ANNEX I U.K.

Extensions of marketing authorisations

1. Changes to the active substance(s):

(a) replacement of a chemical active substance by a different salt/ester complex/ derivative, with the same therapeutic moiety, where the efficacy/safety characteristics are not significantly different;

(b) replacement by a different isomer, a different mixture of isomers, of a mixture by an isolated isomer (e.g. racemate by a single enantiomer), where the efficacy/safety characteristics are not significantly different;

(c) replacement of a biological active substance with one of a slightly different molecular structure where the efficacy/safety characteristics are not significantly different, with the exception of:

— changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza;

— replacement or addition of a serotype, strain, antigen or combination of serotypes, strains or antigens for a veterinary vaccine against avian influenza, foot-and-mouth disease or bluetongue;

— replacement of a strain for a veterinary vaccine against equine influenza;

(d) modification of the vector used to produce the antigen or the source material, including a new master cell bank from a different source, where the efficacy/safety characteristics are not significantly different;

(e) a new ligand or coupling mechanism for a radiopharmaceutical, where the efficacy/ safety characteristics are not significantly different;

(f) change to the extraction solvent or the ratio of herbal drug to herbal drug preparation where the efficacy/safety characteristics are not significantly different.

2. Changes to strength, pharmaceutical form and route of administration:

(a) change of bioavailability;

(b) change of pharmacokinetics e.g. change in rate of release;

(c) change or addition of a new strength/potency;

(d) change or addition of a new pharmaceutical form;

(e) change or addition of a new route of administration[1].

3. Other changes specific to veterinary medicinal products to be administered to food-producing animals: change or addition of target species.

ANNEX II U.K.

Classification of variations

1. The following variations shall be classified as minor variations of type IA:

(a) variations of purely administrative nature that are related to the identity and contact details of:

— the holder;

— the manufacturer or supplier of any starting material, reagent, intermediate, active substance used in the manufacturing process or finished product;

(b) variations related to the deletion of any manufacturing site, including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place;

(c) variations related to minor changes to an approved physico-chemical test procedure, where the updated procedure is demonstrated to be at least equivalent to the former test procedure, appropriate validation studies have been performed and the results show that the updated test procedure is at least equivalent to the former;

(d) variations related to changes made to the specifications of the active substance or of an excipient in order to comply with an update of the relevant monograph of the European Pharmacopoeia or of the national pharmacopoeia of a Member State, where the change is made exclusively to comply with the pharmacopoeia and the specifications for product specific properties are unchanged;

(e) variations related to changes in the packaging material not in contact with the finished product, which do not affect the delivery, use, safety or stability of the medicinal product;

(f) variations related to the tightening of specification limits, where the change is not a consequence of any commitment from previous assessment to review specification limits and does not result from unexpected events arising during manufacture.

2. The following variations shall be classified as major variations of type II:

(a) variations related to the addition of a new therapeutic indication or to the modification of an existing one;

(b) variations related to significant modifications of the summary of product characteristics due in particular to new quality, pre-clinical, clinical or pharmacovigilance findings;

(c) variations related to changes outside the range of approved specifications, limits or acceptance criteria;

(d) variations related to substantial changes to the manufacturing process, formulation, specifications or impurity profile of the active substance or finished medicinal product which may have a significant impact on the quality, safety or efficacy of the medicinal product;

(e) variations related to modifications in the manufacturing process or sites of the active substance for a biological medicinal product;

(f) variations related to the introduction of a new design space or the extension of an approved one, where the design space has been developed in accordance with the relevant European and international scientific guidelines;

(g) variations concerning a change to or addition of a non-food producing target species;

(h) variations concerning the replacement or addition of a serotype, strain, antigen or combination of serotypes, strains or antigens for a veterinary vaccine against avian influenza, foot-and-mouth disease or bluetongue;

(i) variations concerning the replacement of a strain for a veterinary vaccine against equine influenza;

(j) variations related to changes to the active substance of a seasonal, pre-pandemic or pandemic vaccine against human influenza;

(k) variations related to changes to the withdrawal period for a veterinary medicinal product.

ANNEX III U.K.

[F1Cases for grouping variations referred to in Article 7(2)(b) and Article 13d(2)(b)]

Textual Amendments

F1 Substituted by Commission Regulation (EU) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (Text with EEA relevance).

1. One of the variations in the group is an extension of the marketing authorisation.

2. One of the variations in the group is a major variation of type II; all other variations in the group are variations which are consequential to this major variation of type II.

3. One of the variations in the group is a minor variation of type IB; all other variations in the group are minor variations which are consequential to this minor variation of type IB.

4. All variations in the group relate solely to changes of administrative nature to the summary of product characteristics, labelling and package leaflet or insert.

5. All variations in the group are changes to an Active Substance Master File, Vaccine Antigen Master File or Plasma Master File.

6. All variations in the group relate to a project intended to improve the manufacturing process and the quality of the medicinal product concerned or its active substance(s).

7. All variations in the group are changes affecting the quality of a human pandemic influenza vaccine.

8. All variations in the group are changes to the pharmacovigilance system referred to in points (ia) and (n) of Article 8(3) of Directive 2001/83/EC or points (k) and (o) of Article 12(3) of Directive 2001/82/EC.

9. All variations in the group are consequential to a given urgent safety restriction and submitted in accordance with Article 22.

10. All variations in the group relate to the implementation of a given class labelling.

11. All variations in the group are consequential to the assessment of a given periodic safety update report.

12. All variations in the group are consequential to a given post-authorisation study conducted under the supervision of the holder.

13. All variations in the group are consequential to a specific obligation carried out pursuant to Article 14(7) of Regulation (EC) No 726/2004.

14. All variations in the group are consequential to a specific procedure or condition carried out pursuant to Articles 14(8) or 39(7) of Regulation (EC) No 726/2004, Article 22 of Directive 2001/83/EC or Article 26(3) of Directive 2001/82/EC.

ANNEX IV U.K.

Elements to be submitted

1. A list of all the marketing authorisations affected by the notification or application.

2. A description of all the variations submitted, including:

(a) in the case of minor variations of type IA, the date of implementation for each variation described;

(b) in the case of minor variations of type IA which do not require immediate notification, a description of all minor variations of type IA made in the last 12 months to the terms of the concerned marketing authorisation(s) and which have not been already notified.

3. All necessary documents as listed in the guidelines referred to in point (b) of Article 4(1).

4. Where a variation leads to or is the consequence of other variations to the terms of the same marketing authorisation, a description of the relation between these variations.

5. In the case of variations to centralised marketing authorisations, the relevant fee provided for in Council Regulation (EC) No 297/95[(2)].

6. In the case of variations to marketing authorisations granted by the competent authorities of Member States:

(a) a list of those Member States with an indication of the reference Member State if applicable;

(b) the relevant fees provided for in the applicable national rules in the Member States concerned.

ANNEX V U.K.

PART 1 U.K.

Variations concerning a change to or addition of therapeutic indications.

PART 2 U.K.

1. Variations concerning a change to or addition of a non-food producing target species.

2. Variations concerning the replacement or addition of a serotype, strain, antigen or combination of serotypes, strains or antigens for a veterinary vaccine against avian influenza, foot-and-mouth disease or bluetongue.

3. Variations concerning the replacement of a strain for a veterinary vaccine against equine influenza.

[F2ANNEX VI U.K.

List of Member States referred in Article 24a

Textual Amendments

F2 Inserted by Commission Regulation (EU) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (Text with EEA relevance).

the Republic of Bulgaria,
the Federal Republic of Germany.**]**

(**1**) For parenteral administration, it is necessary to distinguish between intra-arterial, intravenous, intramuscular, subcutaneous and other routes. For administration to poultry, respiratory, oral and ocular (nebulisation) routes used for vaccination are considered to be equivalent routes of administration.

(**2**) OJ L 35, 15.2.1995, p. 1.

Status:
Point in time view as at 31/01/2020.

Changes to legislation:
There are currently no known outstanding effects for the Commission Regulation (EC) No 1234/2008.