraph (1), omit “unless either or both of paragraphs (2) and (3) applies”.
- (3) Omit paragraphs (2) and (3).

Amendment of regulation 267 (submission of mock-ups of packaging and leaflets to licensing authority)

206. In regulation 267, in each place where it occurs, for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

Amendment of regulation 268 (offence relating to packaging and package leaflets)

207.—(1) Regulation 268(115) is amended as follows.

- (2) In paragraph (1), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.
- (3) In paragraph (2)(a)—
 - (a) for “Article 28 or 32 of the Paediatric Regulation” substitute “regulation 50C(4), 50D(8) or 58A(2)(b)”; and
 - (b) omit “, Article 9 of Commission Regulation 2016/161”.

Amendment of regulation 269 (offences relating to packaging and package leaflets: other persons)

208.—(1) Regulation 269(116) is amended as follows.

- (2) In paragraph (1), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.
- (3) In paragraph (2)(a)—
 - (a) for “Article 28 or 32 of the Paediatric Regulation” substitute “regulation 50C(4), 50D(8) or 58A(2)(b)”; and
 - (b) omit “, Article 9 of Commission Regulation 2016/161”.

Amendment of regulation 270 (non-compliance with requirements of this Part)

209. In regulation 270(1) and (2), for “marketing authorisation, Article 126a authorisation” substitute “UK marketing authorisation”.

(115) Regulation 268 was amended by [S.I. 2019/62](#).

(116) Regulation 269 was amended by [S.I. 2015/903](#) and [2019/62](#).

Amendment of regulation 273 (child resistant containers for regulated medicinal products)

210.—(1) Regulation 273 is amended as follows.

(2) In paragraph (2), for sub-paragraph (b) substitute—

“(b) any specification for non-reclosable child resistant packaging that the licensing authority is satisfied is of an equivalent or higher technical specification to that specified in sub-paragraph (a).”.

(3) In paragraph (3), for sub-paragraph (b) substitute—

“(b) any specification for reclosable child resistant packaging that the licensing authority is satisfied is of an equivalent or higher technical specification to that specified in sub-paragraph (a).”.

PART 15

Amendment of Part 14 (advertising)

Amendment of regulation 279 (products without a marketing authorisation)

211. In regulation 279—

- (a) in sub-paragraph (a), insert “UK” before “marketing authorisation”;
- (b) at the end of sub-paragraph (b), insert “or”; and
- (c) omit sub-paragraph (d) (and “or” immediately preceding it).

Amendment of regulation 280 (general principles)

212. In regulation 280(1)—

- (a) for “marketing authorisation,” substitute “UK marketing authorisation or”; and
- (b) omit “or Article 126a authorisation”.

Amendment of regulation 281 (duties of authorisation holders and registration holders)

213. In regulation 281(1)—

- (a) in sub-paragraph (a), insert “UK” before “marketing authorisation”;
- (b) at the end of sub-paragraph (b) insert “or”; and
- (c) omit sub-paragraph (d) (and “or” immediately preceding it).

Amendment of regulation 293 (prohibition of supply to the public for promotional purposes)

214. In regulation 293(1)—

- (a) insert “UK” before “marketing authorisation”;
- (b) for “certificate of registration,” substitute “certificate of registration or”; and
- (c) omit “or Article 126a authorisation”.

Amendment of regulation 295 (abbreviated advertisements)

215. In regulation 295(2)(d)—

- (a) insert “UK” before “marketing authorisation”;

- (b) for “certificate of registration,” substitute “certificate of registration or”; and
- (c) omit “or Article 126a authorisation”.

Amendment of Schedule 30 (particulars for advertisements to persons qualified to prescribe or supply)

216. In paragraphs 1, 2 and 6 of Schedule 30(**117**), for “marketing authorisation, certificate of registration, traditional herbal registration or Article 126a authorisation”, substitute “UK marketing authorisation, certificate of registration or traditional herbal registration”.

Amendment of regulation 299 (medical sales representatives)

217. In regulation 299(3), for “marketing authorisation, certificate of registration, traditional herbal registration or Article 126a authorisation”, substitute “UK marketing authorisation, certificate of registration or traditional herbal registration”.

PART 16

Amendment of Part 15 (British Pharmacopoeia)

Amendment of regulation 321 (specified publications)

218. In regulation 321(5)—

- (a) in sub-paragraph (c), insert “UK” before “marketing authorisation”;
- (b) omit sub-paragraph (d).

PART 17

Amendment of Part 16 (enforcement)

Amendment of regulation 322 (validity of proceedings)

219. In regulation 322(1)—

- (a) for “, 7” substitute “or 7”; and
- (b) omit “or 8 (Article 126a authorisations)”.

Amendment of regulation 323 (enforcement in England, Wales and Scotland)

220.—(1) Regulation 323(**118**) is amended as follows.

- (2) In paragraph (1) omit “and the relevant EU provisions”.
- (3) In paragraph (3)—
 - (a) at the end of sub-paragraph (b) insert “and”; and
 - (b) omit sub-paragraph (d).
- (4) Omit paragraph (4A).

(117) Schedule 30 was amended by [S.I. 2014/1878](#).

(118) Regulation 323 was amended [S.I. 2019/62](#).

Amendment of regulation 327 (powers of inspection, sampling and seizure)

221.—(1) Regulation 327(**119**) is amended as follows.

(2) In paragraph (1)(c)—

- (a) in paragraph (v), insert “UK” before “marketing authorisation”;
- (b) insert “or” at the end of paragraph (vi);
- (c) omit paragraph (viii) (and “or” immediately preceding it).

(3) In paragraph (2)—

(a) in sub-paragraph (g)—

- (i) in paragraph (ii), after “Part 11” insert “or Schedule 12A” and insert “and” at the end, and
- (ii) omit paragraphs (iii), (iv) and (v); and

(b) omit sub-paragraph (h).

(4) Omit paragraph (4A).

(5) In paragraph (5)—

- (a) in sub-paragraph (a) for “, (g) or (h)” substitute “or (g)”; and
- (b) in sub-paragraph (b) omit “ or (4A)”.

Amendment of regulation 331 (findings and reports of inspections)

222.—(1) Regulation 331 is amended as follows.

(2) In paragraph (1)—

- (a) insert “UK” before “marketing authorisation”; and
- (b) omit sub-paragraph (c) (and “and” immediately preceding it).

(3) In paragraph (4) for sub-paragraph (c) substitute—

- “(c) in the case of a holder of a UK marketing authorisation or traditional herbal registration, Part 11 (pharmacovigilance).”.

Insertion of regulation 331A (guidelines on inspections)

223. After regulation 331 (finding and reports of inspections) insert—

“Guidelines on inspections

331A.—(1) The licensing authority may publish guidelines specifying the principles applicable to inspections referred to in this Part.

(2) Guidelines under paragraph (1) may include the form and content of reports under regulation 331 and of certificates of good manufacturing practice or good distribution practice.

(3) Until the licensing authority exercises its power under paragraph (1), the guidelines adopted by the European Commission under Article 111a of the 2001 Directive, as they had effect immediately before exit day(**120**), are to continue to apply.”.

(119) Regulation 327 was amended by [S.I. 2013/1855](#) and [2019/62](#).

(120) The guidelines are available at: <https://www.gov.uk/guidance/eu-guidance-documents-referred-to-in-the-human-medicines-regulations-2012> and a hard copy may be obtained from the Medicines and Healthcare products Regulatory Agency at the address given in the Explanatory Note.

PART 18

Amendment of Part 17 (miscellaneous and general)

Amendment of regulation 341 (decisions under the Human Medicines Regulations 2012)

224. In regulation 341(4)(a), insert “UK” before “marketing authorisation”.

Insertion of regulation 344A (modifications to deal with serious shortages) and 344B (regulation making powers)

225. After regulation 344 insert—

“Modifications to deal with serious shortages

344A.—(1) The Ministers may by regulations modify the application of any of the specified provisions in circumstances where the United Kingdom, or any part of the United Kingdom, is experiencing or may experience a serious shortage of medicinal products, or of medicinal products of a specified description, arising from the withdrawal of the United Kingdom from the European Union.

(2) Regulations may only be made under paragraph (1) for the purposes of preventing, remedying or mitigating the serious shortage that is being or may be experienced.

(3) For the purposes of paragraph (1), the “specified provisions” are the provisions of Parts 1, 3 to 5, 10 to 13 and 16, and of the associated Schedules.

(4) The reference in paragraph (1) to a serious shortage arising from the withdrawal of the United Kingdom from the European Union includes reference to a serious shortage where the withdrawal of the United Kingdom from the European Union is one but not the only significant factor contributing to the shortage.

(5) No regulations under paragraph (1) may be made, or have effect, after the end of the period of two years beginning with exit day.

Regulation making powers

344B.—(1) Regulations made under a power in the regulations listed in paragraph (2)—

- (a) are to be made by statutory instrument;
- (b) may make different provision for different purposes and different areas; and
- (c) may include incidental, supplemental, consequential, transitional, transitory or saving provisions, including consequential amendments to these Regulations.

(2) The regulations referred to in paragraph (1) are—

- (a) regulation B17(1) and (4) (good manufacturing practice);
- (b) regulation 50(5A) (Annex I to the 2001 Directive);
- (c) regulation 50G(5) (orphan criteria etc);
- (d) regulations 59(3A) and 61(7A) (post-authorisation efficacy studies);
- (e) regulation 65C(7) (variations of UK marketing authorisations);
- (f) regulation 102(7) (homoeopathic medicinal products);
- (g) regulation 205A(2) (further obligations in respect of pharmacovigilance activities);
- (h) regulation 257E (certain forms of labelling); and

(i) regulation 344A (modifications to deal with serious shortages).

(3) A statutory instrument containing regulations made under the powers listed in paragraph (2) is subject to annulment in pursuance of a resolution of either House of Parliament.”.

Amendment of regulation 345 (immunity from civil liability)

226. In regulation 345(5)—

- (a) insert “UK” before “marketing authorisation”;
- (b) insert “or” after “certificate of registration”; and
- (c) omit “or Article 126a authorisation”.

Amendment of regulation 346 (Secretary of State to carry out a review of certain provisions)

227. In regulation 346(121)—

- (a) in sub-paragraph (c), omit paragraphs (iia), (iiia), (iva), (xixa), (xxviii) and (xxviii); and
- (b) in sub-paragraph (d), omit paragraphs (ia) and (ivab).

PART 19

Transitional and consequential provision and revocations

Transitional provision in relation to EU exit

228.—(1) After regulation 347 insert—

“Transitional provision in relation to EU exit

347A. Schedule 33A contains transitional provision in relation to the EU Exit Regulations.”.

(2) Schedule 7 inserts a new Schedule 33A after Schedule 33.

Consequential amendments

229. Schedule 8 contains consequential amendments.

Revocations of retained direct EU law

230. Schedule 9 contains revocations of retained direct EU law.

(121) Regulation 346 was substituted by S.I. 2013/1855 and then amended by S.I. 2013/2593, 2014/490 and 1878, 2015/323, 903 and 1503, 2016/186, 2017/715, 2018/199 and 2019/62.

Signed by authority of the Secretary of State for Health and Social Care.

Jackie Doyle-Price

Mike Freer

Jeremy Quin

Parliamentary Under-Secretary of State, Two
of the Lords Commissioners of Her Majesty's
Treasury
Department of Health and Social Care
Her Majesty's Treasury

29th March 2019 1st April 2019

SCHEDULE 1

Regulation 3

Amendment of the Medicines (Products for Human Use) (Fees) Regulations 2016

Amendment of regulation 19 (capital fees for applications for variations of authorisations)**1.** In regulation 19—**(a)** in paragraph (1)(a), for paragraph (ii) substitute—

“(ii) 65C (variation of a UK marketing authorisation)”; and

(b) after paragraph (3) insert—

“(4) The reference in paragraph (1)(a)(ii) to an application under regulation 65C of the Human Medicines Regulations includes a reference to an application or notification submitted under paragraph 11(7) or 12(3) of Schedule 33A to the Human Medicines Regulations, or an application or notification which would have been submitted under those paragraphs but for its earlier submission in accordance with paragraph 13(1)(a) of that Schedule.”.

Insertion of regulations 19A-19F (fees for plasma master files, vaccine antigen master files, post-authorisation safety studies, major safety reviews, periodic safety update reports and batch testing)**2.** After regulation 19, insert—**“Fees for certification of plasma master files**

19A.—(1) The fee payable by a person who submits a plasma master file to the licensing authority for scientific and technical evaluation in accordance with paragraph 1.1(c), second indent, of Part III of Annex I to the 2001 Directive, is £8,309.

(2) The fee payable by a person who submits a plasma master file to the licensing authority for re-certification in accordance with paragraph 1.1(c), third indent, of Part III of Annex I to the 2001 Directive is—

- (a) £277, where there are no changes to the plasma master file other than an update to epidemiological data; or
- (b) £734, in any other case.

Fee for certification of vaccine antigen master files

19B. The fee payable by a person who submits a vaccine antigen master file to the licensing authority for scientific and technical evaluation in accordance with paragraph 1.2(c), first indent, of Part III of Annex I to the 2001 Directive, is £8,309.

Fees for assessment of post-authorisation safety studies

19C.—(1) This regulation applies to post-authorisation safety studies initiated, managed or financed by the holder of a marketing authorisation in compliance with obligations imposed under regulation 59 or 61 of the Human Medicines Regulations.

(2) The fee payable by the holder of a marketing authorisation upon submission of the study protocol for a post-authorisation safety study in accordance with paragraph 29(1)(a) of Schedule 12A to the Human Medicines Regulations is £8,309.

(3) The fee payable by the holder of a marketing authorisation upon submission of the final study report for a post-authorisation safety study in accordance with paragraph 29(1) (b) of Schedule 12A to the Human Medicines Regulations is £8,309.

Fee for carrying out a major safety review

19D.—(1) Where the licensing authority conducts a major safety review of a marketing authorisation or traditional herbal registration, or a set of marketing authorisations or traditional herbal registrations, under regulation 196 of the Human Medicines Regulations, a fee is payable in accordance with Part 6A of Schedule 2.

(2) Unless paragraph (3) applies, the fee referred to in paragraph (1) is payable by the holder of the marketing authorisation or registration to which the review relates.

(3) Where the review relates to two or more authorisations or registrations the fee referred to in paragraph (1) is to be divided by the number of authorisations or registrations forming part of the review (“relevant authorisation or registration”) and each holder of a relevant authorisation or registration must pay that reduced fee in respect of each relevant authorisation or registration it holds.

Fee for assessment of periodic safety update reports

19E.—(1) This regulation applies where—

- (a) a periodic safety update report has been submitted to the licensing authority under regulation 191 or 192 of the Human Medicines Regulations; and
- (b) that periodic safety update report relates to a medicinal product which has a UK reference date within the meaning of regulation 193 of the Human Medicines Regulations.

(2) Where this regulation applies, the fee payable by the holder of a marketing authorisation or traditional herbal registration to which the periodic safety update report relates is—

- (a) £890, in the case where no other periodic safety update reports relating to medicinal products with the same UK reference date are submitted; and
- (b) £445, in any other case.

Fee for testing of samples by the appropriate authority

19F.—(1) Where a sample from a batch of a medicinal product is submitted to the appropriate authority in accordance with a batch testing condition imposed under regulation 60A of the Human Medicines Regulations, the fee payable by the holder of the marketing authorisation to which the medicinal product relates is the fee prescribed in Part 6B of Schedule 2 in connection with that submission.

(2) The fee payable by an applicant for a certified copy of a certificate confirming that the appropriate authority is satisfied that the batch is in conformity with the approved specifications is £50.

(3) In this regulation, and in Part 6B of Schedule 2, “appropriate authority” and “batch testing condition” have the same meaning as in regulation 60A of the Human Medicines Regulations.

Status: This is the original version (as it was originally made).

Time for payment of fees under regulations 19A to 19F

19G. All sums payable by way of fees under regulations 19A to 19F are payable on invoice.”.

Amendment of regulation 23 (applications for multiple variations)

3.—(1) Regulation 23 is amended as follows.

(2) For paragraph (3)(b)(i) substitute—

“(i) have agreed should be subject to the procedure for grouping of variations within the meaning of paragraph 5(2)(c) of Schedule 10A to the Human Medicines Regulations; and”.

(3) In paragraph (6), for “Article 5 of [Commission Regulation \(EC\) No 1234/2008](#)” substitute “paragraph 3 of Schedule 10A to the Human Medicines Regulations”.

(4) In paragraph (7)—

(a) in the definition of “Major Variation (Type II) Group Application”—

(i) for sub-paragraph (b) substitute—

“(b) subject to sub-paragraph (c), the variations fall within the scope of paragraph 5(2)(b) or (c) of Schedule 10A to the Human Medicines Regulations;”, and

(ii) for sub-paragraph (c)(i) substitute—

“(i) of a kind referred to in paragraph 5(3)(a) or (c) of Schedule 10A to the Human Medicines Regulations;”;

(b) in the definition of “Major Variation (Type II) Complex Group Application”—

(i) for sub-paragraph (b) substitute—

“(b) subject to sub-paragraph (c), the variations fall within the scope of paragraphs 5(2)(b) or (c) of Schedule 10A to the Human Medicines Regulations;”, and

(ii) for sub-paragraph (c)(i) substitute—

“(i) of a kind referred to in paragraph 5(3)(a) or (c) of Schedule 10A to the Human Medicines Regulations; or”;

(c) in the definition of “Major Variation (Type II) Extended Complex Group Application”—

(i) for sub-paragraph (b) substitute—

“(b) subject to sub-paragraph (c), the variations fall within the scope of paragraph 5(2)(b) or (c) of Schedule 10A to the Human Medicines Regulations;”, and

(ii) for sub-paragraph (c) substitute—

“(c) the variations do not include a variation of a kind referred to in paragraph 5(3)(a) of Schedule 10A to the Human Medicines Regulations; and”;

(d) in the definition of “major variation of type II”, for “Article 2(3) of [Commission Regulation \(EC\) No 1234/2008](#)” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”;

(e) in the definition of “Minor Variation (Type IB) Group Application”—

(i) for sub-paragraph (b) substitute—

- “(b) subject to sub-paragraph (c), the variations fall within the scope of paragraph 5(2)(b) or (c) of Schedule 10A to the Human Medicines Regulations;”, and
- (ii) for sub-paragraph (c)(i) substitute—
 - “(i) a variation of a kind referred to in paragraph 5(3)(a) or (b) of Schedule 10A to the Human Medicines Regulations; or”;
- (f) in the definition of “minor variation of type IA”, for “Article 2(2) of [Commission Regulation \(EC\) No 1234/2008](#)” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”;
- (g) in the definition of “minor variation of type IB”, for “Article 2(5) of [Commission Regulation \(EC\) No 1234/2008](#)” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”; and
- (h) omit the definition of “work sharing”.

Insertion of regulation 27A (fee for renewals of a marketing authorisation)

4. After regulation 27, insert—

“Fee for renewals of a marketing authorisation

27A. Where an application is made to the licensing authority for the renewal of a marketing authorisation and the application for renewal—

- (a) relates to a medicinal product which, at the time the marketing authorisation was granted, contained a new active ingredient; and
- (b) is the first renewal in relation to that product,

the fee payable by the applicant is the fee prescribed in Part 6 of Schedule 2.”.

Omission of Part 8 (Capital Fees for Regulatory Assistance Given by the United Kingdom Acting as Reference Member State Relating to the Assessment of Applications for the Renewal of Specified Marketing Authorisations)

5. Omit Part 8.

Amendment of Schedule 1 (general interpretation provisions)

6. In Schedule 1—

- (a) in paragraph 1—
 - (i) in the definition of “medicinal product”, for “includes any medicinal product for human use to which the 2001 Directive applies and” substitute “has the meaning given by regulation 2 of the Human Medicines Regulations and includes”,
 - (ii) for the definition of “orphan medicinal product” substitute—
 - ““orphan marketing authorisation” has the meaning given by regulation 8(1) of the Human Medicines Regulations;”,
 - (iii) in the definition of “variation”, for “Article 2(1) of [Commission Regulation \(EC\) No 1234/2008](#)” substitute “regulation 8(1) of the Human Medicines Regulations”, and
 - (iv) at the appropriate places insert—
 - ““Annex I to the 2001 Directive” has the meaning given by regulation 8(1) of the Human Medicines Regulations;”,

Status: This is the original version (as it was originally made).

““biological medicinal product” has the meaning given in paragraph 3.2.1.1. (b) of Part I of Annex I to the 2001 Directive;”;

““the Committee for Medicinal Products for Human Use” means the committee established under Article 5(1) of Regulation (EC) No 726/2004;”;

““the EMA” means the European Medicines Agency established by Regulation (EC) No 726/2004;”;

(b) after paragraph 4 insert—

“5.—(1) For the purpose of these Regulations, a company is a medium company if, for the financial year before that in which the application is made, the total value of products it has sold or supplied for the financial year is not more than the amount for the time being specified in item 1 in section 465(3) of the Companies Act 2006(122) (qualification of company as medium) and the conditions in sub-paragraph (2) are met.

(2) The conditions for the purposes of sub-paragraph (1) are—

(a) the company’s balance sheet total as defined in section 465(5) of the Companies Act 2006 is not more than the amount for the time being specified in item 2 in section 465(3) of that Act; or

(b) the average number of persons employed by the company in the financial year before that in which the application is made (determined on a weekly basis) does not exceed the number for the time being specified in item 3 in section 465(3) of that Act.

(3) In this paragraph “financial year” is to be construed in accordance with section 390 of the Companies Act 2006.”.

Amendment of Schedule 2 (capital fees for applications for, and variations to, marketing authorisations, licences, registrations and certificates)

7.—(1) Schedule 2 is amended as follows.

(2) In paragraph 4(a), for “Article 2(4) of Commission Regulation (EC) No 1234/2008” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”.

(3) In paragraph 22—

(a) in sub-paragraph (1), for “Article 2(5) of Commission Regulation (EC) No 1234/2008” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”;

(b) in sub-paragraph (2)(f), for “Article 2(4) of Commission Regulation (EC) No 1234/2008” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”; and

(c) in sub-paragraph (3), for “Article 2(2) of Commission Regulation (EC) No 1234/2008” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”.

(4) In paragraph 23—

(a) in sub-paragraph (a), for “paragraph 1 (changes to active substances) or paragraph 2 (changes to strength, pharmaceutical form and route of administration) of Annex I to Commission Regulation (EC) No 1234/2008 applies” substitute “sub-paragraph (a) (changes to active substances) or sub-paragraph (b) (changes to strength, pharmaceutical form and route of administration) of the definition of “extension of a UK marketing authorisation” in paragraph 1 of Schedule 10A to the Human Medicines Regulations apply”;

(122) Section 465 was amended by S.I. 2015/980

- (b) in sub-paragraph (b), for “Article 2(3) of Commission Regulation [Commission Regulation \(EC\) No 1234/2008](#)” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”; and
- (c) in sub-paragraph (c), for “[Commission Regulation \(EC\) No 1234/2008](#)” substitute “paragraph 1 of Schedule 10A to the Human Medicines Regulations”.
- (5) For the table in paragraph 24, substitute—

“Fees for marketing authorisation applications

<i>Column 1</i>	<i>Column 2</i>
<i>Kind of application</i>	<i>Fee payable</i>
1. Major application	
(a) in respect of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use and in relation to which the applicant has provided such information relating to that opinion as has been requested by the licensing authority	£62,421
(b) in any other case	£92,753
2. Complex application	
(a) in respect of an application to which regulation 53 of the Human Medicines regulations applies, relating to a biological medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use and in relation to which the applicant has provided such information relating to that opinion as has been requested by the licensing authority	£17,330
(b) in any other case	£25,643
3. Standard application	£9,402
4. Simple application	£2,564
5. Parallel import licence applications	
(a) in respect of a simple parallel import licence	£1,792
(b) in respect of a standard parallel import licence	£6,663
(c) in respect of a complex parallel import licence	£18,180
6. Change of ownership application	£442”.

- (6) After paragraph 24, insert—

“Fees where an application for a European Union marketing authorisation had been made before exit day

24A.—(1) This paragraph applies where, before exit day—

- (a) an application has been made to the EMA for a European Union marketing authorisation;

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- (b) day 120 has passed; and
- (c) no final decision has been made by the European Commission in relation to the grant of an European Union marketing authorisation under Article 10 of Regulation (EC) No 726/2004.

(2) Where this paragraph applies and the applicant for the European Union marketing authorisation applies for a UK marketing authorisation in accordance with paragraph 31(2) of Schedule 33A to the Human Medicines Regulations, the fee payable under regulation 12(1) shall be waived.

(3) In this paragraph, “day 120” means the day during the assessment of an application for a European Union marketing authorisation on which the Committee for Medicinal Products for Human Use adopts the list of questions, as well as the overall conclusions and review of the scientific data, to be sent to the applicant.”.

(7) In paragraph 27—

- (a) in sub-paragraph (2), for paragraphs (a) to (c) substitute—
 - “(a) in respect of the first or only marketing authorisation applied for by that secondary applicant—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £17,330; or
 - (ii) in any other case, the amount payable in respect of a complex application under paragraph 24;
 - (b) in respect of each additional marketing authorisation applied for by that secondary applicant which relates to a medicinal product of the same dosage form—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24;
 - (c) in respect of the first additional marketing authorisation applied for by that secondary applicant relating to that medicinal product which is of a different dosage form—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £17,330; or
 - (ii) in any other case, the amount payable in respect of a complex application under paragraph 24;
 - (d) in respect of any other additional marketing authorisation applied for by that secondary applicant relating to that medicinal product which is of a different dosage form—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24.”; and
- (b) in sub-paragraph (3), for paragraph (a), substitute—

- “(a) where the amount payable by the primary applicant is that in respect of a complex application, the fee payable under regulation 12(1)(a) by the secondary applicant is—
 - (i) in the case of an application relating to a biological medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24;”.
- (8) In paragraph 28—
 - (a) in sub-paragraph (2), for paragraphs (a) to (c) substitute—
 - “(a) in respect of each additional marketing authorisation applied for which relates to a medicinal product of a different dosage form with a different route of administration—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £17,330; or
 - (ii) in any other case, the amount payable in respect of a complex application under paragraph 24;
 - (b) in respect of each additional marketing authorisation applied for which relates to a medicinal product of a different dosage form but with the same route of administration—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24; and
 - (c) in respect of each additional marketing authorisation applied for which relates to a medicinal product of the same dosage form but of a different strength of active ingredient or different combination of active ingredients—
 - (i) in the case of an application relating to a medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24.”; and
 - (b) in sub-paragraph (3), for paragraphs (b) and (c), substitute—
 - “(b) in respect of each additional marketing authorisation applied for which relates to a medicinal product of a different dosage form but with the same route of administration—
 - (i) in the case of an application relating to a biological medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24; and

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- (c) in respect of each additional marketing authorisation applied for which relates to a medicinal product of the same dosage form but of a different strength of active ingredient or different combination of active ingredients—
 - (i) in the case of an application relating to a biological medicinal product that has received an opinion favourable to the granting of a marketing authorisation from the Committee for Medicinal Products for Human Use, £6,350; or
 - (ii) in any other case, the amount payable in respect of a standard application under paragraph 24.”.
- (9) In paragraph 38—
 - (a) for sub-paragraph (4) substitute—
 - “(4) In sub-paragraph (1), the appropriate table is—
 - (a) in respect of a reclassification variation application, Table 3;
 - (b) in any other case, Table 2.”; and
 - (b) omit table 1.
- (10) In paragraph 39—
 - (a) in sub-paragraph (1), after “Subject to sub-paragraph (3)” insert “and paragraph 39A”;
 - (b) in sub-paragraph (2), for “in respect of an orphan medicinal product”, substitute “an orphan marketing authorisation”; and
 - (c) in sub-paragraph (3), for “an orphan medicinal product” substitute “a medicinal product which meets the orphan criteria listed in regulation 50G(2) of the Human Medicines Regulations”.
- (11) After paragraph 39, insert—

“Variation of orphan marketing authorisations: small and medium companies

39A.—(1) Subject to sub-paragraph (2), if an application to vary an orphan marketing authorisation is made by, or on behalf of, a small or a medium company within 12 months of the date of grant of the marketing authorisation, the fee payable for that variation application shall be waived.

(2) Sub-paragraph (1) does not apply to an application to authorise use of the medicinal product in a new therapeutic area which does not meet the orphan criteria listed in regulation 50G(2) of the Human Medicines Regulations.”.

- (12) After paragraph 40, insert—

“Fees where an application for a variation or an extension of a European Union marketing authorisation had been made before exit day

40A.—(1) Paragraph (2) applies where, before exit day—

- (a) an application for a variation to which paragraph 11(7) of Schedule 33A to the Human Medicines Regulations applies, has been made to the EMA; and
- (b) the Committee for Medicinal Products for Human Use has adopted a request for supplementary information to be sent to the applicant, or, in the case of an extension, day 120 has passed.

(2) Where this paragraph applies and the holder of a converted EU marketing authorisation submits the application to the licensing authority in order to have the variation made to the converted EU marketing authorisation, the fee payable under regulation 19(1) shall be waived.

(3) In this paragraph—

“day 120” means the day during the assessment of an extension on which the Committee for Medicinal Products for Human Use adopts the list of questions, as well as the overall conclusions and review of the scientific data, to be sent to the applicant;

“converted EU marketing authorisation” has the meaning given in paragraph 6(1) and (2) of Schedule 33A to the Human Medicines Regulations; and

“extension” has the meaning given in paragraph 1 of Schedule 10A to the Human Medicines Regulations.”.

(13) For Part 6 substitute—

“PART 6

Capital Fee for the Renewal of a Marketing Authorisation

Renewal of a marketing authorisation

56. Unless paragraph 57 applies, the fee payable under regulation 27A in connection with an application for the renewal of a United Kingdom marketing authorisation is £9,682.

Renewal of multiple marketing authorisations

57.—(1) This sub-paragraph applies if more than one application falling within regulation 27A is made by the same applicant at the same time, each of which relates to medicinal products which have the same active ingredient or combination of ingredients, dosage form and therapeutic indications, and the marketing authorisations for those products have the same date for renewal.

(2) The fee payable under regulation 27A for applications to which sub-paragraph (1) applies is—

- (a) £9,682 for the first application considered by the licensing authority; and
- (b) £747 for each other application.

PART 6A

Capital Fee for Conducting a Major Safety Review

57A. The fee payable under regulation 19D(1) in connection with the carrying out of a major safety review is—

- (a) £51,286, where one or two active ingredients, or combinations of active ingredients, are included in the assessment;
- (b) £59,595, where three active ingredients, or combinations of active ingredients, are included in the assessment;
- (c) £67,904, where four active ingredients, or combinations of active ingredients, are included in the assessment; or
- (d) £76,213, where five or more active ingredients, or combinations of active ingredients, are included in the assessment.

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PART 6B

Capital Fee for Testing of Samples by the Appropriate Authority

57B.—(1) Unless sub-paragraph (2) applies, the fee payable under regulation 19F(1) in connection with the submission of a sample of a batch of a medicinal product of a kind described in column 1 of the following table is the fee specified in the corresponding entry in column 2 of that table.

(2) This sub-paragraph applies where—

- (a) the holder of the marketing authorisation submits, with a sample of a batch of medicinal product, a certificate issued by a laboratory in a designated country for batch testing and certification of biological medicinal products that relates to the sample of the batch submitted; and
- (b) on the basis of the documentation submitted with the sample, the appropriate authority considers that it is only necessary to carry out a paper based assessment of the sample.

(3) Where sub-paragraph (2) applies, the fee payable under regulation 19F(1) in connection with the submission of a sample of a batch of medicinal product of a kind described in column 1 of the following table is the fee specified in the corresponding entry in column 3 of that table.

(4) Where a product falls within more than one of the Bands referred to in the following table, the product is to be treated as if it only falls within the Band which attracts the highest fee.

Fees for testing of samples

<i>Column 1</i>	<i>Column 2</i>	<i>Column 3</i>
<i>Product Type</i>	<i>Fee payable where the licensing authority carries out a full assessment</i>	<i>Fee payable where the licensing authority carries out a paper-based assessment</i>
1. Plasma pools which require—		
(a) three or fewer tests	£180	£90
(b) four or five tests	£215	£90
(c) six or more tests	£230	£90
2. Band A	£1,660	£305
3. Band B	£1,910	£305
4. Band C	£2,340	£305
5. Band D	£3,690	£677
6. Band E	£6,410	£677
7. Band F	£10,350	£677

(5) In this paragraph—

“Band A” means a single component product, other than Botulinum toxin, requiring five or fewer in vitro tests;

“Band B” means Factor VIII, Factor IX or intravenous Immunoglobulin;

“Band C” means a multi-component product, or Botulinum toxin, requiring five or fewer in vitro tests;

“Band D” means a product requiring six to nine in vitro tests;

“Band E” means a product requiring—

(a) ten or more in vitro tests, or

(b) one or more in vivo tests;

“Band F” means a product—

(a) which requires one or more tests that must be carried out under containment measures applicable to hazard Group 3 or 4 biological agents under the Control of Substances Hazardous to Health Regulations 2002(**123**); or

(b) requires the use of human cells or tissues as part of its testing;

“Multi-component product” means a product containing two or more analytes that require testing; and

“Single component product” means a product containing a single analyte that requires testing.”

Amendment of Schedule 4 (periodic fees for licences)

8. In Schedule 4, in paragraph 1, in the definition of “limited use drug” for “which is in respect of an orphan medicinal product” substitute “in respect of which an orphan marketing authorisation has been granted”.

Amendment of Schedule 7 (waiver, reduction or refund of capital fees)

9. In Schedule 7, after paragraph 7, insert—

“Orphan marketing authorisation

7A. Where the licensing authority grants an orphan marketing authorisation, the following percentage of the fee otherwise payable under regulation 12(1)(a) in connection with the application for that authorisation shall be refunded or, if it has not yet been paid, shall be waived—

(a) in the case of an application made by or on behalf of a small or medium company, 100%;

(b) in the case of a major application that is not made by or on behalf of a small or medium company but to which paragraph 6 of Part II of Annex 1 to the 2001 Directive applies, 50%; or

(c) in any other case, 10%.”.

Amendment of Schedule 8 (Adjustment, reduction or refund of periodic fees)

10.—(1) Schedule 8 is amended as follows.

(2) In the heading, after “Adjustment”, insert “, waiver”.

(3) After paragraph 2, insert—

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“Waiver or refund: converted EU marketing authorisations

2A.—(1) Where the licensing authority revokes a converted EU marketing authorisation in accordance with paragraph 6(3) of Schedule 33A to the Human Medicines Regulations, the periodic fee payable under regulation 38(1) in relation to that authorisation shall be refunded, or if it has not yet been paid, shall be waived.

(2) In this paragraph, “converted EU marketing authorisation” has the meaning given in paragraph 6(1) and (2) of Schedule 33A to the 2012 Regulations.”

Savings

11.—(1) The provisions of the Medicines (Products for Human Use) (Fees) Regulations 2016 (“the 2016 Regulations”) omitted, substituted or amended by this Schedule shall continue to apply as if they had not been omitted, substituted or amended in relation to—

- (a) capital fees payable under the 2016 Regulations in respect of any application or inspection made before the date on which these Regulations come into force; and
- (b) any periodic fee payable under the 2016 Regulations in relation to the fee period during which these Regulations come into force or in relation to a fee period ending before the date on which these Regulations come into force.

(2) The omissions, substitutions and amendments shall not affect any proceedings under the 2016 Regulations for the recovery of any fees due as debts to the Crown and for the purposes of those proceedings, the provisions omitted, substituted or amended by this Schedule shall continue to apply as if they had not been omitted, substituted or amended.

SCHEDULE 2

Regulation 11

Insertion of new Schedule 8B (modifications of Annex I to the 2001 Directive)

1. After Schedule 8A to the Human Medicines Regulations 2012, insert—

“SCHEDULE 8B

Regulation 8(1)

Modifications of Annex I to the 2001 Directive

<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Paragraph (1) of the Introduction and general principles	The reference to “Articles 8 and 10(1)” is to be read as a reference to regulation 50 of the Human Medicines Regulations 2012.
Paragraphs (1) and (2) of the Introduction and general principles	If the licensing authority has published guidelines under regulation 50(5B)(a) of the Human Medicines Regulations 2012, the reference to “the rules governing medicinal products in the European Community, Volume 2B, Notice to applicants, medicinal products for human use, presentation and content of the dossier, Common Technical Document” is to be read as a reference to that guidance.

<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Paragraph (4) of the Introduction and general principles	If the licensing authority has published guidelines under regulation 50(5B)(b) of the Human Medicines Regulations 2012, the reference to “the scientific guidelines relating to the quality, safety and efficacy of medicinal products for human use as adopted by the Committee for Proprietary Medicinal Products (CPMP) and the European Medicines Evaluation Agency (EMA) and the other pharmaceutical Community guidelines published by the Commission in the different volumes of the rules governing medicinal products in the European Community” is to be read as a reference to those guidelines.
Paragraph (6) of the Introduction and general principles	The reference to “the requirements of Commission Directive 91/356/EEC laying down the principles of and guidelines of Good Manufacturing Practice for medicinal products for human use” is to be read as a reference to the Good Manufacturing Practice Directive, as defined in regulation 8(1) of the Human Medicines Regulations 2012.
Paragraph (6) of the Introduction and general principles	If the licensing authority has published principles and guidelines under regulation C17(1) of the Human Medicines Regulations 2012, the reference to “the principles and guidelines on GMP published by the Commission in the rules governing medicinal products in the European Community, Volume 4” is to be read as a reference to those principles and guidelines.
Paragraph (8) of the Introduction and general principles	References to “the European Community” are to be read as references to the United Kingdom.
Paragraph (8) of the Introduction and general principles	The references to “ Directive 2001/20/EC of the European Parliament and of the Council 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” are to be read as references to the Medicinal Products for Human Use (Clinical Trials) Regulations 2004(124).
Paragraph (9) of the Introduction and general principles	The reference to “Council Directives 87/18/EEC on the harmonisation of regulations and administrative provisions relating to the

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<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
	application of the principles of good laboratory practice and the verification of their application for tests in chemical substances and 88/320/EEC on the inspection and verification of good laboratory practice” is to be read as a reference to the Good Laboratory Practice Regulations 1999(125).
Paragraph (10) of the Introduction and general principles	The reference to “Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulation and administrative provisions of the Member States regarding the protection of animals for experimental and other scientific purposes” is to be read as a reference to the Animals (Scientific Procedures) Act 1986(126).
Paragraph (11) of the Introduction and general principles	The paragraph is to be read as follows: “In order to monitor the benefit/risk assessment, any new information not in the original application and all pharmacovigilance information shall be submitted to the licensing authority. After a marketing authorisation has been granted, any change to the data in the dossier shall be submitted to the licensing authority in accordance with the requirements of Schedule 10A to the Human Medicines Regulations 2012, as well as the requirements of Schedule 12A to those Regulations.”
Part I, paragraph 1.2, fourth paragraph	This paragraph is to be read as follows: “Annexed to the administrative data shall be copies of the manufacturing authorisation as defined in regulation 17 of the Human Medicines Regulations 2012.”
Part I, paragraph 1.3.1	The reference to “Article 11” is to be read as a reference to Part 2 of Schedule 8 to the Human Medicines Regulations 2012.
Part I, paragraph 1.3.2	The reference to “Title V” is to be read as a reference to Part I3 of the Human Medicines Regulations 2012, and the references to Articles 63 and 59 are to be read as references to regulations 260 and 266 of the Human Medicines Regulations 2012.
Part I, paragraph 1.3.4	This paragraph is to be read as omitted.

(125) S.I. 1999/3106.

(126) 1986 c. 14, as amended by S.I. 2012/3039.

<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Part I, paragraph 1.4	The reference to “Article 12.2” is to be read as a reference to paragraph 11 of Schedule 8 to the Human Medicines Regulations 2012.
Part I, paragraph 2, first paragraph	The reference to “Article 12” is to be read as a reference to paragraph 11 of Schedule 8 to the Human Medicines Regulations 2012.
Part I, paragraph 3.2(5), first paragraph	The reference to a “Member State” is to be read as including the United Kingdom.
Part I, paragraph 3.2(5), second paragraph	The references to “the national pharmacopoeia of a Member State” are to be read as including references to the British Pharmacopoeia.
Part I, paragraph 3.2(6)	The reference to “the pharmacopoeia of a Member State” is to be read as including a reference to the British Pharmacopoeia.
Part I, paragraph 3.2(12)	The words “which is required by Community legislation” are to be read as omitted.
Part I, paragraph 3.2.1.2	If the licensing authority has published guidelines under regulation 50(5B)(c) of the Human Medicines Regulations 2012, the reference to “guidelines published by the Agency” is to be read as a reference to those guidelines.
Part I, paragraph 3.2.2.1, second paragraph	The reference to “Article 8(3)(c)” is to be read as a reference to paragraph 3 of Schedule 8 to the Human Medicines Regulations 2012.
Part I, paragraph 3.2.2.1, second paragraph, first indent	The reference to “the national pharmacopoeia of one of the Member States” is to be read as including the British Pharmacopoeia.
Part I, paragraph 3.2.2.1, fifth paragraph	The reference to “any Member State” is to be read as a reference to the United Kingdom and the reference to “the Member States” is to be read as a reference to the United Kingdom.
Part I, paragraph 3.2.2.3(a)	The reference to “Article 8(3)(d)” is to be read as a reference to paragraph 5 of Schedule 8 to the Human Medicines Regulations 2012.
Part I, paragraph 4.2.2, fifth paragraph	The reference to “this Directive” is to be read as a reference to the Human Medicines Regulations 2012.
Part I, paragraph 5.2(a)	The reference to “the clinical particulars provided pursuant to Articles 8(3)(i) and 10(1)” is to be read as a reference to those particulars provided pursuant to paragraph 10 of Schedule 8 to, and regulations 51 to 56 of, the Human Medicines Regulations 2012.

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<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Part I, paragraph 5.2(c)	The references to “the European Community” are to be read as references to the United Kingdom.
Part I, paragraph 5.2(c), fifth paragraph	The reference to “ Directive 2001/20/EC and implementing detail guidelines” is to be read as a reference to the Medicinal Products for Human Use (Clinical Trials) Regulations 2004(127).
Part I, paragraph 5.2.1, second paragraph	The reference to “Article 10(1)(a)” is to be read as a reference to regulation 51 of the Human Medicines Regulations 2012.
Part II, paragraph 1, first paragraph	The reference to “Article 10(1)(a)(ii)” is to be read as a reference to regulation 54 of the Human Medicines Regulations 2012.
Part II, paragraph 2(a)	The reference to “Article 10(1)(a)(i)” is to be read as a reference to regulation 56 of the Human Medicines Regulations 2012.
Part II, paragraph 2(b)	The reference to “Article 10(1)(a)(ii)” is to be read as a reference to regulation 51 of the Human Medicines Regulations 2012.
Part II, paragraph 4, first paragraph	The first sentence is to be read as omitted and the words “in accordance with regulation 53 of the Human Medicines Regulations 2012” are to be read as added at the end of the second sentence.
Part II, paragraph 5, first paragraph	The reference to “Article 10(1)(b)” is to be read as a reference to regulation 55 of the Human Medicines Regulations 2012.
Part II, paragraph 6, first paragraph	The reference to “Article 22” is to be read as a reference to regulation 60 of the Human Medicines Regulations 2012.
Part III, paragraph 1.1(a), first indent	The reference to “ Directive 2000/70/EC of the European Parliament and of the Council of 16 November 2000 amending Council Directive 93/42/EC as regards medical devices incorporating stable derivatives of human blood or blood plasma” is to be read as a reference to the Medical Devices Regulations 2002(128).
Part III, paragraph 1.1(a), third indent	The reference to “the Agency or the competent authority” is to be read as a reference to the licensing authority.

(127) S.I. 2004/1157.

(128) S.I. 2002/618.

<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Part III, paragraph 1.1(a), fourth indent	This indent is to be read as omitted.
Part III, paragraph 1.1(b)	The reference to “Article 109, as amended by Directive 2002/98/EC ” is to be read as a reference to the Blood Safety and Quality Regulations 2005(129).
Part III, paragraph 1.1(b)(3), second paragraph	The reference to “medicinal products referred to in Article 2 of Directive 2001/20/EC of the European Parliament and of the Council relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use” is to be read as a reference to investigational medicinal products.
Part III, paragraph 1.1.(c), second indent	This indent is to be read as follows: “The Plasma Master File is subject to a scientific and technical evaluation by the licensing authority.”
Part III, paragraph 1.1(c), fourth indent	This indent is to be read as follows: “Changes subsequently introduced to the terms of a Plasma Master File must follow the variation procedure in Schedule 10A to the Human Medicines Regulations 2012.”
Part III, paragraph 1.1(c), final indent	This indent is to be read as omitted.
Part III, paragraph 1.2(c), first indent	The references to “a competent authority” and to “the Agency” are to be read as references to the licensing authority and the final two sentences are to be read as omitted.
Part III, paragraph 1.2(c), second indent	The reference to “the Community” is to be read as a reference to the United Kingdom.
Part III, paragraph 1.2(c), third indent	This indent is to be read as follows: “Changes in the content of a Vaccine Antigen Master File must follow the variation procedure in Schedule 10A to the Human Medicines Regulations 2012.”
Part III, paragraph 1.2(c), fourth indent	This indent is to be read as omitted.
Part III, paragraph 1.2(c), fifth indent	This indent is to be read as omitted.
Part III, paragraph 2.1	The reference to “applications based on Articles 6(2) and 9” is to be read as a reference to applications in relation to radionuclide generators, radionuclide kits, radionuclide precursors and radiopharmaceuticals.

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<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Part III, paragraph 2.2, fourth paragraph	The reference to “Council Directives 87/18/EEC and 88/320/EEC ” is to be read as a reference to the Good Laboratory Practice Regulations 1999(130).
Part III, paragraph 3, second paragraph	The reference to “Article 15” is to be read as a reference to regulation 103 of the Human Medicines Regulations 2012, the reference to “Article 14(1)” is to be read as a reference to regulation 102 of the Human Medicines Regulations 2012 and the words “referred to in Article 16(1)” are to be read as “which are not registerable homoeopathic medicinal products”.
Part III, paragraph 3(a)	The reference to “an official pharmacopoeia of a Member State” is to be read as including the British Pharmacopoeia and any pharmacopoeia used officially in a country that is included in a list published by the licensing authority for that purpose, and the reference to “the traditional names used in each Member State” is to be read as including the traditional name used in the United Kingdom.
Part III, paragraph 3(b), final paragraph	The reference to “an official pharmacopoeia of a Member State” is to be read as including the British Pharmacopoeia.
Part III, paragraph 3, penultimate paragraph	The reference to “Article 14(1)” is to be read as a reference to regulation 102 of the Human Medicines Regulations 2012.
Part III, paragraph 5, first indent	The reference to “an orphan medicinal product in the meaning of Regulation (EC) No 141/2000 ” is to be read as a reference to a medicinal product to which the orphan criteria are claimed to apply.
Part III, paragraph 5, second indent	The reference to “Article 10(1)(a)(ii)” is to be read as a reference to regulation 54 of the Human Medicines Regulations 2012 and the reference to “Article 5” is to be read as a reference to regulation 167 of the Human Medicines Regulations 2012.
Part IV, paragraph 1, first paragraph	The reference to “point (a) of Article 2(1) of Regulation (EC) No 1394/2007 ” is to be read as a reference to regulation 2A of the Human Medicines Regulations 2012.
Part IV, paragraph 2	This paragraph is to be read as omitted.

<i>Provision of Annex I</i>	<i>Modification subject to which that provision is to be read</i>
Part IV, paragraph 3.1, second paragraph	The reference to “ Directive 2004/23/EC ” is to be read as a reference to the Human Fertilisation and Embryology Act 1990 ⁽¹³¹⁾ and the Human Tissue (Quality and Safety for Human Application) Regulations 2007 ⁽¹³²⁾ and the reference to “ Directive 2002/98/EC ” is to be read as a reference to the Blood Safety and Quality Regulations 2005 ⁽¹³³⁾ .
Part IV, paragraph 3.3.2.1(a)	The reference to “ Directive 2004/23/EC ” is to be read as a reference to the Human Fertilisation and Embryology Act 1990 and the Human Tissue (Quality and Safety for Human Application) Regulations 2007.
Part IV, paragraph 3.4.1, heading	The reference to “devices as referred to in Article 7 of Regulation (EC) No 1394/2007 ” is to be read as a reference to medical devices, bio-materials, scaffolds or matrices.
Part IV, paragraph 3.4.2, heading	The reference to “Article 2(1)(d) of Regulation (EC) No 1394/2007 ” is to be read as a reference to regulation 2A(10) of the Human Medicines Regulations 2012.
Part IV, paragraph 3.4.2(c)	The reference to “Commission Directive 2003/32/EC ” is to be read as a reference to the Medical Devices Regulations 2002.
Part IV, paragraph 3.4.2(d)	The reference to “ Directive 93/42/EEC or Directive 90/385/EEC ” is to be read as a reference to the Medical Devices Regulations 2002 ⁽¹³⁴⁾ .
Part IV, paragraph 3.4.2, final paragraph	The first sentence is to be read as follows: “The applicant shall make available on request of the licensing authority any information related to the assessment by the notified body which has carried out the assessment referred to in point (d) of this section.””.

SCHEDULE 3

Regulation 12

Insertion of new Schedule 2A (modifications of Commission [Directive 2003/94/EC](#))

1. After Schedule 2 to the Human Medicines Regulations 2012, insert—

⁽¹³¹⁾ 1990 c. 37.
⁽¹³²⁾ S.I. 2007/1523.
⁽¹³³⁾ S.I. 2005/50.
⁽¹³⁴⁾ S.I. 2002/618.

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“SCHEDULE 2A

Regulations 8(1) and B17(3)

Modifications of Commission [Directive 2003/94/EC](#)

<i>Provision of Commission Directive 2003/94/EC</i>	<i>Modification subject to which that provision is to be read</i>
Article 1 (scope)	<p>The reference to—</p> <p>(a) “Article 40 of Directive 2001/83/EC” is to be read as a reference to “regulation 17 of the Human Medicines Regulations 2012”; and</p> <p>(b) “Article 13 of Directive 2001/20/EC” is to be read as a reference to “regulation 36 of the Medicines for Human Use (Clinical Trials) Regulations 2004”.</p>
Article 2 (definitions)	<p>In the definition of—</p> <p>(a) “medicinal product”, the reference to “Article 1(2) of Directive 2001/83/EC” is to be read as a reference to “regulation 2 of the Human Medicines Regulations 2012”;</p> <p>(b) “investigational medicinal product”, the reference to “Article 2(d) of Directive 2001/20/EC” is to be read as a reference to “regulation 2(1) of the Medicines for Human Use (Clinical Trials) Regulations 2004”;</p> <p>(c) “manufacturer” the reference to “Article 40(1) and (3) of Directive 2001/83/EC or the authorisation referred to in Article 13(1) of Directive 2001/20/EC” is to be read as a reference to “regulation 17(1) of the Human Medicines Regulations 2012 or the authorisation referred to in regulation 36(1) of the Medicines for Human Use (Clinical Trials) Regulations 2004”;</p> <p>(d) “qualified person” the reference to “Article 48 of Directive 2001/83/EC or in Article 13(2) of Directive 2001/20/EC” is to be read as a reference to “regulation 41 of the Human Medicines Regulations 2012 or regulation 43 of the Medicines for Human Use (Clinical Trials) Regulations 2004”.</p>
Article 3(1) (inspections)	<p>The reference to—</p> <p>(a) “for Article 111(1) of Directive 2001/83/EC” is to be read as a reference to “Part 16</p>

<i>Provision of Commission Directive 2003/94/EC</i>	<i>Modification subject to which that provision is to be read</i>
	<p>of the Human Medicines Regulations 2012 (enforcement)”;</p> <p>(b) “Article 15(1) of Directive 2001/20/EC” is to be read as a reference to “Part 8 of the Medicines for Human Use (Clinical Trials) Regulations 2004 (enforcement)”;</p> <p>(c) “the Member States”, is to be read as a reference to “the licensing authority”;</p> <p>(d) “Member States shall” is to be read as a reference to “The licensing authority may”;</p> <p>(e) “published by the Commission, of Community procedures on inspections and exchanges of information” is to be read as if after it there were inserted “or any guidance published by the licensing authority to replace that Commission guidance”.</p>
Article 3(2) (inspections)	<p>The reference to—</p> <p>(a) “competent authorities” is to be read as a reference to “licensing authority”;</p> <p>(b) “the second paragraph of Article 47 of Directive 2001/83/EC” to the end is to be read as a reference to “regulation C17(1) (a) of the Human Medicines Regulations 2012, or which applies by virtue of regulation C17(2) of those Regulations”.</p>
Article 4(2) (conformity with good manufacturing practice)	<p>The reference to—</p> <p>(a) “third countries” is to be read as a reference to “country other than the United Kingdom”;</p> <p>(b) “Community” is to be read as a reference to “licensing authority”.</p>
Article 5 (compliance with marketing authorisation)	<p>The reference to—</p> <p>(a) “Article 9(2) of Directive 2001/20/EC” in both places it appears is to be read as a reference to “regulation 17 of the Medicines for Human Use (Clinical Trials) Regulations 2004”;</p>

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<i>Provision of Commission Directive 2003/94/EC</i>	<i>Modification subject to which that provision is to be read</i>
Article 9 (documentation)	<p>(b) “competent authorities” in both places it appears is to be read as a reference to “licensing authority”.</p> <p>The reference in—</p> <p>(a) paragraph (1) to “Article 51(3) of Directive 2001/83/EC” is to be read as a reference to “paragraph 15(1) of Schedule 7 to the Human Medicines Regulations 2012”;</p> <p>(b) paragraph (2) to “competent authorities” is to be read as a reference to “licensing authority”.</p>
Article 11 (quality control)	<p>The reference in paragraph (2)—</p> <p>(a) to “point (b) of Article 20 of Directive 2001/83/EC” is to be read as a reference to “paragraph 3 or 17 of Schedule 4 to the Human Medicines Regulations 2012”;</p> <p>(b) to “Article 9(2) of Directive 2001/20/EC” is to be read as a reference to “regulation 17 of the Medicines for Human Use (Clinical Trials) Regulations 2004”;</p> <p>The reference in paragraph (4)—</p> <p>(a) to “Member State” is to be read as a reference to “United Kingdom”;</p> <p>(b) to “competent authority” is to be read as a reference to “licensing authority”;</p>
Article 12(4) (work contracted out)	<p>The reference to—</p> <p>(a) “competent authorities” is to be read as a reference to “licensing authority”;</p> <p>(b) “for Article 111 of Directive 2001/83/EC and Article 15(1) of Directive 2001/20/EC” is to be read as a reference to “Part 16 of the Human Medicines Regulations 2012 or Part 8 of the Medicines for Human Use (Clinical Trials) Regulations 2004”.</p>
Article 13 (complaints, product recall and emergency unblinding)	<p>The reference to “Article 123 of Directive 2001/83/EC” is to be read as a reference to “Part 5 of the Human Medicines Regulations 2012”.</p>

SCHEDULE 4

Regulation 54

Insertion of new Schedule 9A

1. After Schedule 9, insert—

“SCHEDULE 9A

Regulation 50G(4)

Meaning of terms used in the orphan criteria and in regulation 58D

Prevalence of a condition in the United Kingdom

1.—(1) The following provisions apply for the purposes of establishing, pursuant to regulation 50G(2)(a) and (b)(i), that a medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the United Kingdom.

(2) The material provided pursuant to regulation 50G(3) must include—

- (a) material which demonstrates that the disease or condition for which the medicinal product would be authorised affects not more than five in 10,000 persons in the United Kingdom at the time at which the application for an orphan marketing authorisation is submitted, where this is available;
- (b) details of the condition intended to be treated and a justification of the life-threatening or chronically debilitating nature of the condition, supported by scientific or medical references; and
- (c) copies of, or references to, relevant scientific literature, as well as copies of information from relevant databases in the United Kingdom, where available.

(3) If there are no databases as referred to in paragraph (2)(c), information from relevant databases in other countries may be supplied, provided appropriate extrapolations are made.

Potential for return on investment

2.—(1) The following provisions apply for the purposes of establishing, pursuant to regulation 50G(2)(a) and (b)(ii), that a medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition in the United Kingdom and that the medicinal product is unlikely, when marketed, to generate sufficient financial return to justify the necessary investment.

(2) The material provided pursuant to regulation 50G(3) must include—

- (a) details of the condition intended to be treated and a justification of the life-threatening or chronically debilitating nature of the condition, supported by scientific or medical references;
- (b) details of the costs incurred in connection with the development of the medicinal product;
- (c) details of any grants, tax incentives or other cost recovery provisions received in the United Kingdom or any other country in relation to the development of the medicinal product;
- (d) where the medicinal product is already authorised in the United Kingdom for any indication, or where the product is under investigation for one or more other indications, an explanation of, and justification for, the method that is used to apportion the development costs among the various indications;

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- (e) a statement of and justification for all development costs that the applicant expects to incur after the submission of the application for a UK marketing authorisation;
- (f) a statement of and justification for all production and marketing costs that the applicant has incurred in the past and expects to incur in the first ten years that the medicinal product is authorised;
- (g) an estimate of and justification for the expected revenues from sales of the medicinal product in the United Kingdom and elsewhere during the first ten years that the medicinal product is authorised; and
- (h) information on the prevalence and incidence in the United Kingdom of the condition for which the medicinal product would be authorised at the time at which the application for an orphan marketing authorisation application is submitted.

(3) The information concerning costs and revenue referred to in sub-paragraph (2) must be determined in accordance with generally accepted accounting principles and must be certified by a person who is a member of a body of accountants which is established in the United Kingdom and which is approved by the licensing authority for the purposes of this paragraph.

Existence of other methods of diagnosis, prevention or treatment

3.—(1) The following provisions apply for the purposes of establishing, pursuant to regulation 50G(2)(c), that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the United Kingdom, or if such method exists, that the medicinal product will be of significant benefit to those affected by the condition.

(2) The material provided pursuant to regulation 50G(3) must include—

- (a) details of any existing methods of diagnosis, prevention or treatment of the condition in question that have been authorised in the United Kingdom, making reference to scientific or medical literature or other relevant information, including information relating to authorised medicinal products, medical devices or other methods of diagnosis, prevention or treatment which are used in the United Kingdom; and
- (b) a justification as to why either—
 - (i) the methods referred to in paragraph (a) are not considered satisfactory; or
 - (ii) the medicinal product for which an orphan marketing authorisation is sought will be of significant benefit to those affected by the condition.

(3) In this paragraph, “significant benefit” means a clinically relevant advantage or a major contribution to patient care.

Increased safety or effectiveness and clinical superiority

4.—(1) The following provisions apply for the purposes of establishing, pursuant to regulation 58D(6)(c), that a second medicinal product is similar to a medicinal product to which an orphan marketing authorisation relates or is safer or more effective than, or clinically superior to, that product.

(2) The following definitions apply for the purposes of this paragraph—

“clinically superior”, in relation to a medicinal product, means that it is shown to provide a significant therapeutic or diagnostic advantage over and above that provided by an authorised orphan medicinal product in one or more of the following ways—

- (a) greater efficacy;
- (b) greater safety in a substantial portion of the target population, as evidenced where appropriate through comparative clinical trials; or

- (c) in exceptional cases, where neither greater safety nor greater efficacy has been shown, a demonstration that the medicinal product otherwise makes a major contribution to diagnosis or to patient care;

“similar active substance” means an identical active substance, or an active substance with the same principal molecular structural features, but not necessarily all of the same molecular structural features, and which acts via the same mechanism, however, in the case of advanced therapy medicinal products, for which the principal molecular structural features cannot be fully defined, the similarity between two active substances is to be assessed on the basis of the biological and functional characteristics;

“similar medicinal product” means a medicinal product containing a similar active substance or substances as contained in a currently authorised orphan medicinal product, and which is intended for the same therapeutic indication.

(3) For the purposes of the definition of “clinically superior” in relation to a medicinal product which shows that superiority by means of greater efficacy, this is to be assessed by the effect on a clinically meaningful endpoint in adequate and well controlled clinical trials, representing the same kind of evidence needed to support a comparative efficacy claim for two different medicinal products.

(4) The clinical trials referred to in paragraph (3) should be direct comparative clinical trials, unless comparisons based on other endpoints, including surrogate endpoints, can be justified.

(5) Paragraphs 5 to 8 make further provision about the definition of “similar active substance” in relation to certain types of product.

5.—(1) This paragraph applies for the purposes of the definition of “similar active substance” in relation to chemical medicinal products.

(2) The principal molecular structural features are the relevant structural components of an active substance, which may be the whole or part of the molecule.

(3) Whether the principal molecular structural features are the same between two or more molecules will be identified by comparison of their structures.

(4) Isomers, mixtures of isomers, complexes, esters, ethers, salts and derivatives of the original active substance, or an active substance that differs from the original active substance only with respect to minor changes in the molecular structure, such as a structural analogue, are to be considered similar.

(5) Synthetic polynucleotide substances, single or double stranded, consisting of two or more distinct nucleotides where—

- (a) the difference in the nucleotide sequence of the purine and pyrimidine bases or their derivatives is not major, are to be considered similar, therefore for antisense or interfering nucleotide substances, addition, substitution or deletion of a nucleotide not significantly affecting the kinetics of hybridisation to the target are usually to be considered similar; and

- (b) the difference in structure related to modifications of the ribose or deoxyribose backbone sugars or to the replacement of the backbone sugars by synthetic analogues usually result in substances being considered similar, and for antisense or interfering nucleotide substances, changes in the ribose or deoxyribose backbone sugars not significantly affecting the kinetics of hybridisation to the target are usually to be considered similar.

6.—(1) This paragraph applies for the purposes of the definition of “similar active substance” in relation to biological medicinal products other than advanced therapy medicinal products.

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(2) The principal molecular structural features are the structural components of an active substance that are relevant for the functional characteristics of that substance.

(3) The principal molecular structural features may be composed of a therapeutic moiety or a therapeutic moiety in combination with an additional structural element significantly contributing to the functional characteristics of the active substance.

(4) An additional structural element as described in paragraph (3) may be conjugated, fused or linked by other means to the therapeutic moiety or may be an extension of the therapeutic moiety protein backbone by additional amino acids.

(5) Substances with structural elements for which similar methods of modification or conjugation technology are used usually result in similar substances.

(6) Biological active substances which differ from the original biological substance only with respect to minor changes in the molecular structure are to be considered similar.

(7) In relation to proteinaceous substances—

(a) if the difference in structure between them is due to post-translational events, such as different glycosylation patterns, substances are usually to be considered similar; however, exceptionally some post-translational modifications may result in a non-similar substance if there is significant effect on the functional characteristics of the substance;

(b) if the difference in the amino acid sequence is not major, substances are usually to be considered similar; therefore two pharmacologically related protein substances of the same group, for example, having differences related to N-terminal methionine, naturally extracted as opposed to recombinant nucleic acid-derived proteins or other minor variants, are usually to be considered similar; however, the addition of a structural element may result in substances not being considered similar if this significantly affects the functional characteristics of the substance;

(c) monoclonal antibodies binding to the same target epitope are usually to be considered similar; however, two monoclonal antibody conjugates or fusion proteins may be considered not to be similar if either the Complementary Determining Region sequences of the antibody or the additional structural element of the conjugated monoclonal antibody is different.

(8) In relation to polysaccharide substances—

(a) if the substances have identical saccharide repeating units, even if the number of units varies, the substances are usually to be considered similar; and

(b) a conjugated polysaccharide vaccine compared to a non-conjugated polysaccharide vaccine containing the same antigen is considered not to be similar.

7.—(1) This paragraph applies for the purposes of the definition of “similar active substance” in relation to advanced therapy medicinal products.

(2) In relation to cell-based advanced therapy medicinal products, these are not to be considered similar if—

(a) there are differences in starting materials or the final composition of the product which have a significant impact on the biological characteristics or biological activity relevant for the intended therapeutic effect or safety attributes of the product, and the different source of the starting materials, such as in the case of autologous advanced therapy medicinal products, is not sufficient to support a claim that two products are not similar; or

- (b) there are differences in the manufacturing technology having a significant impact on the biological characteristics or the biological activity relevant for the intended therapeutic effect or safety attributes of the product.
- (3) In relation to gene therapy medicinal products—
 - (a) two gene therapy medicinal products are not to be considered similar when there are differences in the therapeutic sequence, viral vector, transfer system, regulatory sequences or manufacturing technology which significantly affect the biological characteristics or biological activity relevant for the intended therapeutic effect or safety attributes of the product; and
 - (b) differences in the therapeutic sequence with a significant impact on the intended therapeutic effect are not sufficient to support a claim that two gene therapy medicinal products are not similar.
- (4) The considerations in paragraphs (2) and (3) also apply in relation to genetically modified cells.

8.—(1) This paragraph applies for the purposes of the definition of “similar active substance” in relation to radiopharmaceuticals.

(2) The same radiopharmaceutical active substance, or one differing from the original in radionuclide, ligand, site of labelling or molecule-radionuclide coupling mechanism linking the molecule and radionuclide which acts via the same mechanism, are to be considered similar substances.”.

SCHEDULE 5

Regulation 73

Insertion of new Schedule 10A (variations to a UK marketing authorisation)

1. After Schedule 10, insert—

“SCHEDULE 10A

Regulation 65C(2)

Variations to a UK marketing authorisation

Interpretation

1. In this Schedule—

“change of, or addition of a new, route of administration”, in relation to parenteral administration, includes any change or addition as between intra-arterial, intra-venous, intramuscular, subcutaneous and any other route;

“extension of a UK marketing authorisation” or “extension” means a variation which consists of—

- (a) a change to one or more active substances that involves—
 - (i) replacement of a chemical active substance by a different salt, ester, complex or derivative, with the same therapeutic moiety, where the efficacy and safety characteristics are not significantly different,
 - (ii) replacement by a different isomer, a different mixture of isomers, of a mixture by an isolated isomer (for example, racemate by a single enantiomer), where the efficacy and safety characteristics are not significantly different,

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- (iii) replacement of a biological active substance with one of a slightly different molecular structure where the efficacy and safety characteristics are not significantly different, with the exception of changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza,
 - (iv) modification of the vector used to produce the antigen or the source material, including a new master cell bank from a different source, where the efficacy and safety characteristics are not significantly different,
 - (v) a new ligand or coupling mechanism for a radiopharmaceutical, where the efficacy and safety characteristics are not significantly different, or
 - (vi) change to the extraction solvent or the ratio of herbal drug to herbal drug preparation where the efficacy and safety characteristics are not significantly different; or
- (b) a change to strength, pharmaceutical form and route of administration that involves—
- (i) change of bioavailability,
 - (ii) change of pharmacokinetics, for example change in rate of release,
 - (iii) change or addition of a new strength or potency,
 - (iv) change or addition of a new pharmaceutical form, or
 - (v) change or addition of a new route of administration;

“holder” means UK marketing authorisation holder;

“major variation of type II” means a variation which is not an extension and which may have a significant impact on the quality, safety or efficacy of the medicinal product concerned namely—

- (a) variations related to the addition of a new therapeutic indication or to the modification of an existing one;
- (b) variations related to significant modifications of the summary of product characteristics due in particular to new quality, pre-clinical, clinical or pharmacovigilance findings;
- (c) variations related to changes outside the range of approved specifications, limits or acceptance criteria;
- (d) variations related to substantial changes to the manufacturing process, formulation, specifications or impurity profile of the active substance or finished medicinal product which may have a significant impact on the quality, safety or efficacy of the medicinal product;
- (e) variations related to modifications in the manufacturing process or sites of the active substance for a biological medicinal product;
- (f) variations related to the introduction of a new design space or the extension of an approved one, where the design space has been developed in accordance with international scientific guidelines; or
- (g) variations related to changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza;

“minor variation of type IA” means a variation which has only a minimal impact, or no impact at all, on the quality, safety or efficacy of the medicinal product concerned namely—

- (a) variations of purely administrative nature that are related to the identity and contact details of—
 - (i) the holder,

- (ii) the manufacturer or supplier of any starting material, reagent, intermediate, active substance used in the manufacturing process or finished product;
- (b) variations related to the identity, location and contact details of the qualified person for pharmacovigilance, or the location of the pharmacovigilance system master file;
- (c) variations related to the deletion of any manufacturing site, including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place;
- (d) variations related to minor changes to an approved physico-chemical test procedure, where the updated procedure is demonstrated to be at least equivalent to the former test procedure, appropriate validation studies have been performed and the results show that the updated test procedure is at least equivalent to the former;
- (e) variations related to changes made to the specifications of the active substance or of an excipient in order to comply with an update of the relevant monograph of the European Pharmacopoeia or of the British Pharmacopoeia, where the change is made exclusively to comply with the pharmacopoeia and the specifications for product specific properties are unchanged;
- (f) variations related to changes in the packaging material not in contact with the finished product, which do not affect the delivery, use, safety or stability of the medicinal product;
- (g) variations related to the tightening of specification limits, where the change is not a consequence of any commitment from previous assessment to review specification limits and does not result from unexpected events arising during manufacture;

“minor variation of type IB” means a variation which is not a minor variation of type IA, a major variation of type II nor an extension; and

“urgent safety restriction” means an interim change in the terms of the UK marketing authorisation due to new information having a bearing on the safe use of the medicinal product.

Classification of variations

2.—(1) Except where sub-paragraph (2) applies, a variation which is not an extension, and whose classification is undetermined after—

- (a) application of the provisions in this Schedule; and
- (b) taking into account—
 - (i) the guidance referred to in regulation 65C(4) or (6) as the case may be), and
 - (ii) where relevant, any recommendations delivered pursuant to paragraph 3,

is to be treated by the licensing authority as a minor variation of type IB.

(2) The licensing authority must treat a variation that would otherwise fall within sub-paragraph (1) as a major variation of type II in the following cases—

- (a) upon request from the holder when submitting the variation; or
- (b) where the licensing authority concludes, following the assessment of validity of a notification in accordance with paragraph 7(1), and taking into account the recommendations given under paragraph 3, that the variation may have a significant impact on the quality, safety or efficacy of the medicinal product concerned.

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Licensing authority recommendation on unclassified variations

3.—(1) Prior to the submission of a variation whose classification is not provided for in this Schedule—

- (a) the holder may request a recommendation on the classification of the variation from the licensing authority; and
- (b) the licensing authority must notify the holder of its recommendation within 45 days of that request, beginning with the date on which the request is received by the licensing authority.

(2) The 45-day period referred to in sub-paragraph (1)(b) may be extended by 25 days where the licensing authority deems it necessary.

Variations leading to the revision of product information

4. Where a variation leads to the revision of the summary of product characteristics, labelling or the package leaflet, the revision must be considered by the licensing authority as part of that variation.

Grouping of variations

5.—(1) Except where sub-paragraph (2) applies, where several variations are notified or applied for, a separate notification or application in accordance with paragraph 6, 7, 8 or 11 of this Schedule is to be submitted in respect of each variation sought.

(2) This sub-paragraph applies—

- (a) where one or more of the same minor variations of type IA to the terms of one or more UK marketing authorisations owned by the same holder are notified at the same time to the licensing authority, in which case a single notification as referred to in paragraph 6 may cover all such variations;
- (b) where several variations to the terms of the same UK marketing authorisation are submitted at the same time, a single submission may cover all such variations provided that the variations concerned fall within one of the relevant circumstances specified in sub-paragraph (3);
- (c) where one or more of the same variation to the terms of one or more UK marketing authorisations held by the same holder are submitted at the same time and the variations do not fall within paragraph (a) or (b), a single submission may cover all such variations provided that the licensing authority agrees to such single submission.

(3) The relevant circumstances are—

- (a) one of the variations in the group is an extension of the UK marketing authorisation;
- (b) one of the variations in the group is a major variation of type II, but all other variations in the group are variations which are consequential to this major variation of type II;
- (c) one of the variations in the group is a minor variation of type IB, but all other variations in the group are minor variations which are consequential to this minor variation of type IB;
- (d) all variations in the group relate solely to changes of an administrative nature to the summary of product characteristics, labelling and package leaflet or insert;
- (e) all variations in the group are changes to an Active Substance Master File, Vaccine Antigen Master File or Plasma Master File;

- (f) all variations in the group relate to a project intended to improve the manufacturing process and the quality of the medicinal product concerned or one or more of its active substances;
 - (g) all variations in the group are changes affecting the quality of a human pandemic influenza vaccine;
 - (h) all variations in the group are changes to the pharmacovigilance system referred to in paragraph 12 of Schedule 8;
 - (i) all variations in the group are consequential to a given urgent safety restriction and submitted in accordance with paragraph 14;
 - (j) all variations in the group relate to the implementation of a given class labelling;
 - (k) all variations in the group are consequential to the assessment of a given periodic safety update report;
 - (l) all variations in the group are consequential to a given post-authorisation study conducted under the supervision of the holder;
 - (m) all variations in the group are consequential to a condition imposed under regulation 59(4C) or (4D).
- (4) The submission referred to in sub-paragraph (2)(b) and (c) must be made by means of the following—
- (a) a single notification in accordance with paragraph 7 where at least one of the variations is a minor variation of type IB and the remaining variations are minor variations;
 - (b) a single application in accordance with paragraph 8 where at least one of the variations is a major variation of type II and none of the variations is an extension; or
 - (c) a single application in accordance with paragraph 11 where at least one of the variations is an extension.

Notification procedure for minor variations of type IA

6.—(1) Subject to sub-paragraph (2), where a minor variation of type IA is made, the holder must submit to the licensing authority a notification containing the elements listed in paragraph 9 within 12 months, beginning with the date on which the variation is implemented by the holder.

(2) The notification referred to in sub-paragraph (1) must be submitted immediately after the implementation of the variation in the case of minor variations requiring immediate notification for the continuous supervision of the medicinal product concerned.

(3) Within 30 days beginning with the date on which the licensing authority receives a notification under this paragraph, the measures provided for in paragraph 10 are to be taken.

Notification procedure for minor variations of type IB

7.—(1) The holder must for minor variations of type IB submit to the licensing authority a notification containing the elements listed in paragraph 9, and if the notification contains those elements, the licensing authority must acknowledge receipt of a valid notification.

(2) If within 30 days beginning with the date on which the licensing authority acknowledges receipt of a valid notification, the licensing authority has not sent the holder an unfavourable opinion, the notification is deemed to be accepted by the licensing authority.

(3) Where the notification is accepted by the licensing authority, the measures provided for in paragraph 10 are to be taken.

(4) Where the licensing authority is of the opinion that the notification cannot be accepted, it must inform the holder, stating the grounds on which its unfavourable opinion is based.

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(5) Within 30 days beginning with the date on which the holder receives the unfavourable opinion, the holder may submit to the licensing authority an amended notification in order to take due account of the grounds laid down in that opinion.

(6) If the holder does not amend the notification in accordance with sub-paragraph (5), the notification is deemed to be rejected.

(7) Where an amended notification has been submitted, the licensing authority must assess it within 30 days beginning with the date on which it receives the amended notification, and the measures provided for in paragraph 10 are to be taken.

(8) This paragraph does not apply where—

- (a) a type IB variation request is submitted in a grouping that includes a variation type II and does not contain an extension: in such a case, the prior approval procedure in paragraph 8 applies; or
- (b) a type IB variation request is submitted in a grouping that includes an extension: in such a case, the procedure in paragraph 11 applies.

Prior approval procedure for major variations of type II

8.—(1) The holder must submit to the licensing authority an application containing the elements listed in paragraph 9, and if the application contains those elements, the licensing authority must acknowledge receipt of a valid application.

(2) Subject to sub-paragraph (3), within 60 days beginning with the date on which the licensing authority acknowledges receipt of a valid application under sub-paragraph (1), the licensing authority must conclude the assessment.

(3) The licensing authority may—

- (a) reduce the period referred to in sub-paragraph (2), having regard to the urgency of the matter; or
- (b) extend it to 90 days for—
 - (i) variations concerning a change to, or addition of, therapeutic indications, or
 - (ii) grouping of variations in accordance with paragraph 5(2)(c).

(4) Within the periods referred to in sub-paragraph (2) or (3), the licensing authority may request the holder to provide supplementary information within a time limit that it specifies, in which case—

- (a) the procedure is suspended from the date on which such a request is made until the date on which that supplementary information has been provided; and
- (b) the licensing authority may extend the period referred to in sub-paragraph (2) by the period for which the procedure is so suspended.

(5) Within 30 days beginning with the date on which the licensing authority concludes its assessment of the application, the measures provided for in paragraph 10 are to be taken.

(6) This paragraph does not apply where a type II variation request is submitted in a grouping that includes an extension: in such case, the procedure in paragraph 11 applies.

Elements to be submitted

9. An application or notification under this Schedule must include—

- (a) a list of all the UK marketing authorisations affected by the notification or application;
- (b) a description of all the variations submitted, including—

- (i) in the case of minor variations of type IA, the date of implementation for each variation described,
- (ii) in the case of minor variations of type IA which do not require immediate notification, a description of all minor variations of type IA made in the last 12 months to the terms of any affected UK marketing authorisation, such period beginning with the day on which the application or notification is submitted, and which have not been already notified,
- (iii) any documents specified in guidance published under regulation 65C(4) or (6) (as the case may be), insofar as relevant to the type of variation notified or applied for,
- (iv) where a variation leads to or is the consequence of other variations to the terms of the same UK marketing authorisation, a description of the relationship between those variations, and
- (v) the relevant fee provided for in the Fees Regulations.

Measures to close the procedures specified in paragraphs 6 to 8

10. Where reference is made to this paragraph, the licensing authority must take the following measures—

- (a) inform the holder as to whether the variation is accepted or rejected;
- (b) where the variation is rejected, inform the holder of the grounds for the rejection; and
- (c) where necessary, amend the decision granting the UK marketing authorisation in accordance with the accepted variation within the time limit laid down in paragraph 15.

Extensions of marketing authorisations

11.—(1) An application for an extension of a UK marketing authorisation must be assessed by the licensing authority in accordance with the same or equivalent procedure that applied under Part 5 to the initial UK marketing authorisation to which it relates.

(2) An extension must either be granted a UK marketing authorisation in accordance with the same or equivalent procedure as for the granting of the initial UK marketing authorisation to which it relates, or be included in that initial UK marketing authorisation.

Human influenza vaccines

12.—(1) By way of exception from paragraph 8, the procedure laid down in sub-paragraphs (2) to (4) applies to the examination of variations concerning changes to the active substance for the purposes of the annual update of a human influenza vaccine.

(2) The holder must submit to the licensing authority an application containing the elements listed in paragraph 9, and if it does so, the licensing authority must acknowledge receipt of a valid application.

(3) The licensing authority must assess the application submitted, and where it deems it necessary, the licensing authority may request additional data from the holder in order to complete its assessment.

(4) The licensing authority must—

- (a) adopt a decision within 45 days, beginning with the date on which it receives a valid application; and
- (b) take the measures provided for in paragraph 10.

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(5) The 45-day period referred to in sub-paragraph (4) is to be suspended from the date on which the additional data referred to in sub-paragraph (3) is requested until the date on which that data is received by the licensing authority.

Pandemic situation with respect to human influenza

13.—(1) By way of exception to the provisions of this Schedule, where a pandemic situation with respect to human influenza is duly recognised by the World Health Organisation, or the licensing authority, the licensing authority may exceptionally and temporarily accept a variation to the terms of a UK marketing authorisation for a human influenza vaccine, where certain non-clinical or clinical data are missing.

(2) Where a variation is accepted pursuant to sub-paragraph (1), the holder must submit the missing non-clinical and clinical data within a time limit set by the licensing authority.

Urgent safety restrictions

14.—(1) Where, in the event of a risk to public health, the holder takes urgent safety restrictions on its own initiative, it must forthwith notify the licensing authority.

(2) If the licensing authority has not raised objections within 24 hours following receipt of that information, the urgent safety restrictions are deemed to be accepted.

(3) In the event of a risk to public health in relation to a medicinal product, the licensing authority may impose urgent safety restrictions on the holder of the UK marketing authorisation in respect of that product.

(4) Where an urgent safety restriction is taken by the holder, or imposed by the licensing authority, the holder must submit the corresponding application for variation within 15 days beginning with the date on which that restriction is initiated.

Amendments to the decision granting the marketing authorisation

15.—(1) Amendments to the decision granting the UK marketing authorisation resulting from the procedures laid down in this Schedule must be made by the licensing authority—

- (a) in the case of major variations of type II, within two months, beginning with the date on which the information referred to in paragraph 10(a) is sent to the holder; or
- (b) in the other cases, within six months, beginning with the date on which the information referred to in paragraph 10(a) is sent to the holder,

and the licensing authority must notify the holder of the amended decision without delay.

(2) The statement indicating compliance with the agreed completed paediatric investigation plan provided for under regulation 58A(2)(a) must be included within the technical dossier of the UK marketing authorisation, and the licensing authority must confirm to the holder that it is so included when it notifies the holder under paragraph 10(a).

Implementation of variations

16.—(1) Minor variations of type IA may be implemented any time before completion of the procedures laid down in paragraph 6.

(2) Where a notification concerning one or several minor variations of type IA is rejected, the holder must cease to apply the rejected variation immediately after receipt of the information referred to in paragraph 10(a).

(3) Minor variations of type IB may only be implemented after the licensing authority has informed the holder that it has accepted the notification pursuant to paragraph 7, or after the notification is deemed accepted pursuant to paragraph 7(2).

(4) Major variations of type II may only be implemented after the licensing authority has informed the holder that it has accepted the variation pursuant to paragraph 10.

(5) An extension may only be implemented after the licensing authority has amended the decision granting the marketing authorisation and notified the holder accordingly.

(6) Urgent safety restrictions, and variations which are related to safety issues, must be implemented within a time frame agreed by the holder and the licensing authority.

Continuous monitoring

17. Where requested to do so by the licensing authority, the holder must supply to the licensing authority without delay any information related to the implementation of a given variation.”

SCHEDULE 6

Regulation 168

Insertion of new Schedule 12A (further provision as to the performance of pharmacovigilance activities)

1. After Schedule 12 insert—

“SCHEDULE 12A

Regulation 205A

Further provision as to the performance of pharmacovigilance activities

PART 1

Pharmacovigilance system master file

Structure of the pharmacovigilance system master file

1.—(1) The information in the pharmacovigilance system master file must be accurate and reflect the pharmacovigilance system in place.

(2) The holder may, where appropriate, use separate pharmacovigilance systems for different categories of medicinal products and if it does so, each such system must be described in a separate pharmacovigilance system master file.

(3) All medicinal products for which the holder obtained a UK marketing authorisation in accordance with these Regulations must be covered by a pharmacovigilance system master file.

Content of the pharmacovigilance system master file

2. The pharmacovigilance system master file must, as a minimum, contain—

(a) the following information relating to the qualified person responsible for pharmacovigilance—

(i) a description of the responsibilities demonstrating that the qualified person for pharmacovigilance has sufficient authority over the pharmacovigilance system

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- in order to promote, maintain and improve compliance with pharmacovigilance tasks and responsibilities,
- (ii) a summary curriculum vitae of the qualified person responsible for pharmacovigilance,
 - (iii) contact details of the qualified person for pharmacovigilance, and
 - (iv) details of back-up arrangements to apply in the absence of the qualified person responsible for pharmacovigilance;
- (b) a description of the organisational structure of the holder, including the list of each site where one or more of the following pharmacovigilance activities are undertaken—
- (i) individual case safety report collection and evaluation,
 - (ii) safety database case entry,
 - (iii) periodic safety update report production,
 - (iv) signal detection and analysis,
 - (v) risk management plan management,
 - (vi) pre and post-authorisation study management, and
 - (vii) management of safety variations to the terms of a UK marketing authorisation;
- (c) a description of the location of, functionality of and operational responsibility for computerised systems and databases used to receive, collate, record and report safety information, and an assessment of their fitness for purpose;
- (d) a description of data handing and recording and of the process used for each of the following pharmacovigilance activities—
- (i) the continuous monitoring of the risk-benefit balance of each medicinal product, the result of that monitoring and the decision-making process for taking appropriate measures,
 - (ii) operation of each risk management system and of the monitoring of the outcome of risk minimisation measures,
 - (iii) collection, assessment and reporting of individual case safety reports,
 - (iv) drafting and submission of periodic safety update reports, and
 - (v) procedures for communicating safety concerns and safety variations to the summary of product characteristics and package leaflet to healthcare professionals and the general public;
- (e) a description of the quality system for the performance of pharmacovigilance activities, including—
- (i) a description of—
 - (aa) the organisational structure for the performance of pharmacovigilance activities,
 - (bb) a summary description of the training concept, including a reference to the location of training files and qualifications records, and
 - (cc) instructions on critical processes,
 - (ii) a description of the record management system referred to in paragraph 12, including the location of the documents used for pharmacovigilance activities,
 - (iii) a description of the system for monitoring the performance of the pharmacovigilance system; and
- (f) where applicable, a description of the activities or services subcontracted by the holder.

Content of the Annex to the pharmacovigilance system master file

3. The pharmacovigilance system master file must have an Annex containing the following documents—

- (a) a list of medicinal products covered by the pharmacovigilance system master file, including the name of each medicinal product, the international non-proprietary name (INN) of each active substance and the countries other than the United Kingdom in which the products covered are authorised to be marketed;
- (b) a list of written policies and procedures for the purpose of complying with Part 11 of these Regulations;
- (c) the list of any sub-contracts falling within paragraph 6(1);
- (d) a list of the tasks that have been delegated by the qualified person for pharmacovigilance;
- (e) a list of all scheduled and completed audits;
- (f) where applicable, a list of the performance indicators that support the quality system for pharmacovigilance specified in paragraph 2(e);
- (g) where applicable, a list of other pharmacovigilance system master files held by the same holder; and
- (h) a logbook containing a record of any alteration of the content of the pharmacovigilance system master file made within the preceding 5 year period, except any alteration of the content that is specified in of paragraph 2(a)(ii) to (iv) or this paragraph.

Maintenance of the pharmacovigilance system master file

4.—(1) The holder must keep the pharmacovigilance system master file up to date and, where necessary, revise it to take account of experience gained, and of technical and scientific progress.

(2) The pharmacovigilance system master file and its Annex must be subject to version control and, in particular, must indicate the date when it was last updated by the holder.

(3) Any deviations from the pharmacovigilance procedures, their impact and their management must be documented in the pharmacovigilance system master file until resolved.

(4) Without prejudice to the requirements set out in regulation 65C and Schedule 10A (variations to a UK marketing authorisation), the holder must notify the licensing authority immediately of any change—

- (a) in the location of the pharmacovigilance system master file; or
- (b) to the contact details and name of the qualified person responsible for pharmacovigilance.

Form of the documents contained in the pharmacovigilance system master file

5.—(1) The pharmacovigilance system master file documents must be complete and legible.

(2) Subject to sub-paragraph (1), in the pharmacovigilance system master file—

- (a) where appropriate, information may be provided in the form of charts or flow diagrams;
- (b) all documents must be indexed and archived so as to ensure their accurate and ready retrieval throughout the period for record-keeping; and
- (c) the particulars and documents may be presented in modules in accordance with the system delineated in detail in the guidance on good pharmacovigilance practices which applies by virtue of regulation 205B.

(3) The pharmacovigilance system master file may be stored in electronic form provided that the media used for storage remain readable over time, and a clearly arranged printed copy can be made available for audits and inspections.

Subcontracting

6.—(1) The holder may subcontract certain activities of the pharmacovigilance system to third parties, but if it does so it must nevertheless retain full responsibility for the completeness and accuracy of the pharmacovigilance system master file.

(2) The holder must draw up a list of the existing subcontracts between it and the third parties referred to in sub-paragraph (1), specifying each product and each country concerned.

Availability and location of the pharmacovigilance system master file

7.—(1) The pharmacovigilance system master file must be—

- (a) located in, or accessible electronically from, the United Kingdom at the single point from which the reports referred to in regulation 187(4) are accessible; and
- (b) permanently and immediately available for inspection at that single point in the United Kingdom.

(2) The holder must ensure that the qualified person for pharmacovigilance has permanent access to the pharmacovigilance system master file.

(3) For the purposes of regulation 182(2)(b), the licensing authority may limit its request to specific parts or modules of the pharmacovigilance system master file and the holder is to bear the costs of submitting the copy of the pharmacovigilance system master file.

(4) The licensing authority may request the holder to submit a copy of the logbook referred to in paragraph 3(h) at regular intervals.

PART 2

Minimum requirements for the quality systems for the performance of pharmacovigilance activities by the licensing authority and holders

Quality system

8.—(1) Any holder, and the licensing authority, must establish and use a quality system that is adequate and effective for the performance of their pharmacovigilance activities.

(2) The quality system must cover organisational structure, responsibilities, procedures, processes and resources, appropriate resource management, compliance management and record management.

(3) The quality system must be based on all of the following activities—

- (a) quality planning: establishing structures and planning integrated and consistent processes;
- (b) quality adherence, namely carrying out tasks and responsibilities in accordance with quality requirements;
- (c) quality control and assurance, namely monitoring and evaluating how effectively the structures and processes have been established and how effectively the processes are being carried out; and

(d) quality improvements, namely correcting and improving the structures and processes where necessary.

(4) All elements, requirements and provisions adopted for the quality system must be documented in a systematic and orderly manner in the form of written policies and procedures, such as quality plans, quality manuals and quality records.

(5) All persons involved in the procedures and processes of the quality systems established by the licensing authority for the performance of pharmacovigilance activities shall be responsible for the good functioning of those quality systems, and must ensure a systematic approach towards quality and towards the implementation and maintenance of the quality system.

Performance indicators

9.—(1) The holder and the licensing authority may use performance indicators to continuously monitor the good performance of pharmacovigilance activities.

(2) The licensing authority may publish a list of performance indicators.

PART 3

Minimum requirements for the quality systems for the performance of pharmacovigilance activities by holders

Management of human resources

10.—(1) The holder must have sufficient competent and appropriately qualified and trained personnel available for the performance of pharmacovigilance activities.

(2) For the purposes of sub-paragraph (1), the holder must—

(a) ensure that the qualified person responsible for pharmacovigilance has acquired adequate theoretical and practical knowledge for the performance of pharmacovigilance activities; and

(b) where the qualified person has not completed basic medical training in accordance with Article 24 of [Directive 2005/36/EC](#) of the European Parliament and of the Council of 7 September 2005 on the recognition of professional qualifications, ensure that the qualified person responsible for pharmacovigilance is assisted by a medically trained person, with such assistance being duly documented.

(3) The duties of the managerial and supervisory staff, including the qualified person responsible for pharmacovigilance, must be defined in job descriptions and their hierarchical relationships must be defined in an organisational chart.

(4) The holder must ensure that the qualified person responsible for pharmacovigilance has sufficient authority to influence the performance of the quality system and the pharmacovigilance activities of the holder.

(5) All personnel involved in the performance of pharmacovigilance activities must receive initial and continued training in relation to their role and responsibilities, and the holder must keep training plans and records for documenting, maintaining and developing the competences of personnel and make them available for audit or inspection.

(6) The holder must provide appropriate instructions on the processes to be used in case of urgency, including business continuity.

Compliance management

11.—(1) Specific quality system procedures and processes must be in place in order to ensure the following—

- (a) the continuous monitoring of pharmacovigilance data, the examination of options for risk minimisation and prevention and that appropriate measures are taken by the holder;
- (b) the scientific evaluation by the holder of all information on the risks of medicinal products, as referred to in regulation 182(4)(a);
- (c) the submission of accurate and verifiable data on serious and non-serious adverse reactions to the licensing authority within the time limits provided for in regulation 188(1)(a) or (b);
- (d) the quality, integrity and completeness of the information submitted on the risks of medicinal products, including processes to avoid duplicate submissions;
- (e) effective communication by the holder with the licensing authority, including communication on—
 - (i) new risks or changed risks,
 - (ii) the pharmacovigilance system master file,
 - (iii) risk management systems,
 - (iv) risk minimisation measures,
 - (v) periodic safety update reports,
 - (vi) corrective and preventive actions, and
 - (vii) post-authorisation studies;
- (f) the update of product information by the holder in the light of scientific knowledge, including the assessments and recommendations made public via the UK web-portal, and on the basis of a continuous monitoring by the holder of information published on that web-portal; and
- (g) appropriate communication by the holder of relevant safety information to healthcare professionals and patients.

(2) Where a holder has subcontracted some of its pharmacovigilance tasks, it must retain responsibility for ensuring that an effective quality system is applied in relation to those tasks.

Record management and data retention

12.—(1) A holder must record all pharmacovigilance information and ensure that it is handled and stored so as to allow for accurate reporting, interpretation and verification of that information.

(2) A holder must put in place a record management system for all documents used for pharmacovigilance activities that ensures—

- (a) the retrievability of those documents; and
- (b) the traceability of the measures taken to investigate safety concerns, of the timelines for those investigations and of decisions on safety concerns, including their date and the decision-making process.

(3) A holder must establish mechanisms enabling the traceability and follow-up of adverse reaction reports.

(4) A holder must arrange for the elements referred to in sub-paragraph (2) to be kept for at least five years, beginning with the day after the system as described in the pharmacovigilance system master file has been formally terminated by the holder.

(5) Pharmacovigilance data and documents relating to individual authorised medicinal products must be retained as long as the product is authorised and for at least 10 years, beginning with the date on which the UK marketing authorisation ceased to exist.

Audit

13.—(1) Risk-based audits of the quality system must be performed at regular intervals to ensure that the quality system complies with the quality system requirements set out in paragraphs 8, 10, 11 and 12, and to determine its effectiveness.

(2) The audits referred to in sub-paragraph (1) must be conducted by individuals who have no direct involvement in or responsibility for the matters or processes being audited.

(3) Following a risk-based audit—

- (a) any corrective action, including a follow-up audit of deficiencies, must be taken where necessary;
- (b) a report on the results of the audit must be drawn up for each audit and follow-up audit;
- (c) the audit report must be sent to the management responsible for the matters audited; and
- (d) the dates and results of audits and follow-up audits must be documented in accordance with regulation 184(1)(b).

PART 4

Minimum requirements for the quality systems for the performance of pharmacovigilance activities by the licensing authority

Management of human resources

14.—(1) The licensing authority must have sufficient competent and appropriately qualified and trained personnel available for the performance of pharmacovigilance activities: the organisational structures and the distribution of tasks and responsibilities must be clear and, to the extent necessary, accessible.

(2) Named contact points in the licensing authority for pharmacovigilance activities must be established.

(3) The licensing authority must ensure that—

- (a) all of its personnel involved in the performance of pharmacovigilance activities receive initial and continued training;
- (b) it keeps training plans and records for documenting, maintaining and developing the competences of personnel; and
- (c) such plans and records are available for audit.

(4) The licensing authority must ensure that it provides to its personnel performing pharmacovigilance activities appropriate instructions on the processes to be used in case of urgency, including business continuity.

Compliance management

15. The licensing authority must establish specific procedures and processes in order to achieve the following objectives—

- (a) ensuring the evaluation of the quality, including completeness, of pharmacovigilance data submitted;

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- (b) ensuring the assessment of pharmacovigilance data and its processing within the timelines provided for in Part 11 of these Regulations;
- (c) ensuring independence in the performance of pharmacovigilance activities;
- (d) ensuring effective communication among regulatory bodies in countries other than the United Kingdom who have the same or similar functions as the licensing authority, as well as with patients, healthcare professionals, marketing authorisation holders and the general public; and
- (e) conducting inspections, including pre-authorisation inspections.

Record management and data retention

16.—(1) The licensing authority must—

- (a) record all pharmacovigilance information, and ensure that it is handled and stored so as to allow for accurate reporting, interpretation and verification of that information; and
- (b) put in place a record management system for all documents used for pharmacovigilance activities that ensures—
 - (i) the retrievability of those documents, and
 - (ii) the traceability of the measures taken to investigate safety concerns, of the timelines for those investigations and of decisions on safety concerns, including their date and the decision-making process.

(2) The licensing authority must arrange for the essential documents describing their pharmacovigilance system to be kept for at least five years, such period beginning with the day after the system has been formally terminated.

(3) Pharmacovigilance data and documents relating to individual authorised medicinal products must be retained by the licensing authority for as long as the product is authorised and for at least 10 years, such period beginning with the day after the UK marketing authorisation has expired.

Audit

17.—(1) Risk-based audits of the quality system must be performed by the licensing authority at regular intervals to ensure that the quality system complies with the requirements set out in paragraphs 8, 14, 15 and 16, and to ensure its effectiveness.

(2) Following a risk-based audit—

- (a) any corrective action, including a follow-up audit of deficiencies, must be taken where necessary;
- (b) a report on the results of the audit must be drawn up for each audit and follow-up audit;
- (c) the audit report must be sent to the management responsible for the matters audited; and
- (d) the dates and results of audits and follow-up audits must be documented.

PART 5

Use of terminology, formats and standards

Use of internationally agreed terminology, formats and standards

18. The licensing authority may publish a list of which of the internationally agreed—

- (a) terminology; and
- (b) formats and standards,

are to be used for the description, classification, retrieval, presentation, risk-benefit evaluation and assessment, electronic exchange and communication of pharmacovigilance and medicinal product information.

PART 6

Transmission of reports of suspected adverse reactions

Individual case safety reports

19. Individual case safety reports must be used for reporting to the licensing authority suspected adverse reactions to a medicinal product that occur in a single patient at a specific point in time.

Content of the individual case safety report

20.—(1) Holders must—

- (a) ensure that individual case safety reports are as complete as possible; and
- (b) communicate the updates of those reports to the licensing authority in an accurate and reliable manner.

(2) In the case of expedited reporting, the individual case safety report must include at least an identifiable reporter, an identifiable patient, one suspected adverse reaction and any medicinal product concerned.

(3) Holders and the licensing authority must record the details necessary for obtaining follow-up information on individual case safety reports and such reports must be adequately documented.

(4) When reporting suspected adverse reactions, holders must provide all available information on each individual case, including—

- (a) administrative information, namely—
 - (i) report type, date and a worldwide unique case identification number as well as unique sender identification and sender type,
 - (ii) the date on which the report was first received from the source and the date of receipt of the most recent information, using a precise date, and
 - (iii) other case identifiers and their sources, as well as references to additional available documents held by the sender of the individual case safety report, where applicable;
- (b) literature reference in accordance with the ‘Vancouver style’ as developed by the International Committee of Medical Journal Editors⁽¹³⁵⁾ for adverse reactions reported in the worldwide literature, including a comprehensive English summary of the article;
- (c) study type, study name and the sponsor’s study number or study registration number for reports from studies not covered by the Clinical Trials Regulations;
- (d) information on any primary source, namely information identifying the reporter, including country of residence and professional qualifications;

⁽¹³⁵⁾International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15.

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- (e) information identifying the patient (and parent in the case of a parent-child report), including age at the time of the onset of the first reaction, age group, gestation period when reaction or event was observed in the foetus, weight, height or gender, last menstrual date and, where relevant, gestation period at time of exposure;
 - (f) relevant medical history and concurrent conditions;
 - (g) the name of any medicinal product suspected to be related to the occurrence of the adverse reaction, including interacting medicinal products or, where the name is not known, any active substance and any other characteristics that allow for the identification of a medicinal product, including—
 - (i) the name of the holder, UK marketing authorisation number, pharmaceutical form and each (parent) route of administration,
 - (ii) any indication for use in the case, dose administered, start date and end date of administration,
 - (iii) actions taken with any medicinal product, and
 - (iv) effect of the dechallenge and rechallenge for suspect medicinal products;
 - (h) for a biological medicinal product, the batch number;
 - (i) concomitant medicinal products, identified in accordance with paragraph (g), which are not suspected to be related to the occurrence of the adverse reaction and past-medical drug therapy for the patient (and for the parent), where applicable;
 - (j) information on any suspected adverse reaction, including—
 - (i) start date and end date of any suspected adverse reaction or duration,
 - (ii) seriousness,
 - (iii) outcome of any suspected adverse reaction at the time of last observation,
 - (iv) time intervals between suspect medicinal product administration and start of any adverse reaction,
 - (v) the original reporter's words or short phrases used to describe any reaction, and
 - (vi) country of occurrence of the suspected adverse reaction;
 - (k) results of tests and procedures relevant to the investigation of the patient;
 - (l) in the event of death of the patient, date and reported cause of death, including autopsy-determined causes;
 - (m) a case narrative, where possible, providing all relevant information for individual cases with the exception of non-serious adverse reactions; and
 - (n) reasons for nullifying or amending an individual case safety report.
- (5) For the purposes of—
- (a) sub-paragraph (4)(b), upon request of the licensing authority, the holder that transmitted the initial report must provide a copy of the relevant article taking into account copyright restrictions, and a full translation of that article into English;
 - (b) sub-paragraph (4)(h), a follow-up procedure must be in place to obtain the batch number where it is not indicated in the initial report;
 - (c) sub-paragraph (4)(m), the information must be presented in a logical time sequence, in the chronology of the patient's experience including clinical course, therapeutic measures, outcome and follow-up information obtained: any relevant autopsy or post-mortem findings must also be summarised in the narrative.
- (6) Suspected adverse reactions must be reported in English.

Format of electronic transmission of suspected adverse reactions

21. Holders must use the formats and terminology specified in the list published under paragraph 18 for the electronic transmission of suspected adverse reactions, if the licensing authority has published a list under that paragraph.

PART 7

Risk management plans

Content of the risk management plan

22.—(1) The risk management plan established by the holder must contain the following elements—

- (a) an identification or characterisation of the safety profile of the medicinal product concerned;
- (b) an indication of how to characterise further the safety profile of the medicinal product(s) concerned;
- (c) a documentation of measures to prevent or minimise the risks associated with the medicinal product, including an assessment of the effectiveness of those measures; and
- (d) a documentation of post-authorisation obligations that have been imposed as a condition of the UK marketing authorisation.

(2) Medicinal products may, where appropriate be subject to the same risk management plan if they—

- (a) contain the same active substance; and
- (b) belong to the same holder.

(3) Where a risk management plan refers to post-authorisation studies—

- (a) it must indicate whether those studies are initiated, managed or financed by the holder voluntarily, or pursuant to obligations imposed by the licensing authority or an equivalent authority to the licensing authority in another country; and
- (b) all post-authorisation obligations must be listed in the summary of the risk management plan referred to in paragraph 23, together with a timeframe for meeting those obligations.

Summary of the risk management plan

23.—(1) The summary of the risk management plan to be made publicly available in accordance with regulation 203(2)(d) (obligations on licensing authority in relation to national medicines web-portal) must include key elements of the risk management plan with a specific focus on risk minimisation activities and, with regard to the safety specification of the medicinal product concerned, important information on potential and identified risks as well as missing information.

(2) Where a risk management plan concerns more than one medicinal product, a separate summary of the risk management plan must be provided by holders for each medicinal product.

Updates of the risk management plan

24.—(1) Subject to sub-paragraph (2), where the holder updates a risk management plan, it must submit the updated risk management plan to the licensing authority.

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- (2) If the licensing authority agrees, the holder may submit only the modules concerned by the update.
- (3) If necessary, the holder must provide the licensing authority with an updated summary of the risk management plan.
- (4) Each submission of the risk management plan must—
 - (a) have a distinct version number; and
 - (b) be dated.

Format of the risk management plan

- 25.** The risk management plan must be in the following format—
- (a) Part I: product overview;
 - (b) Part II: safety specification consisting of—
 - (i) Module SI: epidemiology of each indication and each target population,
 - (ii) Module SII: non-clinical part of the safety specification,
 - (iii) Module SIII: clinical trial exposure,
 - (iv) Module SIV: populations not studied in clinical trials,
 - (v) Module SV: post-authorisation experience,
 - (vi) Module SVI: additional EU requirements for the safety specification,
 - (vii) Module SVII: identified and potential risks, and
 - (viii) Module SVIII: summary of the safety concerns;
 - (c) Part III: pharmacovigilance plan, including post-authorisation safety studies;
 - (d) Part IV: plans for post-authorisation efficacy studies;
 - (e) Part V: risk minimisation measures, including evaluation of the effectiveness of risk minimisation activities;
 - (f) Part VI: summary of the risk management plan; and
 - (g) Part VII: annexes.

PART 8

Periodic safety update reports

Content of periodic safety update reports

- 26.**—(1) The periodic safety update report (“PSUR”) must—
- (a) be based on all available data; and
 - (b) focus on new information which has emerged since the data lock point of the last PSUR.
- (2) The PSUR must provide an accurate estimate of the population exposed to the medicinal product, including all data relating to the volume of sales and volume of prescriptions.
- (3) The estimate of exposure referred to in sub-paragraph (2) must be accompanied by a qualitative and quantitative analysis of actual use, which must indicate, where appropriate, how actual use differs from the indicated use based on all data available to the holder, including the results of observational or drug utilisation studies.

(4) The PSUR must contain the results of assessments of the effectiveness of risk minimisation activities relevant to the risk–benefit assessment.

(5) Where any conditions are imposed under regulation 59(4A) (conditions in relation to UK marketing authorisations to which paediatric specific provisions apply) or 59(4D) (conditions in relation to UK marketing authorisations for advanced therapy medicinal products), the PSUR must also include an assessment of the effectiveness of any risk management system, and the results of any studies performed, in order to comply with those conditions.

(6) Subject to sub-paragraph (7), holders are not required to include systematically detailed listings of individual cases, including case narratives, in the PSUR.

(7) Holders must provide case narratives in the relevant risk evaluation section of the PSUR where integral to the scientific analysis of a signal or safety concern in the relevant risk evaluation section.

(8) Based on the evaluation of the cumulative safety data and the risk-benefit analysis, the holder must draw conclusions in the PSUR as to the need for changes or actions, including implications for the approved summary of product characteristics for each product for which the PSUR is submitted.

(9) Unless otherwise agreed with the licensing authority, a single PSUR must be prepared for all medicinal products which—

- (a) contain the same active substance; and
- (b) are authorised for the same holder,

and sub-paragraph (10) applies to that single PSUR.

(10) Where this sub-paragraph applies—

- (a) the PSUR must cover all indications, routes of administration, dosage forms and dosing regimens, irrespective of whether authorised under different names and through separate procedures; and
- (b) where relevant, data relating to a particular indication, dosage form, route of administration or dosing regimen must be presented in a separate section of the PSUR, with any safety concerns addressed accordingly.

(11) Unless otherwise agreed with the licensing authority, if the substance that is the subject of the PSUR is also authorised as a component of a fixed combination medicinal product, the holder must either—

- (a) submit a separate PSUR for the combination of active substances authorised for the same holder, with cross-references to each relevant single-substance PSUR; or
- (b) provide the combination data within one of the single-substance PSURs.

Format of periodic safety update reports

27. Electronic PSURs must be submitted in the following format—

- (a) Part I: title page including signature;
- (b) Part II: executive summary; and
- (c) Part III: table of contents which contains—
 - (i) introduction,
 - (ii) worldwide marketing authorisation status,
 - (iii) actions taken in the reporting interval for safety reasons,
 - (iv) changes to reference safety information,
 - (v) estimated exposure and use patterns—

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- (aa) cumulative subject exposure in clinical trials,
- (bb) cumulative and interval patient exposure from marketing experience,
- (vi) data in summary tabulations—
 - (aa) reference information,
 - (bb) cumulative summary tabulations of serious adverse events in clinical trials,
 - (cc) cumulative and interval summary tabulations from post-marketing data sources,
- (vii) summaries of significant findings from clinical trials during the reporting interval—
 - (aa) completed clinical trials,
 - (bb) ongoing clinical trials,
 - (cc) long-term follow-up,
 - (dd) other therapeutic use of medicinal product,
 - (ee) new safety data related to fixed combination therapies,
- (viii) findings from non-interventional studies,
- (ix) information from other clinical trials and sources,
- (x) non-clinical data,
- (xi) literature,
- (xii) other periodic reports,
- (xiii) lack of efficacy in controlled clinical trials,
- (xiv) late-breaking information,
- (xv) overview on signals: new, ongoing or closed,
- (xvi) signal and risk evaluation—
 - (aa) summaries of safety concerns,
 - (bb) signal evaluation,
 - (cc) evaluation of risks and new information,
 - (dd) characterisation of risks, and
 - (ee) effectiveness of risk minimisation (if applicable),
- (xvii) benefit evaluation—
 - (aa) important baseline efficacy and effectiveness information,
 - (bb) newly identified information on efficacy and effectiveness, and
 - (cc) characterisation of benefits,
- (xviii) integrated benefit-risk analysis for authorised indications—
 - (aa) benefit-risk context: medical need and important alternatives, and
 - (bb) benefit-risk analysis evaluation,
- (xix) conclusions and actions, and
- (xx) appendices to the PSUR.

PART 9

Post-authorisation safety studies

Scope and interpretation

28.—(1) This Part applies to non-interventional post-authorisation safety studies initiated, managed or financed by a holder under obligations imposed under regulation 59 or 61 (conditions of UK marketing authorisation).

(2) In this Part—

“start of data collection” means the date on which information on the first study subject is first recorded in the study dataset or, in the case of the secondary use of data, the date on which the data extraction starts; and

“end of data collection” means the date on which the analytical dataset is completely available.

Obligations as to post-authorisation safety studies

29.—(1) The holder must submit in English—

- (a) the study protocol; and
- (b) the abstract of the final study report and the final study report.

(2) The holder must ensure that—

- (a) all study information is handled and stored so as to allow for accurate reporting, interpretation and verification of that information;
- (b) the confidentiality of the records of the study subjects remains protected; and
- (c) the analytical dataset and statistical programmes used for generating the data included in the final study report are kept in electronic format and are available for auditing and inspection.

(3) The licensing authority may publish appropriate templates for the protocol, abstract and final study report.

Format of the study protocol

30. The study protocol for a non-interventional post-authorisation safety studies must be submitted in the following format—

- (a) title: informative title including a commonly used term indicating the study design and the medicinal product, substance or drug class concerned, and a sub-title with a version identifier and the date of the last version;
- (b) name of holder;
- (c) responsible parties including a list of all collaborating institutions and other relevant study sites.
- (d) abstract, which must consist of a stand-alone summary of the study protocol, including the following subsections—
 - (i) title with subtitles including version and date of the protocol and name and affiliation of the main author,
 - (ii) rationale and background,
 - (iii) research question and objectives,

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- (iv) study design,
 - (v) population,
 - (vi) variables,
 - (vii) data sources,
 - (viii) study size,
 - (ix) data analysis, and
 - (x) milestones;
- (e) amendments and updates, namely any substantial amendment and update to the study protocol after the start of data collection, including a justification for the amendment or update, the date of the change, and a reference to the section of the protocol where the change has been made.
- (f) milestones, namely a table with planned dates for the following milestones—
- (i) start of data collection,
 - (ii) end of data collection,
 - (iii) any study progress report as referred to in regulation 198(2),
 - (iv) any interim report of study results, if applicable, and
 - (v) final report of study results;
- (g) rationale and background, namely a description of any safety hazard, the safety profile or the risk management measures that led to the study being imposed as an obligation for a UK marketing authorisation;
- (h) research question and objectives in accordance with the decision of the licensing authority in imposing the study as an obligation;
- (i) research methods, namely a description of the research methods, including—
- (i) study design,
 - (ii) setting, namely the study population defined in terms of persons, place, time period, and selection criteria, including the rationale for any inclusion and exclusion criteria: where any sampling from a source population is undertaken, a description of the source population and details of sampling methods must be provided and where the study design is a systematic review or a meta-analysis, the criteria for the selection and eligibility of studies must be explained,
 - (iii) variables,
 - (iv) data sources, namely strategies and data sources for determining exposures, outcomes and all other variables relevant to the study objectives: where the study will use an existing data source, such as electronic health records, any information on the validity of the recording and coding of the data must be reported and in the case of a systematic review or meta-analysis, the search strategy and processes and any methods for confirming data from investigators must be described,
 - (v) study size, namely any projected study size, precision sought for study estimates and any calculation of the study size that can minimally detect a pre-specified risk with a pre-specified interpretative power,
 - (vi) data management,
 - (vii) data analysis,
 - (viii) quality control, and
 - (ix) limitations of the research methods;

- (j) protection of human subjects, namely safeguards in order to comply with national requirements for ensuring the well-being and rights of participants in non-interventional post-authorisation safety studies;
- (k) management and reporting of adverse events or adverse reactions and other medically important events while the study is being conducted;
- (l) plans for disseminating and communicating study results; and
- (m) references.

Format of the abstract of the final study report

31. The abstract of the final study report for a non-interventional post-authorisation safety studies must be submitted in the following format—

- (a) title, with subtitles including date of the abstract and name and affiliation of main author;
- (b) keywords (not more than five keywords indicating the main study characteristics);
- (c) rationale and background;
- (d) research question and objectives;
- (e) study design;
- (f) setting;
- (g) subjects and study size, including dropouts;
- (h) variables and data sources;
- (i) results;
- (j) discussion (including, where relevant, an evaluation of the impact of study results on the risk–benefit balance of the product);
- (k) name of holder; and
- (l) names and affiliations of principal investigators.

Format of the final study report

32. The final study report for a non-interventional post-authorisation safety studies must be submitted in the following format—

- (a) title, including a commonly used term indicating the study design; sub-titles with date of final report and name and affiliation of the main author;
- (b) abstract, namely a stand-alone summary referred to in paragraph 31;
- (c) name and address of the holder;
- (d) investigators, namely the names, titles, degrees, addresses and affiliations of the principal investigator and all co-investigators, and list of all collaborating primary institutions and other relevant study sites;
- (e) milestones, namely the dates for the following milestones—
 - (i) start of data collection (planned and actual dates),
 - (ii) end of data collection (planned and actual dates),
 - (iii) study progress reports,
 - (iv) interim reports of study results, where applicable,
 - (v) final report of study results (planned and actual date), and

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- (vi) any other important milestone applicable to the study, including date of study registration in the electronic study register
- (f) rationale and background, namely a description of the safety concerns that led to the study being initiated, and critical review of relevant published and unpublished data evaluating pertinent information and gaps in knowledge that the study is intended to fill;
- (g) research question and objectives;
- (h) amendments and updates to the protocol, namely a list of any substantial amendments and updates to the initial study protocol after the start of data collection, including a justification for each amendment or update;
- (i) research methods, namely—
 - (i) study design: key elements of the study design and rationale for this choice,
 - (ii) setting: setting, locations, and relevant dates for the study, including periods of recruitment, follow-up, and data collection: in the case of a systematic review or meta-analysis, study characteristics used as criteria for eligibility, with rationale,
 - (iii) subjects: any source population and eligibility criteria for study subjects. Sources and methods for selection of participants shall be provided, including, where relevant, methods for case ascertainment, as well as number of and reasons for dropouts,
 - (iv) variables: all outcomes, exposures, predictors, potential confounders, and effect modifiers, including operational definitions: diagnostic criteria shall be provided, where applicable,
 - (v) data sources and measurement: for each variable of interest, sources of data and details of methods of assessment and measurement; if the study has used an existing data source, such as electronic health records, any information on the validity of the recording and coding of the data must be reported and in the case of a systematic review or meta-analysis, description of all information sources, search strategy, methods for selecting studies, methods of data extraction and any processes for obtaining or confirming data from investigators,
 - (vi) bias,
 - (vii) study size: study size, rationale for any study size calculation and any method for attaining projected study size,
 - (viii) data transformation: transformations, calculations or operations on the data, including how quantitative data were handled in the analyses and which groupings were chosen and why,
 - (ix) statistical methods: description of the following items—
 - (aa) main summary measures,
 - (bb) all statistical methods applied to the study,
 - (cc) any methods used to examine subgroups and interactions,
 - (dd) how missing data were addressed,
 - (ee) any sensitivity analyses, and
 - (ff) any amendment to the plan of data analysis included in the study protocol, with rationale for the change, and
 - (x) quality control: mechanisms to ensure data quality and integrity;
- (j) results: comprising the following subsections—

- (i) participants, namely numbers of study subjects at each stage of study: in the case of a systematic review or meta-analysis, number of studies screened, assessed for eligibility and included in the review with reasons for exclusion at each stage,
 - (ii) descriptive data: characteristics of study participants, information on exposures and potential confounders and number of participants with missing data. In the case of a systematic review or meta-analysis, characteristics of each study from which data were extracted,
 - (iii) outcome data: numbers of study subjects across categories of main outcomes,
 - (iv) main result: unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision and where relevant, estimates of relative risk must be translated into absolute risk for a meaningful time period,
 - (v) other analyses, and
 - (vi) adverse events and adverse reactions;
- (k) discussion which must include—
- (i) key results with reference to the study objectives, prior research in support of and conflicting with the findings of the completed post-authorisation safety study, and, where relevant, the impact of the results on the risk–benefit balance of the product,
 - (ii) limitations of the study taking into account circumstances that may have affected the quality or integrity of the data, limitations of the study approach and methods used to address them, sources of potential bias and imprecision, and validation of the events; both the direction and magnitude of potential biases must be discussed,
 - (iii) interpretation of results, considering objectives, limitations, multiplicity of analyses, results from similar studies and other relevant evidence, and
 - (iv) generalisability; and
- (l) references.”.

SCHEDULE 7

Regulation 228(2)

Insertion of new Schedule 33A (transitional provision)

1. After Schedule 33 insert—

“SCHEDULE 33A

Regulation 347A

Transitional provision in relation to EU Exit

PART 1

Interpretation

1. In this Schedule—

“the COMP” means the Committee for Orphan Medicinal Products of the EMA, established under Article 4 of the Orphan Regulation;

“converted EU marketing authorisation” has the meaning given in paragraph 6(1) and (2);

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“the Paediatric Regulation” means Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004, as it has effect in EU law⁽¹³⁶⁾;

“the Paediatric Committee” means the committee of the EMA established under Article 3 of the Paediatric Regulation;

“the Pharmacovigilance Risk Assessment Committee” means the Committee of the EMA established by Article 56(1)(aa) of Regulation (EC) No 726/2004; and

“Regulation (EC) No 507/2006” means Commission Regulation (EC) No 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 of the European Parliament and of the Council, as it has effect in EU law⁽¹³⁷⁾.

PART 2

Manufacturing, wholesale dealing and brokering

Wholesale dealer’s licence used to distribute a medicinal product imported from an EEA State before exit day

2.—(1) Subject to sub-paragraphs (2) and (3), a person (“P”) who is the holder of a wholesale dealer’s licence which—

- (a) was granted before exit day by the licensing authority;
- (b) was in force immediately before exit day and remains in force on exit day (whether or not it is suspended); and
- (c) was used by P to distribute a medicinal product, which was imported from an EEA State, by way of wholesale dealing, or to possess a medicinal product imported from an EEA State for such a purpose,

is deemed on and after exit day to hold a wholesale dealing licence granted under Part 3 (manufacture and distribution of medicinal products and active substances) that permits the operation of importing medicinal products from an approved country for import for the purposes specified in paragraph (c).

(2) After the end of the period of 6 months beginning with exit day, P is deemed to continue hold a wholesale dealer’s licence that permits the operation of importing medicinal products from an approved country for import by virtue of sub-paragraph (1) only if, before the end of that period, P has notified the licensing authority in writing of—

- (a) P’s intention to continue to import medicinal products from an approved country for import; and
- (b) either—
 - (i) P’s intention to appoint a responsible person (import) who will carry out the functions under regulation 45AA(4) (requirement as to responsible persons where licence holder imports from an approved country for import) in respect of the licence, or
 - (ii) that P will only import medicinal products from an approved country for import to which an exemption in regulation 45AA(2) applies.

⁽¹³⁶⁾OJ No. L 387, 27.12.2006, p. 1.

⁽¹³⁷⁾OJ No. L 92, 30.3.2006, p. 6.

(3) Unless P has notified the licensing authority as provided for in sub-paragraph (2)(b)(ii), after the end of the period of 2 years beginning with exit day, P is deemed to continue to hold a wholesale dealer's licence that permits the operation of importing medicinal products from an approved country for import by virtue of sub-paragraph (1) only if, before the end of that period, P has notified the licensing authority in writing of the name, address and qualifications of a person who—

- (a) is included in the register under regulation 45AB(1); and
- (b) will carry out the functions under regulation 45AA(4) in respect of the licence.

(4) From exit day, until the date on which P notifies the licensing authority of the information specified in sub-paragraph (3), the responsible person in respect of that licence under regulation 45 must carry out the functions under regulation 45AA(4).

(5) As soon as reasonably practicable after receipt of the information specified in paragraph (3), the licensing authority must provide P with written notice that the responsible person (import) is named on the licence.

(6) Where P has notified the licensing authority as provided for in sub-paragraph (2)(b)(ii), the licensing authority must, as soon as reasonably practicable, notify P in writing that the wholesale dealer's licence includes import of a medicinal product from an approved country for import limited to medicinal products to which an exemption in regulation 45AA(2) applies.

Approved country for import list on exit day (regulation 18A)

3.—(1) For the purposes of regulation 18A(1) (approved country for import), during the transitional period, the licensing authority must publish an approved country for import list that includes each EEA State in it.

(2) The licensing authority must not, before the end of the transitional period, exercise its power under regulation 18A(3) to remove an EEA State from the approved country for import list.

(3) In this paragraph, “the transitional period” is the period of two years beginning with exit day.

Qualified persons and approved country for batch testing list on exit day (Schedule 7)

4.—(1) Sub-paragraph (2) applies to a person who—

- (a) is acting as a qualified person immediately before exit day; and
- (b) satisfies the requirements of Part 1 of Schedule 7 (qualification requirements for qualified persons) immediately before exit day as they had effect at that time.

(2) The person is to be treated on and after exit day as continuing to satisfy the requirements of Part 1 of Schedule 7 if the person would otherwise fail to do so as a result of amendments made to that Part by the EU Exit Regulations.

(3) For the purposes of paragraph 14(1)(b) of Schedule 7 (obligations of qualified person), for the transitional period, the licensing authority is deemed to have made appropriate arrangements with—

- (a) each EEA State;
- (b) Australia;
- (c) Canada;
- (d) Israel;
- (e) Japan;

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- (f) New Zealand;
- (g) Switzerland; and
- (h) the United States of America,

and the licensing authority must, on exit day, publish a list that includes those countries under paragraph 14(3) of Schedule 7.

(4) The licensing authority may, in respect of any country specified in sub-paragraph (3) (b) to (h), include that country in the list subject to a condition or restriction as provided for in paragraph 14(4) of Schedule 7, insofar as that condition or restriction was reflected in the appropriate arrangements that existed immediately before exit day under Article 51(2) of the 2001 Directive.

(5) The licensing authority must not, before the end of the transitional period, exercise its powers under paragraph 14(6) of Schedule 7 to remove an EEA State from the list it publishes.

(6) In this regulation, “the transitional period” is the period of two years beginning with exit day.

List of countries with equivalent regulatory standards as to the manufacturing of active substances on exit day (regulation 45O(6) to (9))

5.—(1) For the purposes of regulation 45O(6) (requirements for registration as an importer, manufacturer or distributor of active substances), for the transitional period, the licensing authority must publish a list that includes the following countries—

- (a) each EEA State;
- (b) Australia;
- (c) Brazil;
- (d) Israel;
- (e) Japan;
- (f) Switzerland; and
- (g) the United States of America.

(2) The licensing authority must not, before the end of the transitional period, exercise its power under regulation 45O(9) to remove an EEA State from the list it publishes.

(3) In this paragraph, “the transitional period” is the period of two years beginning with exit day.

PART 3

Transitional provision in respect of conversion of EU marketing authorisations in force immediately before exit day

Conversion of EU marketing authorisations in force before exit day

6.—(1) This paragraph applies in relation to an EU marketing authorisation which was in force immediately before exit day.

(2) An EU marketing authorisation to which this paragraph applies—

- (a) has effect on and after exit day as a UK marketing authorisation granted under regulation 49(1) of these Regulations; and
- (b) is referred to in this Part as a “converted EU marketing authorisation”.

(3) If the holder of an EU marketing authorisation to which this paragraph applies notifies the licensing authority in writing before the end of the period of 21 days beginning with exit day that it does not wish to be the holder of a converted EU marketing authorisation, the licensing authority must revoke the converted EU marketing authorisation with effect from the date of receipt of the notification.

(4) A converted EU marketing authorisation—

- (a) is treated as if it had been granted by the licensing authority under regulation 49(1) on the same terms as those on which the EU marketing authorisation was granted, including any conditions or restrictions subject to which the EU marketing authorisation was granted and which remain in force immediately before exit day;
- (b) is treated, for the purposes of regulations 65 or 65B (validity of UK marketing authorisation), as if it had been granted by the licensing authority on the date that the EU marketing authorisation took effect;
- (c) is treated for the purposes of regulation 67(1) (failure to place on the market) as if it had been granted on exit day, and the period of three years referred to in regulation 67(2) is treated as having started on exit day;
- (d) is treated for the purposes of determining the relevant fee period for the purposes of Schedule 4 to the Fees Regulations (periodic fees for marketing authorisations) as if it had been granted by the licensing authority on the date that the EU marketing authorisation took effect;
- (e) is treated, for the purposes of the reference to the date of grant in regulation 27A(a) of the Fees Regulations (fees for renewals of a marketing authorisation) as if it had been granted on the date that the EU marketing authorisation took effect;
- (f) retains, for the purposes of regulation 51(1) and (2), the benefit of any remaining periods of data or marketing exclusivity (if any) from which the holder benefitted immediately before exit day;
- (g) retains the benefit of any decision by the EMA to exempt the holder from Articles 14(4) or (5) of Regulation (EC) No 726/2004 (failure to place on the market), and that decision is treated as if it had been made by the licensing authority under regulation 67(3); and
- (h) remains subject to—
 - (i) any suspension of the EU marketing authorisation that is in force immediately before exit day,
 - (ii) any post-authorisation obligations imposed after it was granted, and which remain in force immediately before exit day, and
 - (iii) any variation to its terms which were granted or accepted before exit day.

(5) For the purposes of this paragraph, an EU marketing authorisation is in force, even if that authorisation is suspended immediately before exit day.

(6) A converted EU marketing authorisation to which this paragraph applies which—

- (a) was granted as a conditional marketing authorisation within the meaning of Article 1 of Regulation (EC) No 507/2006; and
- (b) remains such a conditional marketing authorisation immediately before exit day,

has effect on and after exit day as a UK marketing authorisation granted under regulation 58F.

(7) A converted EU marketing authorisation to which this paragraph applies which relates to a medicinal product which—

- (a) was designated as an orphan medicinal product by the European Commission pursuant to Article 5 of the Orphan Regulation; and

- (b) remains in the Community register of Orphan Medicinal Products as referred to in that Article immediately before exit day,

has effect on and after exit day as a UK marketing authorisation granted under regulation 58C and retains, for the purposes of regulation 58D, the benefit of any period of marketing exclusivity from which the holder benefitted immediately before exit day under Article 8 of the Orphan Regulation.

Classification of converted EU marketing authorisations

7. For the purposes of regulation 62 (classification of UK marketing authorisation), it is a term of a converted EU marketing authorisation that the product to which the authorisation relates is to be available—

- (a) in a case where the product was classified in its EU marketing authorisation immediately before exit day as a prescription only medicine, the product is to be available only on prescription;
- (b) in a case where the product was not so classified and the licensing authority has determined that the product should be available on general sale, the product is to be available on general sale; or
- (c) in any other case, the product is to be available only from a pharmacy.

Obligations of licensing authority in connection with converted EU marketing authorisations

8.—(1) The licensing authority must, before the end of the period of 7 days beginning with exit day, notify the holders of converted EU marketing authorisations—

- (a) that the EU marketing authorisation is converted to a UK marketing authorisation; and
- (b) that the holder may notify the licensing authority in accordance with paragraph 6(3) that it does not wish to be the holder of a UK marketing authorisation.

(2) The licensing authority must, as soon as reasonably practicable after the end of the period referred to in paragraph 6(3), publish a list of converted EU marketing authorisations.

(3) The list mentioned in sub-paragraph (2) must specify which converted EU marketing authorisations have been revoked in accordance with paragraph 6(3).

Obligations of holders of converted EU marketing authorisations

9.—(1) A holder of a converted EU marketing authorisation must submit to the licensing authority, before the end of the period of one year beginning with exit day, the information described in sub-paragraph (3).

(2) The obligation in sub-paragraph (1) is subject to any requirement imposed by the licensing authority to provide that information before the end of a shorter period specified by the licensing authority under paragraph 10(1).

(3) The information which must be submitted in accordance with sub-paragraph (1) (referred to in this paragraph as the “baseline data”) is—

- (a) such information concerning the product to which the converted EU marketing authorisation relates as may be specified in writing for this purpose and published by the licensing authority on or before exit day;
- (b) notification of whether or not the product to which the converted EU marketing authorisation relates—
 - (i) is on the market in the United Kingdom at the time the notification is given, or

- (ii) if not, whether the product has been on the market in the United Kingdom at any time on or after exit day and if so, the date on which it was withdrawn from the United Kingdom market.

(4) In this Part, the date on which the holder of a converted EU marketing authorisation complies with the obligation in sub-paragraph (1), or with any requirement imposed by the licensing authority under paragraph 10(1) to provide all of the baseline data before the end of a period shorter than the period of one year beginning with exit day, is referred to as “the data submission date”.

Powers of licensing authority in connection with provision of information

10.—(1) If the licensing authority requests a holder of a converted EU marketing authorisation to submit all or part of the baseline data at any time before the expiry of the period of one year beginning with exit day, the holder must supply the information within the time period specified by the licensing authority in its request.

(2) If the licensing authority requests a holder of a converted EU marketing authorisation to provide any other information relating to the EU marketing authorisation, the holder must supply the information within the time period specified by the licensing authority in its request.

Variations of converted EU marketing authorisations notified or applied for before exit day

11.—(1) This paragraph applies where, before exit day—

- (a) a holder of a converted EU marketing authorisation has notified the EMA of, or made an application to the EMA for, a variation of the EU marketing authorisation to which the converted EU marketing authorisation applies under Chapter III of Regulation (EC) No 1234/2008, or has made an application to the EMA for an extension of that EU marketing authorisation in accordance with Article 19 of that Regulation;
- (b) the procedures specified in Article 17 of that Regulation (measures to close the procedures of Articles 14 to 16) have not concluded, or, in the case of an extension, no final decision has been made by the European Commission in relation to the application; and
- (c) the holder of the converted EU marketing authorisation wishes the variation to be made to the converted EU marketing authorisation.

(2) Where the variation is a minor variation of Type IA—

- (a) the variation may be implemented in relation to the converted EU marketing authorisation at any time on or after the time at which it may be implemented in relation to the EU marketing authorisation to which the converted EU marketing authorisation relates;
- (b) the holder of the converted EU marketing authorisation must (subject to paragraph 13), include in the baseline data—
 - (i) a summary of the variation, and
 - (ii) if the notification has been rejected by the EMA, an indication of that fact; and
- (c) the variation to the converted EU marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing before the end of the period of 30 days beginning with the data submission date that the variation is rejected, in which case the holder must cease to apply the rejected variation immediately after receipt of the notification.

(3) Where the variation is a minor variation of Type IB—

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- (a) the variation may be implemented in relation to the converted EU marketing authorisation at any time on or after the time at which it may be implemented in relation to the EU marketing authorisation to which the converted EU marketing authorisation relates;
 - (b) if the variation has not been rejected by the EMA, the holder of the converted EU marketing authorisation must (subject to paragraph 13) include a copy of the notification in the baseline data; and
 - (c) the variation to the converted EU marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing before the end of the period of 30 days beginning with the data submission date that the variation is rejected, in which case the holder must cease to apply the rejected variation immediately after receipt of the notification.
- (4) Sub-paragraph (5) applies where—
- (a) the variation is a major variation of Type II or an extension; and
 - (b) before exit day the Committee for Medicinal Products for Human Use gave a positive final opinion in relation to the application with which the United Kingdom concurred.
- (5) Where this sub-paragraph applies—
- (a) the variation may be implemented in relation to the converted EU marketing authorisation at any time on or after the time at which it may be implemented in relation to the EU marketing authorisation to which the converted EU marketing authorisation relates;
 - (b) the holder of the converted EU marketing authorisation must (subject to paragraph 13) include a copy of the application in the baseline data; and
 - (c) the licensing authority must either—
 - (i) treat the variation as accepted, and, if the variation affects the terms of the converted EU marketing authorisation, amend those terms accordingly; or
 - (ii) notify the holder of the converted EU marketing authorisation before the end of the period of 30 days beginning with the data submission date that the variation is rejected, in which case the holder must cease to apply the rejected variation immediately after receipt of the notification.
- (6) Sub-paragraph (7) applies where—
- (a) the variation is a major variation of Type II or an extension; and
 - (b) before exit day the Committee for Medicinal Products for Human Use had not given any opinion in relation to the application, or had given a negative final opinion in relation to it, or had given a positive final opinion but the United Kingdom recorded a divergent opinion.
- (7) Where this paragraph applies—
- (a) the holder of the converted EU marketing authorisation must submit to the licensing authority—
 - (i) the application for the variation; and
 - (ii) (subject to paragraph 13) the baseline data; and
 - (b) the licensing authority must consider the application in accordance with Schedule 10A.
- (8) In this paragraph and paragraph 12, “minor variation of Type IA”, “minor variation of Type IB”, “major variation of Type II” and “extension” have the meanings given in paragraph 1 of Schedule 10A.

Variations of converted EU marketing authorisations submitted to EMA after exit day but before the data submission date

- 12.—(1) This paragraph applies where a holder of a converted EU marketing authorisation—
- (a) notifies the EMA of, or applies to the EMA for, a variation of the EU marketing authorisation to which the converted EU marketing authorisation relates during the period beginning with exit day and ending on the day before the data submission date; and
 - (b) wishes the variation to be made in relation to the converted EU marketing authorisation.
- (2) Where the variation is a minor variation of Type IA—
- (a) the variation may be implemented in relation to the converted EU marketing authorisation at the same time as it may be implemented in relation to the EU marketing authorisation to which the converted EU marketing authorisation relates;
 - (b) the holder of the converted EU marketing authorisation must (subject to paragraph 13), include in the baseline data—
 - (i) a summary of the variation, and
 - (ii) if the notification has been rejected by the EMA, an indication of that fact; and
 - (c) the variation to the converted EU marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing within the period of 30 days beginning with the data submission date that the variation is rejected, in which case the holder must cease to apply the rejected variation immediately after receipt of the notification.
- (3) Where the variation is a minor variation of Type IB, a major variation of Type II or an extension which has not been rejected by the EMA—
- (a) the holder of the converted EU marketing authorisation must submit to the licensing authority—
 - (i) the notification of, or application for, the variation, and
 - (ii) (subject to paragraph 13) the baseline data; and
 - (b) the licensing authority must consider the application in accordance with Schedule 10A.

Variations of converted EU marketing authorisations sought in advance of the data submission date

- 13.—(1) If a holder of a converted EU marketing authorisation wishes the licensing authority to consider a notification of, or an application for, a variation to the authorisation before the data submission date, the holder must—
- (a) submit the notification or application to the licensing authority; and
 - (b) unless sub-paragraph (2) applies, provide to the licensing authority at the same time such information concerning the product to which the converted EU marketing authorisation relates as may be specified in writing by the licensing authority for this purpose and published on or before exit day.
- (2) If a holder of a converted EU marketing authorisation wishes the licensing authority to consider a notification of, or an application for, a variation to the authorisation before the data submission date but does not provide the information described in sub-paragraph (1)(b) with the notification or application, the licensing authority may agree to consider the notification or application if it is satisfied that—
- (a) the variation may be necessary on urgent safety grounds;

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- (b) the variation may be necessary in order to maintain supplies of a particular medicinal product to patients in the United Kingdom; or
- (c) there are other good reasons for considering the variation in advance of the submission of the information described in sub-paragraph (1).

(3) Where the licensing authority considers a notification of, or an application for, a variation in advance of the data submission date in accordance with this paragraph, the references in paragraphs 11(2)(c), (3)(c) and (5)(c)(ii) and 12(2)(c) to the data submission date are to be read as references to the date on which—

- (a) the notification of, or the application for, the variation is submitted to the licensing authority in accordance with sub-paragraph (1); or
- (b) the licensing authority notifies the holder that it will consider the notification or application, in accordance with sub-paragraph (2), without the information referred to in sub-paragraph (2)(b).

Applications for renewals of converted EU marketing authorisations made before exit day

14.—(1) This paragraph applies where a holder of a converted EU marketing authorisation has, before exit day, made an application to the EMA for renewal of the EU marketing authorisation in accordance with Article 14 of Regulation (EC) No 726/2004 but no final decision has been made in relation to that application by the European Commission before exit day.

(2) Where this paragraph applies—

- (a) the holder of the converted EU marketing authorisation must (subject to paragraph 18) submit the application for renewal to the licensing authority with the baseline data; and
- (b) the licensing authority must—
 - (i) where before exit day the Committee for Medicinal Products for Human Use has given a positive final opinion in relation to the application with which the United Kingdom concurred, treat the renewal application as accepted for the purposes of regulation 66 (application for renewal of authorisation), or
 - (ii) where before exit day the Committee for Medicinal Products for Human Use has not given any opinion or has given a negative final opinion in relation to the application, or where a positive final opinion has been given but the United Kingdom recorded a divergent opinion, treat the application as an application made in relation to the converted EU marketing authorisation under regulation 66 and consider the application in accordance with that regulation.

Applications for renewals of conditional marketing authorisations made before exit day

15.—(1) This paragraph applies where before exit day—

- (a) a holder of a converted EU marketing authorisation which was granted as a conditional marketing authorisation within the meaning of Article 1 of Regulation (EC) No 507/2006 has made an application to the EMA for renewal of the authorisation in accordance with Article 6 of that Regulation; but
- (b) no final decision has been made in relation to that application by the European Commission.

(2) Where this paragraph applies—

- (a) the holder of the converted EU marketing authorisation must (subject to paragraph 18) submit the application for renewal to the licensing authority with the baseline data; and

- (b) the licensing authority must—
 - (i) where before exit day the Committee for Medicinal Products for Human use has given a positive final opinion in relation to the application with which the United Kingdom concurred, treat the renewal application as accepted for the purposes of regulation 66B, or
 - (ii) where before exit day the Committee for Medicinal Products for Human Use has not given any opinion or has given a negative final opinion in relation to the application, or where a positive final opinion has been given but the United Kingdom recorded a divergent opinion, treat the application as an application made in relation to the converted EU marketing authorisation under regulation 66B (renewal of conditional marketing authorisation) and consider the application in accordance with that regulation.

Applications for renewals of converted EU marketing authorisations made after exit day

16.—(1) This paragraph applies where a holder of a converted EU marketing authorisation is due to make an application for renewal of the authorisation in accordance with regulation 66 (application for renewal of authorisation) during the period of one year beginning with exit day.

- (2) Where this paragraph applies—
 - (a) the holder of the converted EU marketing authorisation must (subject to paragraph 18) submit the baseline data so that it is received by the licensing authority at the same time as the application for renewal is made;
 - (b) the licensing authority must consider the renewal application in accordance with regulation 66; and
 - (c) the converted EU marketing authorisation remains in force until the licensing authority notifies the holder of its decision on the renewal application.

Applications for renewals of conditional marketing authorisations made after exit day

17.—(1) This paragraph applies where the holder of a converted EU marketing authorisation which was granted as a conditional marketing authorisation within the meaning of Article 1 of Regulation (EC) No 507/2006 is due to make an application for renewal of the authorisation in accordance with regulation 66B during the period beginning with exit day and ending on the data submission date.

- (2) Where this paragraph applies—
 - (a) the holder of the converted EU marketing authorisation must (subject to paragraph 18) submit the baseline data so that it is received by the licensing authority at the same time as the application for renewal is made;
 - (b) the licensing authority must consider the renewal application in accordance with regulation 66B (renewal of conditional marketing authorisation); and
 - (c) the authorisation remains in force until the licensing authority notifies the holder of its decision on the renewal application.

Renewals of converted EU marketing authorisations sought in advance of the data submission date

18.—(1) If a holder of a converted EU marketing authorisation submits an application for renewal in accordance with regulation 66 or 66B before the data submission date, it must, unless

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sub-paragraph (2) applies, provide to the licensing authority with the application such information concerning the product to which the converted EU marketing authorisation relates as may be specified in writing by the licensing authority for this purpose and published on or before exit day.

(2) If a holder of a converted EU marketing authorisation wishes the licensing authority to consider a renewal application before the data submission date but does not provide the information described in sub-paragraph (1) with the application, the licensing authority may agree to consider the application if it is satisfied that—

- (a) the renewal may be necessary on urgent safety grounds;
- (b) the renewal may be necessary in order to maintain supplies of a particular medicinal product to patients in the United Kingdom; or
- (c) there are other good reasons for considering the renewal in advance of the data submission date.

Article 61(3) notifications made before exit day in relation to converted EU marketing authorisations

19.—(1) This paragraph applies where, before exit day—

- (a) a holder of a converted EU marketing authorisation has, in accordance with Article 61(3) of the 2001 Directive, notified the EMA of a proposed change to an aspect of the labelling or the package leaflet of the EU marketing authorisation to which the converted EU marketing authorisation relates; but
- (b) the period of 90 days referred to in Article 61(3) has not elapsed and the EMA has not objected to the proposed change.

(2) Where this paragraph applies, and where the holder wishes the proposed change to apply in relation to the converted EU marketing authorisation—

- (a) the holder may put the change into effect in relation to the converted EU marketing authorisation at the same time as it may be put into effect in relation to the EU marketing authorisation;
- (b) the holder must (subject to paragraph 21) include with the baseline data—
 - (i) a copy of the notification, and
 - (ii) an indication of whether the EMA has opposed the proposed change; and
- (c) the proposed change to the labelling or the package leaflet of the converted EU marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing within the period of 30 days beginning with the data submission date that the proposed change is opposed, in which case the holder must cease to apply the opposed change immediately after receipt of the notification.

Article 61(3) notifications made in relation to converted EU marketing authorisations after exit day but before the data submission date

20.—(1) This paragraph applies where, during the period beginning with exit day and ending on the day before the data submission date, a holder of a converted EU marketing authorisation notifies the EMA in accordance with Article 61(3) of the 2001 Directive of a proposed change to an aspect of the labelling or the package leaflet of the EU marketing authorisation to which the converted EU marketing authorisation relates.

(2) Where this paragraph applies, and where the holder wishes the proposed change to apply in relation to the converted EU marketing authorisation—

- (a) the holder of the converted EU marketing authorisation may put the change into effect at the same time as it may be put into effect in relation to the EU marketing authorisation;
- (b) the holder must (subject to paragraph 21) include with the baseline data—
 - (i) a copy of the notification, and
 - (ii) an indication of whether the EMA has opposed the proposed change; and
- (c) the proposed change to the labelling or the package leaflet of the converted EU marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing within the period of 30 days beginning with the data submission date that the proposed change is opposed, in which case the holder must cease to apply the opposed change immediately after receipt of the notification.

Article 61(3) notifications sought in advance of the data submission date

21.—(1) If a holder of a converted EU marketing authorisation wishes to notify the licensing authority of a proposed change to an aspect of the labelling or the package leaflet of the EU marketing authorisation to which the converted EU marketing authorisation relates in advance of the data submission date, the holder must—

- (a) submit the notification of the proposed change to the licensing authority; and
- (b) unless sub-paragraph (2) applies, at the same time provide the licensing authority with such information concerning the product to which the converted EU marketing authorisation relates as may be specified in writing by the licensing authority for this purpose and published on or before exit day.

(2) If a holder of a converted EU marketing authorisation wishes the licensing authority to consider a proposed change before the data submission date but does not provide the information described in sub-paragraph (1)(b) with the notification, the licensing authority may agree to consider the notification if it is satisfied that—

- (a) the proposed change may be necessary on urgent safety grounds;
- (b) the proposed change may be necessary in order to maintain supplies of a particular medicinal product to patients in the United Kingdom; or
- (c) there are other good reasons for considering the proposed change in advance of the data submission date.

(3) Where the licensing authority considers a proposed change in accordance with this paragraph, the references in paragraph 19(2)(c) and 20(2)(c) to the data submission date are to be read as references to the date on which—

- (a) the proposed change is notified to the licensing authority in accordance with sub-paragraph (1); or
- (b) the licensing authority notifies the holder that it will consider the notification, in accordance with sub-paragraph (2), without the information referred to in sub-paragraph (1)(b).

Place of establishment for converted EU marketing authorisation holder established in EEA state before exit day

22.—(1) Subject to sub-paragraph (2), a person who—

- (a) holds a converted EU marketing authorisation on exit day (whether or not it is suspended); and
- (b) was, immediately before exit day, established in an EEA State, and remains established there on and after exit day,

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is to be treated, for the transitional period, as satisfying the requirements of regulation 49(3) or 66(2) (as the case may be), notwithstanding the amendments made to those provisions by the EU Exit Regulations.

(2) But sub-paragraph (1) continues to apply to a person after the end of the specified period only if the person has, before the end of that period, notified the licensing authority in writing of—

- (a) a named individual who resides and operates in the United Kingdom who the licensing authority may contact in respect of any matter relating to the converted EU marketing authorisation during the transitional period; and
- (b) that individual's address, telephone number and email address.

(3) In this paragraph—

“the specified period” means 4 weeks beginning with exit day; and

“the transitional period” means the period of 21 months beginning with exit day.

Temporary exemption as to packaging requirements for converted EU marketing authorisations

23.—(1) A holder of a converted EU marketing authorisation does not commit an offence under regulation 268 during the period of 33 months beginning with exit day to the extent that—

- (a) the packaging and package leaflet do not comply with the requirements of Part 13 by reason only of the fact that the outer or immediate packaging, or the package leaflet, do not include the correct information as to—
 - (i) the name and address of the holder of the UK marketing authorisation, or, where applicable, the name of the holder's representative,
 - (ii) the number of the UK marketing authorisation, or
 - (iii) the name and address of the manufacturer of the product; and
- (b) the outer and immediate packaging, or the package leaflet, do not include the correct information specified in paragraph (a)(i) to (iii) solely because—
 - (i) the number of the marketing authorisation is the number of the EU marketing authorisation to which the converted EU marketing authorisation relates, or
 - (ii) the UK marketing authorisation holder has established itself in the United Kingdom before the end of the period of 21 months beginning with exit day in order to comply with regulation 49(3), and the information specified in paragraph (a)(i) or (iii) is no longer correct as a consequence of that establishment in the United Kingdom.

(2) Sub-paragraph (1) only applies if—

- (a) the packaging and package leaflet met the requirements of Part 13 as to the matters specified in sub-paragraph (1)(a)(i) to (iii) immediately before exit day; and
- (b) the holder of the converted EU marketing authorisation, having been notified of the number of the UK marketing authorisation and having established itself in the United Kingdom, does not otherwise need to make any changes to the outer or immediate packaging, or the package leaflet, during the period referred to in sub-paragraph (1).

Referrals made under Article 20 of Regulation (EC) No 726/2004 that have not concluded or been implemented before exit day

24.—(1) Sub-paragraph (2) applies where—

- (a) the European Commission has requested the opinion of the EMA in accordance with Article 20(2) of Regulation (EC) No 726/2004 in relation to a specified matter; but
 - (b) no final decision has been adopted by the European Commission in accordance with Article 20(3) of that Regulation immediately before exit day.
- (2) Where this sub-paragraph applies, the licensing authority must make a decision in respect of the specified matter in accordance with regulation 68 (revocation, variation and suspension of UK marketing authorisation) as soon as reasonably practicable.
- (3) In making a decision under regulation 68 in accordance with sub-paragraph (2), the licensing authority must have regard to—
- (a) any relevant information obtained by it before exit day in relation to the specified matter as a consequence of its involvement in the procedure under Article 20 of Regulation (EC) No 726/2004;
 - (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a member State in the making of that decision or agreement, under any procedure provided for in the Council Decision of 28 June 1999 laying down the procedure for the exercise of implementing powers conferred on the Commission; and
 - (c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11.
- (4) Sub-paragraph (5) applies if the licensing authority is making a decision under regulation 68 in accordance with sub-paragraph (2) in a case where the Committee for Medicinal Products for Human Use has given a final opinion in relation to the specified matter.
- (5) Where this sub-paragraph applies, the licensing authority may treat the opinion as if it were the opinion of the appropriate committee for the purposes of paragraph 5 of Schedule 11.
- (6) Sub-paragraph (7) applies where—
- (a) the European Commission has requested the opinion of the EMA in accordance with Article 20(2) of Regulation (EC) No 726/2004 in relation to a specified matter;
 - (b) a final decision has been adopted by the European Commission in accordance with Article 20(3) of that Regulation immediately before exit day; but
 - (c) the necessary steps to give effect to the decision referred to in paragraph (b) have not been taken before exit day.
- (7) Where this sub-paragraph applies, the licensing authority must, where a Commission decision or opinion requires steps to be taken in respect of an EU marketing authorisation that is a converted EU marketing authorisation, take the steps necessary as a result of the decision or opinion to suspend, revoke or vary a converted EU marketing authorisation as soon as reasonably practicable.
- (8) In this paragraph, “specified matter” means a matter in relation to which the opinion of the EMA has been requested by the European Commission under Article 20(2) of Regulation (EC) No 726/2004 before exit day that might result in the suspension, revocation or variation of an EU marketing authorisation which is a converted EU marketing authorisation.

Enforcement

25. If a holder of a converted EU marketing authorisation fails to comply with an obligation imposed on the holder by or under this Part, the licensing authority may suspend the authorisation until the holder complies with the obligation.

PART 4

Transitional provision in respect of UK marketing authorisations, parallel import licences and parallel distribution notices

Place of establishment for UK marketing authorisation holder or parallel import licence holder established in an EEA State before exit day

- 26.—(1) Subject to sub-paragraphs (2) and (3), any person—
- (a) who—
 - (i) holds a UK marketing authorisation immediately before exit day which remains in force on exit day (whether or not it is suspended),
 - (ii) holds a parallel import licence immediately before exit day which remains in force on exit day (whether or not it is suspended),
 - (iii) has made an application for, or to renew, a UK marketing authorisation or parallel import licence before exit day, which has not been determined before that date, or
 - (iv) makes such an application on or after exit day but before the end of the transitional period; and
 - (b) who was, immediately before exit day, established in an EEA State and remains established there on and after exit day,

is to be treated, for the transitional period, as satisfying the requirements of regulation 49(3), 66(2) or 66A(2) (as the case may be), notwithstanding the amendments made to those provisions by the EU Exit Regulations.

(2) But sub-paragraph (1) continues to apply to a person only if the person has notified the licensing authority in writing of—

- (a) a named individual who resides and operates in the United Kingdom who the licensing authority may contact in respect of any matter relating to the UK marketing authorisation or parallel import licence, or application for a UK marketing authorisation or parallel import licence (as the case may be), during the transitional period; and
 - (b) that individual's address, telephone number and email address.
- (3) A person must notify the licensing authority under sub-paragraph (2)—
- (a) where sub-paragraph (1)(a)(i) to (iii) applies, within the period of 4 weeks beginning with exit day; or
 - (b) where sub-paragraph (1)(a)(iv) applies, at the time of making the application.

(4) This paragraph does not apply to a UK marketing authorisation that is a converted EU marketing authorisation within the meaning of paragraph 6.

(5) In this paragraph “the transitional period” means the period of 21 months beginning with exit day.

Temporary exemption as to packaging requirements: change of place of establishment

27.—(1) Subject to sub-paragraph (2), a person to whom paragraph 26 applies does not commit an offence under regulation 268 (offence relating to packaging and package leaflets: holder of authorisation etc) during the transitional period to the extent that—

- (a) the packaging and package leaflet do not comply with the requirements of Part 13 (packaging and leaflets) by reason only of the fact that the outer or immediate

packaging, or the package leaflet (as the case may be), do not include the correct information as to—

- (i) the name and address of the holder of the UK marketing authorisation, or, where applicable, the name of that holder’s representative,
 - (ii) the number of the UK marketing authorisation, or
 - (iii) the name and address of the manufacturer of the product; and
- (b) the outer and immediate packaging, or the package leaflet, do not include the correct information specified in paragraph (a)(i) to (iii) solely because—
- (i) the UK marketing authorisation holder has established itself in the United Kingdom before the end of the period of 21 months beginning with exit day in order to comply with regulation 49(3), and
 - (ii) the information specified in paragraph (a)(i) to (iii) is no longer correct as a consequence of that establishment in the United Kingdom.
- (2) Sub-paragraph (1) only applies if—
- (a) the packaging and package leaflet met the requirements of Part 13 as to the matters specified in paragraph (1)(a)(i) to (iii) immediately before exit day; and
 - (b) the UK marketing authorisation holder, having established itself in the United Kingdom, does not otherwise need to make any changes to the outer or immediate packaging, or the package leaflet, as the case may be, during the transitional period.
- (3) In this paragraph “the transitional period” means the period of 33 months beginning with exit day.

Conversion of parallel distribution notices in to parallel import licences

- 28.**—(1) Sub-paragraph (2) applies where—
- (a) a person holds a parallel distribution notice, issued by the EMA, for a medicinal product in respect of which there is an EU marketing authorisation;
 - (b) that distribution notice, and that EU marketing authorisation, are in force immediately before exit day; and
 - (c) that parallel distribution notice specifies the United Kingdom as a member state of destination in respect of that medicinal product.
- (2) Subject to sub-paragraph (3), a person who falls within sub-paragraph (1) is deemed, on and after exit day, to have a parallel import licence granted under Part 5 in respect of the medicinal product specified in the parallel distribution notice.
- (3) A person who falls within sub-paragraph (1) continues to hold a parallel import licence pursuant to sub-paragraph (2) only if that person notifies the licensing authority—
- (a) before the end of the period of 21 days beginning with exit day, of each medicinal product, and each country from which it is intended to import that product on or after exit day; and
 - (b) of any other information that the licensing authority requests, within such time period as the licensing authority may specify.
- (4) The licensing authority must as soon as reasonably practicable after receipt of the information specified in sub-paragraph (3), issue a parallel import licence to the holder of the parallel distribution notice.

Inclusion of the batch testing condition in relevant UK marketing authorisations, and batch testing of biological medicinal products in the EEA before exit day (regulation 60A)

- 29.—(1) Sub-paragraph (2) applies where—
- (a) a marketing authorisation was in force before exit day,
 - (b) that authorisation is in force as a UK marketing authorisation on exit day (whether or not it is suspended); and
 - (c) that authorisation is for a medicinal product of a type that is specified in regulation 60A(2)(a) to (e) (condition as to the submitting of samples and other information to the appropriate authority).
- (2) Where this sub-paragraph applies, the UK marketing authorisation is deemed to include the batch testing condition on and after exit day.
- (3) Sub-paragraph (4) applies where a holder of a UK marketing authorisation has, before exit day, submitted to a competent authority of an EEA State samples for testing from a batch of a medicinal product (“the relevant batch”) that—
- (a) is the subject of that authorisation; and
 - (b) is of a type specified in regulation 60A(2)(a) to (e).
- (4) Where this sub-paragraph applies, the holder of the UK marketing authorisation is deemed to have satisfied the batch testing condition in respect of the relevant batch if, before exit day—
- (a) the competent authority of that EEA State examines the sample from the relevant batch; and
 - (b) that authority declared it to be in conformity with the approved specifications (within the meaning of Article 114 of the 2001 Directive) before exit day.
- (5) The appropriate authority—
- (a) must include each EEA State on the list it publishes under regulation 60A(5) on exit day; and
 - (b) must not, before the end of the transitional period, exercise its powers under regulation 60A(8) to remove an EEA State from the list it publishes under regulation 60A(5).
- (6) For the purposes of regulation 60A(9), the appropriate authority must, on exit day—
- (a) include Switzerland and Israel in the list it publishes under that paragraph; and
 - (b) include in respect of those countries any conditions or restrictions in the arrangement with those countries that affect the applicability of the batch testing exemption.
- (7) In this paragraph—
- (a) “the transitional period” means the period of 21 months beginning with exit day; and
 - (b) “the batch testing condition” and “the batch testing exemption” have the same meaning as in regulation 60A.

Existing data and marketing exclusivity and global marketing authorisations

- 30.—(1) Sub-paragraph (2) applies in relation to a UK marketing authorisation which, immediately before exit day, is part of a global marketing authorisation with one or more EU marketing authorisations or marketing authorisations granted by the competent authority of an EEA state.
- (2) Where this sub-paragraph applies, the provisions of regulation 48(5) (definitions for Part 5), in so far as they describe a global marketing authorisation by reference to UK marketing

authorisations only, do not affect the periods of data and marketing exclusivity to which the holder of a UK marketing authorisation to which this paragraph applies is entitled immediately before exit day.

Applications for EU marketing authorisations made before exit day

31.—(1) Sub-paragraph (2) applies where, before exit day—

- (a) an application has been made to the EMA for an EU marketing authorisation; but
- (b) no final decision has been made by the European Commission in relation to the grant of an EU marketing authorisation under Article 10 of Regulation (EC) No 726/2004.

(2) Where this sub-paragraph applies, the applicant may apply to the licensing authority for the grant of a UK marketing authorisation by submitting to the licensing authority—

- (a) a copy of the application for the EU marketing authorisation; and
- (b) if requested by the licensing authority, such material or information that the licensing authority reasonably considers necessary for dealing with the application.

(3) Sub-paragraph (4) applies where, before exit day and in relation to an application to which sub-paragraph (2) applies, a final opinion favourable to the granting of an EU marketing authorisation has been given by the Committee for Medicinal Products for Human Use and the United Kingdom concurred with that opinion.

(4) Where this sub-paragraph applies, the licensing authority must grant a UK marketing authorisation in response to an application as described in sub-paragraph (2) as soon as reasonably practicable after it is received.

(5) Sub-paragraph (6) applies where before exit day, in relation to an application to which sub-paragraph (2) applies—

- (a) no final opinion favourable to the granting of an EU marketing authorisation has been given by the Committee for Medicinal Products for Human Use; or
- (b) such an opinion has been given but the United Kingdom recorded a divergent opinion.

(6) Where this sub-paragraph applies, the licensing authority must consider an application made under sub-paragraph (2) in accordance with Part 5 of these Regulations (marketing authorisations).

Place of establishment for UK marketing authorisation holder established in EEA state before exit day (pre-exit EU marketing authorisation applications)

32.—(1) Subject to sub-paragraph (2), a person—

- (a) who applied to the EMA for an EU marketing authorisation before exit day;
- (b) to whom the licensing authority grants a UK marketing authorisation on or after exit day in response to that application in accordance with paragraph 31; and
- (c) who was, immediately before exit day, established in an EEA State, and remains established there on and after exit day,

is to be treated, for the transitional period, as satisfying the requirements of regulation 49(3), notwithstanding the amendments made to those provisions by the EU Exit Regulations.

(2) Sub-paragraph (1) applies to a person only if, when submitting a copy of the application for the EU marketing authorisation to the licensing authority in accordance with paragraph 31, the person notifies the licensing authority in writing of—

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- (a) a named individual who resides and operates in the United Kingdom whom the licensing authority may contact in respect of any matter relating to the UK marketing authorisation during the transitional period; and
- (b) that individual's address, telephone number and email address.

(3) In this paragraph, "the transitional period" means the period which beginning with the date on which the licensing authority grants a UK marketing authorisation as described in paragraph 31(4) and ending 21 months after exit day.

Packaging in relation to UK marketing authorisations granted in response to application for EU marketing authorisation made before exit day

33.—(1) Subject to sub-paragraph (2), a person to whom paragraph 32(1) applies does not commit an offence under regulation 268 (offence relating to packaging and package leaflets: holder of authorisation etc) during the transitional period to the extent that—

- (a) the packaging and package leaflet do not comply with the requirements of Part 13 (packaging and leaflets) by reason only of the fact that the outer or immediate packaging, or the package leaflet, do not include the correct information as to—
 - (i) the name and address of the holder of the marketing authorisation, or, where applicable, the name of the holder's representative,
 - (ii) the number of the marketing authorisation, or
 - (iii) the name and address of the manufacturer of the product; and
- (b) the outer and immediate packaging, or the package leaflet, do not include the correct information specified in paragraph (a)(i) to (iii) solely because—
 - (i) the number of the marketing authorisation is the number of the EU marketing authorisation to which the application for the EU marketing authorisation related, or
 - (ii) the UK marketing authorisation holder has established itself in the United Kingdom before the end of the period of 21 months beginning with exit day in order to comply with regulation 49(3), and the information specified in paragraph (a)(i) or (iii) is no longer correct as a consequence of that establishment in the United Kingdom.

(2) Sub-paragraph (1) only applies if—

- (a) the packaging and package leaflet met the requirements of Part 13 as to the matters specified in sub-paragraph (1)(a)(i) to (iii) immediately before exit day; and
- (b) the UK marketing authorisation holder, being aware of the number of the UK marketing authorisation and having established in the United Kingdom, does not otherwise need to make any changes to the outer or immediate packaging, or the package leaflet, as the case may be, during the transitional period.

(3) In this paragraph, "the transitional period" means the period beginning with the date on which the licensing authority grants a UK marketing authorisation as described in paragraph 31(4) and ending 33 months after exit day.

Applications made for a UK marketing authorisation before exit day to which Chapter 4 of Title III of the 2001 Directive applied

34.—(1) Sub-paragraph (2) applies where an application for a UK marketing authorisation has been made before exit day and—

- (a) regulation 58(6) and (7) of the 2012 Regulations (applications to be determined under Chapter 4 of Title III of the 2001 Directive) applied to that application before exit day; but
 - (b) a decision as specified in Article 28(5) of the 2001 Directive has not been adopted by the licensing authority before exit day.
- (2) Where this sub-paragraph applies, the licensing authority must—
- (a) where the procedure specified in Article 28(4) of the 2001 Directive has concluded before exit day in relation to that application, grant a UK marketing authorisation in respect of that application as soon as reasonably practicable, and in any event before the end of the period of 30 days, beginning with exit day; or
 - (b) where the procedure specified in Article 28(4) of the 2001 Directive has not concluded before exit day, determine that application in accordance with Part 5 of these Regulations (marketing authorisations) as soon as reasonably practicable, unless the applicant notifies the licensing authority in writing that they no longer want the application to proceed.
- (3) In making a determination under sub-paragraph (2)(b), the licensing authority must have regard to—
- (a) any relevant information obtained by it before exit day in relation to the application as a consequence of its involvement in any procedure provided for in Chapter 4 of Title III of the 2001 Directive;
 - (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a reference member state or concerned member state in the making of that decision or agreement, under any procedure provided for in Chapter 4 of Title III of the 2001 Directive; and
 - (c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11 (advice and representations).
- (4) In making a determination under sub-paragraph (2)(b), the licensing authority must take all reasonable steps to ensure that it makes a decision to grant or refuse a UK marketing authorisation in the time period specified in regulation 58(1) (consideration of application) as if it had applied to that application on the date on which the application was submitted.

Transitional provision in respect of Plasma Master Files

35.—(1) This paragraph applies in relation to a UK marketing authorisation or EU marketing authorisation—

- (a) which was granted before exit day;
- (b) the application for which made reference to a Plasma Master File within the meaning of paragraph 1.1(a), first indent, of Part III of Annex I to the 2001 Directive which was certified by the EMA in accordance with paragraph 1.1(c) of that Part of the Annex; and
- (c) which remains in force as a UK marketing authorisation on and after exit day.

(2) A holder of the UK marketing authorisation to which this paragraph applies may, subject to complying with the obligations in sub-paragraph (3), continue to refer to the Plasma Master File as certified by the EMA, notwithstanding the modifications to paragraph 1.1(c) of Part III of Annex I to the 2001 Directive in Schedule 8B, subject which that paragraph is to be read on and after exit day.

(3) The holder of a UK marketing authorisation to which this paragraph applies must notify the licensing authority of—

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- (a) the outcome of the annual update and recertification of the Plasma Master File by the EMA within 4 weeks beginning with the completion of that update and recertification;
 - (b) any application for changes to the terms of the Plasma Master File which the holder seeks from the EMA, within 4 weeks beginning with the date of the application; and
 - (c) the outcome of any application referred to in paragraph (b), within 4 weeks beginning with the date on which the holder is notified of that outcome.
- (4) The licensing authority may at any time review the terms of a Plasma Master File to which reference is made in accordance with sub-paragraph (2), with a view to exercising its powers under these Regulations in relation to the UK marketing authorisation.

Suspensions of UK marketing authorisations that have effect immediately before exit day that were imposed under Chapter 4 of Title III of the 2001 Directive or Regulation (EC) No 726/2004

36. Where, immediately before exit day, a marketing authorisation, which is a UK marketing authorisation on exit day, has been suspended pursuant to the procedures in Chapter IV of Title III of 2001 Directive or Regulation (EC) No 726/2004, the suspension—

- (a) continues to have effect on and after exit day in accordance with the terms on which it was imposed; and
- (b) is to be treated as if it had been imposed by the licensing authority under Part 5 (marketing authorisations).

Referrals made under Article 31 of the 2001 Directive concerning the suspension, variation or revocation of an EU marketing authorisation or a UK marketing authorisation that have not concluded before exit day

37.—(1) Sub-paragraph (2) applies where—

- (a) a specified matter has been referred under Article 31 of the 2001 Directive before exit day; but
- (b) that procedure has not concluded before exit day.

(2) Where this sub-paragraph applies, the licensing authority must make a decision in respect of the specified matter in accordance with regulation 68 (revocation, variation and suspension of UK marketing authorisation) as soon as reasonably practicable.

(3) In making a decision under regulation 68 in accordance with sub-paragraph (2), the licensing authority must have regard to—

- (a) any relevant information obtained by it before exit day in relation to the specified matter as a consequence of its involvement in any procedure provided for in Chapter 4 of Title III of the 2001 Directive;
- (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a member state in the making of that decision or agreement, under any procedure provided for in Chapter 4 of Title III of the 2001 Directive; and
- (c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11.

(4) Sub-paragraph (5) applies if the licensing authority is making a decision under regulation 68 in accordance with sub-paragraph (2) in a case where the Committee for Medicinal Products for Human Use or the Co-ordination Group for Mutual Recognition and Decentralised Procedures (as the case may be) has given a final opinion in relation to the matter referred under Article 31 of the 2001 Directive.

(5) Where this sub-paragraph applies, the licensing authority may treat the opinion as if it were the opinion of the appropriate committee for the purposes of paragraph 5 of Schedule 11 (advice and representations).

(6) Sub-paragraph (7) applies where—

- (a) a specified matter has been referred under Article 31 of the 2001 Directive before exit day;
- (b) that referral has concluded before exit day; but
- (c) the licensing authority has not, before exit day, taken the steps necessary to give effect to that decision or that opinion (as the case may be).

(7) Where this sub-paragraph applies, the licensing authority must take the steps necessary as a result of the decision or opinion to suspend, revoke or vary the UK marketing authorisation—

- (a) as soon as reasonably practicable; and
- (b) in the case of a UK marketing authorisation that is not a converted EU marketing authorisation, within the period specified in Article 34(3) of the 2001 Directive (if relevant).

(8) In this paragraph—

“concluded before exit day”, in relation to an Article 31 referral, means—

- (a) a Commission decision as provided for in Article 34(3) of the 2001 Directive has been taken before exit day; or
- (b) an opinion of the Co-ordination Group for Mutual Recognition and Decentralised Procedures, which constituted the end of the Article 31 referral procedure, has been given before exit day; and

“specified matter” means—

- (a) a matter referred under Article 31 of the 2001 Directive before exit day that concerns a proposal to suspend, revoke or otherwise vary a UK marketing authorisation or an EU marketing authorisation; but
- (b) does not include a referral made under Article 107i of the 2001 Directive.

PART 5

Transitional provision in relation to variations of marketing authorisations other than converted EU marketing authorisations

Application or notification made before exit day in respect of a variation under Chapter IIa of Regulation (EC) No 1234/2008 (variations to purely national marketing authorisations)

38.—(1) Sub-paragraph (2) applies where—

- (a) an application or notification in respect of a variation to a UK marketing authorisation has been submitted to the licensing authority under Chapter IIa of Regulation (EC) No 1234/2008 before exit day; but
- (b) the procedures specified in Article 13e of that Regulation (measures to close the variation procedures in Chapter IIa of that Regulation) have not concluded before exit day.

(2) Where this sub-paragraph applies, the licensing authority must—

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- (a) determine which of the provisions specified in Schedule 10A that are relevant to that application or notification need to be taken on or after exit day, having regard to the steps that have already been undertaken under Chapter IIa of Regulation (EC) No 1234/2008 before exit day;
 - (b) assess the application or notification in accordance with the provisions of that Schedule the authority has determined are relevant to the application, as if the application or notification had been made under them; and
 - (c) take all reasonable steps to ensure that it assesses the notification or application in accordance with any relevant time period specified in that Schedule, as if the application had been made under the provisions in that Schedule before exit day.
- (3) Paragraphs 15 and 16 of Schedule 10A apply to any variation that falls under sub-paragraph (1)(a) or (b).

Application or notification made before exit day in respect of a variation under Chapter II of Regulation (EC) No 1234/2008 (variations to marketing authorisations granted in accordance with Chapter 4 of the 2001 Directive)

39.—(1) This paragraph applies where an application or notification in respect of a variation to a marketing authorisation has been submitted to the licensing authority, as a relevant authority, under Chapter II of Regulation (EC) No 1234/2008 before exit day.

(2) If the procedures specified in Article 11(1) of Regulation (EC) No 1234/2008 have not concluded before exit day, the licensing authority must—

- (a) assess the application or notification in accordance with regulation 65C and Schedule 10A to these Regulations, as if the application or notification had been made under those provisions; and
- (b) make such an assessment having regard to the matters specified in sub-paragraph (5).

(3) If the procedures specified in Article 11(1) of Regulation (EC) No 1234/2008 have concluded before exit day—

- (a) the licensing authority must take the steps specified in Article 11(2) of Regulation (EC) No 1234/2008 within the time limit specified in Article 23(1) of that Regulation; and
- (b) paragraphs 15 and 16 of Schedule 10A apply to the variation.

(4) In making a determination under sub-paragraph (2), the licensing authority must—

- (a) determine which steps of the procedures specified in Schedule 10A that are relevant to that application or notification need to be taken on or after exit day, having regard to the matters specified in sub-paragraph (5); and
- (b) take all reasonable steps to ensure that it assesses the notification or application in accordance with any time period specified in that Schedule, as if the application had been made under the provisions in that Schedule before exit day.

(5) In making a determination under sub-paragraph (2), the licensing authority must have regard to—

- (a) any recommendation in relation to that application or notification given before exit day pursuant to Article 5 of Regulation (EC) No 1234/2008;
- (b) any relevant information obtained by it before exit day, as a relevant authority, in relation to the application or notification by virtue of any procedure provided for in Chapter II of that Regulation; and
- (c) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a relevant authority, including any matter referred under the procedure specified in Article 13 of that Regulation.

Application or notification in respect of a variations made before exit day under Article 20 of Regulation (EC) No 1234/2008 (work-sharing procedure)

- 40.**—(1) Sub-paragraph (2) applies where—
- (a) an application or notification in respect of a variation to a UK marketing authorisation has been submitted to the licensing authority, as a relevant authority or the reference authority, under Article 20 of Regulation (EC) No 1234/2008;
 - (b) the marketing authorisation is one to which Chapter II or IIa of that Regulation applied; and
 - (c) the procedure in Article 20(8) has not been completed before exit day.
- (2) Where this sub-paragraph applies, the licensing authority must—
- (a) determine which of the provisions specified in Schedule 10A that are relevant to that application or notification need to be taken on or after exit day, having regard to the steps that have already been undertaken under Article 20 of Regulation (EC) No 1234/2008 before exit day;
 - (b) assess the application or notification in accordance with the relevant provisions in that Schedule, as if the application or notification had been made under them; and
 - (c) take all reasonable steps to ensure that it assesses the notification or application in accordance with any relevant time period specified in that Schedule, as if the application had been made under the provisions in that Schedule before exit day.
- (3) In making a determination or assessment under sub-paragraph (2), the licensing authority must have regard to—
- (a) any opinion given by the reference authority before exit day in relation to that application;
 - (b) any relevant information obtained by it before exit day, as a reference authority or relevant authority, in relation to the application or notification by virtue of any procedure provided for in regulation 20 of Regulation (EC) No 1234/2008; and
 - (c) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a relevant authority.
- (4) Paragraphs 15 and 16 of Schedule 10A apply to any variation that falls under sub-paragraph (1).

PART 6

Transitional provision in relation to the Paediatric Regulation

Transitional provision in relation to applications made to EMA before exit day under the Paediatric Regulation

- 41.**—(1) Where a paediatric investigation plan has been agreed by the EMA in accordance with the Paediatric Regulation before exit day, that plan, including any modifications agreed by the EMA before exit day, has effect on and after exit day as an agreed paediatric investigation plan.
- (2) Sub-paragraph (3) applies where—
- (a) a paediatric investigation plan has been submitted to the EMA with a request for agreement before exit day;
 - (b) the proposed paediatric plan is valid in accordance with the provisions of Article 15(2) of the Paediatric Regulation; but

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- (c) the EMA has not adopted a decision to agree the plan before exit day.
- (3) Where this sub-paragraph applies, the licensing authority must—
 - (a) where an opinion favourable to agreeing the paediatric investigation plan with which the United Kingdom concurred has been given by the Paediatric Committee before exit day, treat the plan as an agreed paediatric investigation plan;
 - (b) where an opinion against agreeing the paediatric investigation plan with which the United Kingdom concurred has been given by the Paediatric Committee before exit day, decide that it cannot agree the plan under regulation 50B(5) (agreement and modification of paediatric investigation plan); or
 - (c) where before exit day no opinion in relation to the paediatric investigation plan has been given by the Paediatric Committee, or where such an opinion has been given but the United Kingdom recorded a divergent opinion, treat it as a request for agreement under regulation 50B(1) and determine that request as soon as reasonably practicable, unless the applicant notifies the licensing authority in writing that they do not want the application to proceed as a request for agreement of a paediatric investigation plan under these Regulations.
- (4) Sub-paragraph (5) applies where—
 - (a) a paediatric investigation plan has been agreed by the EMA in accordance with the Paediatric Regulation before exit day;
 - (b) the person to whom the EMA's decision to agree the plan was addressed has, before exit day, made a proposal under Article 22 of the Paediatric Regulation to modify the plan, or to request a waiver; but
 - (c) the EMA has not adopted a decision to agree to the modification or waiver before exit day.
- (5) Where this sub-paragraph applies, the licensing authority must—
 - (a) where an opinion favourable to agreeing the modification or waiver with which the United Kingdom concurred has been given by the Paediatric Committee before exit day, agree to the modification or waiver as if it had been requested under regulation 50B(6);
 - (b) where an opinion against agreeing the modification or waiver with which the United Kingdom concurred has been given by the Paediatric Committee before exit day, decide that it cannot agree to the modification or waiver as if it had been requested under regulation 50B(6); or
 - (c) where before exit day no opinion in relation to the modification or waiver has been given by the Paediatric Committee, or where such an opinion has been given but the United Kingdom recorded a divergent opinion, treat the proposal as one made under regulation 50B(6) and consider it accordingly, unless the applicant notifies the licensing authority in writing that they do not want the proposal to proceed as a proposal under regulation 50B(6).
- (6) Where the EMA has adopted a decision to grant, and has not revoked, a waiver of the obligation to produce the information in Article 7(1)(a) of the Paediatric Regulation before exit day, that waiver has effect on and after exit day as a waiver granted by the licensing authority under regulation 50D (waiver of production of information in a paediatric investigation plan).
- (7) Sub-paragraph (8) applies where—
 - (a) an application has been made to the EMA for a waiver of the obligation to produce the information in Article 7(1)(a) of the Paediatric Regulation before exit day;
 - (b) the application has been accepted as valid by the EMA; but
 - (c) the EMA has not adopted a decision to grant the waiver before exit day.

- (8) Where this sub-paragraph applies, the licensing authority must—
- (a) where an opinion favourable to agreeing the waiver with which the United Kingdom concurred has been given by the Paediatric Committee before exit day, grant the waiver under regulation 50D(2);
 - (b) where an opinion against agreeing the waiver with which the United Kingdom concurred has been given by the Paediatric Committee before exit day, decide that it cannot grant the waiver under regulation 50D(2); or
 - (c) where before exit day no opinion in relation to the waiver has been given by the Paediatric Committee, or where such an opinion has been given but the United Kingdom recorded a divergent opinion, treat the proposal as one made under regulation 50D and consider it accordingly, unless the applicant notifies the licensing authority in writing that they do not want the proposal to proceed as a proposal under regulation 50D.

PART 7

Transitional provision in relation to orphan medicinal products

Transitional provision in relation to applications made to EMA before exit day for orphan medicinal products

- 42.**—(1) This sub-paragraph applies where—
- (a) before exit day—
 - (i) an application has been made to the EMA for an EU marketing authorisation in relation to a medicinal product which has been approved as an orphan medicinal product by the European Commission pursuant to Article 5 of the Orphan Regulation and which appears in the Orphan Register, but
 - (ii) no final decision has been made by the European Commission in relation to maintaining the product’s inclusion in the Orphan Register following the grant of an EU marketing authorisation, and
 - (b) on or after exit day, the licensing authority is granting or considering an application for a UK marketing authorisation in relation to the product in accordance with paragraph 31(4) or (6).
- (2) Where sub-paragraph (1) applies, the licensing authority must—
- (a) where an opinion favourable to the maintenance of the inclusion of the medicinal product in the Orphan Register with which the United Kingdom concurred has been given by the COMP before exit day in relation to the application, decide for the purposes of regulation 58C(1)(a) (consideration of applications relating to orphan medicinal products) that the orphan criteria are met in relation to the product, or
 - (b) where no opinion favourable to such maintenance has been given by the COMP before exit day in relation to the application, or where such an opinion has been given but the United Kingdom recorded a divergent opinion, reach its own view for the purposes of regulation 58C(1)(a) as to whether the orphan criteria are met in relation to the product.
- (3) In this paragraph, “Orphan Register” means the Community register of Orphan Medicinal Products as referred to in Article 5 of the Orphan Regulation.

PART 8

Transitional provision in respect of homoeopathic medicinal products

List of countries for the purposes of the definition of “homoeopathic medicinal product” on exit day

43.—(1) For the purposes of the definition of “homoeopathic medicinal product” in regulation 8 (general interpretation: accepted Pharmacopoeias for homoeopathic manufacturing procedures), during the transitional period, the licensing authority must publish a list of countries that includes each EEA State in it.

(2) The licensing authority must not, before the end of the transitional period, remove an EEA State from the list described in sub-paragraph (1).

(3) In this paragraph, “the transitional period” is the period of two years beginning with exit day.

Place of establishment for holders of certificates of registration established in EEA before exit day

44.—(1) Subject to sub-paragraph (2), any person—

(a) who—

- (i) holds a certificate of registration immediately before exit day which remains in force on exit day (whether or not it is suspended),
- (ii) has made an application for, or to renew, a certificate of registration before exit day, which has not been determined by the licensing authority before that date, or
- (iii) makes such an application on or after exit day but before the end of the transitional period; and

(b) who was, immediately before exit day, established in an EEA State and who remains there on and after that day,

is to be treated, for the transitional period, as satisfying the requirements of regulation 103(4) or 108(2) (as the case may be), notwithstanding the amendments made to those provisions by the EU Exit Regulations.

(2) But sub-paragraph (1) continues to apply to a person only if the person has notified the licensing authority in writing of—

- (a) a named individual who resides and operates in the United Kingdom who the licensing authority may contact in respect of any matter relating to the certificate of registration, or application for a certificate of registration, during the transitional period; and
- (b) that individual’s address, telephone number and email address.

(3) A person must notify the licensing authority under sub-paragraph (2)—

- (a) where sub-paragraph (1)(a)(i) or (ii) applies, within the period of 4 weeks beginning with exit day; or
- (b) where sub-paragraph (1)(a)(iii) applies, at the time of making the application.

(4) In this paragraph “the transitional period” means the period of 21 months beginning with exit day.

Temporary exemption as to packaging requirements: change of place of establishment

45.—(1) Subject to sub-paragraph (2), a person to whom paragraph 44 applies does not commit an offence under regulation 268 (offence relating to packaging and package leaflets) during the transitional period in relation to a product to the extent that—

- (a) the packaging and package leaflet do not comply with the requirements of Part 13 (packaging and leaflets) by reason only of the fact that the outer or immediate packaging, or the package leaflet (as the case may be), do not include the correct information as to—
 - (i) the name and address of the holder of the certificate of registration,
 - (ii) the number of the certificate of registration, or
 - (iii) the name and address of the manufacturer of the product if different from the holder of the certificate of registration; and
- (b) the outer and immediate packaging, or the package leaflet, do not include the correct information specified in paragraph (a)(i) to (iii) solely because—
 - (i) the holder of the certificate of registration has established itself in the United Kingdom before the end of the period of 21 months beginning with exit day in order to comply with regulation 103(4) or 108(2), and
 - (ii) the information specified in paragraph (a)(i) to (iii) is no longer correct as a consequence of that establishment in the United Kingdom.

(2) Sub-paragraph (1) only applies if—

- (a) the packaging and package leaflet met the requirements of Part 13 as to the matters specified in sub-paragraph (1)(a)(i) to (iii) immediately before exit day; and
- (b) the certificate of registration holder, having established itself in the United Kingdom, does not otherwise need to make any changes to the outer or immediate packaging, or the package leaflet, as the case may be, during the transitional period.

(3) In this paragraph “the transitional period” means the period of 33 months beginning with exit day.

Applications made for a certificate of registration for a registrable homoeopathic product before exit day to which Chapter 4 of Title III of the 2001 Directive applied

46.—(1) Sub-paragraph (2) applies where an application for a certificate of registration has been made before exit day and—

- (a) regulation 104(5) and (6) (applications to be determined under Chapter 4 of Title III of the 2001 Directive) applied to that application before exit day; but
- (b) a decision as specified in Article 28(5) of the 2001 Directive has not been adopted by the licensing authority before exit day.

(2) Where this sub-paragraph applies, the licensing authority must—

- (a) where the procedure specified in Article 28(4) of the 2001 Directive has concluded before exit day in relation to that application, grant a certificate of registration in respect of that application as soon as reasonably practicable, and in any event before the end of the period of 30 days, beginning with exit day; or
- (b) where the procedure specified in Article 28(4) of the 2001 Directive has not concluded before exit day, determine that application in accordance with Part 6 of these Regulations as soon as reasonably practicable, unless the applicant notifies the licensing authority in writing that they no longer want the application to proceed.

(3) In making a determination under sub-paragraph (2)(b), the licensing authority must have regard to—

- (a) any relevant information obtained by it before exit day in relation to the application as a consequence of its involvement in any procedure provided for in Chapter 4 of Title III of the 2001 Directive; and
- (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a reference member state or concerned member state in the making of that decision or agreement, under any procedure provided for in Chapter 4 of Title III of the 2001 Directive.

(4) In making a determination under sub-paragraph (2)(b), the licensing authority must take all reasonable steps to ensure that it makes a decision to grant or refuse a certificate of registration in the time period specified in regulation 104(1) as if it had applied to that application on the date on which the application was submitted.

Suspensions of certificates of registration that have effect immediately before exit day that were imposed under Chapter 4 of Title III of the 2001 Directive

47. Where, immediately before exit day, a certificate of registration has been suspended pursuant to the procedures in Chapter IV of Title III of 2001 Directive, the suspension—

- (a) continues to have effect on and after exit day in accordance with the terms on which it was imposed; and
- (b) is to be treated as if it had been imposed by the licensing authority under Part 6 of these Regulations (certification of homeopathic medicinal products).

Referrals made under Article 31 of the 2001 Directive concerning the suspension, variation or revocation of a certificate of registration that have not concluded before exit day

48.—(1) Sub-paragraph (2) applies where—

- (a) a specified matter has been referred under Article 31 of the 2001 Directive before exit day; but
- (b) the procedure has not concluded before exit day.

(2) Where this sub-paragraph applies, the licensing authority must make a decision in respect of the specified matter in accordance with regulation 110 (revocation, variation and suspension of certificate of registration) as soon as reasonably practicable.

(3) In making a decision under regulation 110 in accordance with sub-paragraph (2), the licensing authority must have regard to—

- (a) any relevant information obtained by it before exit day in relation to the specified matter as a consequence of its involvement in any procedure provided for in Chapter 4 of Title III of the 2001 Directive;
- (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a member state in the making of that decision or agreement, under any procedure provided for in Chapter 4 of Title III of the 2001 Directive;
- (c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11 (advice and representations).

(4) Sub-paragraph (5) applies if the licensing authority is making a decision under regulation 110 in accordance with sub-paragraph (2) in a case where the Co-ordination Group for Mutual Recognition and Decentralised procedures has given an opinion in relation to the matter under Article 31 of the Directive.

(5) Where this sub-paragraph applies, the licensing authority may treat the opinion as if it were the opinion of the appropriate committee for the purposes of paragraph 5 of Schedule 11.

(6) Sub-paragraph (7) applies where—

- (a) a specified matter has been referred under Article 31 of the 2001 Directive before exit day;
- (b) the referral has concluded before exit day; but
- (c) the licensing authority has not, before exit day, taken the steps necessary to give effect to that decision or that opinion (as the case may be).

(7) The licensing authority must take the steps necessary as a result of the decision or opinion to suspend, revoke or vary the certificate of registration within the time period specified in Article 34(3) of the 2001 Directive where the decision or opinion requires steps to be taken in relation to a certificate of registration.

(8) In this paragraph—

“concluded before exit day”, in relation to an Article 31 referral, means—

- (a) a Commission decision as provided for in Article 34(3) of the 2001 Directive has been taken before exit day; or
- (b) an opinion of the Co-ordination Group for Mutual Recognition and Decentralised Procedures, which constituted the end of the Article 31 referral procedure, has been given before exit day;

“specified matter” means—

- (a) a matter referred under Article 31 of the 2001 Directive before exit day that concerns a proposal to suspend, revoke or otherwise vary a certificate of registration; but
- (b) does not include a referral made under Article 107i of the 2001 Directive.

PART 9

Transitional provision in respect of traditional herbal registrations

Place of establishment for holders of traditional herbal registrations established in EEA before exit day

49.—(1) Subject to sub-paragraph (2), any person—

- (a) who—
 - (i) holds a traditional herbal registration immediately before exit day which remains in force on exit day (whether or not it is suspended),
 - (ii) has made an application for, or to renew, a traditional herbal registration before exit day, which has not been determined by the licensing authority before that date, or
 - (iii) makes such an application on or after exit day but before the end of the transitional period; and
- (b) who was, immediately before exit day, established in an EEA State and who remains there on and after that day,

is to be treated, for the transitional period, as satisfying the requirements of regulation 127(3) or 133(2) (as the case may be), notwithstanding the amendments made to those provisions by the EU Exit Regulations.

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(2) But sub-paragraph (1) continues to apply to a person only if the person notifies the licensing authority in writing of—

- (a) a named individual who resides and operates in the United Kingdom who the licensing authority may contact in respect of any matter relating to the traditional herbal registration, or application for a traditional herbal registration, during the transitional period; and
- (b) that individual's address, telephone number and email address.

(3) A person must notify the licensing authority under sub-paragraph (2)—

- (a) where sub-paragraph (1)(a)(i) or (ii) applies, within the period of 4 weeks beginning with exit day; or
- (b) where sub-paragraph (1)(a)(iii) applies, at the time of making the application.

(4) In this paragraph “the transitional period” means the period of 21 months beginning with exit day.

Temporary exemption as to packaging requirements: change of place of establishment

50.—(1) Subject to sub-paragraph (2), a person to whom paragraph 49 applies does not commit an offence under regulation 268 (offence relating to packaging and package leaflets) during the transitional period in relation to a product to the extent that—

- (a) the packaging and package leaflet do not comply with the requirements of Part 13 (packaging and leaflets) by reason only of the fact that the outer or immediate packaging, or the package leaflet (as the case may be), do not include the correct information as to—
 - (i) the name and address of the holder of the traditional herbal registration, or, if applicable, the holder's representative,
 - (ii) the number of the traditional herbal registration, or
 - (iii) the name and address of the manufacturer of the product; and
- (b) the outer and immediate packaging, or the package leaflet, do not include the correct information specified in paragraph (a)(i) to (iii) solely because—
 - (i) the holder of the traditional herbal registration has established itself in the United Kingdom before the end of the period of 21 months beginning with exit day in order to comply with regulation 127(3) or 133(2), and
 - (ii) the information specified in paragraph (a)(i) to (iii) is no longer correct as a consequence of that establishment in the United Kingdom.

(2) Sub-paragraph (1) only applies if—

- (a) the packaging and package leaflet met the requirements of Part 13 as to the matters specified in sub-paragraph (1)(a)(i) to (iii) immediately before exit day; and
- (b) the holder of the traditional herbal registration, having established itself in the United Kingdom, does not otherwise need to make any changes to the outer or immediate packaging, or the package leaflet, as the case may be, during the transitional period.

(3) In this paragraph “the transitional period” means the period of 33 months beginning with exit day.

List of approved countries for traditional use of a herbal medicinal product on exit day

51.—(1) For the purpose of regulation 125A (list of approved countries for traditional use of a herbal medicinal product), the licensing authority must, for the transitional period, include each EEA State in the list it publishes under regulation 125A(1).

(2) The licensing authority must not, before the end of the transitional period, exercise its power under regulation 125A(3) to remove an EEA State from the list.

(3) In this paragraph, the transitional period is two years beginning with exit day.

Applications made for a traditional herbal registration before exit day to which Chapter 4 of Title III of the 2001 Directive applied

52.—(1) Sub-paragraph (2) applies where an application for a traditional herbal registration has been made before exit day and—

(a) regulation 130(12) and (13) (applications to be determined under Chapter 4 of Title III of the 2001 Directive) applied to that application before exit day; but

(b) a decision as specified in Article 28(5) of the 2001 Directive has not been adopted by the licensing authority before exit day.

(2) Where this sub-paragraph applies, the licensing authority must—

(a) where the procedure specified in Article 28(4) of the 2001 Directive has concluded before exit day in relation to that application, grant a traditional herbal registration in respect of that application as soon as reasonably practicable, and in any event before the end of the period of 30 days, beginning with exit day; or

(b) where the procedure specified in Article 28(4) of the 2001 Directive has not concluded before exit day, determine that application in accordance with Part 7 of these Regulations as soon as reasonably practicable, unless the applicant notifies the licensing authority in writing that they no longer want the application to proceed.

(3) In making a determination under sub-paragraph (2)(b), the licensing authority must have regard to—

(a) any relevant information obtained by it before exit day in relation to the application as a consequence of its involvement in any procedure provided for in Chapter 4 of Title III of the 2001 Directive;

(b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a reference member state or concerned member state in the making of that decision or agreement, under any procedure provided for in Chapter 4 of Title III of the 2001 Directive;

(c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11 (advice and representations).

(4) In making a determination under sub-paragraph (2)(b), the licensing authority must take all reasonable steps to ensure that it makes a decision to grant or refuse a traditional herbal registration in the time period specified in regulation 130(1) as if it had applied to that application on the date on which the application was submitted.

Suspensions of traditional herbal registrations that have effect immediately before exit day that were imposed under Chapter 4 of Title III of the 2001 Directive

53. Where, immediately before exit day, a traditional herbal registration has been suspended pursuant to the procedures in Chapter IV of Title III of 2001 Directive, the suspension—

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- (a) continues to have effect on and after exit day in accordance with the terms on which it was imposed; and
- (b) is to be treated as if it had been imposed by the licensing authority under Part 7 of these Regulations (traditional herbal registrations).

Referrals made under Article 31 of the 2001 Directive concerning the suspension, variation or revocation of a traditional herbal registration that have not concluded before exit day

54.—(1) Sub-paragraph (2) applies where—

- (a) a specified matter has been referred under Article 31 of the 2001 Directive before exit day; but
- (b) the procedure has not concluded before exit day.

(2) Where this sub-paragraph applies, the licensing authority must make a decision in respect of the specified matter in accordance with regulation 135 (revocation, variation and suspension of traditional herbal registration) as soon as reasonably practicable.

(3) In making a decision under regulation 135 in accordance with sub-paragraph (2), the licensing authority must have regard to—

- (a) any relevant information obtained by it before exit day in relation to the specified matter as a consequence of its involvement in any procedure provided for in Chapter 4 of Title III of the 2001 Directive;
- (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a member state in the making of that decision or agreement, under any procedure provided for in Chapter 4 of Title III of the 2001 Directive;
- (c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11 (advice and representations).

(4) Sub-paragraph (5) applies if the licensing authority is making a decision under regulation 135 of these Regulations in accordance with sub-paragraph (2) in a case where the Co-ordination Group for Mutual Recognition and Decentralised procedures has given an opinion in relation to the matter under Article 31 of the Directive.

(5) Where this sub-paragraph applies, the licensing authority may treat the opinion as if it were the opinion of the appropriate committee for the purposes of paragraph 5 of Schedule 11.

(6) Sub-paragraph (7) applies where—

- (a) a specified matter has been referred under Article 31 of the 2001 Directive before exit day;
- (b) the referral has concluded before exit day; but
- (c) the licensing authority has not, before exit day, taken the steps necessary to give effect to that decision or that opinion (as the case may be).

(7) Where this sub-paragraph applies, the licensing authority must take the steps necessary as a result of the decision or opinion to suspend, revoke or vary the traditional herbal registration within the time period specified in Article 34(3) of the 2001 Directive where the decision or opinion requires steps to be taken in relation to a traditional herbal registration.

(8) In this paragraph—

“concluded before exit day”, in relation to an Article 31 referral, means—

- (a) a Commission decision as provided for in Article 34(3) of the 2001 Directive has been taken before exit day; or

- (b) an opinion of the Co-ordination Group for Mutual Recognition and Decentralised Procedures, which constituted the end of the Article 31 referral procedure, has been given before exit day; and

“specified matter” means—

- (a) a matter referred under Article 31 of the 2001 Directive before exit day that concerns a proposal to suspend, revoke or otherwise vary a traditional herbal registration; but
- (b) does not include a referral made under Article 107i of the 2001 Directive.

Proposals to refer an application for a traditional herbal registration to the Committee for Herbal Medicinal Products and the procedure in Part 3 of Schedule 11 that were on-going at exit day

55.—(1) This paragraph applies where—

- (a) the licensing authority has proposed to refer an application for a traditional herbal registration to the Committee on Herbal Medicinal Products in accordance with Article 16c(4) of the 2001 Directive before exit day; but
- (b) that application has not been determined in accordance with Part 7 of these Regulations before exit day.

(2) Where the licensing authority has received an opinion of the Committee for Herbal Medicinal Products before exit day in relation to the application, it must take that decision in to account and determine that application.

(3) Where the licensing authority has not received an opinion of the Committee for Herbal Medicinal Products before exit day, notwithstanding the amendments made to Part 3 of Schedule 11 by the EU Exit Regulations, it may—

- (a) proceed to determine the application, taking into account any proceedings that took place before exit day under Part 3 of Schedule 11 (prior to its amendment by the EU Exit Regulations), or any opinion of the Committee on Herbal Medicinal Products in relation to the application that is given on or after exit day; or
- (b) it may refer the matter under regulation 130A in order to obtain the findings and advice of the appropriate committee before determining the application.

PART 10

Transitional provision in respect of pharmacovigilance

Interpretation of Part

56. In this Part, references to a “holder” are to the holder of a UK marketing authorisation or a traditional herbal registration.

Temporary exemption as to the location of an appropriately qualified person for pharmacovigilance

57.—(1) Sub-paragraph (2) applies to a holder of a UK marketing authorisation or traditional herbal registration—

- (a) which was granted before exit day;
- (b) that remains in force on exit day as a UK marketing authorisation or traditional herbal registration (as the case may be); and

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(c) in respect of which, the holder had an appropriately qualified person for pharmacovigilance in respect of that authorisation or registration who, immediately before exit day, resided and operated in an EEA State.

(2) Where this sub-paragraph applies to a holder, that holder is to be treated as satisfying the requirements of regulation 182(2)(a), notwithstanding the amendments made to that provision by the EU Exit Regulations, for the transitional period, insofar as that holder would otherwise not meet those requirements solely because the appropriately qualified person responsible for pharmacovigilance in respect of that authorisation or registration resides and operates in an EEA State.

(3) In this regulation “the transitional period” means the period of 21 months beginning with exit day.

Referrals made under Article 107i of the 2001 Directive concerning the evaluation of data from pharmacovigilance activities which are not concluded before exit day

58.—(1) Sub-paragraph (2) applies where—

- (a) a specified matter has been referred under Article 107i of the 2001 Directive (urgent Union procedure) before exit day; but
- (b) that procedure has not concluded before exit day.

(2) Where this sub-paragraph applies, the licensing authority must make a decision in respect of the specified matter in accordance with regulation 68 or 135 (revocation, variation and suspension of UK marketing authorisation or traditional herbal registration) as soon as reasonably practicable.

(3) In making a decision under regulation 68 or 135 in accordance with sub-paragraph (2), the licensing authority must have regard to—

- (a) any relevant information obtained by it before exit day in relation to the specified matter as a consequence of its involvement in any procedure provided for by, or referred to in, Section 4 of Chapter 3 of the 2001 Directive;
- (b) any relevant decision made, or agreement reached, before exit day, where the United Kingdom participated as a member state in the making of that decision or agreement, under any procedure provided for by, or referred to in, Section 4 of Chapter 3 of the 2001 Directive; and
- (c) any advice it receives from the appropriate committee pursuant to the procedures in Schedule 11 (advice and representations).

(4) Sub-paragraph (5) applies if the licensing authority is making a decision under regulation 68 or 135 in accordance with sub-paragraph (2) in a case where the Committee for Medicinal Products for Human Use or the Co-ordination Group for Mutual Recognition and Decentralised Procedures (as the case may be) has given a final opinion in relation to the matter.

(5) Where this sub-paragraph applies, the licensing authority may treat the opinion as if it were the opinion of the appropriate committee for the purposes of paragraph 5 of Schedule 11 (advice and representations).

(6) In making a determination under regulation 68 or 135 in accordance with sub-paragraph (2), the licensing authority may adopt or have regard to any decision made, or agreement reached, in relation to the specified matter under Section 4 of Chapter 3 of the 2001 Directive on or after exit day, notwithstanding that the United Kingdom did not participate in the making of that decision or agreement.

(7) Sub-paragraph (8) applies where—

- (a) a specified matter has been referred under Article 107i of the 2001 Directive before exit day; and
 - (b) that referral has concluded before exit day; but
 - (c) the licensing authority has not, before exit day, taken the steps necessary to give effect to that decision or that opinion (as the case may be).
- (8) Where this sub-paragraph applies, the licensing authority must take the steps necessary as a result of the decision or opinion to suspend, revoke or vary the UK marketing authorisation or traditional herbal registration—
- (a) as soon as reasonably practicable, and, where relevant, within the time period specified in Article 34(3) of the 2001 Directive where a Commission decision requires steps to be taken in relation to a UK marketing authorisation that is not a converted EU marketing authorisation, or traditional herbal registration; or
 - (b) as soon as reasonably practicable, where a Commission decision or opinion requires steps to be taken in respect of a UK marketing authorisation that is a converted EU marketing authorisation.
- (9) In this paragraph—
- “concluded before exit day”, in relation to an Article 107i referral, means—
- (a) a Commission decision as provided for in Article 107k of the 2001 Directive has been taken before exit day; or
 - (b) an opinion of the Co-ordination Group for Mutual Recognition and Decentralised Procedures, which constituted the end of the Article 107i referral procedure in accordance with Article 107k(2), has been given before exit day;
- “specified matter” means a referral made under Article 107i of the 2001 Directive on the basis of concerns resulting from the evaluation of data from pharmacovigilance activities.

Matters on-going at exit day in respect of periodic safety update reports

- 59.**—(1) Sub-paragraph (2) applies where—
- (a) a holder has submitted a periodic safety update report under regulation 191 before exit day;
 - (b) that periodic safety report is, immediately before exit day, to be assessed in accordance with the single assessment procedure in Article 107e of the 2001 Directive;
 - (c) the procedure described in Article 107e(3) of the 2001 Directive has been completed before exit day; but
 - (d) the licensing authority has not yet taken the steps described in regulation 194 before exit day.
- (2) Where this sub-paragraph applies, notwithstanding the revocation of regulation 194 (responding to a single assessment of PSUR under Article 107e of the 2001 Directive) by the EU Exit Regulations, the licensing authority must take the steps specified in regulation 194 in respect of the UK marketing authorisation or traditional herbal registration as soon as reasonably practicable.
- (3) Sub-paragraph (4) applies where—
- (a) a holder has submitted a periodic safety update report under regulation 191 before exit day;
 - (b) that periodic safety report is, immediately before exit day, to be assessed in accordance with the single assessment procedure in Article 107e of the 2001 Directive; and

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- (c) the procedure described in Article 107e(3) of the 2001 Directive has not been completed before exit day.
- (4) Where this sub-paragraph applies, the licensing authority—
 - (a) may notify a holder falling within sub-paragraph (3)(a) of the need to provide to it such further information that the licensing authority specifies; and
 - (b) must, subject to sub-paragraph (5), assess the periodic safety update report in accordance with regulation 195 (obligations on licensing authority to assess PSURs) (as amended by the EU Exit Regulations) as soon as reasonably practicable.
- (5) Information required under sub-paragraph (4)(a) must be provided before the end of whatever period the licensing authority may specify.
- (6) In making a determination under regulation 195, where sub-paragraph (4) applies, the licensing authority may adopt or have regard to—
 - (a) any relevant information obtained by it before exit day in relation to the periodic safety report and the assessment of that report as a consequence of its involvement in any procedure provided for in Section 2 of Chapter III of the 2001 Directive;
 - (b) any relevant decision made, or agreement reached, in relation to the periodic safety update report or its assessment before exit day, where the United Kingdom participated as a member state in the making of that decision or agreement, under any procedure provided for in Section 2 of Chapter III of the 2001 Directive;
 - (c) any decision made, or agreement reached, in relation to that marketing authorisation or certificate of registration under Section 2 of Chapter III of the 2001 Directive on or after exit day, notwithstanding that the United Kingdom did not participate in the making of that decision or agreement.

Matters on-going at exit day in relation to draft study protocols under Article 107n and 107o of the 2001 Directive (submission of, and amendment to, draft study protocols for required studies)

- 60.**—(1) Where the Pharmacovigilance Risk Assessment Committee has, before exit day—
- (a) issued a letter endorsing a draft study protocol under Article 107n(2)(a) of the 2001 Directive;
 - (b) informed a holder that the study is a clinical trial under Article 107n(2)(c) of the 2001 Directive; or
 - (c) informed a holder of its endorsement of a substantial amendment to that protocol under Article 107o of the 2001 Directive,

the licensing authority is deemed to have accepted the draft study protocol, or the amended draft study protocol, or made that decision (as the case may be) under regulation 199(5) (submission of draft study protocols for required studies) or 200(5)(b) (amendment to study protocols for required studies).

(2) Where sub-paragraph (1) applies, the licensing authority may request the holder to provide to it any information in relation to the procedures under Article 107n or 107o of the 2001 Directive within a specified time period, and that holder must provide that information within that time period.

- (3) Sub-paragraph (4) applies where, before exit day—
 - (a) a holder is proposing to, or pursuant to Article 21a or 22a of the 2001 Directive, is under a duty to, undertake a non-interventional post-authorisation safety study; and

- (b) the procedure specified in Article 107n or 107o of the 2001 Directive has not concluded before exit day.
- (4) Where this sub-paragraph applies, on and after exit day, the holder must—
 - (a) submit any further information that has been required of it by the Pharmacovigilance Risk Assessment Committee to the licensing authority; and
 - (b) submit to the licensing authority such further information that it may request in relation to the procedures under Article 107n or 107o of the 2001 Directive within a time period specified by the licensing authority, whether or not that information has already been submitted to, or received from, that Committee before exit day,and the licensing authority must assess that information in accordance with regulation 199 or 200 (as the case may be).
- (5) In this paragraph, “not concluded before exit day” means that—
 - (a) a holder is proposing to, or, pursuant to Article 21a or 22a of the 2001 Directive, is under a duty to, undertake a non-interventional post-authorisation safety study;
 - (b) the Pharmacovigilance Risk Assessment Committee has not taken any of the steps specified in sub-paragraph (1)(a) to (c).

Matters on-going at exit day in respect of the follow up of final study reports

- 61.**—(1) Sub-paragraph (2) applies where—
- (a) a final study report has been submitted to the Pharmacovigilance Risk Assessment Committee under Article 107p of the 2001 Directive; but
 - (b) that committee has not, before exit day, made recommendations under Article 107q(1) of the 2001 Directive.
- (2) Where this sub-paragraph applies—
- (a) the licensing authority may, on or after exit day, request the holder to submit to it the information specified in regulation 201(2) (submission and evaluation of final study reports for required studies), and such further information relating to the final study report, or the procedure provided for in Chapter 4 of Title IX of the 2001 Directive, as the licensing authority may require; and
 - (b) that holder must, in any event, undertake the steps specified in regulation 201(5) in respect of that final study report.
- (3) Sub-paragraph (4) applies where—
- (a) regulation 202(1) (follow-up of final study reports) applied before exit day in respect of a final study report; but
 - (b) the licensing authority has not, before exit day, taken the steps specified in regulation 202(2).
- (4) Where this paragraph applies, notwithstanding the revocation of regulation 202 by the EU Exit Regulations, the licensing authority must take the steps specified in regulation 202(2) in accordance with the time period specified in that paragraph.
- (5) Sub-paragraph (6) applies where—
- (a) regulation 202(3) applied before exit day; but
 - (b) the holder has not taken the steps specified in regulation 202(4) before exit day.
- (6) Where this sub-paragraph applies, notwithstanding the revocation of regulation 202—
- (a) the holder must take the steps specified in regulation 202(4); and

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- (b) the licensing authority must determine that application for a variation in accordance with Part 5 (marketing authorisations) or 7 (traditional herbal registrations).

PART 11

Transitional provision in respect of Part 12

Approved country health professional list on exit day (regulation 214(6A))

62.—(1) For the purposes of regulation 214(6A), for the transitional period, the licensing authority must include on the list published under that paragraph, professions of equivalent professional status to an appropriate practitioner under regulation 214(3) to (5D) in each EEA State.

- (2) In this paragraph, “transitional period” is the period of one year beginning with exit day.

PART 12

General provision in relation to transitional provisions

Licensing authority power to require information

63.—(1) Notwithstanding any other power to require information under this Schedule, the licensing authority may require in writing that a holder of, or an applicant for, a UK marketing authorisation, parallel import licence, manufacturing licence, wholesale dealing licence, certificate of registration or traditional herbal registration provides it with any information which—

- (a) is relevant to the exercise of the licensing authority’s functions under this Schedule; and
- (b) is either in the holder’s or applicant’s possession or is information which the holder or applicant may reasonably access,

within such time period as the licensing authority specifies in that written request.

(2) If the holder of an authorisation, licence, certificate or registration mentioned in sub-paragraph (1) fails to comply with a request made pursuant to that sub-paragraph, the licensing authority may suspend the authorisation, licence, certificate or registration until the holder complies with the obligation.

(3) Nothing in this Schedule requires a person to supply information in contravention of requirements imposed under the data protection legislation (within the meaning of Part 1 of the Data Protection Act 2018(**138**)).”.

SCHEDULE 8

Regulation 229

Consequential provision

PART 1

Amendment of primary legislation

Amendment of the National Health Service Act 2006

1.—(1) Section 88 of the National Health Service Act 2006(**139**) (GMS contracts: prescription of drugs, etc) is amended as follows.

(2) In subsection (3), for “Community marketing authorization or United Kingdom” substitute “UK”.

(3) For subsection (4) substitute—

“(4) “UK marketing authorisation” has the meaning given by regulation 8(1) of the Human Medicines Regulations 2012 ([S.I. 2012/1916](#))(**140**).”.

Amendment of the Access to Medical Treatments (Innovation) Act 2016

2. In section 3(2)(b) and (4)(a), (b) and (c) of the Access to Medical Treatments (Innovation) Act 2016(**141**) (provision supplementary to section 2: database of innovative treatments) insert “UK” before “marketing authorisation”.

PART 2

Amendment of secondary legislation

Amendment of the Medicines (Bal Jivan Chamcho Prohibition) (No 2) Order 1977

3. In article 2 of the Medicines (Bal Jivan Chamcho Prohibition) (No 2) Order 1977 (prohibition of sale, supply and importation of Bal Jivan Chamcho)(**142**)—

(a) for paragraph (4) substitute—

“(4) The prohibition imposed by paragraph (1) does not apply where the medicinal product—

(a) is imported from an approved country for import; and

(b) is being, or is to be, exported to a country other than the United Kingdom.”; and

(b) for paragraph (5) substitute—

“(5) In paragraph (4), “approved country for import” has the meaning given in regulation 8(1) of the Human Medicines Regulations 2012.”.

(139) 2006 c.41.

(140) S.I. 2012/1916.

(141) 2016 c.9.

(142) S.I. 1977/670. Article 2 was amended by S.I. 1990/2487, 1997/856, 2008/548 and 2012/1809.

Amendment of the Prescription Only Medicines (Human Use) Order 1997

4. In article 5(1) of the Prescription Only Medicines (Human Use) Order 1997 (exempt medicinal products)(**143**), insert “UK” before “marketing authorisation”.

Amendment of the Medicines (Aristolochia and Mu Tong etc) (Prohibition) Order 2001

5.—(1) The Medicines (Aristolochia and Mu Tong etc) (Prohibition) Order 2001(**144**) is amended as follows.

(2) In article 1 (citation, commencement and interpretation)(**145**)—

- (a) omit the definitions of “free circulation in member States” and “third country”; and
- (b) insert at the appropriate place—

““approved country for import” has the meaning given in regulation 8(1) of the Human Medicines Regulations 2012;”.

(3) In article 4 (exceptions to the prohibition imposed by articles 2 and 3)(**146**)—

(a) for paragraph (3) substitute—

“(3) The prohibition imposed by articles 2 and 3 does not apply where the medicinal product—

- (a) is imported from an approved country for import; and
- (b) is being, or is to be, exported to a country other than the United Kingdom.”; and

(b) in paragraph (4), for “marketing authorisation, certificate of registration, traditional herbal registration or Article 126a authorisation” substitute “UK marketing authorisation, certificate of registration or traditional herbal registration”.

Amendment of the Medicines for Human Use (Kava-kava) (Prohibition) Order 2002

6.—(1) The Medicines for Human Use (Kava-kava) Prohibition) Order 2002(**147**) is amended as follows.

(2) In article 1 (citation, commencement and interpretation)(**148**)—

- (a) omit the definitions of “free circulation in member States” and “third country”; and
- (b) insert at the appropriate place—

““approved country for import” has the meaning given in regulation 8(1) of the Human Medicines Regulations 2012;”.

(3) In article 3 (exceptions to the prohibition imposed by article 2)(**149**)—

(a) for paragraph (c) substitute—

“(c) imported from an approved country for import, and is being, or is to be, exported to a country other than the United Kingdom; or”; and

(b) in paragraph (d), for “marketing authorisation, certificate of registration, traditional herbal registration or Article 126a authorisation” substitute “UK marketing authorisation, certificate of registration or traditional herbal registration”.

(143) S.I. 1997/1830. Article 5(1) was amended by S.I. 2012/1916.

(144) S.I. 2001/1841.

(145) Article 1 was amended by S.I. 2008/548 and 2012/1809.

(146) Article 4 was amended by S.I. 2008/548 and 2012/1916.

(147) S.I. 2002/3170.

(148) Article 1 was amended by S.I. 2008/548 and 2012/1809.

(149) Article 3 was amended by S.I. 2008/548 and 2012/1916.

Amendment of the Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003

7. In regulation 1(2) of the Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003 (citation, commencement and interpretation)(150), in the definition of “unlicensed product”—

- (a) in paragraph (a) for “marketing authorization” substitute “UK marketing authorisation”; and
- (b) omit paragraphs (a)(ii) and (d).

Amendment of the Blood Safety and Quality Regulations 2005

8. In regulation 1A of the Blood Safety and Quality Regulations 2005(151), after paragraph (10) insert—

“(10A) Paragraph 7.1 is to be read as if reference to “[Directive 2003/94/EC](#)” were to “the Good Manufacturing Practice Directive, within the meaning of regulation 8(1) of the Human Medicines Regulations 2012.”.

Amendment of the Natural Mineral Water, Spring Water and Bottled Drinking Water (England) Regulations 2007

9. In regulation 3(1)(a) of the Natural Mineral Water, Spring Water and Bottled Drinking Water (England) Regulations 2007 (exemptions)(152) for “Directive” to the end substitute “regulation 2(1) of the Human Medicines Regulations 2012”.

Amendment of the Medicines for Human Use (Prohibition) (Senecio and Miscellaneous Amendments) Order 2008

10.—(1) The Medicines for Human Use (Prohibition) (Senecio and Miscellaneous Amendments) Order 2008(153) is amended as follows.

(2) In article 1 (citation, commencement and interpretation)(154)—

- (a) omit the definitions of “free circulation in member States” and “third country”; and
- (b) insert at the appropriate place—

““approved country for import” has the meaning given in regulation 8(1) of the Human Medicines Regulations 2012;”.

(3) In article 3 (exceptions to the prohibition imposed by article 2)(155)—

(a) for paragraph (c) substitute—

“(c) is imported from an approved country for import, and is being, or is to be, exported to a country other than the United Kingdom; or”; and

- (b) in paragraph (d), for “marketing authorisation, certificate of registration, traditional herbal registration or Article 126a authorisation” substitute “UK marketing authorisation, certificate of registration or traditional herbal registration”.

(150) S.I. 2003/1680. Regulation 2(1) has been previously amended by S.I. 2004/3224, 2005/2750 and 2754 and 2012/1916.

(151) S.I. 2005/50. Regulation 1A was inserted by S.I. 2019/4.

(152) S.I. 2007/2785. Regulation 3(1)(a) was substituted by S.I. 2018/352.

(153) S.I. 2008/548.

(154) Article 1 was amended by S.I. 2012/1809.

(155) Article 3 was amended by S.I. 2012/1916.

Amendment of the National Health Service (Pharmaceutical and Local Pharmaceutical Services) Regulations 2013

11.—(1) The National Health Service (Pharmaceutical and Local Pharmaceutical Services) Regulations 2013(**156**) are amended as follows.

(2) In paragraph 8(10) of Schedule 4 (terms of service of NHS pharmacists: providing ordered drugs or appliances), insert “UK” before “marketing authorisation” in both places it appears.

(3) In paragraph 6(8) of Schedule 7 (mandatory terms for LPS schemes: providing ordered drugs or appliances), insert “UK” before “marketing authorisation” in both places it appears.

Amendment of the Genetically Modified Organisms (Contained Use) Regulations 2014

12. In regulation 3(2)(b) of the Genetically Modified Organisms (Contained Use) Regulations 2014 (application)(**157**), at the end insert—

“; or

(iv) a medicinal product for human use marketed in accordance with the Human Medicines Regulations 2012;”.

Amendment of the Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015

13.—(1) The Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015(**158**) are amended as follows.

(2) In regulation 1(4) (citation, commencement and interpretation), insert “UK” before “marketing authorisation”.

(3) In regulation 5(2)(c)(i) (exception for medicines indicated for the treatment of persons under 18), insert “UK” before “marketing authorisation”.

Amendment of the Genetically Modified Organisms (Contained Use) Regulations (Northern Ireland) 2015

14. In regulation 3(2)(b) of the Genetically Modified Organisms (Contained Use) Regulations (Northern Ireland) 2015 (application)(**159**), at the end insert—

“; or

(iv) a medicinal product for human use marketed in accordance with the Human Medicines Regulations 2012;”.

Amendment of the Health Service Products (Provision and Disclosure of Information) Regulations 2018

15. In regulation 29(4) of the Health Service Products (Provision and Disclosure of Information) Regulations 2018(**160**)—

(a) in the definition of “notifiable presentation”—

(i) insert “UK” before “marketing authorisation”, and

(ii) omit from “other than” to the end;

(156) S.I. 2013/349.

(157) S.I. 2014/1663.

(158) S.I. 2015/895.

(159) S.R. 2015 No. 339.

(160) S.I. 2018/677.

- (b) in the definition of “designated producer” insert “UK” before “marketing authorisation”; and
- (c) in the definition of “marketing authorisation” insert “UK” before “marketing”.

Amendment of the Branded Health Service Medicines (Costs) Regulations 2018

16.—(1) The Branded Health Service Medicines (Costs) Regulations 2018(**161**) are amended as follows.

- (2) In regulation 1(2) (interpretation)—
 - (a) in the definition of “marketing authorisation” insert “UK” before “marketing” and re-insert the definition at the appropriate place;
 - (b) in the definition of “marketing authorisation holder” insert “UK” before “marketing” in and re-insert the definition at the appropriate place;
 - (c) omit the definition of “parallel distributed presentation”;
 - (d) in paragraph (b) of the definition of “relevant medicine” insert “UK” before “marketing authorisation”; and
 - (e) in the definition of “supplementary protection certificate” omit from “means” to the end and insert “has the meaning given by section 128B(2) of the Patents Act 1977”.
- (3) In regulation 3 (payment scheme)—
 - (a) in paragraph (3)(a), insert “UK” before “marketing authorisation holder”;
 - (b) omit paragraph (4)(c).
- (4) In regulation 9 (new presentation)—
 - (a) in paragraph (10)—
 - (i) in sub-paragraph (a), insert at the beginning “in relation to a product in respect of which there is a converted EU marketing authorisation”,
 - (ii) in sub-paragraph (b), for “Article 21” to the end substitute “regulation 64(6) of the 2012 Regulations”; and
 - (b) in paragraph (12), insert before the definition of “licensing authority”—
““converted EU marketing authorisation” has the meaning given in paragraph 6(1) and (2) of Schedule 33A to the 2012 Regulations;”.
- (5) In regulation 21 (sales report), omit paragraph (1)(h).
- (6) In regulation 22 (presentation report), omit sub-paragraph (h).

SCHEDULE 9

Regulation 230

Retained EU law: revocations

1. Insofar as they apply to medicinal products for human use, and subject to the transitional provisions in Schedule 33A to the Human Medicines Regulations 2012(**162**), the following instruments are revoked—

- (a) Council [Decision 75/320/EEC](#) of 20 May 1975 setting up a Pharmaceutical Committee;

(161) S.I. 2018/345.

(162) S.I. 2012/1916.

Status: This is the original version (as it was originally made).

- (b) Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Agency for the evaluation of medicinal products;
- (c) Commission Regulation (EC) No 1662/95 of 7 July 1995 laying down certain detailed arrangements for implementing the Community decision-making procedures in respect of marketing authorisations for products for human or veterinary use;
- (d) Commission Regulation (EC) No 2141/96 of 7 November 1996 concerning the examination of an application for the transfer of a marketing authorisation for a medicinal product falling within the scope of Council Regulation (EC) No 2309/93;
- (e) Council Regulation (EC) No 2743/98 of 14 December 1998 amending Regulation (EC) No 297/95 on fees payable to the European Agency for the Evaluation of Medicinal Products;
- (f) Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products;
- (g) Commission Regulation (EC) No 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts 'similar medicinal product' and 'clinical superiority';
- (h) 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;
- (i) Council Regulation (EC) No 1905/2005 of 14 November 2005 amending Regulation (EC) No 297/95 on fees payable to the European Medicines Agency;
- (j) Commission Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises;
- (k) Commission Regulation (EC) No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 of the European Parliament and of the Council;
- (l) Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004;
- (m) Regulation (EC) No 1902/2006 of the European Parliament and of the Council of 20 December 2006 amending Regulation (EC) No 1901/2006 on medicinal products for paediatric use;
- (n) Commission Regulation (EC) No 658/2007 of 14 June 2007 concerning financial penalties for infringement of certain obligations in connection with marketing authorisations granted under Regulation (EC) No 726/2004 of the European Parliament and of the Council;
- (o) Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) NO 726/2004;
- (p) Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicines;
- (q) Commission Regulation (EC) No 668/2009 of 24 July 2009 implementing Regulation (EC) No 1394/2007 of the European Parliament and of the Council with regard to the

- evaluation and certification of quality and non-clinical data relating to advanced therapy medicinal products developed by micro, small and medium-sized enterprises;
- (r) 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;
 - (s) [Commission Regulation \(EU\) No 488/2012](#) of 8 June 2012, amending Regulation (EC) no 658/2007 concerning financial penalties for infringement of certain obligations in connection with marketing authorisations granted under Regulation (EC) No 726/2004 of the European Parliament and of the Council;
 - (t) Commission Implementing Regulation (EU) No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and [Directive 2001/83/EC](#) of the European Parliament and of the Council;
 - (u) [Commission Regulation \(EU\) No 712/2012](#) of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products;
 - (v) Regulation (EU) No 1027/2012 of the European Parliament and of the Council of 25 October 2012 amending Regulation (EC) No 726/2004 as regards pharmacovigilance;
 - (w) Commission Implementing Decision of 22 November 2012 establishing a list of third countries with a regulatory framework applicable to active substances for medicinal products for human use and the respective control and enforcement activities ensuring a level of protection of public health equivalent to that in the Union, in accordance with [Directive 2001/83/EC](#);
 - (x) Commission Implementing Decision of 23 January 2013 on the assessment of a third country's regulatory framework applicable to active substances of medicinal products for human use and of the respective control and enforcement activities pursuant to Article 111b of [Directive 2001/83/EC](#);
 - (y) Commission Implementing Regulation (EU) No 198/2013 of 7 March 2013 on the selection of a symbol for the purpose of identifying medicinal products for human use that are subject to additional monitoring;
 - (z) Commission implementing Decision of 24 April 2013 amending implementing [Decision 2012/715/EU](#) establishing a list of third countries with a regulatory framework applicable to active substances for medicinal products for human use and the respective control and enforcement activities ensuring a level of protection of public health equivalent to that in the Union;
 - (aa) Commission implementing Decision of 4 June 2013 amending implementing [Decision 2012/715/EU](#) establishing a list of third countries with a regulatory framework applicable to active substances for medicinal products for human use and the respective control and enforcement activities ensuring a level of protection of public health equivalent to that in the Union;
 - (bb) Commission implementing Decision of 11 June 2013 amending implementing [Decision 2012/715/EU](#) establishing a list of third countries with a regulatory framework applicable to active substances for medicinal products for human use and the respective control and enforcement activities ensuring a level of protection of public health equivalent to that in the Union;

- (cc) Commission Delegated Regulation (EC) No 357/2014 of 3 February 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council as regards situations in which post-authorisation efficacy studies may be required;
- (dd) Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use⁽¹⁶³⁾;
- (ee) Commission Delegated Regulation (EU) No 1252/2014 of 28 May 2014 supplementing Directive 2001/83 with regard to principles and guidelines of good manufacturing practice for active substances for medicinal products for human use;
- (ff) Commission Implementing Regulation (EU) No 699/2014 of 24 June 2014 on the design of the common logo to identify persons offering medicinal products for sale at a distance to the public and the technical, electronic and cryptographic requirements for verification of its authenticity;
- (gg) Commission implementing Decision of 1 July 2015 amending implementing Decision 2012/715/EU establishing a list of third countries with a regulatory framework applicable to active substances for medicinal products for human use and the respective control and enforcement activities ensuring a level of protection of public health equivalent to that in the Union;
- (hh) Commission Delegated Regulation (EU) No 2016/161 of 2 October 2015 supplementing Directive 2001/83 of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use;
- (ii) Commission Regulation (EU) 2018/781 of 29 May 2018 amending Regulation (EC) No 847/2000 as regards the definition of the concept “similar medicinal product”.

EXPLANATORY NOTE

(This note is not part of the Regulations)

These Regulations are made in exercise of the powers conferred by section 8(1) of the European Union (Withdrawal) Act 2018 (c. 16) in order to address failures of retained EU law to operate effectively and other deficiencies (in particular under section 8(2)(a), (b), (c), (d), (f) and (g) and (6)) arising from the withdrawal of the United Kingdom from the European Union. They are also made under paragraphs 1(1) and 7(2) of Schedule 4 to the European Union (Withdrawal) Act 2018, insofar as they make provision in relation to fees.

These Regulations make amendments to legislation in the field of the regulation of medicinal products for human use. The main body of the Regulations amends the Human Medicines Regulations 2012 (S.I. 2012/1916) and Schedule 1 amends the Medicines (Products for Human Use) (Fees) Regulations 2016 (S.I. 2016/190). Transitional provision is made in new Schedule 33A to the Human Medicines Regulations 2012. Consequential amendments are made in Schedule 8 and revocations of retained EU law are made in Schedule 9.

⁽¹⁶³⁾OJ No, L 189, 27.6.2014, p. 112.

An impact assessment of the effect that this instrument will have on the costs of business, the voluntary sector and the public sector is available from the Medicines and Healthcare products Regulatory Agency, 10 South Colonnade, Canary Wharf, London, E14 4PU and is published alongside this instrument at .