SCHEDULES

SCHEDULE 2

Amendment of the Human Medicines (Amendment etc.) (EU Exit) Regulations 2019

PART 10

Amendment of Part 11 (amendment of Part 11 (Pharmacovigilance))

107. In regulation 139 (amendment of regulation 177 (application of part and interpretation))—

(a) for paragraph (2) substitute—

"(2) After paragraph (1) insert—

"(1A) Schedule 12A applies in relation to medicinal products that are the subject of a UKMA(GB) ora THR(GB).".'"

(b) in paragraph (3) omit sub-paragraphs (b) and (c);

(c) in paragraph (4) omit sub-paragraphs (b) and (c);

(d) omit paragraph (5);

(e) for paragraph (6) substitute—

"(6) In paragraph (5)—

(a) for "Schedule 33" substitute "Schedules 33 and 33A";

(b) in paragraph (c) of the definition of "relevant post-authorisation safety study", omit "and"; and

(c) after that definition, insert—

""signal" means, in relation to a UKMA(GB) or THR(GB), information arising from one or multiple sources, including observations and experiments, which suggests a new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial, which is judged to be of sufficient likelihood to justify verificatory action; and".".

108. After regulation 139 (amendment of regulation 177 (application of part and interpretation)) insert—

"**Amendment of regulation 179 (obligation on licensing authority to operate pharmacovigilance system)**

139A. In regulation 179—

(a) in paragraph (1), after "pharmacovigilance system" insert "in relation to medicinal products for sale or supply in Great Britain";

(b) after paragraph (1) insert—

"(1A) The licensing authority must operate a pharmacovigilance system in relation to medicinal products for sale or supply in Northern Ireland.";

(c) in paragraph (2) for "The pharmacovigilance system" substitute "Each pharmacovigilance system"; and

(d) in paragraph (3)(a) for "the pharmacovigilance system" substitute "each pharmacovigilance system".".

109. In regulation 140 (amendment of regulation 180 (obligation on licensing authority to audit pharmacovigilance system))—

(a) in paragraph (2)—

(i) before "omit" insert—

"(a) after "its pharmacovigilance system" insert "relating to medicinal products for sale or supply in Great Britain" and";

(ii) from "omit" to the end becomes sub-paragraph (b);

(b) after paragraph (2) insert—

"(2A) After paragraph (1) insert—

"(1A) The licensing authority must perform a regular audit of its pharmacovigilance system relating to medicinal products for sale or supply in Northern Ireland and report the results of that audit to the European Commission.".";

(c) after paragraph (3) insert—

"(4) After paragraph (2) insert—

"(3) The results of the audit referred to in paragraph (1A) must be reported to the European Commission—

(a) on the first occasion no later than 21st September 2021;

(b) every two years after the first occasion.".".

110. For regulation 141 (omission of regulation 181 (delegation of obligations under Part 11)) substitute—

"**Amendment of regulation 181 (delegation of obligations under Part 11)**

141. In regulation 181(1), for "to another EEA State" substitute "in connection with its pharmacovigilance system in relation to medicinal products for sale or supply in Northern Ireland to an EEA State".".

111. In regulation 142 (amendment of regulation 182 (obligation on holder to operate a pharmacovigilance system))—

(a) in paragraph (2) for "for "resides and operates" to the end substitute "after "in the EU" insert "or United Kingdom"";

(b) after paragraph (2) insert—

"(2A) In paragraph (2)(b), after "pharmacovigilance system master file" insert "and ensure it is permanently and immediately available for inspection electronically in the United Kingdom at the single point from which the reports referred to in regulation 187(4) are accessible".

(2B) After paragraph (2) insert—

"(2A) Where the person the holder has permanently and continuously at its disposal under paragraph (2)(a) ("the qualified person") does not reside and operate in the United Kingdom, the holder must nominate a contact person for pharmacovigilance at a national level who reports to the qualified person,

resides and operates in the United Kingdom and has permanent access to the pharmacovigilance system master file.

(2B) Paragraph (2A) has effect from the day twelve months after IP completion day.".";

(c) for paragraph (3) substitute—

"(3) For paragraph (3) substitute—

"(3) Without prejudice to the requirements set out in regulation 65C and Schedule 10A (variations to a UK marketing authorisation) the holder must keep the licensing authority informed at all times of the name and contact details of—

(a) the appropriately qualified person mentioned in paragraph (2)(a); and

(b) the nominated person mentioned in paragraph (2A).

(3A) The holder must—

(a) ensure that the pharmacovigilance system master file is accessible electronically from the single point within the United Kingdom from which the reports referred to in regulation 187(4) are accessible; and

(b) immediately notify the licensing authority of any change to the single point where the pharmacovigilance system master file may be accessed electronically.".".

112. In regulation 143 (amendment of regulation 184 (obligation on holder to audit pharmacovigilance system)), in the inserted paragraph (3) after "The holder" insert "of a UKMA(GB) or THR(GB)".

113. For regulation 145 (amendment of regulation 186 (reporting obligations on the licensing authority)) substitute—

"**145.** In regulation 186—

(a) in paragraph (1), for sub-paragraphs (d) and (e) substitute—

"(d) submit reports of serious suspected adverse reactions in Northern Ireland that it has recorded under regulation 185 in relation to—

(i) a UKMA(NI),

(ii) a UKMA(UK),

(iii) a THR(NI),

(iv) a THR(UK), or

(v) an Article 126a authorisation,

to the EMA before the end of the period of 15 days beginning on the day following the day on which the report was received; and

(e) submit reports of non-serious suspected adverse reactions in Northern Ireland that it has recorded under regulation 185 in relation to—

(i) a UKMA(NI),

(ii) a UKMA(UK),

(iii) a THR(NI),

(iv) a THR(UK), or

(v) an Article 126a authorisation,

to the EMA before the end of the period of 90 days beginning on the day following the day on which the report was received.";

(b) omit paragraph (4).".

114. In regulation 147 (amendment of regulation 187 (recording obligations on holders)) for paragraph (2) substitute—

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

115. In regulation 148 (amendment of regulation 188 (reporting obligations on holders))—

(a) in paragraph (3), before sub-paragraph (a) insert—

"(za) for "Subject to paragraph (2), the holder" substitute "The holder of a UK marketing authorisation, traditional herbal registration or Article 126a authorisation";";

(b) after paragraph (3) insert—

"(3A) After paragraph (1) insert—

"(1A) The holder of a UKMA(UK), a UKMA(NI), a THR(UK), a THR(NI) or an Article 126a authorisation must, in relation to the product—

(a) submit electronically to the Eudravigilance database a report on all serious suspected adverse reactions that occur in the UK and other countries before the end of the period of 15 days beginning on the day on which the holder gained knowledge of the reaction;

(b) submit electronically to the Eudraviligance database a report on all non-serious suspected adverse reactions that occur in an EEA State or Northern Ireland before the end of the period of 90 days beginning on the day on which the holder gained knowledge of the reaction;

(c) collect follow-up information on reports submitted under sub-paragraphs (a) or (b) and submit it electronically to the Eudravigilance database by way of an update to the original report within the specified time period; and

(d) collaborate with the EMA and the competent authorities of the EEA States in the detection of duplicates of suspected adverse reaction reports.".";

(c) for paragraph (4) substitute—

"(4) In paragraph (2)—

(a) after "holder" insert "of a UKMA(NI), a UKMA(UK), a THR(NI), a THR(UK) or an Article 126a authorisation";

(b) for "paragraph (1)(a) or (b)" substitute "paragraph (1A)(a) or (b)"; and

(c) for "paragraph (1)(d)" substitute "paragraph (1A)(c)".

(4A) In paragraph (3) for "paragraph (4)" substitute "paragraph (4A)".";

(d) after paragraph (5) insert—

"(5A) After paragraph (4) insert—

"(4A) The holder of a UKMA(NI), a UKMA(UK), a THR(NI), a THR(UK) or an Article 126a authorisation must—

(a) monitor medical literature other than the monitored publications for reports of suspected adverse reactions to the product; and

(b) report suspected adverse reactions identified under sub-paragraph (a) in accordance with paragraph (1A).".".

116. In regulation 149 (amendment of regulation 189 (signal detection: licensing authority obligations)) for paragraph (3) substitute—

"(3) In paragraphs (2) and (3), for "The licensing" insert "In relation to medicinal products subject to a UKMA(UK), a UKMA(NI), a THR(UK), a THR(NI) or an Article 126a authorisation, the licensing".".

117. For regulation 150 (amendment of regulation 190 (signal detection: holder obligation)) substitute—

"**150.** For regulation 190(1) substitute—

"(1) The holder must inform—

(a) the licensing authority, and

(b) in respect of a UKMA(UK), a UKMA(NI), a THR(UK), a THR(NI) or an Article 126a authorisation, the EMA,

without delay if it detects any relevant changes in relation to the product.".".

118. In regulation 151 (amendment of regulation 191 (obligation on holder to submit periodic safety update reports: general requirements))—

(a) in paragraph (2) for "for "EMA" substitute "licensing authority"" substitute "after "EMA" insert "and the licensing authority or, in the case of a holder of a UKMA(GB), to the licensing authority only,";

(b) omit paragraph (4);

(c) in paragraph (5), in the inserted paragraph (4A), after "A PSUR" insert "in relation to a product authorised under a UKMA(GB)";

(d) in paragraph (6), in the inserted paragraph (8A), after "conditional marketing authorisation" insert "in relation to a product authorised under a UKMA(GB)";

(e) for paragraph (7) substitute—

"(7) In paragraph (10)—

(a) for sub-paragraph (b) substitute—

"(b) where—

(i) in relation to a product authorised under a UKMA(NI) or UKMA(UK), the product has not yet been placed on the market within the EEA or Northern Ireland, at least every six months following authorisation until the placing on the market within the EEA or Northern Ireland, or

(ii) in relation to a product authorised under a UKMA(GB), the product has not yet been placed on the market in Great Britain, at least every six months following authorisation until the placing on the market within Great Britain; and";

(b) for sub-paragraph (c) substitute—

"(c) where—

(i) in relation to a product authorised under a UKMA(NI) or UKMA(UK), the product has been placed on the market within the EEA or Northern Ireland—

(aa) at least every six months during the first two years following the initial placing on the market,

(bb) once a year for the following two years, and

(cc) every three years after that;

(ii) in relation to a product authorised under a UKMA(GB), the product has been placed on the market in Great Britain—

(aa) at least every six months during the first two years following the initial placing on the market,

(bb) once a year for the following two years, and

(cc) every three years after that.".".

119. In regulation 152 (amendment of regulation 192 (obligation to submit periodic safety reports: derogation from general requirements))—

(a) in paragraph (3), for "for "EMA" to the end substitute "after "EMA" insert "and the licensing authority or, in the case of a holder of a UKMA(GB), to the licensing authority only,";

(b) for paragraph (4) substitute—

"(4) In paragraph (9), after "paragraph (3)(a)" insert "from the holder of a UKMA(UK), UKMA(NI), THR(UK), THR(NI) or Article 126a authorisation".".

120. In regulation 153 (amendment of regulation 193 (harmonisation of PSUR frequency or date of submission))—

(a) for paragraph (2) substitute—

"(2) In paragraph (1) substitute—

"(1) Where products that are subject to different authorisations or registrations contain the same active substance or the same combination of active substances, the frequency and dates of submission may be amended and harmonised in accordance with—

(a) Article 107c(4) of the 2001 Directive, where—

(i) any of the authorisations or registrations is a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation; and

(ii) none of the authorisations or registrations is a UKMA(GB) or THR(GB); or

(b) paragraphs (2A), (3) and (4A), where—

(i) any of the authorisations or registrations is a UKMA(GB) or THR(GB); and

(ii) none of the authorisations or registrations is a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation.";";

(b) after paragraph (2) insert—

"(2A) In paragraph (2), after "holder" insert "of a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation".";

(c) in paragraph (3)—

(i) for "For paragraph (2) substitute—" substitute "After paragraph (2) insert—";

(ii) the text to be inserted is renumbered as paragraph (2A);

(iii) in the text to be inserted, after "the holder" insert "of a UKMA(GB) or THR(GB)";

(d) in paragraph (4)—

(i) for "For paragraph (4) substitute—" substitute "After paragraph (4) insert—";

(ii) the text to be inserted is renumbered as paragraph (4A);

(iii) in the text to be inserted, after "from a holder" insert "of a UKMA(GB) or THR(GB)";

(e) in paragraph (5)—

(i) for sub-paragraph (a) substitute—

"(a) after "of the 2001 Directive" insert "or paragraph (2A) (as the case may be)""; and

(ii) for sub-paragraph (b) substitute—

"(b) after "EMA" insert "or licensing authority (as the case may be)"";

(f) in paragraph (6)—

(i) for "For paragraph (6) substitute" substitute "After paragraph (6) insert"; and

(ii) the substituted paragraphs (6) and (6A) become paragraphs (6A) and (6B) respectively; and

(iii) in the substituted paragraph (6) for "(6A)" substitute "(6B)"; and

(g) in paragraph (7) for "(6A)" substitute "(6B)".

121. In regulation 154 (omission of regulation 194 (responding to a single assessment of PSUR under Article 107e of the 2001 Directive))—

(a) in the heading, for "omission" substitute "amendment"; and

(b) for "Omit regulation 194." substitute "In regulation 194(1) after "medicinal product" insert "authorised under a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation".".

122. In regulation 155 (amendment of regulation 195 (obligation on licensing authority to assess PSURs)—

(a) after paragraph (2) insert—

"(2A) Before paragraph (1) insert—

"(A1) This regulation applies in the circumstances specified in paragraphs (1) and (1A).".

(2B) In paragraph (1)—

(a) after "relating to a medicinal product" insert "authorised for sale or supply authorised under a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation"; and

(b) in sub-paragraph (a)(i) omit "other than the United Kingdom".";

(b) in paragraph (3)—

(i) for "For" substitute "After";

(ii) for "substitute" substitute "insert";

(iii) the inserted paragraph (1) becomes inserted paragraph (1A);

(iv) in the inserted paragraph (1A), after "to a medicinal product" insert "authorised for sale or supply under a UKMA(GB) or THR(GB)";

(c) omit paragraph (5).

123. Before regulation 156 insert—

"**Amendment of regulation 196 (urgent action)**

156ZA. In regulation 196—

(a) in the italic heading immediately preceding it, after "Urgent action" insert "and major safety review";

(b) in paragraph (1), for "The licensing authority must initiate the Section 4 procedure by informing" substitute "In the case of a medicinal product authorised for sale or supply under a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation, the licensing authority must inform";

(c) omit sub-paragraph (2B);

(d) omit paragraphs (4) to (7);

(e) in paragraph (8), omit the definition of "EU urgent action procedure" and "Section 4 procedure".".

124. In regulation 156 (substitution of regulation 196 (urgent action))—

(a) for the heading to the regulation, substitute "Insertion of new regulation 196A (major safety review by the licensing authority)";

(b) for "For regulation 196 and the italic heading immediately preceding it" substitute "After regulation 196 insert";

(c) in the text to be inserted by that regulation—

(i) omit the italic heading "Major safety review";

(ii) renumber the regulation as regulation 196A.

125. In regulation 157 (omission of regulation 197 (EU urgent action procedure))—

(a) in the heading for "Omission" substitute "Amendment";

(b) for "Omit" substitute "In;

(c) after "regulation 197" insert ", in paragraph (1), after "class of medicinal products" insert "authorised for sale or supply under a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation"".

126. In regulation 158 (amendment of regulation 198 (post-authorisation safety studies: general provisions))—

(a) in paragraph (2), for "for "competent authorities" to the end substitute—

"—

(a) "the competent authorities" to the end becomes sub-paragraph (a);

(b) in sub-paragraph (a), at the end insert "and the licensing authority, where the product is subject to a marketing authorisation, traditional herbal registration or Article 126a authorisation for sale or supply in Northern Ireland;"

(c) after sub-paragraph (a) insert—

"(b) the licensing authority, where the product is subject to a marketing authorisation or traditional herbal registration for sale or supply in Great Britain only.".";

(b) in paragraph (3)—

(i) in sub-paragraph (a) for "for "relevant competent authorities" to the end substitute—

"(i) "for "the relevant competent authorities" substitute—

"—

(i) the relevant competent authorities and the licensing authority, where paragraph (2)(a) applies;

(ii) the licensing authority where paragraph (2)(b) applies,"

(ii) "any new information" to the end becomes full-out words;"; and

(ii) in sub-paragraph (b) for "for "competent authorities" to the end substitute—

"—

(i) "the competent authorities of the EEA States in which the study was conducted" becomes paragraph (i);

(ii) in paragraph (i), after "the study was conducted" insert "and the licensing authority, where paragraph (2)(a) applies;"

(iii) after paragraph (i) insert—

"(ii) the licensing authority, where paragraph (2)(b) applies,";

(iv) "before the end of the period" to the end becomes full-out words.".

127. In regulation 159 (amendment of regulation 199 (submission of draft study protocols for required studies))—

(a) for paragraph (2) substitute—

"(2) In paragraph (2) for "to the body specified in paragraph (3)" to the end substitute—

"to—

(a) the body specified in paragraph (3) and the licensing authority (where not otherwise required by paragraph (3)), where the authorisation is a UKMA(NI) or UKMA(UK);

(b) the licensing authority, where the authorisation is a UKMA(GB),

before the study is commenced.".";

(b) for paragraph (3) substitute—

"(3) In paragraph (4)—

(a) after "protocol is submitted" insert "only";

(b) after "paragraphs (2) and (3)(a)" insert "(and is not submitted to the Pharmacovigilance Risk Assessment Committee)".";

(c) omit paragraphs (4) to (6).

128. In regulation 160 (amendment of regulation 200 (amendment to study protocols for required studies))—

(a) for paragraph (2) substitute—

"(2) In paragraph (2) for "to the body specified in paragraph (3)" to the end substitute—

"to—

(a) the body specified in paragraph (3) and the licensing authority (where not otherwise required by paragraph (3)), where the authorisation for the product is a UKMA(NI) or UKMA(UK);

(b) the licensing authority, where the authorisation for the product is a UKMA(GB),

before their implementation.".";

(b) for paragraph (3) substitute—

"(3) In paragraph (4)—

(a) after "protocol is submitted" insert "only";

(b) after "paragraphs (2) and (3)(a)" insert "(and is not submitted to the Pharmacovigilance Risk Assessment Committee)".";

(c) omit paragraphs (4) and (5).

129. In regulation 161 (amendment of regulation 201 (submission and evaluation of final study reports for required studies))—

(a) for paragraph (2) substitute—

"(2) In paragraph (2) for "to the body specified in paragraph (3)" to the end substitute—

"to—

(a) the body specified in paragraph (3) and the licensing authority (where not otherwise required by paragraph (3)), where the authorisation for the product is a UKMA(NI) or UKMA(UK);

(b) the licensing authority, where the authorisation for the product is a UKMA(GB),

a final study report and an abstract of the study results.".";

(b) omit paragraph (3);

(c) in paragraph (4) for "omit from" to the end substitute "omit "for reports falling under paragraph (3)(a)" and "for reports falling under paragraph (3)(b)".

130. For regulation 162 (omission of regulation 202 (follow up of final study reports)) substitute—

"**Amendment of regulation 202 (follow up of final study reports)**

162. In regulation 202(1), after "This regulation applies" insert "in respect of a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation".".

131. For regulation 164(3) (amendment of regulation 203 (obligations on licensing authority in relation to national medicines web-portal)) substitute—

"(3) In paragraph (2), after sub-paragraph (d) insert—

"(da) the list published by the licensing authority under, or which applies by virtue of, regulation 202A;".".

132. In regulation 165 (omission of regulation 204 (obligation on licensing authority in relation to public announcements))—

(a) in the heading for "Omission" substitute "Amendment";

(b) for "Omit" substitute "In";

(c) after "regulation 204" insert ", in paragraph (1), after "pharmacovigilance concerns" insert "which relate to products authorised under a UKMA(NI) or UKMA(UK)".

133. In regulation 166 (amendment of regulation 205 (obligations on holders in relation to public announcements))—

(a) in paragraph (2) for "for "bodies listed" to the end substitute "after "bodies listed in paragraph (3)" insert "where the product is subject to a UKMA(NI), UKMA(UK), THR(NI), THR(UK) or Article 126a authorisation, or the licensing authority where the product is subject to a UKMA(GB) or THR(GB),"";

(b) omit paragraph (3).

134. In regulation 167 (insertion of regulation 205A (further obligations in respect of pharmacovigilance activities)), in the inserted regulation 205A—

(a) in paragraph (1), after "Schedule 12A" insert "applies in relation to medicinal products for sale or supply under a UKMA(GB) or THR(GB) and";

(b) in paragraph (2)—

(i) for "The Ministers" substitute "The Secretary of State";

(ii) after "by regulations" insert "in respect of Great Britain".

135. In regulation 170 (amendment of regulation 206 (infringement notices)) for paragraphs (2) and (3) substitute—

"(2) In paragraph (3), after "paragraph (1)" insert "in relation to a product authorised for sale or supply under a UKMA(NI), UKMA(UK), THR(NI) or THR(UK)".

(3) In paragraph (4) after sub-paragraph (a) insert—

"(aa) Schedule 12A;".".

136. Omit regulations 172 (amendment regulation 208 (false and misleading information)), 173 (amendment of regulation 209 (penalties)) and 174 (Omission of regulation 210 (offences relating to pharmacovigilance obligations under Regulation (EC) No 726/2004)).

137. In regulation 175 (amendment of regulation 210A (offences in relation to pharmacovigilance obligations under the Implementing Regulation))—

(a) in paragraph (2)—

(i) for "for" substitute "after";

(ii) for "substitute "Schedule 12A"" substitute "insert "and Schedule 12A"";

(b) in paragraph (3) for sub-paragraphs (a) and (b) substitute—

"(a) in sub-paragraph (a), at the beginning insert "in relation to a UKMA(NI), UKMA(UK), THR(NI) THR(UK) or Article 126a authorisation,";

(b) after sub-paragraph (a) insert—

"(aa) in relation to a UKMA(GB) or THR(GB), fails to comply with any requirement or obligation contained in a provision of Schedule 12A listed in paragraph (2A); or".";

(c) in paragraph (4)—

(i) for "For paragraph (2) substitute" substitute "After paragraph (2) insert";

(ii) the inserted paragraph (2) becomes inserted paragraph (2A);

(iii) omit the inserted paragraphs (3) and (4);

(d) after paragraph (4) insert—

"(5) In paragraph (4), after "Implementing Regulation" insert ", or of paragraph 26(8) or 29(1) of Schedule 12A,".".

138. Omit regulation 176 (amendment of regulation 211 (persons liable)).

139. For regulation 177 (amendment of regulation 212 (transitional amendments)) substitute—

"**177.** In regulation 212, omit "182, 186, 188, 191, 192".".

140. In regulation 178 (amendment of Schedule 33 (transitional arrangements: pharmacovigilance)) for "4" substitute "5".