Draft legal text for Medicines, Clinical Trials and Medical Devices EU Exit No Deal Statutory Instruments

Introduction

1. The text in this document relates to the three EU Exit No Deal Statutory Instruments (SIs) required to update the:

    - Human Medicines Regulations 2012 ("HMRs")
    - Medicines (Products for Human Use) (Fees) Regulations 2016
    - Medicines for Human Use (Clinical Trials) Regulations 2004 ("CTRs")
    - Medical Devices Regulations 2002 ("MDRs")

2. The changes to the first two instruments are proposed to be combined in a single SI.

3. This document should be read as an accompaniment to the MHRA consultation being held on the relevant Department of Health and Social Care consultation webpage.

4. This **draft** text is provided to aid the understanding of what is being proposed within the consultation.

5. However, **this text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.**

6. SI text is only provided in relation to the areas being actively consulted upon.

7. It should be noted that no legal text is being provided for the fees elements as the drafting is consequential on the legislative changes for the associated functions, which are still to be settled. The proposed fee levels that are being consulted upon are contained within the consultation.

8. References in the draft amendments to "exit day" are references to 29 March 2019 at 11.00 p.m.

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Medicines SI Draft Text

Change M1: Legal presence

Question 6: Do you have any views on how the proposed transition period for UK MAH and QPPV establishment should be managed by the MHRA in order to reduce any impact or burden in terms of meeting the requirements?

Amendment of regulation 49 of the HMRs (application for grant of UK marketing authorisation)

X. In paragraph (3), for "European Union" substitute "United Kingdom."

Amendment of regulation 66 of the HMRs (application for renewal of authorisation)

X. In regulation 66, in paragraph (2), for "European Union" substitute "United Kingdom".

Place of establishment for UK marketing authorisation holder: transitional provision *[proposed to be part of a new Schedule to the HMRs]*

X.—(1) Subject to sub-paragraph (2), any person—

(a) who—

(i) holds a marketing authorisation immediately before exit day which remains in force as a UK marketing authorisation on exit day (whether or not it is suspended);

(ii) has made an application for, or to renew, a marketing authorisation 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 other than the United Kingdom,

(c) remains established in that EEA State on and after exit day,

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 [*see the proposed amendments to those Regulations above*].

(2) A person only continues to fall within sub-paragraph (1) if, within the specified time, 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 UK marketing authorisation, or application for a marketing authorisation (as the case may be), during the transitional period; and

(b) that individual's address, telephone number and email address.

(3) In this regulation—

"the specified time" means—

(a) [*x weeks]* beginning on exit day; or

(b) where sub-paragraph (1)(a)(iii) applies, at the time of making the application; and

"the transitional period" means the period beginning on exit day and ending on 31st December 2020.

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Amendment of regulation 182 of the HMRs (obligation on marketing authorisation holder to operate a pharmacovigilance system)

X. In paragraph (2)(a) of regulation 182, for "EU" substitute "United Kingdom".

Transitional provision in respect of an appropriately qualified person for pharmacovigilance *[proposed to be part of a new Schedule to the HMRs]*

X.—(1) Paragraph (2) applies where, immediately before exit day, a marketing authorisation holder had, pursuant to regulation 182(2)(a), an appropriately qualified person for pharmacovigilance who resided and operated in an EEA State other than the United Kingdom.

(2) Subject to paragraph (3), a UK marketing authorisation holder is to be treated as satisfying the requirements of regulation 182(2)(a), notwithstanding the amendments made to that provision by [*see the proposed amendments to that Regulation above*], for the transitional period, insofar as that holder would otherwise not meet those requirements solely because the qualified person responsible for pharmacovigilance resides and operates in an EEA State.

(3) In this regulation "the transitional period" begins on exit day and ends on 31st December 2020.

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Change M2: New Marketing Authorisation (MA) assessment routes

Question 7: Do you agree with the proposed new targeted assessment process?

Amendment of regulation 58 of the HMRs (consideration of application)

X.—(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 one or more of—

(a) a decision by the European Commission to grant a marketing authorisation;

(b) an opinion of the Committee for Medicinal Products for Human Use; or

(c) a decision by the competent authority of a country other than the United Kingdom to grant a marketing authorisation;

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 decisions described in sub-paragraphs (a) to (c) 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 decisions to grant a marketing authorisation should be relevant for the purposes of paragraph (4A)(c)."

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Change M3: Converting centrally authorised products (CAPs) to UK MAs – commonly referred to as 'grandfathering' of licences

Question 9: Do you agree with the requirements for data provision for grandfathered CAPs?
Question 10: Do you agree with the proposed approach to handling variations for CAP grandfathered products?
Question 11: Do you envisage any problems?

Transitional provision in respect of conversion of EU marketing authorisations in force immediately before exit day *[Proposed to be part of a new Schedule to the HMRs]*

Conversion of EU marketing authorisations in force before exit day

1.—(1) This paragraph applies in relation to an EU marketing authorisation which—

(a) was granted before exit day;

(b) remains in force immediately before exit day; and

(c) in relation to which no notification as described in sub-paragraph (3) has been received by the licensing authority 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 these Regulations; and

(b) is referred to in this Part as a "converted EU marketing authorisation".

(3) A notification as described in this sub-paragraph is a written notification given before exit day by the holder of an EU marketing authorisation informing the licensing authority that it does not wish to become the holder of a UK marketing authorisation in accordance with sub-paragraph (2)(a).

(4) A converted EU marketing authorisation—

(a) is treated as if it had been granted by the licensing authority under these Regulations on the same date and on the same terms as 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) retains the benefit of any remaining periods of data or marketing exclusivity from which the holder benefitted immediately before exit day;

(c) retains the benefit of any decision by the European Medicines Agency ("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);

(d) 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;

(iii) any variation to its terms which were granted or approved before the 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 in accordance with Regulation (EC) No 507/2006; and

(b) remains a conditional marketing authorisation immediately before exit day,

has effect on and after exit day as a UK marketing authorisation granted under [*cross-reference to the regulation which transposes the Conditional Marketing Authorisation Regulation*].

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(7) A converted EU marketing authorisation to which this paragraph applies and which relates to a medicinal product which—

(a) has been 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.

(8) If before exit day the licensing authority suspended the use of a medicinal product under Article 20(4) of Regulation (EC) No 726/2004, and that suspension remains in place immediately before exit day, the suspension of use is treated on and after exit day as if it had been done in relation to the converted EU marketing authorisation under regulation 69(1), in reliance on regulation 69(2)(a) or (b).

Classification of converted EU marketing authorisations

2. 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) only on prescription, if the product was classified in its EU marketing authorisation immediately before exit day as a prescription only medicine;

(b) only from a pharmacy, if the product was not classified in its EU marketing authorisation immediately before exit day as a prescription only medicine and paragraph (c) does not apply; or

(c) on general sale, if the product was not classified in its EU marketing authorisation immediately before exit day as a prescription only medicine and the licensing authority has determined that the product should be available on general sale.

Obligation of licensing authority in connection with converted EU marketing authorisations

3.The licensing authority must, as soon as reasonably practicable after exit day, publish a list of EU marketing authorisations—

(a) that are not converted EU marketing authorisations, by virtue of paragraph 1(1)(c); and

(b) that are converted EU marketing authorisations by virtue of paragraph 1(2).

Obligations of holders of converted EU marketing authorisations

4.—(1) The holder of a converted EU marketing authorisation must submit to the licensing authority, before the end of the period of one year beginning on exit day, the information described in sub-paragraph (3).

(2) The date on which the holder of a converted EU marketing authorisation complies with the obligation in sub-paragraph (1) is referred to in this Part as "the data submission date".

(3) The information which must be submitted in accordance with sub-paragraph (1) is—

(a) such information concerning the product to which the converted EU marketing authorisation relates as may be specified by the licensing authority in guidance published for that purpose on or before exit day; and

(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 after exit day and if so, the date on which it was withdrawn from the United Kingdom market.

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(4) The holder of a converted EU marketing authorisation must provide to the licensing authority on or before 31st December 2021 a mock up, in accordance with Part 13 (packaging and leaflets) of—

(i) the outer packaging of the medicinal product;

(ii) the immediate packaging of the medicinal product; and

(iii) the package leaflet for the medicinal product.

Powers of licensing authority in connection with provision of information

5.—(1) If the licensing authority requests the holder of a converted EU marketing authorisation to submit all or part of the information described in paragraph 4(3) at any time before the expiry of the period of one year beginning on exit day, the holder must submit the information without delay.

(2) If the licensing authority requests the holder of a converted EU marketing authorisation to provide any other information relating to the authorisation, the holder must provide the information without delay.

Variations of converted EU marketing authorisations applied for before exit day

6.—(1) This paragraph applies where the holder of a converted EU marketing authorisation has, before exit day, notified the EMA of, or made an application to the EMA for, a variation of the EU marketing authorisation.

(2) Where the variation is a minor variation of Type IA which has not been rejected by the EMA before the data submission date—

(a) the holder of the converted EU marketing authorisation must include a summary of the variation in the information submitted in accordance with paragraph 4(1); and

(b) the variation to the UK marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing within 30 days of the data submission date that the variation to the UK marketing authorisation is rejected.

(3) Where the variation is a minor variation of Type IB or a major variation of Type II—

(a) the holder of the converted EU marketing authorisation must include a copy of the notification of, or the application for, the variation with the information submitted in accordance with paragraph 4(1); and

(b) the licensing authority must—

(i) where the Committee for Medicinal Products for Human Use ("CHMP") has given a positive opinion in relation to the application with which the licensing authority agrees, treat the variation as accepted; and

(ii) where the CHMP has not given any opinion or has given a negative opinion in relation to the application, or where the licensing authority disagrees with the CHMP opinion, consider the application in accordance with [*insert cross-reference to the variation procedure*].

(4) If the holder of a converted EU marketing authorisation wishes the licensing authority to consider an application for a variation to the authorisation before the data submission date, the licensing authority may consider it if it is of the view that—

(a) the variation is necessary on urgent safety grounds;

(b) the variation is 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 receipt of the information submitted in accordance with paragraph 4(1).

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Variations of converted EU marketing authorisations applied for after exit day but before the data submission date

7.—(1) This paragraph applies where the holder of a converted EU marketing authorisation wishes to apply for a variation of the authorisation during the period which begins on exit day and ends on the data submission date.

(2) Where the variation is a minor variation of Type IA—

(a) the holder of the converted EU marketing authorisation must include a notification of the variation in the information submitted in accordance with paragraph 4(1); and

(b) the variation to the UK marketing authorisation is deemed to be accepted unless the licensing authority notifies the holder in writing within 30 days of the data submission date that the variation to the UK marketing authorisation is rejected.

(3) Where the variation is a minor variation of Type IB or a major variation of Type II—

(a) the holder of the converted EU marketing authorisation must include the notification of, or the application for, the variation with the information submitted in accordance with paragraph 4(1); and

(b) the licensing authority must consider the application in accordance with [*insert cross-reference to the variation procedure*].

(4) If the holder of a converted EU marketing authorisation wishes the licensing authority to consider an application for a variation to the authorisation before the data submission date, the licensing authority may consider it if it is of the view that—

(a) the variation is necessary on urgent safety grounds;

(b) the variation is 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 receipt of the information submitted in accordance with paragraph 4(1).

Applications for renewal of converted EU marketing authorisations made before exit day

8.—(1) This paragraph applies where the 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(2) of Regulation (EC) No 726/2004 but that application has not been determined by the EMA before exit day.

(3) Where this paragraph applies—

(a) the holder of the converted EU marketing authorisation must include a copy of the application for renewal with the information supplied in accordance with paragraph 4(1); and

(b) the licensing authority must treat the application as an application made in relation to the converted EU marketing authorisation under regulation 66 (application for renewal of authorisation) and must—

(i) where the CHMP has given a positive opinion in relation to the application with which the licensing authority agrees, treat the renewal application as accepted; or

(ii) where the CHMP has not given any opinion or has given a negative opinion in relation to the application, or where the licensing authority disagrees with the CHMP opinion, consider the application in accordance with regulation 66.

Applications for renewals of converted EU marketing authorisations made after exit day

9.—(1) This paragraph applies where the 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 beginning on exit day and ending on the data submission date.

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(2) Where this paragraph applies—

(a) the holder of the converted EU marketing authorisation must include the application for renewal with the information supplied in accordance with paragraph 4(1), including where the data submission date is later than the date specified in regulation 66(5); and

(b) the licensing authority must consider the application in accordance with regulation 66.

Applications for renewals of conditional marketing authorisations made before exit day

10.—(1) This paragraph applies where—

(a) the holder of a converted EU marketing authorisation which was granted as a conditional marketing authorisation under Regulation (EC) No 507/2006 has, before exit day, made an application to the EMA for renewal of the authorisation in accordance with Article 6 of that Regulation; but

(b) that application has not been determined by the EMA before exit day.

(2) Where this paragraph applies—

(a) the holder of the converted EU marketing authorisation must include a copy of the application for renewal with the information supplied in accordance with paragraph 4(1); and

(b) the licensing authority must treat the application as an application made in relation to the converted EU marketing authorisation under [*insert cross reference to provisions on renewal of conditional marketing authorisations*] and must—

(i) where the CHMP has given a positive opinion in relation to the application with which the licensing authority agrees, treat the renewal application as accepted; and

(ii) where the CHMP has not given any opinion [or has given a negative opinion] in relation to the application, or where the licensing authority disagrees with the CHMP opinion, consider the application in accordance with [*insert cross reference to provisions on renewal of conditional marketing authorisations*].

Applications for renewals of converted conditional EU marketing authorisations made after exit day

11.—(1) This paragraph applies where the holder of a converted EU marketing authorisation which was granted as a conditional marketing authorisation under Regulation (EC) No 507/2006 is due to make an application for renewal of the authorisation in accordance with [*insert cross reference to provisions on renewal of conditional marketing authorisations*] during the period beginning on exit day and ending on the data submission date.

(2) Where this paragraph applies—

(a) the holder of the converted EU marketing authorisation must include the application for renewal with the information supplied in accordance with paragraph 4(1), including where the data submission date is later than the date specified in [*insert cross reference to provisions on renewal of conditional marketing authorisations*]; and

(b) the licensing authority must consider the application in accordance with [*insert cross reference to provisions on renewal of conditional marketing authorisations*].

Failure to place on the market etc

12. For the purposes of regulation 67 (failure to place on the market)—

(a) a converted EU marketing authorisation is treated as if it had been granted on exit day for the purposes of regulation 67(1); and

(b) the period of three years referred to in regulation 67(2) is treated as having started on exit day.

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Packaging of converted EU marketing authorisations

13.—(1) No offence is committed by the holder of a converted EU marketing authorisation under regulation 268 during the period beginning on exit day and ending on 31st December 2021 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 marketing authorisation, or, where applicable, the name of the holder's representative;

(ii) the number of the marketing authorisation; or

(ii) 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 (ii) solely because that information refers to the EU marketing authorisation to which the converted EU marketing authorisation relates.

(2) Sub-paragraph (1) only applies if the holder of the converted EU marketing authorisation, having established in the United Kingdom and having been notified of the number of the UK marketing authorisation, 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).

Enforcement

14. If the holder of a converted EU marketing authorisation fails to comply with an obligation in this Part, or fails to comply with any requirement imposed by the licensing authority pursuant to this Part, the licensing authority may suspend the converted EU marketing authorisation until the holder complies with the obligation.

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Change M4: Packaging

A: Amending packaging and leaflets for a product on the market

Question 12: Do you agree with the proposed approach on packaging, including the period of time proposed to allow for changes?

Transitional provision as to packaging (change of place of establishment) *[proposed to be part of a new Schedule to the HMRs]*

X.—(1) Subject to paragraph (2), no offence is committed under regulation 268, by a person to whom [*the transitional provisions for those established in an EEA State other than the UK immediately before exit day – see Change M1]* apply during the transitional period 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 (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 31st December 2020 in order to comply with [*Change M1*], and

(ii) because of that establishment in the United Kingdom, the information specified in paragraph (a)(i) to (iii) is no longer correct.

(2) Paragraph (1) only applies if—

(a) the packaging and package leaflet did meet 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, during the transitional period.

(3) In this paragraph "the transitional period" begins on exit day and ends on 31st December 2021.

B) Safety Features under the Falsified Medicines Directive (FMD)

Question 13: Do you agree with the proposed approach?

Revocations of retained EU law

X. The following instrument is revoked and does not form part of retained EU law—

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Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC 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.

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Change M5: Paediatric investigation plans (PIPs) and studies

Question 14: Do you agree with the proposal for UK paediatric investigation plans (PIPs) and newly completed paediatric studies?

X. After regulation 50 of the HMRs, 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(4) *[as inserted by change M7]*; 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 and 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 application.

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

(5) The licensing authority must—

(a) decide whether or not—

(i) 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

(ii) the expected therapeutic benefits of the medicinal product justify the studies proposed; and

(b) in doing so 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) On receipt of a request under paragraph (6), the licensing authority must consider the request and reach a decision in relation to it as soon as reasonably practicable.

Deferral of initial 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 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, 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.

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 medicinal 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 pharmaco-kinetic 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.

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 the licensing authority with 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."

X. After regulation 58, insert—

"Paediatric rewards

58A.—(1) This paragraph applies if—

(a) an application to which regulation 50A 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) complies with the agreed paediatric investigation plan.

(2) Where paragraph (1) applies, the licensing authority must—

(a) include in the 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 (1) 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 Article 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.

(4) Paragraph (3) does not apply if the grant of the application referred to in paragraph (1)(a) entitles the holder of the UK marketing authorisation to a one year extension of the ten year period referred to in regulation 51(2), in accordance with regulation 51(2)(a).

(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) applies.

(6) This paragraph applies if the licensing authority grants a UK marketing authorisation in response to an application to which regulation 50E applies (paediatric use marketing authorisation).

(7) Where paragraph (6) 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 same marketing authorisation holder has been granted a UK marketing authorisation for use in adults.

(8) Where paragraph (6) applies, the holder of the paediatric use marketing authorisation—

(a) is entitled to benefit from the periods of data and marketing exclusivity referred to in regulation 51(2) in relation to the material supplied pursuant to regulation 50E(2); but

(b) is not entitled to any period of data or marketing exclusivity in relation to any material to which reference was made, in accordance with regulations 51 to 55, in the application for the paediatric use marketing authorisation.

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 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).

(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 (6);

(b) regulation 50C(2); and

(c) regulation 50D(2) 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."

Amendment of regulation 59 of the HMRs (conditions of UK marketing authorisation)

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

(2) After paragraph (4), insert—

"(4A) Where the application is one to which regulation 50A, 50E or 50F (applications with paediatric aspects) 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.

(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, 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).

Post authorisation requirements in relation to UK marketing authorisations with paediatric indications

X. After regulation 78 of the HMRs, insert—

"Post authorisation requirements in relation to UK marketing authorisations with paediatric indications

78A.—(1) This paragraph applies where—

(a) the holder of a UK marketing authorisation intends to discontinue supply of the product to which the authorisation relates; and

(b) the holder of the authorisation benefited from a reward or incentive under regulation 58A or 58D(5) in relation to the product and the period of protection provided pursuant to those regulations has expired.

(2) Where paragraph (1) applies, the holder of the UK marketing authorisation must—

(a) either—

(i) transfer the 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 as provided for in 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) This paragraph applies to the holder of a UK marketing authorisation if—

(a) the 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 the holder obtained that paediatric indication.

(4) Where paragraph (3) 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) This paragraph applies if—

(a) a decision by the licensing authority in respect of a paediatric investigation plan is addressed to a person; and

(b) the plan refers to clinical trials carried out in a country other than the United Kingdom ("third country clinical trials").

(6) Where paragraph (5) applies, the person to whom the licensing authority's decision was addressed must send to the licensing authority the details set out in Article 11 of the Clinical Trials Directive in relation to the third country 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 (5) applies, the person to whom the licensing authority's decision was addressed 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.

(8) Where paragraph (9) applies, paragraph (7) does not apply, and paragraph (10) applies.

(9) This paragraph applies 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 paragraph (9) applies, the sponsor must submit the results of the clinical trial to the licensing authority within the period of twelve months beginning on the day on which the trial ended.

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

(11) This paragraph 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 the authorisation relates.

(12) Where paragraph (11) applies, the holder 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) This paragraph 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 the 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 paragraph (13) applies, the marketing authorisation holder 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 on the date on which the deferral decision was made.".

Transitional provision in relation to the Paediatric Regulation *[proposed to be part of a new Schedule to the HMRs]*

X.—(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

(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 of the EMA ("PDCO") 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 PDCO before exit day, decide that it cannot agree the plan under regulation 50B(5); or

(c) where before exit day no opinion in relation to the paediatric investigation plan has been given by the PDCO, 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 PDCO before exit day, agree to the modification or waiver under regulation 50B(7);

(b) where an opinion against agreeing the modification or waiver with which the United Kingdom concurred has been given by the PDCO before exit day, decide that it cannot agree to the request under regulation 50B(7); or

(c) where before exit day no opinion in relation to the modification or waiver has been given by the PDCO, 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.

(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 PDCO before exit day, agree to 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 PDCO before exit day, decide that it cannot agree to the request under regulation 50D(2); or

(c) where before exit day no opinion in relation to the waiver has been given by the PDCO, 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."

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Change M6: Orphan designation

Question 15: Do you agree with the proposal to explore incentivising submission of MA applications for products intended to treat rare diseases in UK?

To be inserted after new regulation 50F of the HMRs-

"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.

(6) Regulations under paragraph (5)—

(a) are to be made by statutory instrument;

(b) may make different provision for different purposes;

(c) may include incidental, supplementary, consequential, transitional, transitory or saving provision.

(7) A statutory instrument containing regulations under paragraph (5) is subject to annulment in pursuance of a resolution of either House of Parliament."

X. After Schedule 9 to the HMRs, 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 application 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;

(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 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 established in the United Kingdom and 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 diagnosis, prevention or treatment methods 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 sub-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;

"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) For the purposes of the definition of "similar active substance", an active substance which acts via the same mechanism includes—

(a) isomers, mixtures of isomers, complexes, esters, salts and non-covalent 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;

(b) the same macromolecule or one that differs from the original macromolecule only with respect to changes in the molecular structure, such as—

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(i) proteinaceous substances where—

(aa) the difference is due to infidelity of transcription or translation;

(bb) the difference in structure between them is due to post-translational events (such as different glycosylation patters) or different tertiary structures;

(cc) the difference in the amino acid sequence is not major, with the effect that two pharmacologically related protein substances of the same group (for example, two biological compounds having the same international non-proprietary name sub-stem) could be considered similar; and

(dd) the monoclonal antibodies bind to the same target epitope;

(ii) polysaccharide substances having identical saccharide repeating units, even if the number of units varies and even if there are post-polymerisation modifications, including conjugation;

(iii) polynucleotide substances, including gene transfer and antisense substances, consisting of two or more distinct nucleotides where—

(aa) the difference in the nucleotide sequence of the purine and pyrimidine bases or their derivatives is not major, with the effect that for anti-sense substances, the addition or deletion of nucleotides not significantly affecting the kinetics of hybridisation to the target could be considered similar;

(bb) the difference in structure relates to modifications to the ribose or deoxyribose sugar backbone or to the replacement of the backbone by synthetic analogues; and

(cc) the difference is in the vector or transfer system;

(iv) closely related complex partly definable substances, such as two related viral vaccines or two related cell therapy products; or

(c) 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, provided that it acts via the same mechanism.".

To be inserted after new reg 58B of the HMRs-

"Consideration of applications relating to orphan medicinal products

58C. If the licensing authority is satisfied in relation to an application for a UK marketing authorisation for a medicinal product that—

(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 58,

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

Orphan rewards

58D.—(1) 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 was granted in relation to the medicinal product to which an orphan marketing authorisation relates;

(b) the EU marketing authorisation was granted before the licensing authority granted the orphan marketing authorisation; and

(c) the EU marketing authorisation was granted on the basis that the product was an orphan medicinal product within the meaning of Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, as it has effect in EU law from time to time.

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

(a) the date from which the EU marketing authorisation took effect; and

(b) 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 if, at the end of the fifth year, 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 (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 of a UK marketing authorisation 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) the second applicant can establish to the satisfaction of the licensing authority that the second medicinal product, 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."

Transitional provision in relation to Orphan Regulation *[proposed to be part of a new Schedule to the HMRs]*

X.—(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 designated as an orphan medicinal product by the European Commission pursuant to Article 5 of Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products and which appears in the Community register of Orphan Medicinal Products as referred to in that Article; but

(ii) no final decision has been made by the European Commission in relation to the maintenance of the orphan status of the product; and

(b) on or after exit day, the licensing authority is considering an application for a UK marketing authorisation in relation to the product in accordance with [*the transitional provisions in relation to central MA applications*].

(2) Where sub-paragraph (1) applies, the licensing authority must—

(a) where an opinion favourable to the maintenance of orphan status of the medicinal product 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) that the orphan criteria are met in relation to the product; or

(b) where no opinion favourable to the maintenance of orphan status of the medicinal product 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 making a determination under sub-paragraph (2)(b), the licensing authority must have regard to any relevant information obtained by it before exit day in relation to the application as a consequence of its involvement in the procedure for considering applications concerning products of the kind described in sub-paragraph (1).

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Change M7: Abridged applications

Question 16: Do you agree with the proposal for abridged applications?

Amendment of regulation 48 of the HMRs (application of Part 5)

X.—(1) Regulation 48 is amended as follows.

(2) In paragraph (2)—

(a) for the definition of "generic medicinal product", substitute—

""generic medicinal product" means a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies;";

(b) for the definition of "reference medicinal product", substitute—

""reference medicinal product" means a medicinal product authorised under regulation 49(1), in accordance with the provisions of regulation 50;".

(3) At the end insert—

"(3) 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.

(4) When a medicinal product has been granted an initial UK marketing authorisation under regulation 49(1)(a) in accordance with the provisions of regulation 50, 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, in particular for the purposes of the application of regulation 51(1) and (2)."

Amendment of regulation 51 of the HMRs (applications relating to generic medicinal products)

X.—(1) Regulation 51 is amended as follows.

(2) In paragraph (1), for the words from "provide information" to the end, substitute ", 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 under regulation 49(1)(a) for not less than eight years".

(3) After paragraph (1), insert—

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

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

(1C) 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

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.

(1D) 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 guidelines published by the licensing authority for that purpose.".

(4) For paragraph (2) substitute—

"(2) 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 from the date on which the reference medicinal product was granted a UK marketing authorisation, or the date referred to in paragraph (1A) or (1B), if earlier."

(5) After paragraph (2) insert—

"(3) Paragraph (4) applies if, during the first eight of the ten years referred to in paragraph (2) the marketing authorisation holder for the reference medicinal product obtained a UK marketing authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, the licensing authority considers bring a significant clinical benefit in comparison with existing therapies.

(4) Where this paragraph applies, the period of ten years referred to in paragraph (2) is extended to eleven.

(5) This paragraph 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.

(6) Where paragraph (5) applies, the applicant for a UK marketing authorisation under paragraph (1) or regulation 52 or 53 may not, for the period of one year after the licensing authority has granted or varied a UK marketing authorisation in relation to the new indication, refer in its application to the studies mentioned in paragraph (5)(b).

(7) 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 (6) is reduced by the period of time which has elapsed between –

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

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

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

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

(2) 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.

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

(3) For paragraph (2), substitute—

"(2) The applicant 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—

(a) demonstrate that the reference medicinal product is or has been authorised under regulation 49(1)(a) for not less than eight years; and

(b) provide the results of appropriate pre-clinical tests or clinical trials in relation to the applicable circumstance in paragraph (1)(b).".

(4) In paragraph (3) —

(a) for "Regulation 51(2)" substitute "Paragraphs (1A) to (2) of regulation 51"; and

(b) for "it applies" substitute "they apply".

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

X.—(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 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—

(a) demonstrate that the reference medicinal product is or has been authorised under regulation 49(1)(a) for not less than eight years; and

(b) 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 the related detailed guidelines.".

(4) In paragraph (3)—

(a) for "Regulation 51(2)" substitute "Paragraphs (1A) to (2) of regulation 51"; and

(b) for "it applies" substitute "they apply".

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

X.—(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 and clinical trials with appropriate scientific literature."

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

X.—(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—

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

"(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 of the HMRs (applications containing information supplied in relation to another product with consent)

X. In paragraph (2) of regulation 56, omit ", in accordance with Article 10c of the 2001 Directive".

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Change M8: Increased requirements for needing a manufacturer's licence for import or a wholesale dealer's licence

Question 17: The transitional provision for this area is still to be considered. Have you views on the length of time that should be allowed for organisations to obtain MIAs, and what arrangements should be put in place during that period?

Amendment of regulation 41 of the HMRs (requirements as to qualified persons)

X.—(1) Regulation 41 is amended as follows.

(2) After paragraph (2) insert—

"(2A) Subject to paragraph (2B), a qualified person must reside and operate in the United Kingdom.

(2B) Where a manufacturing licence is used by the holder to distribute a medicinal product, which is imported from a country that is included in the list mentioned in paragraph (2C), or to possess a medicinal product for such purpose, a qualified person who undertakes that role in respect of such a product must reside and operate in the United Kingdom or in a country that is included in that list.

(2C) The licensing authority must—

(a) publish a list of designated countries in respect of qualified persons ("designated country in respect of qualified persons list");

(b) only include in that list a country which is included in the designated country for batch testing list.

(2D) In order to determine whether a country should be included in the designated country in respect of qualified persons list, the licensing authority may, in particular, take into account—

(a) the mechanisms that country has in place to assist the licensing authority in obtaining information in respect of a qualified person that resides in that country; and

(b) that country's ability to assist the licensing authority in any action it may need to take in respect of a qualified person that resides in that country in relation to the matters for which that person is responsible for under these Regulations.

(2E) The licensing authority must—

(a) remove a country from the designated country in respect of qualified persons list if that country is removed from the list of designated countries for batch testing;

(b) in any event review the countries it has included in the list of designated countries in respect of qualified persons to determine if it is still satisfied that the country should remain on that list; and

(c) undertake that review at least every three years beginning on the date on which that country is included in that list.".

Transitional provision in respect of regulation 41 of the HMRs (designated country in respect of qualified persons list) *[proposed to be part of a new Schedule to the HMRs]*

X—(1) For the purposes of regulation 41(2C), for the transitional period, the licensing authority must include each EEA State in the designated country in respect of qualified persons list.

(2) Notwithstanding regulation 41(2E)(c), the licensing authority must, before the end of the transitional period, determine in respect of each EEA State if it is satisfied that that State should remain on the designated country in respect of qualified persons list .

(3) In this regulation, "the transitional period" begins on exit day and ends on [*x date*].

Amendment of regulation 8 of the HMRs (general interpretation)

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

1. In regulation 8(1), at the appropriate place, insert—

""designated country for batch testing list" means a country included in the list published by the licensing authority under paragraph 14(3) of Schedule 7 (obligations of qualified persons) and "designated country for batch testing" is to be construed accordingly;".

Amendment of Schedule 7 to the HMRs (obligations of qualified persons)

X. In paragraph 14 of Schedule 7—

(a) in sub-paragraph (1)(a) omit "from a country other than an EEA State",

(b) in sub-paragraph (1)(b)—

(i) for "European Union" substitute "licensing authority",

(ii) "that country" substitute "the country from which those products are imported"; and

(c) at the end insert—

"(3) The licensing authority must publish a list of the countries with whom it has made appropriate arrangements under paragraph 14(1)(b).

(4) 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.

(5) 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

(b) undertake such a review at least every three years beginning on the date on which the country is included in the list referred to in sub-paragraph (3).".

Transitional provision for wholesale dealer's licence used solely for import from an EEA State

[proposed to be part of a new Schedule to the HMRs]

X.—(1) Subject to paragraph (2), a wholesale dealer's licence which—

(a) was granted before exit day by the licensing authority;

(b) remains in force immediately before exit day;

(c) was used solely by the holder to distribute a medicinal product, which was imported from an EEA State, by way of wholesale dealing, or possess a medicinal product imported from an EEA State for such a purpose,

has effect on and after exit day as a manufacturer's licence granted under Part 3 of the HMRs for the sole purpose of distributing a medicinal product imported from an EEA State, or possessing such a product for that purpose.

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(2) The holder of a wholesale dealer's licence falling within paragraph (1) must, as soon as reasonably practicable and in any event within [*x period of time*] beginning on exit day, notify the licensing authority of the name of a qualified person who meets the requirements of regulation 41 of the HMRs.

Transitional provision for wholesale dealer's licence used for import from an EEA State and other purposes *[proposed to be part of a new Schedule to the HMRs]*

X.—(1) Paragraph (2) applies to the holder of a wholesale dealer's licence which—

(a) was granted before exit day by the licensing authority;

(b) remains in force immediately before exit day;

(c) was used by the holder before exit day for purposes including, but not limited to, the distribution of a medicinal product, which was imported from an EEA State, by way of wholesale dealing, or possessing a medicinal product imported from an EEA State for such a purpose.

(2) Subject to paragraph (3), the holder of a wholesale dealer's licence falling within paragraph (1) is deemed to also have a manufacturing licence granted under Part 3 of the HMRs for the sole purpose of distributing a medicinal product imported from an EEA State, or possessing a medicinal product imported from an EEA state for such a purpose, on exit day.

(3) The holder of a wholesale dealer's licence falling within paragraph (1) only continues to benefit from the provision in paragraph (2) if that holder notifies the licensing authority of—

(a) the name of a qualified person who meets the requirements of regulation 41 of the HMRs as soon as reasonably practicable and in any event within [*x time period*] beginning on exit day; and

(b) 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 paragraph (3), issue a manufacturer's licence to the holder of a wholesale dealer's licence.

Transitional provision for manufacturer's licence used solely for importing a medicinal product from a non-EEA State for use in an EEA State *[proposed to be part of a new Schedule to the HMRs]*

X—(1) A manufacturer's licence which—

(a) was granted before exit day by the licensing authority;

(b) remains in force immediately before exit day;

(c) was used by the holder solely for the activity of importing a medicinal product into the United Kingdom from a non-EEA State for use in an EEA State other than the United Kingdom,

has effect, subject to paragraph (2), on and after exit day, as a wholesale dealer's licence granted under regulation 18 of the HMRs.

(2) The holder of a manufacturer's licence falling within paragraph (1) must, as soon as reasonably practicable and in any event within [*x period of time*] beginning on exit day, notify the licensing authority of the name of a responsible person who meets the requirements of regulation 45 (requirement as to responsible persons).

Transitional provision for manufacturer's licence used for importing a medicinal product from a non-EEA State for use in an EEA State and other purposes *[proposed to be part of a new Schedule to the HMRs]*

X—(1) Paragraph (2) applies to the holder of a manufacturer's licence which—

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

(a) was granted before exit day by the licensing authority;

(b) remains in force immediately before exit day;

(c) was used by the holder before exit day for purposes including, but not limited to, the import of a medicinal product from a non-EEA State for use in an EEA State.

(2) Subject to paragraph (3), the holder of a manufacturer's licence falling within paragraph (1) is deemed, on exit day, to also have a wholesale dealer's licence granted under Part 3 for the sole purpose of the import of a medicinal product from a non-EEA State for use in an EEA State.

(3) The holder of a manufacturer's licence falling within paragraph (1) only continues to benefit from the provision in paragraph (2) if that holder notifies the licensing authority of—

(a) the name of a responsible person who meets the requirements of regulation 45 as soon as reasonably practicable and in any event within [*x time period*] beginning on exit day; and

(b) 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 paragraph (3), issue a wholesale dealer's licence to the holder of the manufacturer's licence.

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Change M9: Recognition of prescriptions

Question 18: Do you agree with the proposal to enable continued recognition of prescriptions issued in an EU / EEA country?

Amendment of regulation 213 of the HMRs (interpretation)

X. In regulation 213(1), for "EEA health professional" substitute—

"designated country health professional" means—

(a) a person in a country that is included in the list mentioned in regulation 214(6A); and

(b) who is a person of equivalent professional status to a profession included in that list;".

Amendment of regulation 214 of the HMRs (sale and supply of prescription only medicines)

X.—(1) Regulation 214 is amended as follows.

(2) In paragraph (6), for "EEA health professional" substitute "designated country health professional";

(3) After paragraph (6) insert —

"(6A) The licensing authority must publish a list of designated countries and professions in respect of prescriptions.

(6B) The licensing authority must—

(a) review the countries and professions it has included in the list referred to in paragraph (6A) to determine if it is still satisfied that they should remain on that list; and

(b) undertake such a review at least every [X] years beginning on the date on which that country or profession is included in that list.".

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Clinical Trials SI Draft Text

Change CT1: Legal presence – clinical trials

Question 23: Do you agree with the approach proposed, for a sponsor or legal representative to be established in the UK or a designated country?

Amendment of regulation 3 of the CTRs (sponsor of a clinical trial)

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

(2) In paragraph (11)(a), for "an EEA State" substitute "the United Kingdom or a country that is included in the list mentioned in paragraph (11A)."

(3) After paragraph (11), insert—

"(11A) The licensing authority must publish a list of designated countries where a sponsor of a clinical trial, or their legal representative, can be established for the purpose of paragraph (11).

(11B) In order to determine whether a country should be included in the list mentioned in paragraph (11A), the licensing authority may, in particular, take into account—

(a) the mechanisms the country has in place to assist the licensing authority in contacting, or obtaining information in respect of, a sponsor or legal representative that is established there; and

(b) that country's ability to assist the licensing authority in any action it may need to take in respect of a sponsor or legal representative that is established there.

(11C) The licensing authority must—

(a) review the countries it has included in the list referred to in paragraph (11A) to determine if it is still satisfied that the country should remain on that list; and

(b) undertake such a review at least every three years beginning on the date on which that country is included in that list. "

Transitional provision in respect of regulation 3 (designated country where a sponsor of a clinical trial, or their legal representative, can be established)

X.—(1) For the purposes of regulation 3, for the transitional period, the licensing authority must include in the list mentioned in paragraph (11A) of that regulation each EEA State.

(2) Notwithstanding regulation 3(11C), the licensing authority must, before the end of the transitional period, determine in relation to each EEA State if it is satisfied that that country should remain on the list mentioned in regulation 3(11A).

(3) In this regulation, "transitional period" begins on exit day and ends on [*x date*].

Question 24: Do you agree with the additional requirement on the sponsor to ensure that, where both the sponsor and legal representative are not UK-based, a CI is continuously available to assist with the actioning of any relevant licensing authority or sponsor required changes to the conduct of the trial?

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Amendment of regulation 3 of the CTRs (sponsor of a clinical trial)

X. After paragraph (11C), insert—

"(11D) Where neither the sponsor nor legal representative is established in the United Kingdom, the sponsor must ensure that the chief investigator is available as a point of contact for the licensing authority.".

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Change CT2: Transparency

Question 25: Do you agree with this approach?

Publication of information *[provision proposed to be inserted into the CTRs]*

X.—(1) Subject to paragraph (3), the licensing authority may make accessible to the public information contained in the items listed in paragraph (2) insofar as it relates to a clinical trial carried out, or being carried out, under these Regulations.

(2) The items listed in this paragraph are-

(a) the request for authorisation made under regulation 17;

(b) any amended request for authorisation made under regulation 18, 19 or 20;

(c) any amendment to the protocol made under regulation 23, 24 or 25;

(d) the favourable opinion of the ethics committee given in accordance with regulation 15 or the favourable opinion given by an appeal panel in accordance with paragraph 4 of Schedule 4; and

(e) the notification of the end of the clinical trial made under regulation 27.

(3) Prior to making information available to the public under paragraph (1), the licensing authority must, after consulting such persons as the licensing authority considers appropriate, publish a list of the information which may be made accessible to the public under paragraph (1).

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Change CT3: Use of designated country lists, including for legal presence and importation of investigational medicinal products (IMPs)

Question 26: Do you agree with the proposed designated country lists?

- Designated country list 1:

(see CT1)

- Designated country list 2:

Amendment of regulation 2 of the CTRs (interpretation)

X. In regulation 2(1), at the appropriate place, insert—

"designated country marketing authorisation" means an authorisation granted by a regulatory body responsible for licensing medicinal products in a country that is included in the list mentioned in regulation 15(11).".

Amendment of regulation 15 of the CTRs (ethics committee opinion)

X.—(1) Regulation 15 is amended as follows.

(2) In paragraph (5)(e)—

(a) for "marketing authorisation" substitute "UK marketing authorisation, or designated country marketing authorisation,"; and

(b) after "summary of product characteristics" insert ", or equivalent document,".

(3) After paragraph (10) insert—

"(11) The licensing authority must publish a list of designated countries from which a summary of product characteristics, or equivalent document, will be accepted for the purpose of paragraph (5)(e).

(12) In order to determine whether a country should be included in the list mentioned in paragraph (11), the licensing authority may, in particular, take into account the regulatory equivalence of that country to the UK in assessing the safety, quality and efficacy of the medicinal product.

(13) The licensing authority must—

(a) review the countries it has included in the list referred to in paragraph (11) to determine if it is still satisfied that the country should remain on that list; and

(b) undertake such a review at least every three years beginning on the date on which that country is included in that list".

Amendment of regulation 20 of the CTRs (authorisation procedure for clinical trials involving medicinal products with special characteristics)

X. In regulation 20(1)(a)(i) for "marketing authorisation" substitute "UK marketing authorisation or a designated country marketing authorisation".

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Transitional provision in respect of regulation 15 (designated country from which a summary of product characteristics, or equivalent document, will be accepted for the purpose of regulation 15(5)(e))

X.—(1) For the purposes of regulation 15, for the transitional period, the licensing authority must include in the list mentioned in paragraph (11) of that regulation each EEA State.

(2) Notwithstanding regulation 15(13), the licensing authority must, before the end of the transitional period, determine in relation to each EEA State if it is satisfied that that country should remain on the list mentioned in regulation 15(11).

(3) In this regulation, "transitional period" begins on exit day and ends on [*x date*].

- Designated country list 3:

Amendment of regulation 43 of the CTRs (qualified persons)

X. In regulation 43, after paragraph (1) insert—

"(1A) Subject to paragraph (1B), a qualified person must reside and operate in the United Kingdom.

(1B) Where a manufacturing authorisation is used solely by the holder to distribute an investigational medicinal product which is imported from a country that is included in the list mentioned in regulation 41(2C) of the HMRs, or to possess a medicinal product for such purpose, a qualified person who undertakes that role in respect of such a product must reside and operate in the United Kingdom or in a country that is included in that list."

This text is indicative drafting only and may not be representative of the final legal provisions. The drafting may change for reasons including, but not limited to, any changes considered necessary as a result of consultation, and to complete, refine and finalise the drafting.

Medical Devices SI Draft Text

Change D1: Registration of medical devices

Question 31: Do you agree with this approach and what do you think the timetable for transition period should be?

In Part II of the MDRs

"7A.—Registration of persons placing general medical devices on the market

(1) No person may place a relevant device on the market in accordance with this Part unless that person—

(a) is established in the United Kingdom; and

(b) has complied with paragraph (2).

(2) A person complies with this paragraph if, before placing a relevant device on the market, the person—

(a) informs the Secretary of State of the address of that person's registered place of business in the United Kingdom or, if the person does not have a registered address, an address in the United Kingdom at which service of any document relating in any way to the person's placing of a relevant device on the market will be effective;

(b) if they are not the manufacturer of the relevant device, provides the Secretary of State with sufficient written evidence that they have the manufacturer's authority to place the relevant device on the market;

(c) supplies the Secretary of State with a description of each device concerned; and

(d) pays to the Secretary of State the relevant fee in accordance with regulation [53]."

In Part III of the MDRs

"21A Registration of persons placing active implantable medical devices on the market

(1) No person may place a relevant device on the market in accordance with this Part [or Part VIII insofar as it applies to relevant devices] unless that person—

(a) is established in the United Kingdom; and

(b) has complied with paragraph (2).

(2) A person complies with this paragraph if, before placing a relevant device on the market, the person —

(a) informs the Secretary of State of the address of his registered place of business in the United Kingdom or, if the person does not have a registered address, an address in the United Kingdom at which service of any document relating in any way to the person's placing of a relevant device on the market will be effective;

(b) if they are not the manufacturer of the relevant device, provides the Secretary of State with sufficient written evidence that they have the manufacturer's authority to place the relevant device on the market;

(c) supplies the Secretary of State with a description of each device concerned; and

(d) pays to the Secretary of State the relevant fee in accordance with regulation [53]."

In Part IV of the 2002 Regulations.

"33A—Registration etc. of persons placing in vitro diagnostic medical devices on the market

(1) No person may place a relevant device, on the market in accordance with this Part [or Part IX insofar as it applies to relevant devices] unless that person—

(a) is established in the United Kingdom; and

(b) has complied with paragraph (2).

(2) A person complies with this paragraph if, before placing a relevant device on the market, the person —

(a) informs the Secretary of State of the address of his registered place of business in the United Kingdom or, if the person does not have a registered address, an address in the United Kingdom at which service of any document relating in any way to the person's placing of a relevant device on the market will be effective;

(b) if they are not the manufacturer of the relevant device, provides the Secretary of State with sufficient written evidence that they have the manufacturer's authority to place the relevant device on the market;

(c) supplies the Secretary of State with relevant information in relation to each device concerned; and

(d) pays to the Secretary of State the relevant fee in accordance with regulation [53].

(3) In this regulation "relevant information" means—

(a) in relation to a new relevant device, a statement indicating that the device is a new relevant device;

(b) if the device consists wholly or partly of reagents, reagent products or calibration and control materials, appropriate information in terms of common technological characteristics and /or analytes;

(c) if the device does not wholly or partly consist of reagents, reagent products or calibration and control materials, the appropriate indications;

(d) in relation to devices in a list in Annex II and devices for self-testing—

(i) all data allowing for identification of such devices, the analytical and, where appropriate, diagnostic parameters as referred to in Section 3 of Part A of Annex I;

(ii) [if requested by the Secretary of State,] the labelling and instructions for use for when the device is placed on the market or put into service;

(e) in relation to devices for performance evaluation which relate either to devices referred to in a list in Annex II or to devices for self-testing, all data allowing for identification of such devices, the analytical and where appropriate, diagnostic parameters as referred to in Section 3 of Part A of Annex I.

(4) Where justified and within two years of the placing of a new relevant device on the market, the Secretary of State may request a report relating to the experience gained with the device subsequent to it being placed on the market.

(5) In this regulation a device is a "new relevant device" if—

(i) there has been no such device continuously available on another market (other than the UK market) during the previous three years for the relevant analyte or other parameter, or

(ii) use of the device involves analytical technology not continuously used in connection with a given analyte or other parameter on another market during the previous three years."

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NIBSC SI Draft Text

Change N1: Independent UK batch testing of biological medicines and associated fees

Question 42: Do you agree that, as a standalone national control laboratory, NIBSC certifies batches of biological medicines used in the UK, taking a risk-based approach and accepting evidence of testing by an EU 27 OMCL as discussed above?

Question 43: Do you agree with this proposal for NIBSC OMCL batch testing fees? Y/N. Please give reasons for your answer.

Insertion of new regulation 60A of the HMRs (condition - submitting samples for testing)

X. After regulation 60, insert—

"Condition as to testing of samples by the appropriate authority

60A.—(1) In this regulation—

"the appropriate authority" has the same meaning as in section 57 of the Health and Social Care Act 2012;

"appropriate documentation" means any certificate issued by a laboratory in a designated country for batch testing and certification of biological medicinal products, and such other documentation as the appropriate authority may require;

"the batch testing condition" is a condition to the effect that the holder of the 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 the sample from that batch, the appropriate documentation, or both, and confirmed that it is satisfied that it is in conformity with the approved specifications;

"designated country list for batch testing and certification of biological medicinal products" means the list described in paragraph (5), and designated country for batch testing and certification of biological medicinal products is to be construed accordingly.

(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) a new immunological product manufactured using new or altered kinds of technology or new for a particular manufacturer, during a transitional period of time to be specified by the licensing authority in the condition to be imposed; or

(e) derived from human blood or human plasma.

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

(4) If the appropriate authority requests the UK marketing authorisation holder to provide any further information or material during the period referred to in paragraph (3), the period referred to in that paragraph is suspended for the period—

(a) beginning on the date on which the request is made; and

(b) ending with the date on which the information or material is provided.

(5) The appropriate authority must—

(a) publish the designated country list for the batch testing and certification of biological medicinal products; and

(b) take in to account, in addition to any other factors the appropriate authority considers relevant, whether the appropriate documentation submitted by the UK marketing authorisation holder includes a certificate issued by a laboratory in a designated country for batch testing and certification of biological medicinal products in determining whether the appropriate authority needs to undertake any further testing of the medicinal product submitted to it.

(6) In order to determine whether a country should be included in the designated country list for batch testing and certification of biological medicinal products, the appropriate authority may, in particular, take into account whether the relevant certification 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.

(7) The appropriate authority must—

(a) review the countries it has included in the designated 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

(b) undertake that review at least every three years beginning on the date on which that country is included in the list.".

Transitional provision in respect of new regulation 60A (batch testing condition) *[proposed to be part of a new Schedule to the HMRs]*

X—(1) Sub-paragraph (2) applies where—

(a) a marketing authorisation remains in force as a UK marketing authorisation on exit day (whether or not it is suspended);

(b) that authorisation is for a medicinal product of a type that is specified in regulation 60A(2)(a) to (e).

(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 marketing authorisation holder has, before exit day, submitted to a competent authority of an EEA State (other than the United Kingdom) samples for testing from a batch of a medicinal product ("the relevant batch") that—

(a) is the subject of that authorisation;

(b) is of a type specified in regulation 60A(2)(a) to (e); and

(c) was manufactured in an EEA State other than the United Kingdom.

(4) Where this sub-paragraph applies, the UK marketing authorisation holder 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) For the purposes of regulation 60A(5), the appropriate authority must include each EEA State in the designated country list for batch testing and certification of biological medicinal products for the transitional period.

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(6) Notwithstanding regulation 60A(7)(b), the appropriate authority must, before the end of the transitional period, determine in relation to each EEA State if it is satisfied that that country should remain on the designated country list for batch testing and certification of biological medicinal products.

(7) In this regulation, the transitional period begins on exit day and ends on [*x date*].