VELFERÐARRÁÐUNEYTIÐ

Ministry of Welfare

REGULATION
on Marketing Authorisations for Proprietary Medicinal Products, their Labelling and Package Leaflets, No. 141/2011,
as amended by Regulations No. 1021/2011 and No. 943/2012.

CHAPTER I
General provisions.

Article 1
Scope and definitions.

This Regulation applies to marketing authorisation for proprietary medicinal products, their labelling and package leaflets. Provisions of Articles 21-41 on labelling and package leaflets shall also apply, as applicable, to other medicinal products.

Marketing authorisation holders shall, as appropriate, use recognised names of pharmaceutical forms, routes of administration, etc. in accordance with the latest edition of Pharmeuropa, Standard Terms, published by the European Pharmacopoeia Commission (Ph. Eur.).

For the purposes of this Regulation, the following terms shall have these meanings:

1. *Proprietary medicinal product:* All medicinal products, ready or almost ready for use, for which a marketing authorisation has been granted, with a special name and in a special packaging of the manufacturer (marketing authorisation holder).
2. *Medicinal product:* Any type of substance or combination of substances which:
   a) is said to possess characteristics useful for treating or preventing diseases in humans or animals, or
   b) can be used for or administered to humans or animals, either for the purpose of restoring, correcting or modifying physiological functions through pharmacological or immunological effects or effects on metabolism, or to confirm diagnosis of illness.
3. *Substance:* Any matter, irrespective of origin which may be: human, e.g. human blood or human blood products; animal, e.g. micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products, etc.; vegetable, e.g. micro-organisms, plants, parts of plants, vegetable secretions, extracts, etc.; or chemical, e.g. elements, naturally occurring chemical materials and chemical products obtained by chemical reaction or synthesis.
4. *Magistral formula:* Any medicinal product prepared in a pharmacy in accordance with a physician‘s prescription for an individual patient.
5. *Officinal formula:* Any medicinal product which is prepared by a pharmacy or pharmaceutical manufacturing facility in accordance with a prescription approved by the Icelandic Medicines Agency and dispensed by pharmacies. A pharmaceutical manufacturing facility is a production plant where medicinal products are produced in accordance with good manufacturing practice for medicinal products and which has been granted a manufacturing license in accordance with the provisions of the Medicinal Products Act.
6. *Reference medicinal product:* A medicinal product which has been recognised by the Icelandic Medicines Agency and has obtained a marketing authorisation as referred to in Article 2, based on an application according to Articles 12 and 13 of this Regulation.

7. *Generic medicinal product:* A medicinal product which has the same qualitative and quantitative composition of 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. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy.
8. *Homeopathic medicinal product:* Any medicinal product prepared from substances called homeopathic stocks in accordance with the homeopathic manufacturing procedure described by the European Pharmacopoeia or, in absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.
9. *Immunological medicinal product:* All medicinal products which are vaccines, toxins, serums or allergen products:
   a) "Vaccines, toxins and serums" shall, among other things, include:
      i. Agents used to produce active immunity, such as cholera vaccine, BCG, polio vaccine and smallpox vaccine.
      ii. Agents used to diagnose the state of immunity, including tuberculin and tuberculin PPD, toxins for the Schick and Dick Tests, brucellin.
      iii. Agents used to produce passive immunity, such as diphtheria antitoxin, anti-smallpox globulin, antilymphocytic globulin.
   b) "Allergen product": Any medicinal product which is intended to identify or induce a specific acquired alteration in the immunological response to an allergising agent.
   c) *Veterinary immunological medicinal product:* A veterinary medical product administered to animals in order to produce active or passive immunity or to diagnose the state of immunity.
10. *Radiopharmaceutical:* Any ready-to-use medicinal product which contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose.
11. *Radionuclide generator:* Any system incorporating a fixed parent radionuclide from which is produced a daughter radionuclide which is to be obtained by elution or by any other method and used in a radiopharmaceutical.
12. *Radionuclide kit:* Any preparation to be reconstituted or combined with radionuclides or medicinal products to create a final radiopharmaceutical, usually prior to its administration.
13. *Radionuclide precursor:* Any other radionuclide produced for the radio-labelling of another substance prior to administration.
14. *Medicinal products derived from human blood or human plasma:* Medicinal products based on blood constituents which are prepared industrially by public or private establishments, such medicinal products including, in particular, albumin, coagulating factors and immunoglobulins of human origin.
15. *Premixture for medicated feed:* All veterinary medicinal products prepared in advance for the purpose of subsequently producing medicated feed.
16. *Medicated feed:* Any mixture of a veterinary medicinal product or products and feed or feeds which is ready prepared for marketing and intended to be fed to animals without further processing, because of its curative or preventive properties or other properties as a medicinal product referred to in item 1.
17. *Agent of marketing authorisation holder:* A representative appointed by a marketing authorisation holder in the Member State concerned.
18. *Risk connected with use of the medicinal product:*
   a) All risks to patients‘ health or public health with regard to the quality, safety and efficacy of the medicinal product.
   b) All risks of undesirable environmental impacts.
19. *Risk-benefit balance:* An assessment of the balance between the positive effects of the medicinal product and the risk, as defined in item 18a.
20. *Withdrawal period:* The period necessary between the last administration of the veterinary medicinal product to animals under normal conditions of use until foodstuffs may be produced

from such animals, in order to protect public health by ensuring that such foodstuffs do not contain residues in quantities in excess of the maximum limits laid down in application of Regulation (EEC) No. 2377/90.

21. *EU Commission's guidelines ("Notice to applicants"):* Detailed guidelines from the EU to applicants for marketing authorisations for medicinal products currently in effect.
22. *European Medicines Agency (EMA):* The European Medicines Agency established by Regulation (EC) No. 726/2004.

CHAPTER II
Marketing authorisations for medicinal products.

Article 2
Requirement for a marketing authorisation.

Ready-to-use medicinal products for human and veterinary use and medicated mixtures for use in feeds must have obtained the approval of the Icelandic Medicines Agency and been granted a marketing authorisation before being placed on the market.

A marketing authorisation is required for each concentration and each pharmaceutical form even if the medicinal products are in other respects identical.

The requirement for a marketing authorisation does not apply to homeopathic medicinal products, *cf.* Regulation No. 967/2000, on the import, sale and distribution of homeopathic medicinal products and their labelling, for products with valid marketing authorisation in another Member State of the European Economic Area (EEA).

Article 3
Exemptions from the requirement for a marketing authorisation.

Exempt from the requirement for a marketing authorisation are:

a) Any physician's magistral formula and officinal formula.
b) Medicinal products intended for research and development trials, *cf.* however the provisions of Directive 2001/20/EC, on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
c) Intermediate products intended for further processing by an authorised manufacturer.
d) Any radionuclides in the form of sealed sources.
e) Whole blood, plasma or blood cells of human origin, with the exception of plasma produced through industrial processes.
f) Medicated feed as defined in Directive 90/167/EEC, of 26 March 1990, laying down the conditions governing the preparation, placing on the market and use of medicated feeding-stuffs.
g) Inactivated immunological veterinary medicinal products which are manufactured from pathogens and antigens obtained from an animal or animals from the same holding and used for the treatment of that animal or the animals of that holding in the same locality.
h) Veterinary medicinal products based on radioactive isotopes; additives in feedingstuffs and supplementary feedingstuffs covered by other legislation.

The Icelandic Medicines Agency may decide that specific medicinal products shall have marketing authorisations as provided for in Article 2, even if covered by paragraph 1.

Article 4.
Authorisation for use of a medicinal product without a marketing authorisation based on an application by a physician or dentist.

The Icelandic Medicines Agency may, after receiving a reasoned application from a physician or dentist and on the latter's responsibility, grant authorisation to use a medicinal product which does not have a marketing authorisation, *cf.* Article 2. The Icelandic Medicines Agency shall set detailed instructions for handling such applications, which must be published on the Agency's website together with the application form.

Article 5

Special authorisation for use of a medicinal product based on an application from a veterinarian.

The Icelandic Medicines Agency may, after receiving a reasoned application from a veterinarian and on the latter‘s (personal) responsibility, grant authorisation to use a veterinary medicinal product covered by Article 2 which does not have a marketing authorisation. Authorisation may be granted for a medicinal product which a veterinarian must use. The Icelandic Medicines Agency may also grant a veterinarian authorisation to use a medicinal product with or without marketing authorisation for purposes other than its registered indications or for other animal species than it is intended.

Authorisation according to paragraph 1 may not be granted for a veterinary medicinal product for animals if their products are used for human consumption, unless the medicinal product has a marketing authorisation in at least one Member State of the EEA Agreement and the active ingredient is on the list in Annexes I, II or III of Regulation (EEC) 2377/90. The Icelandic Medicines Agency may, however, derogate from this provision if serious epidemics arise in animals and a suitable medicinal product with a marketing authorisation within the EEA is not available.

Article 6

Exemptions from the requirement for a marketing authorisation in exceptional circumstances.

The Icelandic Medicines Agency may, on the basis of a marketing authorisation in another Member State of the EEA Agreement, according to Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC, and if the requirements of the Medicinal Products Act for granting a marketing authorisation are satisfied, issue a marketing authorisation for a medicinal product which has been removed from the register or for which no marketing authorisation has been sought, if the Icelandic Medicines Agency considers it justified on grounds of national health or public interest to have the medicinal product in question on the market.

If the Icelandic Medicines Agency grants an authorisation according to paragraph 1, the Agency must ensure that provisions of the Medicinal Products Act and Regulations adopted on its basis, concerning labelling and package leaflets, dispensing classification of the medicinal product, advertisements and pharmacovigilance are satisfied.

If the Icelandic Medicines Agency intends to avail itself of the authorisation according to paragraph 1, it must notify the holder of the marketing authorisation in the state where the medicinal product is registered of its intention and at the same time request a copy of the evaluation report and the valid marketing authorisation of the medicinal product from the authorities in that state.

The Icelandic Medicines Agency may authorise temporary distribution of a medicinal product for which a marketing authorisation has not been granted, provided it is intended to protect against bacteria, toxins, chemical agents or nuclear radiation which are believed or known to have spread or to be likely to do so.

The Icelandic Medicines Agency may grant other exemptions from the requirement for a marketing authorisation in exceptional circumstances (compassionate use).

The Icelandic Medicines Agency shall notify the EFTA Surveillance Authority of medicinal products for which it has granted an authorisation on the basis of paragraph 1, and of all modifications made to such an authorisation or if it is cancelled temporarily or permanently.

Article 7

Information disclosure concerning medical products exempt from the requirement for a marketing authorisation.

Any party placing on the market a medicinal product according paragraph 1 of Article 3 must, if requested, inform the Icelandic Medicines Agency of the nature and scope of the activity. The same shall apply to any party granted an authorisation to use a medicinal product without a marketing authorisation, according to Article 4 or 5 as appropriate.

CHAPTER III

Application for a marketing authorisation.

A. General provisions.

Article 8

Rules on applications for a marketing authorisation etc.

The provisions of this Chapter shall apply to applications for a marketing authorisation while Chapter V shall apply to handling of applications. If approval is sought for a medicinal product based on a marketing authorisation issued in another Member State of the EEA Agreement, the rules of Chapter IV shall also apply. In the case of a medicinal product for which approval is sought on the basis of a marketing authorisation issued by the European Commission, only the provisions of Chapter VI shall apply.

Article 9

Special definitions.

For the purposes of this Chapter, the following meanings shall apply:

a) *The name of the medicinal product*: The name given to a medicinal product, which cannot be confused with the common name, or a common or scientific name, together with a trade mark or the name of the manufacturer.
b) *Generic name:* The international non-proprietary name (INN) recommended by the World Health Organisation or, if one does not exist, the usual common name.
c) *Strength of the medicinal product:* The content of the active substances expressed quantitatively per dosage unit, per unit of volume or weight according to the dosage form.
d) *Immediate packaging:* The container or other form of packaging immediately in contact with the medicinal product.
e) *Outer packaging:* The packaging into which the immediate packaging is placed.
f) *Labelling:* Information on the immediate or outer packaging.
g) *Package leaflet/instructions for use:* A leaflet containing information for the user which accompanies the medicinal product.

B. Application requirements.

Article 10

Applicant, location and requirement for an agent.

An application for a marketing authorisation must be submitted to the Icelandic Medicines Agency by the prospective holder of the marketing authorisation or its agent. If an applicant is not established within the European Economic Area the application must be submitted by an agent of the applicant according to Article 96.

Article 11

Minimum application requirements.

An application for a marketing authorisation must provide the information and documentation on quality, safety and efficacy of a medicinal product provided for in applicable rules and which is considered necessary to assess whether the risk-benefit balance of the medicinal product is positive.

Applications must be submitted to the Icelandic Medicines Agency on application forms available there. A single copy of supporting documentation and data for an application shall be submitted, unless otherwise specified, together with a receipt for payment of the fee for a marketing authorisation.

Article 12

Data and supporting documents for an application.

An application for a marketing authorisation must be accompanied by the following particulars and documents:

a) Administrative data.
b) Name of the medicinal product.
c) Qualitative and quantitative information on all the contents of the medicinal product, including a reference to its international generic name recommended by the World Health Organisation, if available, or a reference to the relevant chemical name.

d) An assessment of possible environmental risk resulting from the product and proposals to limit the risk. The impact shall be assessed and specific measures taken in each case to reduce it.
e) A description of the method of production.
f) Therapeutic indications, contraindications and adverse reactions.
g) Posology, pharmaceutical form, method and route of administration and estimated shelf life.
h) Reasons for precautionary and safety measures, which need to be taken when a medicinal product is stored, administered to patients or waste is disposed of, together with suggestions of possible risk to the environment which could result from the medicinal product.
i) Description of the control methods employed by the manufacturer.
j) Results of pharmaceutical (physico-chemical, biological or microbiological) tests, pre-clinical (toxicological and pharmacological) tests and clinical trials and, with regard to medicinal products for human consumption, a declaration that clinical trials which have been conducted outside the European Union fulfil the ethical requirements laid down in Directive 2001/20/EC.
k) A detailed description of pharmacovigilance and, if applicable, the risk management system which the applicant intends to implement.
l) A statement, according to paragraph 1 of Article 88, that the applicant employs the services of a party who is responsible for the undertaking‘s pharmacovigilance.
m) A proposal for a summary of product characteristics, in accordance with the provisions of subchapter C.
n) Proposals for labels for the immediate and outer packaging, in accordance with the provisions of subchapter D.
o) A proposal for a package leaflet, in accordance with the provisions of subchapter E.
p) Certificates/documents showing that the manufacturer holds a valid authorisation in its own country to produce the medicinal product.
q) Copies of marketing authorisations which the product has been granted in the EEA or a third country, together with a list of those states where a marketing application for the medicinal product is under examination.
r) Copies of the summaries of product characteristics and package leaflets approved in an EEA Member State or proposals for summaries of product characteristics and package leaflets submitted there for approval.
s) If an application for a marketing authorisation has been refused or withdrawn in any EEA Member State or third country, notification must be given thereof and the reasons for such a decision.
t) Copies of all designations of a medicinal product as an orphan medicinal product, as referred to in Regulation (EC) No. 141/2000 of the European Parliament and of the Council from 16 December 1999, on orphan medicinal products, together with a copy of the relevant opinion of the European Medicines Agency.

The form and contents of the application shall in other respects comply with the guidelines of the European Commission (“Notice to Applicants for marketing authorisation for medicinal products for human use” and, in the case of veterinary medicinal products, “Notice to Applicants for marketing authorisation for veterinary medicinal products”) currently in effect, *cf.* Annex 1 to Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC or, in the case of a veterinary medicinal product, Annex 1 of Directive 2001/82/EC, as amended by Directive 2004/28/EC and Directive 2009/9/EC.

The information referred to in items q), r) and s) of paragraph 1 must be updated on a regular basis while the application is being evaluated by the Icelandic Medicines Agency. Prior to the issuance of a marketing authorisation samples of the medicinal product in its final form must be submitted.

Article 13

Special requirements for an application for a veterinary medicinal product

An application for a marketing authorisation for veterinary medicinal products must also be accompanied by, in addition to the documentation listed in Article 12:

a) An assessment of the potential risk the medicinal product could pose to the environment or to human and animal health with normal use, the report on which this assessment is based, and proposals to limit such risk.
b) A proposal for the withdrawal period from the time the medicinal product is administered until products of the animal can be utilised without danger to human health. Necessary reports shall be included which justify a reasonable withdrawal period and propose maximum residue limits (MRLs) for slaughter products, eggs and milk.
c) Copies of documentation submitted to the European Commission in accordance with the provisions of Regulation (EEC) No. 2377/90, when a medicinal product for which a marketing authorisation is sought contains a new active substance which is not listed in Annexes I, II or III to Regulation (EEC) No. 2377/90.

With regard to the provisions of item b) of paragraph 1, the Icelandic Medicines Agency may require that an application be accompanied by a description of a suitable method of measurement to enable the monitoring of maximum residue limits in products.

In special instances when application is made for a marketing authorisation for an immunological veterinary medicinal product, an applicant may be exempted from the requirement for certain tests on the animal species for which the medicinal product is intended if the said tests cannot be carried out on the basis of EEA legislation.

Article 14
Simplified application.
(Generic medicinal product).

Toxicological, pharmacological and clinical data will not be required, *cf.* item j) of paragraph 1 of Article 12, if an applicant can demonstrate that a medicinal product is a generic version of a reference medicinal product which holds or has held a valid marketing authorisation in Iceland or the European Economic Area for no less than eight years (simplified application). If a marketing authorisation has not been granted for the reference medicinal product in Iceland, the applicant must specify in its application in what EEA Member State the reference medicinal product holds or has held a valid marketing authorisation.

A generic medicinal product, for which a marketing authorisation has been granted in accordance with paragraph 1, may not be marketed until ten years have passed since the original marketing authorisation was obtained for the reference medicinal product.

The ten-year period according to paragraph 2 may be extended to a maximum of 11 years if the marketing authorisation holder is granted, during the first eight of these ten years, authorisation for one or more new indications for use, which are considered to involve a substantial clinical advantage compared to available treatments. If an application is submitted for new indications for a substance which has a well established use, data exclusivity shall furthermore be provided for a period of one year, which may not be extended, provided that extensive preclinical or clinical trials have been carried out in connection with the new indication.

When a medicines control agency in the respective state within the European Economic Area where an application for a generic medicinal product is submitted requests confirmation that the reference medicinal product has or has had a marketing authorisation in Iceland, and that information be provided on the composition of the reference medicinal product and, if necessary, information on other documentation, such confirmation or information must be provided within one month of the receipt of such request.

If a medicinal product is not covered by the definition of a generic medicinal product, or if it is not possible to show through tests of bioavailability that it is equivalent to the reference medicinal product, or if amendments have been made to the active substance or substances, indications, concentration, pharmaceutical form or route of administration compared to the reference medicinal product, the conclusions of relevant toxicological, pharmacological and clinical tests must be submitted.

If a biological medicinal product fails to fulfil all the conditions to be considered a generic medicinal product, in particular due to discrepancies connected to the raw materials or to a difference in the manufacturing process of the biological medicinal product and the biological reference

medicinal product, the conclusions of relevant tests to fulfil requirements of safety (preclinical trials) or efficacy (clinical trials) or both must be submitted.

Carrying out of tests and trials, which are necessary in connection with the application of this provision and actual requirements resulting from them, shall not be considered to infringe against patent rights or supplementary protection certificates for medicinal products.

This provision shall not limit the obligation to submit relevant toxicological, pharmacological or clinical tests on a medicinal product in the case of new indications for its use, new posology or new routes of administration.

If a change in the classification of a medicinal product has been approved based on extensive preclinical or clinical trials, the Icelandic Medicines Agency shall not take into consideration the results of these tests for a period of one year after the change was originally approved when it evaluates an application by another applicant or holder of a marketing authorisation for changes in classification of the same substance.

A medicinal product for which a marketing authorisation has been granted according to Article 67 shall enjoy data exclusivity for eight years and market protection for ten years, which shall be extended to 11 years if the marketing authorisation holder obtains, during the first eight years of this ten-year period, approval for one or more new indications which can be considered a significant advantage over the treatment currently available.

If a medicinal product intended for animals for human consumption contains a new active substance which was not approved within the EEA prior to 30 April 2004, the ten-year period of data exclusivity shall be extended by one year for each amendment to a marketing authorisation which implies recognition of use of the medicinal product for another species for human consumption, if such amendment is authorised within five years from the time the original marketing authorisation was granted. This period shall not, however, be longer than 13 years in total in the case of a marketing authorisation valid for four or more animal species which provide products for human consumption. The extension of the ten-year period to 11, 12 or 13 years for veterinary medicinal products intended for animal species which provide products for human consumption shall only be authorised if the holder of the marketing authorisation originally applied for a decision on MRLs for those species included under the scope of the application.

The above-mentioned time limits for data exclusivity apply to reference medicinal products for which application is made within the EEA after 1 November 2005.

Article 15

Well established use.

Toxicological, pharmacological and clinical data will not be required, *cf.* item j) of paragraph 1 of Article 12, if an applicant can demonstrate that there is at least a ten-year well established therapeutic use of the active substances in the medicinal product within the EEA, that their efficacy is recognised and their safety is satisfactory, having regard to the requirements laid down in Annex 1 to Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC.

The same shall apply to natural medicinal products for veterinary use, but having regard to the requirements laid down in Annex 1 to Directive 2001/82/EC, as amended by Directive 2004/28/EC and Directive 2009/9/EC. In the case of veterinary medicinal products, no demands will be made for the data listed in items a) and b) of paragraph 1 of Article 13.

An applicant as referred to in this provision shall instead of the data referred to in paragraphs 1 and 2 provide relevant scientific publications instead of conclusions from research and trials.

An applicant may refer to an evaluation report published by the European Medical Agency on maximum residue limits as provided for in Regulation (EEC) No. 2377/1990.

Article 16

Combinations.

In the case of medicinal products, which contain active substances which are used in the combination for which authorisation has been obtained, but which have up until now not been used in combination for therapeutic purposes, then as provided for in item j) of paragraph 1 of Article 12 for a medicinal product with a marketing authorisation, conclusions must be submitted from new preclinical trials or new clinical trials connected with this combination. It is not necessary to submit scientific

references connected with each of the individual active substances. For veterinary medicinal products, documentation must be submitted on a withdrawal period for the new combination.

Article 17

Approval of marketing authorisation holder.

Physical and chemical data, biological and microbiological data, data on toxicological and pharmacological tests and other tests on the efficacy of the medicinal product (preclinical tests) as well as clinical data, *cf.* item j) of paragraph 1 of Article 12 for a medicinal product with a marketing authorisation, can be referred to if an applicant can:

a) demonstrate that a generic medicinal product has the same qualitative and quantitative composition of active substances and the same pharmaceutical form as a medicinal product with a marketing authorisation in the European Economic Area and
b) the marketing authorisation holder for the medicinal product referred to has granted its approval for reference to be made to this data in the discussion of the application.

If the application concerns a medicinal product for a food-producing animal species, data from safety tests and test of medicinal product residues may be used in the same manner, *cf.* paragraph 1.

Article 18

Summaries and reports.

To support the documentation listed in Articles 12 and 13, summaries and reports of experts shall be included on:

a) Physical and chemical, biological and microbiological data.
b) Summaries and reports on toxicological studies and studies of pharmaco-dynamics/pharmacokinetics.
c) Clinical data.

The above reports must be prepared by qualified experts in the subjects concerned, as provided for in Annex 1 to Directive 2001/83/EC and Annex 1 to Directive 2001/82/EC. The author must sign each report. A brief curriculum vitae of the expert shall be attached.

C. Summary of Product Characteristics (SPC).

Article 19

Proposal for a summary of product characteristics (SPC) for a medicinal product for human use.

The proposal for a summary of product characteristics shall contain the following information in the order specified below:

1. Name of the medicinal product, strength and pharmaceutical form.
2. Qualitative and quantitative composition in terms of the active substances and constituents of the excipients, 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 information:
   - 4.1. indications,
   - 4.2. posology and method of administration for adults and, if necessary, for children,
   - 4.3. counter-indications,
   - 4.4. special 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,
   - 4.5. interactions with other medicinal products and other interactions,
   - 4.6. use during pregnancy and lactation,
   - 4.7. effect on ability to drive a vehicle and operate machinery,
   - 4.8. adverse reactions,
   - 4.9. overdose (symptoms, emergency measures, antidotes).
5. Pharmacological characteristics:
   - 5.1. pharmacodynamic characteristics,
   - 5.2. pharmacokinetic characteristics,

5.3. preclinical safety data.

6. Pharmaceutical particulars:
   6.1. list of excipients,
   6.2. major incompatibilities,
   6.3. shelf life, when necessary, after reconstitution of the medicinal product or when the immediate packaging is opened for the first time,
   6.4. special precautions for storage,
   6.5. nature and contents of the immediate packaging,
   6.6. special precautions for disposal of opened medicinal products or waste materials derived from such medicinal products, if appropriate.
7. Marketing authorisation holder.
8. Number of the marketing authorisation.
9. Date of first issue of the marketing authorisation or of its renewal.
10. Date of the latest review 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.

With respect to the granting of a marketing authorisation according to Article 14, those parts of the summary of product characteristics referring to indications or pharmaceutical forms, which were still covered by patent rights at the time the generic medicinal product was placed on the market, need not be included.

Article 20

A proposal for a summary of product characteristics (SPC) for a veterinary medicinal product.

The proposal for a summary of product characteristics for a veterinary medicinal product must include the information listed in Article 19, with the exception of those particulars mentioned in items 4, 5.3, 11 and 12. Item 4 of the summary of product characteristics for a veterinary medicinal product shall include the following information in the order specified below:

4. Clinical information:
   4.1. target species,
   4.2. therapeutic indications, specifying the target species,
   4.3. counter-indications,
   4.4. special precautions for each target species,
   4.5. special precautions for use, including special precautions to be taken by the person administering the medicinal product to animals,
   4.6. adverse reactions (frequency and seriousness),
   4.7. use during pregnancy and lactation or laying time,
   4.8. interactions with other medicinal products and other interactions,
   4.9. posology and method of administration,
   4.10. overdose (symptoms, emergency procedures, antidotes) if necessary,
   4.11. withdrawal periods for various foods, including foods where the withdrawal period is zero days.

With respect to the granting of a marketing authorisation as referred to in Article 14, those parts of the summary of product characteristics referring to indications or pharmaceutical forms, which were still covered by patent rights at the time the generic medicinal product was placed on the market, need not be included.

D. Labelling.

Article 21

Outer packaging.

The following information must 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, its strength and pharmaceutical form and, if applicable, whether it is intended for infants, children or adults. If the medicinal product contains three active substances or fewer, the international non-proprietary names (INNs) shall be specified, or the common name if the former is not available. The proprietary name of the medicinal product shall not be liable to confusion with the generic name of the product or other medicinal products, or liable to risk of incorrect use of the medicinal product. If a medicinal product is available in several pharmaceutical forms and/or strengths, the pharmaceutical form and/or the strength must be included in the name of the medicinal product. The name of the medicinal product must also appear on the packaging in Braille, together with its strength, if the medicinal product is available in more than one strength. The marketing authorisation holder must ensure that patients‘ associations can obtain the package leaflet in a form which is accessible to the blind and visually handicapped, if requested.
b) All active substances and their concentrations shall be specified. The concentration shall be indicated per dosage unit or given volume or weight, depending upon the pharmaceutical form.
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 recognized action or effect according to the guidelines published by the European Commission on excipients (“Notice to Applicants”). If the product is injectable, or a topical or eye preparation, all excipients must be stated.
e) Instructions for use, including the method and, if necessary, the route of administration. The packaging must have a space to specify the prescribed dosage.
f) A special warning that the medicinal product must be stored out of reach of children.
g) Special warnings, if this is necessary.
h) The expiry date.
i) Special storage precautions.
j) Instructions on the disposal of unused medicinal products or packaging, if applicable, together with a reference to an appropriate disposal system.
k) The name and address of the holder of the marketing authorisation for the medicinal product and agent if applicable.
l) The number of the marketing authorisation (MT no.).
m) The manufacturer‘s batch number.
n) In the case of non-prescription medicinal products, instructions on use.
o) Other information of significance for the correct use of the medicinal product.

Article 22

Outer packaging of veterinary medicinal products.

Information as referred to in Article 21 shall also appear on the outer packaging of a medicinal product intended for veterinary use or on the immediate packaging if there is no outer packaging. The following information must be also provided:

a) The species for which the medicinal product is intended.
b) The withdrawal period, even if nil, in the case of veterinary medicinal products intended for food-producing animals.
c) The words “Veterinary medicinal product”.

If a medicinal product has been granted a centralised marketing authorisation, *cf.* Chapter VI, the Icelandic Medicines Agency may decide on labelling with detailed information for outer packaging concerning handling, storage, sale or precautions, as long as such information does not infringe against the EEA Agreement or the marketing authorisation, or appear to be an advertisement.

Article 23

Illustrations and symbols.

Outer packaging may have labelling with illustrations or symbols intended to explain in more detail the information listed in Articles 21 and 22, together with other information in accordance with the approved SPC of the medicinal product and which is useful to patients, excluding information which is considered an advertisement.

Article 24

Immediate packaging.

Information according to Articles 21 and 22 shall also appear on the immediate packaging of a medicinal product, unless the provisions of Article 25 or 26 apply.

Article 25

Immediate packaging, blister packs.

On blister packs, which are in outer packaging and which fulfil the requirements of Articles 21 and 22, the following information at least must appear:

a) Name of the medicinal product, *cf.* item a) of Article 21.
b) Strength and pharmaceutical form.
c) Name of the marketing authorisation holder.
d) Expiry date.
e) Manufacturer‘s batch number.
f) The label “Veterinary medicinal product”, if the medicinal product is intended exclusively for animals.

Article 26

Small immediate packaging.

When the immediate packaging of medicinal products is so small that the products cannot be labelled satisfactorily, according to Articles 21 and 22, at least the following information must appear:

a) Name of the medicinal product, *cf.* item a) of Article 21.
b) Route of administration, if necessary.
c) Concentration, if necessary.
d) Expiry date.
e) Manufacturer‘s batch number.
f) Contents by weight, volume or number of dosage units.
g) The label “Veterinary medicinal product”, if the medicinal product is intended exclusively for animals.

Article 27

Requirements of legibility and language.

The particulars referred to in Articles 21 and 26 shall be easily legible, as comprehensible as possible and indelible.

The particulars referred to in Articles 21 and 22 shall be in Icelandic, with the exception of the list of ingredients, *cf.* items b) and d) of Article 21, which may be in English or Latin. This provision shall not exclude labelling in other languages, as long as this includes the same information.

In the case of orphan medicinal products, if a reasoned application is made to this effect, the particulars specified in Article 21 may appear only in one of the official languages of the European Economic Area.

The Icelandic Medicines Agency may, in special circumstances, authorise labelling on packaging in English or a Nordic language.

Article 28

Requirements for special labelling.

The Icelandic Medicines Agency may require special labelling on the packaging of a medical product, concerning for instance:

a) The price of the medicinal product.
b) Information on the social security contribution.
c) Conditions for dispensing the medicinal product.
d) Identification.

In the case of a medicinal product with a centralised marketing authorisation, as provided for in Chapter VI, the Icelandic Medicines Agency shall comply with the guidelines issued by the European Commission for labelling and packaging.

Article 29

Labelling exemptions.

The Icelandic Medicines Agency may grant exemptions from the above requirements for labelling of specific particulars and from the requirement of labelling in Icelandic for specific medicinal products if the medicinal product is not dispensed directly to a patient for self-treatment, or to the owner or guardian of an animal for its treatment.

E. Package leaflets.

Article 30

Package leaflets.

Package leaflets with information intended for users shall be included in the packaging of all medicinal products. If space permits, this information may be printed on the packaging itself, provided this does not detract from the legibility of other labelling which is to appear on the packaging.

Article 31

Information in package leaflets and format.

The text of a package leaflet shall comply with an approved SPC and shall in other respects fulfil the conditions laid down in Articles 32-41.

If a medicinal product has been awarded a marketing authorisation as provided for in Chapter IV under varying proprietary names in other states of the EEA Agreement, the package leaflet must include a list of the proprietary names which have been authorised in each respective Member State.

The package leaflet must give the date of its latest review.

Article 32

Identification of a medicinal product.

The package leaflet shall include the following particulars for the identification of the medicinal product:

a) The name of the medicinal product, its strength and pharmaceutical form and, if applicable, whether it is intended for infants, children or adults. The generic name shall appear if the product contains only one active substance and if its name is a proprietary name.
b) The classification of the medicinal product or its type of activity, in terms easily comprehensible to the patient or owner of an animal.
c) The contents of the pharmaceutical form, including all active substances and excipients, and a statement of the active substances expressed quantitatively. The generic names shall be used.
d) The pharmaceutical form and strength, together with details of the contents by weight, by volume or by number of doses of the product, for each presentation of the product.
e) The name and address of the holder of the marketing authorisation and the manufacturer, as well as that of the Icelandic agent, if available.

Article 33

Therapeutic indications.

Information on approved indications for the medicinal product shall appear on the package leaflet.

The Icelandic Medicines Agency may decide that information on certain indications shall not appear on a package leaflet if such information could cause serious distress to a patient or is considered undesirable for other reasons.

Article 34

Warnings and precautionary rules.

The following information which is necessary for a patient before taking the medicinal product shall appear on the package leaflet:

a) Contra-indications.
b) Precautions for use.
c) Forms of interaction with other medicinal products and other substances (e.g. alcohol, tobacco, foods) which may affect the action of the medicinal product.
d) Special warnings, taking into consideration:

1) Certain categories of patients (e.g. children, pregnant or breastfeeding women, the elderly, persons with specific pathological conditions).
2) Effects on the ability to drive vehicles or operate machinery.
3) Those excipients, knowledge of which is important for the safe and effective use of the medicinal product and included in the guidelines of the European Commission ("Notice to Applicants") on excipients.

Article 35

Information on the proper use of the medicinal product.

Information must appear on the package leaflet on the proper use of the medicinal product, including the following in particular:

a) The dosage.
b) Instructions for use.
c) The frequency of administration and other necessary information on treatment with the medicinal product. If necessary, the following shall also be mentioned:
    1) The duration of treatment, where it should be limited.
    2) Actions to be taken in the case of an overdose (symptoms and treatment of an overdose).
    3) Information on what to do if one or more doses have been forgotten.
    4) Information on the danger of withdrawal effects when treatment ceases or is altered.
    5) Special instructions to consult a physician or pharmacist, as appropriate, to obtain further information on use of the medicinal product.

Article 36

Adverse reactions.

Adverse reactions which can occur under normal use of the medicinal product and suitable actions in response shall be described on the package leaflet.

The user shall be expressly encouraged to communicate any serious adverse reactions and undesirable effects which are not mentioned in the leaflet to a physician (dentist) or pharmacist.

The owner or guardian of an animal shall be encouraged to notify a veterinarian of any undesirable effects of a medicinal product.

Article 37

Storage conditions and other information.

A reference to the expiry date shall be indicated on the package leaflet with:

a) A warning against using the product after this date.
b) Special storage precautions as appropriate.
c) Information on possible visible signs of deterioration.
d) A full statement of the active substances and excipients expressed qualitatively and a statement of the active substances expressed quantitatively, using their common names, in the case of each presentation of the medicinal product.
e) The pharmaceutical form and the contents by weight, volume or number of doses of the product, in the case of each presentation of the product.
f) The name and address of the holder of the marketing authorisation and, as applicable, names of agents.
g) The name and address of the manufacturer.

Article 38

Illustrations and symbols.

Special symbols or illustrations may be used to further clarify the information in Articles 31-37 and other information which accords with the approved SPC and is useful to patients without in any way being an advertisement.

Article 39

Package leaflets for veterinary medicinal products.

Package leaflets with information intended for animals‘ owners or guardians shall be included in the packaging of veterinary medicinal products. If space permits, this information may be printed on the packaging itself, provided this does not detract from the legibility of other labelling which is to appear on the packaging.

Package leaflets for veterinary medicinal products shall in addition to the information listed in Articles 31-37 include the following particulars:

a) The animal species for which the medicinal product is intended, method of administration and instructions for use as necessary.
b) The withdrawal period, even if nil, in the case of veterinary medicinal products for animals intended for human consumption.
c) Instructions on the handling and disposal of used or expired medicinal products as appropriate.

Article 40

Requirements of legibility and language.

The information on package leaflets must be written so as to be clear and comprehensible to the consumer and owner or guardian of an animal. The information must be in Icelandic. This provision shall not exclude labelling in other languages, as long as this includes the same information.

The package leaflet shall reflect consultation with target groups of patients to ensure that it is easily legible, clear and simple to use.

To ensure access to necessary medicinal products and information on these products, the Icelandic Medicines Agency may authorise information on package leaflets in English or a Nordic language, provided the information in question is available in Icelandic on the website of the Icelandic Medicines Agency and can be printed out in a pharmacy and provided to the patient when the medicinal product concerned is dispensed. When the patient receives the package leaflet he/she shall be informed that this is an Icelandic translation of the package leaflet.

Article 41

Exemptions.

The Icelandic Medicines Agency may grant an exemption from the provision of certain particulars on the package leaflet and from having the package leaflet in Icelandic if the medicinal product is not dispensed directly to a patient for self-treatment or to the owner or guardian of an animal for its treatment.

F. Renewal and transfer of a marketing authorisation.

Article 42

Application for renewal of a marketing authorisation.

An application for renewal of a marketing authorisation for a medicinal product must be sent to the Icelandic Medicines Agency no later than 180 days before the authorisation expires.

An applicant must submit, for instance, updated documentation on the quality, safety and efficacy of the medicinal product, including documentation concerning any changes which have been made since the marketing authorisation was granted.

The marketing authorisation will be renewed if it can be concluded from the application documentation that the risk-benefit balance of the medicinal product is positive.

The Icelandic Medicines Agency shall provide further instructions on the requirements for documentation when application is made for renewal of a marketing authorisation. The provisions of Chapter V shall apply to the procedure.

Article 43

Application for transfer of a marketing authorisation.

An application to transfer a marketing authorisation to a new authorisation holder shall be sent to the Icelandic Medicines Agency at least 90 days before the transfer.

The marketing authorisation holder and the party to which the authorisation is to be transferred must attest with their signatures that the documentation, which is considered necessary in the

assessment of the Icelandic Medicines Agency for the transfer, is correct and genuine and, as appropriate, complies with Regulation (EC) No. 2141/96.

CHAPTER IV
Recognition on the basis of a marketing authorisation from other EEA Member States.

Article 44
Basis for recognition.

Mutual recognition procedure: A marketing authorisation granted by a reference Member State may be used as a basis for recognition of a medicinal product for which a marketing authorisation is sought. An application for a marketing authorisation based on such recognition must be sent to the Icelandic Medicines Agency in accordance with the requirements of this Chapter and Chapter III.

Article 45
Documentation on the medicinal product and procedure.

An applicant must demonstrate that the documentation which is provided with an application is identical to that which the reference Member State has recognised and to the documentation which was made available in other EEA Member States concerned.

"Reference Member State" shall mean a Member State of the EEA Agreement which has prepared an assessment of a specific medicinal product and issued a marketing authorisation which forms the basis for its recognition in another Member State of the EEA Agreement.

A "participating Member State" shall mean a Member State of the EEA Agreement to which application has been made for recognition of the assessment and the marketing authorisation of the reference Member State.

An applicant for a marketing authorisation for a medicinal product in more than one EEA Member State must request that one EEA Member State assume the role of a reference Member State and prepare an assessment report for the medicinal product.

If a marketing authorisation has already been granted when an application is submitted, the Icelandic Medicines Agency shall recognise the marketing authorisation granted by the reference Member State. To this end the holder of a marketing authorisation shall request that the reference Member State prepare an assessment report or, if necessary, update an existing assessment report. The reference Member State shall prepare an assessment report or update it within 90 days of receipt of a valid application. The assessment report, together with an approved SPC, labelling and package leaflet, must be sent to the states concerned and to the applicant.

Decentralised procedure: If a marketing authorisation has not been granted in any EEA Member State when an application is submitted, and the applicant is concurrently applying for a marketing authorisation in more than one EEA Member State, identical applications shall be submitted to the states where a marketing authorisation is sought in accordance with the provisions of Chapter III. The application must be accompanied by a list of all the states where application has been made for a marketing authorisation. In its application, the applicant shall request one Member State to act as "reference Member State" and to prepare an assessment report on the medicinal product and drafts of an SPC, labelling and package leaflet. The reference Member State shall prepare these draft documents within 120 days after receipt of a valid application and shall send them to the concerned Member States and to the applicant.

An application for a marketing authorisation for a veterinary medicinal product according to paragraph 6 must include an assessment as to whether the requirements of paragraph 11 of Article 14 are satisfied.

Article 46
Information provision to the European Medicines Agency (EMA).

An applicant must, in tandem with submitting an application, inform the European Medicines Agency (EMA), either through the Committee for Medicinal Products for Human Use (CHMP) or the Committee for Medicinal Products for Veterinary Use (CVMP), that an application has been submitted as well as information on EEA Member States where applications have been submitted. An applicant must provide the date of the application and send the Agency a copy of a marketing authorisation issued by the reference Member State. In addition, an applicant must send the Committee referred to in

the first sentence a copy of all marketing authorisations which have been granted for the medicinal product in question in other EEA Member States and provide information on other applications which are being processed.

Article 47

Decision on recognising a medicinal product.

The Icelandic Medicines Agency shall recognise the medicinal product based on the decision of the reference Member State within 90 days of receiving the assessment of that state and an approved SPC, labelling and package leaflet, unless recognition of the medicinal product could, in the estimation of the Icelandic Medicines Agency, pose a serious threat to human health in general. The Icelandic Medicines Agency may refuse to recognise a veterinary medicinal product if the product could, in the estimation of the Icelandic Medicines Agency, pose a serious threat to human or animal health.

The Icelandic Medicines Agency shall issue a marketing authorisation for a medicinal product which has been recognised no later than 30 days after an agreement is reached between the reference Member State and participating Member States. The Icelandic Medicines Agency shall concurrently notify the reference Member State of its decision.

Article 48

Objections to documentation submitted on medicinal products.

If the Icelandic Medicines Agency is of the opinion that it cannot approve an assessment report, SPC, labelling and package leaflet within the period laid down in Article 47, for reasons which concern a potential serious risk to public health, the Agency must send the reference Member State, other participating Member States and the applicant detailed grounds for its position.

The points of disagreement shall forthwith be referred to the co-ordination group of medicines control agencies in the European Economic Area, which is located at the EMA. The applicant shall be given the opportunity to make its point of view known orally or in writing, as provided for in the procedure laid down in Article 29 of Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC.

If agreement is reached within 60 days of the communication of the points of disagreement referred to in paragraph 1, the reference Member State shall record the agreement, close the procedure and inform the applicant accordingly. The Icelandic Medicines Agency shall then issue a marketing authorisation for the medicinal product within 30 days.

Article 49

Referral procedure to resolve disputes.

If no agreement can be reached in the co-ordination group according to Article 48 within 60 days, the matter shall be referred to the relevant EMA committee (CHMP or CVMP) for resolution in accordance with the procedure laid down in Articles 32, 33 and 34 of Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC, or Articles 36, 37 and 38 of Directive 2001/82/EC, as amended by Directive 2004/28/EC.

In the circumstances referred to in paragraph 1, Member States which have approved the assessment report, the draft SPC and the labelling and package leaflet may, at the applicant‘s request, grant an authorisation for the medicinal product without waiting for the outcome of the procedure; the authorisation granted shall be valid until a final outcome according to paragraph 1 is available. In that event, the authorisation granted shall be without prejudice to the outcome of that procedure.

Article 50

Submission of documentation on a medicinal product in the case of disputes.

As soon as the applicant is informed that a disputed case has been referred to the EMA for resolution, according to Article 49, it must send the relevant Committee of the Agency, according to paragraph 1 of Article 49, which is intended to discuss the case, copies of documentation submitted according to Articles 12 and 13.

When the decision of the European Commission in cases of dispute is available, in accordance with the procedure in Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC

and Directive 2004/27/EC or Directive 2001/82/EC, as amended by Directive 2004/28/EC, the Icelandic Medicines Agency shall take the appropriate decision within 30 days.

CHAPTER V
Procedures relevant to the marketing authorisation.
A. Handling of an application.

Article 51
Valid application.

A valid application for a marketing authorisation is considered to have been received when the Icelandic Medicines Agency has ascertained that the application complies with requirements.

If an application is not considered valid, the Icelandic Medicines Agency shall inform the applicant as to which requirements are not deemed to be satisfied. In such cases, the applicant may withdraw its application within 30 days of the date of the notification or request to submit additional documentation or data.

Article 52
Handling of an application.

The Icelandic Medicines Agency shall make a preliminary examination of an application and obtain all information considered necessary for an application to be able to be considered. If the Icelandic Medicines Agency considers that the requirements for granting a marketing authorisation are not satisfied, it shall inform the applicant thereof and grant it a suitable time limit to express its opinion or withdraw its application before the Icelandic Medicines Agency confirms receipt of the application.

Article 53
Time limits in application procedure.

A decision on the approval or refusal of authorisation for a medicinal product must be taken within 210 days of the submission of a valid application, *cf.* Article 59. If the Icelandic Medicines Agency requests that an applicant rectify any deficiencies in an application, the time limit shall be extended until rectification has been made.

If an application is based on a marketing authorisation issued in another state of the EEA Agreement, the rules in Chapter IV shall apply.

Article 54
Suspension of application procedure due to an application in another EEA Member State.

The Icelandic Medicines Agency may suspend examination of an application in cases where an application has been sought for a marketing authorisation for the same medicinal product in another EEA Member State, unless the application has been submitted in accordance with the rules in Chapter IV.

If examination has been suspended for this reason the Icelandic Medicines Agency shall inform the reference Member State and the applicant thereof.

Article 55
Suspension of application procedure due to a marketing authorisation granted in another EEA Member State.

If another EEA Member State has already granted a marketing authorisation for a medicinal product which is the subject of an application for a marketing authorisation in Iceland, the Icelandic Medicines Agency shall suspend its examination of the application, unless the application has been submitted in accordance with the rules in Chapter IV.

Article 56
Referral procedure to resolve different decisions by EEA Member States.

In instances where EEA Member States have taken different decisions on the authorisation, temporary suspension or revocation of a marketing authorisation for a medicinal product, the Icelandic

Medicines Agency, European Commission, applicant or marketing authorisation holder may refer the case to the relevant EMA Committee (CHMP or CVMP) to resolve the disagreement in accordance with the procedure laid down in Articles 32, 32 and 34 of Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC, or Articles 36, 37 and 38 of Directive 2001/82/EC, as amended by Directive 2004/28/EC.

Article 57

Referral to resolve disagreement in other special instances.

The Icelandic Medicines Agency, European Commission, applicant or holder of a marketing authorisation can also, in other special instances than those referred to in Article 56, refer a case for resolution in accordance with the same rules.

B. Granting of a marketing authorisation.

Article 58

Requirement for granting a marketing authorisation.

If an application satisfies the requirements for documentation on the quality, safety and efficacy of a medicinal product, a marketing authorisation shall be granted once the Icelandic Medicines Agency has approved the SPC, labelling and package leaflet and decided whether the medicinal product shall be subject to prescription, arrangements for dispensing, maximum amounts which may be prescribed and limitations on dispensing, as provided for in Chapter VII.

When the Icelandic Medicines Agency grants a marketing authorisation for a medicinal product the applicant will receive an approved SPC.

Article 59

Refusal to grant a marketing authorisation.

An application for a marketing authorisation shall be refused if:

a) The medicinal product is not considered to fulfil the requirements for quality, safety or efficacy.
b) The medicinal product is intended for food-producing animals and contains active substances which are not listed in Annexes I, II or III to Regulation (EEC) No. 2377/90, or if it is not possible to determine a maximum residue limit authorised.
c) The withdrawal period is not sufficient in length to ensure that animal products do not contain residues which could be dangerous to consumers or data is insufficient.
d) In the case of a veterinary medicinal product, the product is considered to present an unacceptable risk to human or animal health.
e) A veterinary medicinal product contains substances which may not be given to animals under other legislation.
f) The application does not fulfil currently applicable requirements and the deficiencies have not been rectified within a reasonable time limit as provided for in Article 51.
g) Documentation accompanying the application does not demonstrate a positive risk-benefit balance.

An application may not be rejected on the basis of labelling or a package leaflet, provided it complies in other respects with the requirements of Chapter III of this Regulation.

An applicant or holder of a marketing authorisation is responsible for the reliability of the documents and data submitted.

Although an application for a marketing authorisation may not be refused due to unsatisfactory labelling of the medicinal product or its package leaflet, as referred to in subchapters D and E of Chapter III, this shall be without prejudice to the general legal liability of the manufacturer or holder of the marketing authorisation.

Article 60

Special marketing authorisations.

The Icelandic Medicines Agency may, in exceptional circumstances, grant a marketing authorisation for a medicinal product which does not fulfil the requirements for documentation laid down in Chapter III, *cf.* Chapter IV.

Such special marketing authorisations will only be granted temporarily and may be subject to special conditions, including that the applicant undertake special obligations concerning in particular the safety of the medicinal product.

The application of this provision apply to medicinal products for human use must comply with the requirements laid down in Annex 1 to Directive 2001/83/EC, as amended by Directive 2003/63/EC, Directive 2004/24/EC and Directive 2004/27/EC.

A marketing authorisation granted with reference to this provision shall be valid for one year and may be renewed.

Information must be available on the conditions which apply to the marketing authorisation in question and the relevant time limits.

C. Revocation of marketing authorisations.

Article 61

Revocation, cancellation, amendment and invalidation of a marketing authorisation.

A marketing authorisation granted as provided for in Article 58 can be revoked, invalidated, suspended or amended if:

a) It is revealed that a medicinal product on the market in Iceland does not satisfy current acts and rules on medicinal products or the requirements for obtaining a marketing authorisation.
b) The medicinal product is no longer considered to fulfil the requirements for quality, safety or efficacy.
c) Information which has bee provided in connection with an application is incorrect or has not been amended in accordance with Chapter IX of this Regulation.
d) Quality control is not carried out in accordance with the requirements of an applicable quality description as provided for in rules.
e) The obligations laid down in Article 80 to make the necessary changes to production or control, or to an SPC, are not satisfied.
f) The withdrawal period for animals after administration of a medicinal product is no longer considered sufficient to ensure no residues remain in animal products which could be harmful to consumers.
g) Notification of the agent referred to in Article 96 was not sent within the specified time limits, after parties had been warned that such failure to comply with the time limits would result in revocation of the marketing authorisation.
h) The medicinal product is considered to be harmful under normal conditions of use.
i) The medicinal product does not possess therapeutic efficacy.
j) The risk-benefit balance is no longer positive for the conditions of use specified in the marketing authorisation.
k) The qualitative and quantitative composition of the medicinal product is not as specified.

If the provisions of Articles 21-41, on labelling and package leaflets, and instructions in this regard, are not complied with, the Icelandic Medicines Agency may revoke the marketing authorisation until the provisions on labelling and the package leaflet have been complied with.

If the Icelandic Medicines Agency, following an assessment of documentation on pharmacovigilance, decides that a marketing authorisation should be revoked, suspended, amended or invalidated, it must immediately notify the EMA, EEA Member States and the marketing authorisation holder.

If it is necessary to take actions to protect public health, the Icelandic Medicines Agency can suspend the marketing authorisation for a medicinal product. This must be notified to EMA, the European Commission and other EEA Member States no later than the next working day.

Article 62

Revocation of special marketing authorisations.

A special marketing authorisation granted according to Article 60 may be revoked in accordance with the rules of Article 61, as appropriate.

D. Grounds, notifications and publication.

Article 63

Assessment reports.

The Icelandic Medicines Agency prepares assessment reports and comments on the documentation of applications with regard to the outcome of toxicological, pharmaceutical and clinical studies on the medicinal product. The assessment reports must be reviewed and updated whenever new information is available which could be of significance for the quality, safety or efficacy of a medicinal product.

Article 64

Grounds and notifications.

When an application is refused according to Article 59, grounds for the refusal must accompany the notification to the applicant together with information on routes of appeal. The same shall apply when a marketing authorisation is revoked.

Article 65

Notifications to the European Medicines Agency (EMA).

When it grants a marketing authorisation as provided for in Article 58, the Icelandic Medicines Agency shall concurrently send a copy of the marketing authorisation and approved SPC to the EMA.

Article 66

Publication in the Legal Gazette.

A list of marketing authorisations issued shall be published in the Legal Gazette (Icel. *Lögbirtingablaðið*) and on the website of the Icelandic Medicines Agency. The same shall apply when a marketing authorisation is revoked.

CHAPTER VI

Rules on centralised marketing authorisations for medicinal products in the European Economic Area (EEA).

Article 67

Application for a centralised marketing authorisation for the EEA.

The EEA Agreement, Annex 2, Chapter XIII, No. 15zb, Regulation (EC) No. 726/2004, laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, as amended by Regulation (EC) No. 1394/2007, applies in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects, *cf.* Regulation No. 794/2010, on the entry into force of EU Regulations on medicinal products (X).

The EEA Agreement, Annex 2, Chapter XIII, No. 15zd, Regulation (EC) No. 507/2006, on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No. 726/2004, applies in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects, *cf.* Regulation No. 418/2008, on the entry into force of EU Regulations on medicinal products (VIII).

The EEA Agreement, Annex 2, Chapter XIII, No. 15zh, Regulation (EC) No. 1394/2007, on advanced therapy medicinal products and amending Directive 2001/83/EEC and Regulation (EC) No. 726/2004, applies in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects, *cf.* Regulation No. 418/2008, on the entry into force of EU Regulations on medicinal products (VIII).

The EEA Agreement, Annex 2, Chapter XIII, No. 15zj, Regulation (EC) No. 658/2007 concerning financial penalties for infringement of certain obligations in connection with marketing authorisations granted under Regulation (EC) No. 726/2004, enters into force in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects. The Icelandic Medicines Agency determines penalties in accordance with the proposal of the European Commission.

Medicinal products covered by the Annex to Regulation (EC) No. 726/2004, can only be granted a marketing authorisation in accordance with this chapter. Medicinal products covered by Regulation (EC) No. 726/2004 (Point 2 of Article 3), may be granted a marketing authorisation in the same manner.

Applications for marketing authorisations shall be sent to the EMA.

If the European Commission has taken a decision on a marketing authorisation according to paragraph 1, 2 or 3, the Icelandic Medicines Agency shall take the relevant decision within 30 days.

Article 68

Application for renewal and transfer of a marketing authorisation.

The EEA Agreement, Annex 2, Chapter XIII, No. 15l, Regulation (EC) No. 214/96 on handling of applications for the transfer of marketing authorisations covered by Regulation (EC) No. 726/2004, enters into force in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects.

The marketing authorisation holder shall send an application for transfer of a marketing authorisation which has been granted on the basis of Article 67 to the EMA.

The marketing authorisation holder shall send an application for renewal of a marketing authorisation which has been granted on the basis of Article 67 to the EMA in accordance with the provisions of the Regulation (EC) 726/2004.

If the European Commission has taken a decision on the renewal, transfer or revocation of a marketing authorisation according to paragraph 2 or 3, the Icelandic Medicines Agency shall take the relevant decision within 30 days.

Article 69

Publication in the Legal Gazette.

The provisions of Article 66 on publication in the Legal Gazette or on the website of the Icelandic Medicines Agency shall apply to the relevant decisions referred to in this chapter.

CHAPTER VII

Decision on prescription requirements, special reporting requirements and restrictions on dispensing medicinal products.

Article 70

Decision on dispensing arrangements.

When a medicinal product is granted a marketing authorisation the Icelandic Medicines Agency shall decide whether it should be subject to medical prescription and whether there should be any other restrictions on arrangements for dispensing the product. The Icelandic Medicines Agency shall also decide whether mixtures containing a medicinal product (i.e. medicinal products which do not have a marketing authorisation, e.g. officinal formula) shall be subject to prescription.

Article 71

Decision on prescription requirements for medicinal products for humans and veterinary medicinal products for non-food-producing animals.

The following aspects are of main consideration in determining whether medicinal products shall be subject to prescription:

a) If a medicinal product is likely to be able to cause damage to health either directly or indirectly, even when used correctly, if utilised without the supervision of a physician/dentist.
b) If the incorrect use of a medicinal product could cause damage to health either directly or indirectly.
c) If experience of the medicinal product is so brief that it can be assumed that the effects of the medicinal product and its adverse reactions are not fully known.
d) If the medicinal product is injectable and generally prescribed by a physician or dentist.

If the attention of the Icelandic Medicines Agency is drawn to new information it shall examine such and change the classification of a medicinal product as appropriate.

Article 72

Decision on exemption from prescription requirements for veterinary medicinal products for food-producing animals.

The Icelandic Medicines Agency may authorise the exemption of veterinary medicinal products intended for food-producing animals from prescription if all of the following conditions are met:

a) Administration of the veterinary medicinal product is limited to combinations which are used without special expertise or knowledge.
b) The veterinary medicinal product presents neither a direct or indirect risk to the animal or animals treated, for the person administering the product or for the environment, even if administered incorrectly.
c) The SPC for the veterinary medicinal product contains no warnings on potential serious adverse reactions from its proper use.
d) Neither the veterinary medicinal product nor other medicinal products containing the same active substance have previously been the subject of frequent notifications of serious adverse reactions.
e) The SPC does not mention any counter-indications in connection other veterinary medicinal products which are generally used without prescription.
f) The veterinary medicinal product does not require special storage conditions.
g) There is no risk for consumers from residues in products from animals which have received treatment, even if the veterinary medicinal product is used incorrectly.
h) There is no risk for healthy persons or animals with regard to developing immunities to antibiotics or antihelmintics, even if the medicinal product containing these substances is used incorrectly.

Article 73

Decision on special reporting requirements for medicinal products or other restrictions on dispensing.

The following factors are of main importance in determining special reporting requirements for medicinal products or other restrictions on dispensing, such as a decision on the maximum amount which may be prescribed in each instance:

a) The medicinal product contains a substance classified as a habit-forming or addictive substance under international conventions and national rules.
b) Incorrect use of the medicinal product can result in a serious risk of abuse or cause a habit and/or addiction, or there is a risk of illegal use of the medicinal product.
c) The medicinal product contains an active substance which, by reason of its novelty or properties, should have special reporting requirements as a precautionary measure.

Article 74

Restrictions on use of a medicinal product and its prescription.

The Icelandic Medicines Agency shall decide whether use of a medicinal product requiring prescription shall be limited only to hospitals and healthcare institutions, in which case this shall be specially indicated in pharmacopoeia. The Icelandic Medicines Agency may also limit authorisations to prescribe medicinal products to specialists in certain fields, in which case this shall be specially indicated in pharmacopoeia. The principal reasons for the above-mentioned restrictions are:

a) Because of its characteristics, use of a medicinal product outside of healthcare institutions is considered risky or it is considered safer to limit its use to healthcare institutions because of its novelty.
b) The medicinal product is used to treat conditions which must be diagnosed in specialised healthcare institutions with the necessary facilities, even though administration may then be carried out elsewhere.
c) The medicinal product is intended for outpatients but it is considered necessary, with regard to the action of the medicinal product and possible adverse reactions, that treatment be controlled by a specialist from beginning to follow-up.

CHAPTER VIII

Legal effect of marketing authorisations.

A. General provisions.

Article 75

Right to place on the market.

A marketing authorisation grants the holder of the authorisation the right to place a medicinal product on the market as a proprietary medicinal product as provided for in the authorisation and the decisions and rules which apply in other respects.

The marketing authorisation shall be valid for five years and renewable upon expiry, according to Article 42 or 68. Before a reassessment is made, the marketing authorisation holder must, at least six months prior to the expiration of the marketing authorisation according to paragraph 2, have submitted to the Icelandic Medicines Agency complete and updated documentation of the quality, safety and efficacy of the medicinal product, including all changes which have been made to it since the marketing authorisation was granted.

A marketing authorisation which is renewed on the basis of an application according to Article 42 shall be valid for an unlimited period if the marketing authorisation which was renewed was valid on 1 July 2006 or later.

The Icelandic Medicines Agency may decide, giving valid grounds concerning pharmacovigilance, that the renewed marketing authorisation shall be limited to a five-year period of validity.

A marketing authorisation shall become invalid if the medicinal product for which the authorisation was granted has not in fact been placed on the market within three years of its granting or if the medicinal product for which the marketing authorisation was granted and which was placed on the market has not in fact been on the market for a continuous three-year period. The Icelandic Medicines Agency may, in special circumstances and for reasons of public health, grant exemptions from this. Such exemptions must be supported by suitable grounds.

A marketing authorisation shall not affect the liability of the authorisation holder under other legislation.

Article 76

Prohibition against marketing of a medicinal product for which a marketing authorisation has been granted.

The Icelandic Medicines Agency may immediately ban the marketing of a medicinal product and demand that a medicinal product, for which a marketing authorisation has been granted, be removed from the market if it considers;

a) that the medicinal product is harmful with normal use; or
b) that the medical product does not have a therapeutic effect; or
c) that the risk-benefit balance is not positive under the conditions for use specified in the authorisation; or
d) that the qualitative and quantitative composition of the medicinal product is not as specified; or
e) that control testing has not been carried out of the medicinal product and/or its ingredients, or at intermediate production stages, or other requirements or obligations connected with the granting of the manufacturing authorisation have not been satisfied; or
f) if such deficiencies are revealed in the medicinal product that this is deemed to warrant revocation of its marketing authorisation.

If possible, the marketing authorisation holder shall be warned that such a decision is imminent. A decision on an immediate ban against the marketing of a medicinal product must be reasoned and information provided on routes of appeal.

The Icelandic Medicines Agency may prohibit the marketing of an individual production batch if defects in the medicinal product are revealed.

The Icelandic Medicines Agency may, on its own initiative or at the request of the European Commission, temporarily suspend the marketing of a medicinal product for which a marketing authorisation has been granted as provided for in Chapter VI in cases of urgency, to protect public health or the environment.

If the Icelandic Medicines Agency takes a decision according to paragraph 1 or 3 concerning a medicinal product with a marketing authorisation as provided for in Chapter VI, EMA must be informed of the decision no later than the following working day.

If the Icelandic Medicines Agency takes a decision according to paragraph 4 concerning a medicinal product with a marketing authorisation as provided for in Chapter VI, it must ensure that healthcare personnel are informed of the decision and the reasons for it and notify EMA and the European Commission of the decision no later than the following working day.

When a decision on a ban on the marketing or sale of a medicinal product holding a marketing authorisation as provided for in Chapter VI is taken by the European Commission as provided for in Regulation (EC) No. 726/2004, as amended by Regulation (EC) No. 649/98/EC, the Icelandic Medicines Agency shall take the relevant decision within 30 days.

Article 77

Marketing of a medicinal product after expiry of a marketing authorisation.

Unless otherwise indicated, a medicinal product may be on the market for up to 90 days after the marketing authorisation has expired.

B. Special obligations of marketing authorisation holders.

Article 78

Surveillance obligations.

Holders of marketing authorisations must monitor the risks which may arise from the use of a medicinal product. All adverse reactions which appear in humans or animals from use of a medicinal product shall be recorded and notified in accord with the provisions of Chapter X.

Article 79

Information disclosure.

After a marketing authorisation has been granted, the holder of the marketing authorisation must inform the Icelandic Medicines Agency of the date the marketing of a medicinal product for human use actually begins for each respective package size and type for which authorisation was granted. If authorisation has been granted as provided for in Chapter VI, such a notification must be sent to EMA.

The marketing authorisation holder shall furthermore inform the Icelandic Medicines Agency, or EMA in the case of authorisation granted as provided for in Chapter VI, if it ceases to market the medicinal product in the Member State, either temporarily or permanently. Such notification must be sent no later than two months before the marketing of a medical product is suspended except in special circumstances.

The marketing authorisation holder must immediately submit to the Icelandic Medicines Agency any new information which could result in changes to those aspects or documents referred to in Articles 12, 14, 19 or 50 or in Annex 1 of Directive 2001/83/EC and Annex 1 to Directive 2001/82, as subsequently amended. It must, in particular, notify the Icelandic Medicines Agency immediately of any prohibitions or restrictions which may be imposed by competent authorities in countries where a medicinal product for human use is placed on the market, and of any new information which could affect an assessment of the risk and benefit of use of the medicinal product in question.

The Icelandic Medicines Agency may at any time request the holder of a marketing authorisation to provide data showing that the risk-benefit balance is still positive, making it possible to continuously assess this balance.

A marketing authorisation holder must inform the Icelandic Medicines Agency of its knowledge of any new information on clinical effects and adverse reactions, of toxicology and the quality of the medicinal product and of all defects or flaws which come to light.

At the request of the Icelandic Medicines Agency the marketing authorisation holder must provide the Agency with all information, in particular in connection with pharmacovigilance, on the extent of sales of the medicinal product and all information it possesses on the number of prescriptions of the medicinal product.

Article 80

Obligation to recommend changes.

A marketing authorisation holder is obliged to follow technical and scientific innovations concerning medicinal products and to make any necessary changes to ensure current best manufacturing and testing practices are always applied.

All such changes must be approved in accordance with the provisions of Chapter IX.

Article 81

Control of medicinal products for which a marketing authorisation has been granted.

The Icelandic Medicines Agency may at any time carry out quality control of medicinal products for which a marketing authorisation has been granted.

The Icelandic Medicines Agency shall ensure that current legal requirements for medicinal products are complied with through regular examinations and, if deemed necessary, examinations without prior notice and, as appropriate, by entrusting an official laboratory carrying out control of medicinal products, or a laboratory designated for this purpose by a Member State, to conduct tests of samples.

C. Recognition in another EEA Member State based on an Icelandic marketing authorisation.

Article 82

Requirements for recognition in another Member State of the EEA Agreement.

If an applicant or holder of a marketing authorisation for a medicinal product in Iceland requests to use this authorisation as the basis for recognition in another EEA Member State, the party concerned must inform the Icelandic Medicines Agency thereof and account for any possible changes or additions to the documentation submitted in Iceland.

The Icelandic Medicines Agency may demand to receive all information and documentation required to determine whether the documentation submitted in the EEA Member State concerned is identical to that which was used in Iceland.

Article 83

Summary and updating of assessment reports.

An applicant for a marketing authorisation or marketing authorisation holder may request that the Icelandic Medicines Agency prepare an assessment report for a medicinal product or carry out the necessary revision of an existing assessment report. A request to this effect shall be dealt with within 90 days of receipt.

Article 84

Forwarding of assessment reports.

The Icelandic Medicines Agency shall see to the forwarding of assessment reports to those EEA Member States specified by the marketing authorisation holder at the same time as the latter submits its application for a marketing authorisation in these states.

CHAPTER IX

Changes to the conditions of a marketing authorisation.

Article 85

Changes to the conditions of a marketing authorisation.

The EEA Agreement, Annex 2, Chapter XIII, No. 15zi, 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, applies in Iceland with the adaptation resulting from Annex 2, Protocol 1 to the EEA Agreement and the agreement in other respects, *cf.* Regulation (EC) No. 418/2010, on the entry into force of EU Regulations on medicinal products (VIII).

Applications for changes to the conditions of a marketing authorisation, which has been granted on the basis of Articles 47, 50 or 67, shall be handled according to paragraph 1.

If the European Commission has taken a decision on changes to the conditions of a marketing authorisation on the basis of the rules in Chapter VI, as provided for in Regulation (EC) No. 1234/2008, the Icelandic Medicines Agency shall take the relevant decision within 30 days.

Article 86

Changes to labelling or package leaflets.

An application for changes to labelling or a package leaflet which does not require change to the SPC shall be considered to be approved if the marketing authorisation holder has not received comments from the Icelandic Medicines Agency within 90 days after a valid application was received.

CHAPTER X

Pharmacovigilance.

Article 87

Special definitions.

For the purpose of this Chapter these concepts shall have the following meanings:

a. *Adverse reaction:* A response to a medicinal product which is noxious and unintended and which occurs at doses normally used in humans or animals for the prophylaxis, diagnosis or therapy of disease or modification of physiological function.
b. *Serious adverse reaction:* An adverse reaction which results in death, is life-threatening, results in disability, absence from work or a congenital anomaly, requires inpatient hospitalisation or prolongation of existing hospitalisation, or results in the death of an animal or incurable or lasting disease symptoms.
c. *Unexpected adverse reactions:* Adverse reactions, the nature, severity or outcome of which is not consistent with the summary of product characteristics (SPC).
d. *Serious unexpected adverse reactions:* Adverse reactions which are both serious and unexpected.
e. *Pharmacovigilance:* Monitoring of adverse reactions to medicinal products. In co-operation with other medicinal product authorities in the EEA Member States, the Icelandic Medicines Agency shall establish a database to facilitate the flow of information on pharmacovigilance for medicinal products marketed in the EEA, for the purpose of ensuring that information is received by the authorities of the Member States at the same time.
f. *Periodic Safety Update Report (PSUR):* Reports issued regularly which contain the information referred to in Article 104.
g. *Post-authorisation safety study:* A pharmacoepidemiological study carried out in accordance with the terms of the marketing authorisation with the aim of identifying or quantifying a safety hazard which could arise from an authorised medicinal product.
h. *Abuse of medicinal products:* Persistent or sporadic, intentional excessive use of a medicinal product which is accompanied by harmful physical or psychological effects.

Article 88

Requirements made of marketing authorisation holders for a pharmacovigilance system.

The marketing authorization holder shall have continuously at his disposal an appropriately qualified person responsible for pharmacovigilance within the company. This person shall be domiciled in the European Economic Area.

The qualified person shall be responsible for:

a) The establishment and maintenance of a system which ensures that all suspected adverse reactions of which employees of a company are aware are reported to the responsible person of the company, collected and assessed and made accessible at least at one point within the EEA.
b) The establishment and maintenance of a system which ensures that all suspected adverse reactions of which employees of a company are aware are reported to the responsible person of the company, collected and assessed and made accessible at least at one point within the EEA.

c) The preparation of reports and notifications, according to Articles 90-94, which are sent to the Icelandic Medicines Agency and EMA in the requested format, *cf.* Article 106 of Directive 2001/83/EC, Article 77 of Directive 2001/82 and Article 26 of Regulation (EC) No. 726/2004.
d) Ensuring that any request from the Icelandic Medicines Agency for the provision of additional information considered necessary for the evaluation of the benefits and risks afforded by a medicinal product is answered fully and promptly, including the provision of information about the volume of sales or prescriptions of the medicinal product concerned.
e) The provision to the Icelandic Medicines Agency of any other documentation relevant to the evaluation of the benefits and risks afforded by a medicinal product, including appropriate information on post-authorisation safety studies.
f) To ensure that all suspected serious adverse reactions to medicinal products for which a marketing authorisation has been granted as provided for in Chapter IV are notified, so that they will be accessible to the reference Member State.

Adverse reactions to medicinal products for humans shall be notified in electronic format as provided for in Article 106 of Directive 2001/83/EC. Adverse reactions to medicinal products for animals shall be notified in electronic format as provided for in Article 77 of Directive 2001/82/EC. Adverse reactions to medicinal products which have been approved as provided for in Chapter VI shall be notified in electronic format as provided for in Article 26 of Regulation (EC) No. 726/2004.

A marketing authorisation holder may not provide information in connection with pharmacovigilance for an authorised medicinal product to the public if it has not previously or concurrently notified this to the Icelandic Medicines Agency, or EMA in the case of a marketing authorisation as referred to in Article 67. In all cases the marketing authorisation holder must ensure that such information is presented objectively and is not misleading.

If a medicinal product has been granted a marketing authorisation as provided for in Chapter VI, notification shall be sent to EMA, *cf.* item a) of this Article.

Article 89

Forwarding of notifications of suspected serious adverse reactions.

The Icelandic Medicines Agency must record all suspected serious adverse reactions in Iceland of which it is informed. The Icelandic Medicines Agency shall immediately and in any case no later than 15 days after receiving information send notification to EMA and to the marketing authorisation holder.

The Icelandic Medicines Agency shall make a concerted effort to ensure that physicians and other healthcare personnel send notification of suspected serious adverse reactions to the respective authorities.

The Icelandic Medicines Agency may adopt rules for physicians and other healthcare personnel on notifications of suspected serious adverse reactions, especially if such control is a condition for a marketing authorisation.

Article 90

Notifications of marketing authorisation holders of serious adverse reactions.

A marketing authorisation holder which has been granted a marketing authorisation according to Article 58, must record all suspected serious adverse reactions brought to its attention by the healthcare personnel concerned or of which it becomes aware by other means (scientific literature etc.). The information must be notified to the Icelandic Medicines Agency immediately and in any case no later than 15 days after receipt of the information.

A marketing authorisation holder which has been granted a marketing authorisation according to Article 67 must record all suspected serious adverse reactions within the EEA brought to its attention by the healthcare personnel concerned. The marketing authorisation holder must without delay and in any case no later than 15 days after receiving the information inform the competent health authorities in the EEA Member States from which notifications were received of adverse reactions.

A marketing authorisation holder which has been granted a marketing authorisation according to Article 67 must record all other suspected serious adverse reactions within the EEA which it can justifiably be expected to be aware of through other means (scientific literature etc.). The marketing authorisation holder must without delay and in any case no later than 15 days after receiving the

information inform the competent health authorities in the EEA Member States concerned and EMA of these adverse reactions.

Article 91

Notification of serious adverse reactions of veterinary medicinal products.

A marketing authorisation holder which has been granted a marketing authorisation for a veterinary medicinal product must record all serious adverse reactions and adverse reactions in humans, which are suspected to be connected to use of veterinary medicinal products and of which it is notified or of which it can be expected to be aware. The marketing authorisation holder must immediately and in any case no later than 15 days after receipt of the information send a report to the Icelandic Medicines Agency.

A marketing authorisation holder which has been granted a marketing authorisation for a veterinary medicinal product must record all serious unexpected adverse reactions, and suspected adverse reactions in humans, together with any instances where it is suspected that a pathogen has been spread with a veterinary medicinal product to the territory of a third country. The marketing authorisation holder must immediately and in any case no later than 15 days after receiving the information send a report to EMA and the competent healthcare authorities in the EEA Member States where the medicinal product has been granted a marketing authorisation, as provided for in paragraph 1 of Article 77 of Directive 2001/82, or where the medicinal product has been recognised on the basis of Chapter VI, as provided for in Article 26 of Regulation (EC) No. 726/2004.

A marketing authorisation holder which has obtained a marketing authorisation for a veterinary medicinal product covered by Directive 87/22/EEC, or which has been recognised as provided for in Articles 44-47, or which is covered by a procedure referred to in Article 49, must ensure that all suspected serious adverse reactions and adverse reactions in humans which arise in EEA Member States are notified so that this information is accessible to the reference Member State.

The Icelandic Medicines Agency shall without delay and in any case no later than 15 days after receiving information on suspected serious adverse reactions to use of the medicinal product in Iceland notify this to the marketing authorisation holder.

Article 92

Notifications of marketing authorisation holders of suspected unexpected serious adverse reactions.

A marketing authorisation holder which has obtained a marketing authorisation must record all suspected unexpected serious adverse reactions to medicinal products outside the EEA and if there is reason to suspect that a medicinal product bears a transmissible agent. The marketing authorisation holder shall immediately and in any case no later than 15 days after receiving information send notification to this effect to EMA and to the healthcare authorities concerned within the EEA.

Article 93

Periodic Safety Update Report (PSUR).

A marketing authorisation holder must prepare a detailed report of all suspected adverse reactions.

The report shall be sent to healthcare authorities within the EEA, the Icelandic Medicines Agency and EMA, if the authorisation was granted according to Article 67, if requested.

Unless otherwise required in the marketing authorisation, the report shall be sent to healthcare authorities of the Member States of the EEA either immediately when a request to this effect is submitted or at six-month intervals from the granting of the authorisation for the medicinal product until the medicinal product is placed on the market. The report shall also be provided immediately when a request to this effect is submitted and no less frequently than at six-month intervals during the first two years after the medicinal product is placed on the market and annual for the next two years. After that the report shall be submitted at three-year intervals or immediately when a request is made to this effect.

If authorisation has been granted for a medicinal product according to Article 67, the summary shall also be sent to EMA. After a marketing authorisation has been granted, the marketing authorisation holder may request a change to the schedule referred to above.

The report shall be accompanied by a scientific assessment of the risk-benefit balance for the medicinal product.

The report must include information received during the period referred to in paragraph 3. The report must be sent to the healthcare authorities concerned within 60 days of the end of the specified time limit.

Article 94

Suspected unexpected adverse reactions which are not considered serious.

Unless otherwise indicated specifically in the marketing authorisation, the recording and notification of suspected unexpected adverse reactions to a medicinal product which are not considered serious shall be carried out as provided for in Article 104. The information shall be placed in the intended chapter in the report.

Regulation (EC) No. 540/95 laying down the arrangements for reporting suspected unexpected adverse reactions which are not serious, whether arising in the Community or in a third country, to medicinal products for human or veterinary use authorized in accordance with the provisions of Council Regulation (EEC) No. 726/2004, applies in Iceland with the adaptation resulting from Annex 2, Chapter XIII, Protocol 1 to the EEA Agreement.

CHAPTER XI

Miscellaneous provisions.

Article 95

Requirement for a manufacturing license.

Icelandic manufacturers of medicinal products must hold a valid manufacturing license, according to Article 34 of the Medicinal Products Act, No. 93/1994, in order for the medicinal products they manufacture to obtain a marketing authorisation in Iceland.

Manufacturers of medicinal products in other EEA Member States must have a similar license, issued by the healthcare authorities in the state concerned.

Manufacturers outside the EEA must have a license to manufacture the specific medicinal product for which a marketing authorisation is sought, issued by the healthcare authorities of that country. They must also have available documentation describing the manufacturing process and quality control in manufacturing the medicinal product. Furthermore, they must provide access to reports on supervision by the healthcare authorities of their own country or another country and grant Icelandic inspectors access to the manufacturing location and documentation on the manufacturing process and quality control.

Article 96

Agents of marketing authorisation holders.

A marketing authorisation holder which is not established in the EEA must have an agent established in Iceland. The agent must provide the Icelandic Medicines Agency with proof of its agency. If this agency ceases, the Icelandic Medicines Agency must be notified thereof without delay. In such instances a new agency must be notified within a suitable time limit determined by the Icelandic Medicines Agency, otherwise the marketing authorisation may be revoked, according to item g) of paragraph 1 of Article 61, *cf.* Article 62.

An agent must ensure that the marketing authorisation holder complies with currently applicable provisions on the import, marketing, advertising and clinical testing of proprietary medicinal products in Iceland and must be authorised by the authorisation holder to represent it in national courts or to authorities in cases concerning the conditions for granting a marketing authorisation for a medicinal product.

If an agent or its agency fails to fulfil the prescribed conditions, or if an agent repeatedly neglects its duties in other respects, the Icelandic Medicines Agency may demand a new agency be provided within a reasonable time limit.

In specific instances the Icelandic Medicines Agency may waive the requirement of an agent.

The marketing authorisation holder is responsible for marketing of the medicinal product. The appointment of an agent does not absolve the marketing authorisation holder from its legal liability.

Article 97

Fees payable to the Icelandic Medicines Agency and EMA.

The Icelandic Medicines Agency shall collect fees in accordance with the tariff in the Regulation on marketing authorisations, annual fees and other fees for authorisations for medicinal products which apply at any given time, *cf.* Article 3 of the Medicinal Products Act. The fees are non-refundable even if an application is refused or withdrawn.

[The EEA Agreement, Annex 2, Chapter XIII, No. 15h, Regulation (EC) No. 297/95, on fees payable to EMA, as amended by Regulation (EC) No. 2743/98, Regulation (EC) No. 494/2003, Regulation (EC) No. 1905/2005, regulation (EC) No. 249/2009, Regulation (EU) No. 301/2011 and Regulation (EU) No. 273/2012 enters into force in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects.][1)]

The EEA Agreement, Annex 2, Chapter XIII, No. 15zc, Regulation (EC) No. 2049/2005, laying down, pursuant to Regulation (EC) No. 726/2004, of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the EMA by micro, small and medium-sized enterprises, enters into force in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects.

For handling by EMA a fee is paid according to paragraphs 2 and 3.

[1)] *Regulation No. 943/2012, Article 1.*

Article 98

Orphan medicinal products.

The EEA Agreement, Annex 2, Chapter XIII, No. 15m, Regulation (EC) No. 141/2000, on orphan medicinal products, and the EEA Agreement, Annex 2, Chapter XIII, No. 15n, Regulation (EC) No. 847/2000, laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product enters into force in Iceland with the adaptation resulting from Annex 2, Protocol 1 of the Agreement and the Agreement in other respects.

An application for status as an orphan medicinal product and application for a marketing authorisation for a medicinal product designated as an orphan medicinal product must be sent to EMA in accordance with the rules referred to in paragraph 1.

Article 99

Application for price.

Application for a maximum wholesale price and for all changes in the prices of human and veterinary medicinal products subject to prescription must be made to the Medicinal Products Pricing Committee, as provided for in Chapter XV of the Medicinal Products Act.

Article 100

Register of proprietary medicinal products.

Information on proprietary medicinal products will only be published in the register of proprietary medicinal products if a valid marketing authorisation exists and samples of the packaging and package leaflet in their final form are available.

Article 101

Provision on impartiality.

To ensure independence and transparency the Icelandic Medicines Agency must ensure that its employees who are responsible for granting authorisations, reporters or experts, who are involved in granting authorisations and control of medicinal products have neither financial nor other interests at stake in the pharmaceutical industry which could affect their impartiality. These persons must provide a statement of their financial interests annually.

Article 102

Limitations of liability.

A marketing authorisation holder, manufacturers or professional healthcare workers shall not bear civil or administrative liability for consequences which may result from the use of a medicinal product which does not conform with approved indications or from the use of a medicinal product which has

not been granted an authorisation, if the competent authority has requested or demanded this use to prevent damage by pathogens, toxins, chemical agents or radioactivity which is suspected or confirmed to have spread.

This provision does not limit the liability for damages for defective medicinal products resulting from rules on the liability for damages from defective products.

Article 103

The period of protection referred to in Article 14 shall not apply to a reference medicinal product if the application for a marketing authorisation for the product was submitted prior to 30 October 2005.

CHAPTER XII

Entry into force Repeal.

Article 104

Entry into force and repeal.

The provisions of this Regulation are based in particular on:

The EEA Treaty, Annex II, Subcategory XIII, and in the EEA Supplement to the *Official Journal of the European Union,* Book 3, ISSN 1022-9337, EFTA Publication Unit.

Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use.

Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products.

Directive 2004/27/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use.

Directive 2004/28/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products.

Council Regulation (EEC) No. 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin.

Regulation (EC) No. 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

Commission 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.

Commission Regulation (EC) No. 540/95 of laying down the arrangements for reporting suspected unexpected adverse reactions which are not serious, whether arising in the Community or in a third country, to medicinal products for human or veterinary use authorized in accordance with the provisions of Council Regulation (EEC) No. 726/2004.

Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.

Commission Directive 2003/63/EC amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use.

Commission Directive 2006/130/EC of 11 December 2006 implementing Directive 2001/82/EC of the European Parliament and of the Council as regards the establishment of criteria for exempting certain veterinary medicinal products for food-producing animals from the requirement of a veterinary prescription.

Commission Directive 2009/9/EC of 10 February 2009 amending Directive 2001/82/EC of the European Parliament and of the Council on the Community code relating to veterinary medicinal products.

[Directive 2009/53/EC of the European Parliament and of the Council, of 18 June 2009, amending Directive 2001/82EC and Directive 2001/83/EC as regards the amendments on terms of marketing authorisations for medicinal products;

Commission Directive 2009/120/EC of 14 September 2009 amending, as regards advanced therapy medicinal products, the Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use.][1)]

This Regulation, which is set by authority of Articles 5, 7 and 49 of the Medicinal Products Act, No. 93/1994, as subsequently amended, shall enter into force upon publication.

At the same time Regulation No. 462/2000, on marketing authorisation for proprietary medicinal products, their labelling and package leaflets, as subsequently amended, is repealed.

[1)] *Regulation No. 1021/2011, Article 2.*

Ministry of Welfare, 1 February 2011

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[*This translation is published for information only.*
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