ANNEX III
CONDITIONS FOR QUALIFICATION OF A QUALIFIED PERSON

[Former Article 48]

1. **The qualified person referred to in paragraph 1 shall hold a university degree in one or more** of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology.

2. **The qualified person shall have acquired practical experience over at least two years, in one or more undertakings that are authorised manufacturers, obtaining sufficient knowledge of manufacture, testing, supply chains, good manufacturing practice and pharmaceutical quality systems as well as regulatory processes and dossier content for ensuring the quality of medicinal products.**

3. **The Commission may publish guidelines outlining the practical experience requirements.**

4. A qualified person shall be in possession of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course of study, or a course **recognised** as equivalent by the Member State concerned, extending over a period of at least four years of theoretical and practical study in one of the following scientific disciplines: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology.

   However, the minimum duration of the university course may be three and a half years where the course is followed by a period of theoretical and practical training of a minimum duration of one year and including a training period of at least six months in a pharmacy open to the public, corroborated by an examination at university level.

   Where two university courses or two courses **recognised** by the State as equivalent co-exist in a Member State and where one of these extends over four years and the other over three years, the three-year course leading to a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course or its **recognised** equivalent shall be considered to fulfil the condition of duration referred to in the second subparagraph in so far as the diplomas, certificates or other evidence of formal qualifications awarded on completion of both courses are **recognised** as equivalent by the **Member** State in question.

   The course shall include theoretical and practical study bearing upon at least the following basic subjects:

   (a) Experimental physics

   (b) General and inorganic chemistry

   (c) Organic chemistry

   (d) Analytical chemistry

   (e) Pharmaceutical chemistry, including analysis of medicinal products

   (f) General and applied biochemistry (medical)

   (g) Physiology

   (h) Micro biology

   (i) Pharmacology

(j) Pharmaceutical technology

(k) Toxicology

(l) Pharmacognosy (study of the composition and effects of the natural active substances of plant and animal origin).

Studies in these subjects should be so balanced as to enable the person concerned to fulfil the obligations specified in **Article 151**.

In so far as certain diplomas, certificates or other evidence of formal qualifications mentioned in the first subparagraph do not fulfil the criteria laid down in this paragraph, the competent authority of the Member State shall ensure that the person concerned provides evidence of adequate knowledge of the subjects involved.

5. The qualified person shall have acquired practical experience over at least two years, in one or more undertakings **or not-for-profit entities that** are **authorised** to manufacture medicinal products, in the activities of qualitative analysis of medicinal products, of quantitative analysis of active substances and of the testing and checking necessary to ensure the quality of medicinal products.

6. A person engaging in the activities of the person referred to in **Article 150** from the time of the application of Second Council Directive 75/319/EEC[2], in a Member State without complying with the provisions of **this Annex** shall be eligible to continue to engage in those activities within the **Union**.

7. The holder of a diploma, certificate or other evidence of formal qualifications awarded on completion of a university course — or a course **recognised** as equivalent by the Member State concerned — in a scientific discipline allowing **them** to engage in the activities of the person referred to in Article 48 in accordance with the laws of that **Member** State may — if **they** began **their** course prior to 21 May 1975 — be considered as qualified to carry out in that **Member** State the duties of the person referred to in **Article 150** provided that **they have** previously engaged in the following activities for at least two years before 21 May 1985 following notification of this directive in one or more undertakings **or not-for-profit entities authorised** to manufacture: production supervision **or** qualitative and quantitative analysis of active substances, and the necessary testing and checking under the direct authority of the person referred to in **Article 150** to ensure the quality of the medicinal products.

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2 Second Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products (OJ L 147, 9.6.1975, p. 13). Directive is not in force anymore.

ANNEX IV
LABELLING PARTICULARS

[Former Article 54]

The following particulars shall appear on the outer packaging of medicinal products or, where there is no outer packaging, on the immediate packaging:

(a) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults; where the product contains up to three active substances, the international non-proprietary name (INN) shall be included, or, if one does not exist, the common name;

(b) a statement of the active substances expressed qualitatively and quantitatively per dosage unit or according to the form of administration for a given volume or weight, using their common names;

(c) the pharmaceutical form and the contents by weight, by volume or by number of doses of the product;

(d) a list of those excipients known to have a **recognised** action or effect and included in the detailed guidance published pursuant to **Article 68**;

(e) the method of administration and, if necessary, the route of administration. Space shall be provided for the prescribed dose to be indicated;

(f) a special warning that the medicinal product must be stored out of the reach and sight of children;

(g) a special warning, if this is necessary for the medicinal product;

(h) the expiry date in clear terms (month/year);

(i) special storage precautions, if any;

(j) specific precautions relating to the disposal of unused medicinal products or waste derived from medicinal products, where appropriate, as well as reference to any appropriate collection system in place;

(k) the name and address of the marketing authorisation holder and, where applicable, the name of the representative appointed by the holder to represent **them**;

(l) the number of the **authorisation** for placing the medicinal product on the market;

(m) the manufacturer's batch number;

(n) in the case of non-prescription medicinal products, instructions for use;

(o) for medicinal products other than radiopharmaceuticals referred to in **Article 55(1)**, safety features enabling wholesale distributors and persons authorised or entitled to supply medicinal products to the public to:

(i) verify the authenticity of the medicinal product, and

(ii) identify individual packs,

as well as a device allowing verification of whether the outer packaging has been tampered with.

ANNEX V
CONTENTS OF SUMMMARY PRODUCT CHARACTERISTICS

[former Article 11]

The summary of the product characteristics shall contain, in the order indicated below, the following information:

(1) name of the medicinal product followed by the strength and the pharmaceutical form.

(2) qualitative and quantitative composition in terms of the active substances and constituents of the excipient, knowledge of which is essential for proper administration of the medicinal product. The usual common name or chemical description shall be used.

(3) pharmaceutical form.

(4) clinical particulars:

- (a) therapeutic indications,
- (b) posology and method of administration for adults and, where necessary for children,
- (c) contra-indications,
- (d) special warnings and precautions for use and, in the case of immunological medicinal products, any special precautions to be taken by persons handling such products and administering them to patients, together with any precautions to be taken by the patient,
- (e) interaction with other medicinal products and other forms of interactions,
- (f) use during pregnancy and lactation,
- (g) effects on ability to drive and to use machines,
- (h) undesirable effects,
- (i) overdose (symptoms, emergency procedures, antidotes).

(5) pharmacological properties:

- (a) pharmacodynamic properties,
- (b) pharmacokinetic properties,
- (c) preclinical safety data.

(6) pharmaceutical particulars:

- (a) list of excipients,
- (b) major incompatibilities,
- (c) shelf life, when necessary after reconstitution of the medicinal product or when the immediate packaging is opened for the first time,
- (d) special precautions for storage,
- (e) nature and contents of container,
- (f) special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product, if appropriate. **In case of antimicrobial medicinal products in addition to the precautions a**

warning that inappropriate disposal of the medicinal product contributes to antimicrobial resistance.

(7) marketing authorisation holder.

(8) marketing authorisation **numbers**.

(9) date of the first authorisation or renewal of the authorisation.

(10) date of revision of the text.

(11) for radiopharmaceuticals, full details of internal radiation dosimetry.

(12) for radiopharmaceuticals, additional detailed instructions for extemporaneous preparation and quality control of such preparation and, where appropriate, maximum storage time during which any intermediate preparation such as an eluate or the ready-to-use pharmaceutical will conform with its specifications.

For authorisations under **Articles 19, 20, 21, 22 and subsequent variations**, those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms **that are** still covered by patent law at the time when a generic **or biosimilar medicinal product is placed on the market** need not be included.

ANNEX VI
CONTENTS OF PACKAGE LEAFLET

[former Article 59]

The package leaflet shall contain, in the order indicated below, the following information:

(1) for the identification of the medicinal product:

(a) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults. The common name shall be included where the product contains only one active substance and if its name is an invented name;

(b) the pharmaco-therapeutic group or type of activity in terms easily comprehensible for the patient;

(2) the therapeutic indications;

(3) a list of information **that** is necessary before the medicinal product is taken:

(a) contra-indications;

(b) appropriate precautions for use;

(c) forms of interaction with other medicinal products and other forms of interaction (e.g. alcohol, tobacco, **food**) **that** may affect the action of the medicinal product;

(d) special warnings;

(4) the necessary and usual instructions for proper use, and in particular:

(a) the dosage,

(b) the method and, if necessary, route of administration;

(c) the frequency of administration, specifying if necessary the appropriate time at which the medicinal product may or must be administered;

and, as appropriate, depending on the nature of the product:

(d) the duration of treatment, where it should be limited;

(e) the action to be taken in case of an overdose (such as symptoms, emergency procedures);

(f) what to do when one or more doses have not been taken;

(g) indication, if necessary, of the risk of withdrawal effects;

(h) a specific recommendation to consult the doctor or the pharmacist, as appropriate, for any clarification on the use of the product;

(5) a description of the adverse reactions **that** may occur under normal use of the medicinal product and, if necessary, the action to be taken in such a case;

(6) a reference to the expiry date indicated on the label, with:

(a) a warning against using the product after that date;

(b) where appropriate, special storage precautions;

(c) if necessary, a warning concerning certain visible signs of deterioration;

(d) the full qualitative composition (in active substances and excipients) and the quantitative composition in active substances, using common names, for each presentation of the medicinal product;

(e) for each presentation of the product, the pharmaceutical form and content in weight, volume or units of dosage;

(f) the name and address of the marketing authorisation holder and, where applicable, the name of **their** appointed representatives in the Member States;

(i) the name and address of the manufacturer;

(7) the date on which the package leaflet was last revised.

(8) **for antimicrobials, a warning that improper use and disposal of the medicinal product contributes to antimicrobial resistance.**

ANNEX VII
AREAS FOR ADAPTED FRAMEWORKS REFERRED TO IN ARTICLE 18

Phage therapies

ANNEX VIII LIST OF COLOURS PERMITTED FOR USE IN THE MEDICINAL PRODUCTS OTHER THAN THOSE INCLUDED IN THE UNION LIST OF AUTHORISED FOOD ADDITIVES IN TABLE 1 OF PART B OF ANNEX II TO REGULATION (EC) 1333/2008.

ANNEX IX AVAILABILITY

I. For the purpose of the notification in accordance with Article 40(2), point (e) of the Directive, the marketing authorisation holder shall notify the following information as referred to in Article 177 of this Directive and Article 122(1) of [revised Regulation (EC) No 726/2004]:

(1) Product details

(a) Product name;

(b) Active substance(s);

(c) Procedure type;

(d) Authorisation procedure, National/ EMA Authorisation number;

(e) Country of authorisation;

(f) Human/ Veterinary medicine;

(g) ATC code;

(h) Pharmaceutical form;

(i) Strength;

(j) Route(s) of administration;

(k) Pack size.

(2) Details of shortage

(a) Shortage status (anticipated, current);

(b) Available stock;

(c) Date of beginning of shortage [by Member State];

(d) Expected end date [by Member State], if applicable;

(e) Reason for shortage;

(f) Impacted countries;

(g) Reference number of any Rapid Alert (quality/ safety) related to the issue or other reference to NCAs, EMA Quality Defect Report if relevant;

(h) Reference to related pending regulatory action, if relevant;

(i) Other competent authorities notified, including reference to Quality Defect report if relevant;

(j) Shortage mitigation plan, detailing the risk assessment of impact of shortage, including where available:

- Potential alternative medicinal products;
- Estimated size of population affected by the shortage of this product;
- Quantities already delivered (in previous 12 months);
- Manufacturing capacity and forecast of supply (in next 6 months);
- Anticipated demand for the medicinal product (in next 6 months);
- Impact on the supply of other medicinal products;
- Impact on the consumption of/ demand for other medicinal products;

(k) Any actions required to be completed, at the request of competent authorities of Member States concerned.

(3) Contact details

(a) Marketing authorisation holder name and address;

(b) Name and contact details of person notifying.

II. For the purpose of the notification in accordance with Article 40(2), points (b),(c) and (d) of the Directive, the marketing authorisation holder shall notify the following minimum set of information, as referred to in Article 177 this Directive and Article 122(1) of [revised Regulation (EC) No 726/2004]:

(1) Product details

(a) Product name;

(b) Active substance(s);

(c) Procedure type;

(d) Authorisation procedure, National/ EMA Authorisation number;

(e) Country of authorisation;

(f) Human/ Veterinary medicine;

(g) ATC code;

(h) Pharmaceutical form;

(i) Strength;

(j) Route(s) of administration;

(k) Pack size;

(2) Details of suspension, cessation or withdrawal

(a) Type (suspension, cessation or withdrawal);

(b) Available stock up to suspension, cessation or withdrawal;

(c) Date of suspension, cessation or withdrawal [by Member State];

(d) Reason ;

(e) Impacted countries;

(f) Reference number of any Rapid Alert (quality/ safety) related to the issue or other reference to NCAs, EMA Quality Defect Report if relevant;

(g) Reference to related pending regulatory action, if relevant;

(h) Other competent authorities notified, including reference to Quality Defect report if relevant.

(i) Risk assessment of impact of suspension, cessation or withdrawal, including where available:

- Potential alternative medicinal products;

- Estimated size of population affected by the withdrawal of this product;
- Quantities already delivered (in previous 12 months);
- Projected deliveries until suspension, cessation or withdrawal occurs;
- Anticipated demand for the medicinal product (in next 6 months);
- Impact on the supply of other medicinal products;
- Impact on the consumption of/ demand for other medicinal products;

(j) Any actions required to be completed, at the request of competent authorities of Member States concerned.

(3) Contact details

(a) Marketing authorisation holder name and address;

(b) Name and contact details of person notifying.

III The Shortage Prevention Plan referred to in Article 40(1) of the Directive and Article 122(1) of [revised Regulation (EC) No 726/2004] shall contain the following minimum set of information:

(1) Product details

(a) Product name;

(b) Active substance(s);

(c) Authorisation procedure, National/ EMA Authorisation number;

(d) Country of authorisation;

(e) Human/ Veterinary medicine;

(f) ATC code;

(g) Pharmaceutical form;

(h) Strength;

(i) Route(s) of administration;

(j) Pack size.

(2) Risk assessment, including:

(a) Risk prioritisation;

(b) Supply chain map, with particular attention on vulnerabilities in the supply chain;

(c) Risk control strategy in place.

(3) Shortage prevention measures

(a) Process for detection and notification of shortages;

(b) Mitigating initiatives.

(4) Process for review and update of the Shortage Prevention Plan

(5) Contact details

(a) Marketing authorisation holder name and address;

(b) Name and details of contact person.