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STATUTORY INSTRUMENTS

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**1993 No. 2538**

**MEDICINES**

**The Medicines (Applications for Grant of Product Licences—Products for Human Use) Regulations 1993**

<i>Made</i>	- - - -	<i>21st October 1993</i>
<i>Laid before Parliament</i>		<i>28th October 1993</i>
<i>Coming into force</i>	- -	<i>29th November 1993</i>

The Secretary of State concerned with health in England, the Secretaries of State respectively concerned with health and with agriculture in Wales and in Scotland, the Minister of Agriculture, Fisheries and Food, the Department of Health and Social Services for Northern Ireland and the Department of Agriculture for Northern Ireland, acting jointly, in exercise of powers conferred upon them by sections 18, 129(1) and (5) and 132(1) of the Medicines Act 1968<sup>(1)</sup> or, as the case may be, those conferred by the said provisions and now vested in them<sup>(2)</sup> and of all other powers enabling them in that behalf, after consulting such organisations as appear to them to be representative of interests likely to be substantially affected by these Regulations<sup>(3)</sup>, hereby make the following Regulations:

**Citation, commencement and interpretation**

1.—(1) These Regulations may be cited as the Medicines (Applications for Grant of Product Licences—Products for Human Use) Regulations 1993, and shall come into force on 29th November 1993.

(2) In these Regulations—

“the Act” means the Medicines Act 1968;

“application”, except in regulation 2 below and in sub-paragraph (a) of paragraph 6 of Schedule 2, means an application to which these Regulations apply by virtue of that regulation;

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- (1) 1968 c. 67. The expression “the Ministers”, used in section 129(1), is defined in section 1(1) of that Act as amended by S.I.1969/388, Schedule 1. Section 132(1) is cited for the definition of “prescribed”.
- (2) In the case of the Secretaries of State concerned with health in England and in Wales by virtue of Article 2(2) of, and Schedule 1 to, the Transfer of Functions (Wales) Order 1969 (S.I.1969/388); in the case of the Secretary of State concerned with agriculture in Wales by virtue of Article 2(3) of, and Schedule 1 to, the Transfer of Functions (Wales) (No. 1) Order 1978 (S.I.1978/272); in the case of the Northern Ireland Departments by virtue of section 40 of, and Schedule 5 to, the Northern Ireland Constitution Act 1973 (c. 36) and section 1(3) of, and paragraph 2(1)(b) of Schedule 1 to, the Northern Ireland Act 1974 (c. 28).
- (3) (See section 129(6) of the Medicines Act 1968 (c. 67).)

“the Directives” means the Directives made by, as the case may be, the Council or Commission of the European Economic Community, numbered [75/318/EEC\(4\)](#), [75/319/EEC\(5\)](#), [89/342/EEC\(6\)](#) and [89/381/EEC\(7\)](#) and any reference to any of those Directives is to the Directive as in force immediately before the date on which these Regulations are made;

“expert” means an expert with suitable technical or professional qualifications and experience for the purposes of drawing up any description or particulars referred to in paragraphs 7 and 8 of, or any report referred to in paragraph 12 of, Schedule 1;

“product” means any medicinal product and any other article, product or substance in relation to which section 7(2) of the Act for the time being has effect (with or without modification) as it has effect in relation to medicinal products, by virtue of an order under section 104 or 105 of the Act made before the date on which these Regulations were made or regulations under section 2(2) of the European Communities Act 1972(8) made before that date.

(3) Expressions used in these Regulations which are also used in any relevant Community Directive(9) shall, except where the contrary intention appears and except in the case of “medicinal product”, have the same meaning as they have in the relevant Directive, and related expressions shall be construed accordingly.

(4) Any reference in these Regulations to a numbered Schedule is a reference to the Schedule to these Regulations bearing that number.

### **Application of these Regulations**

2.—(1) Subject to paragraph (2) below, these Regulations shall apply to any application, made after the coming into force of these Regulations, for the grant (but not renewal) of a product licence in relation to a product for human use.

(2) These Regulations shall not apply where the application is one which is deemed to be an application by virtue of section 18(3) of the Act.

### **Manner of applications**

3.—(1) Every application shall be made in writing and shall be signed by or on behalf of the applicant.

(2) Twenty-six copies, or such lesser number as the licensing authority may direct, of each application and of any accompanying material shall be supplied to the licensing authority in the English language, and where the application or any accompanying material has been translated from another language, also one copy of the application or the accompanying material, as the case may be, in the original language.

(3) A separate application shall be made in respect of each product of a particular description, except that a single application may be made—

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(4) OJ No.L147, 9.6.75, p.1. The Directive was amended by Directive [89/341/EEC](#) (OJ No.L142, 25.5.89, p.11), and the Annex to it was substituted by Directive [91/507/EEC](#) (OJ No.L270, 26.9.91, p.32).

(5) OJ No.L147, 9.6.75, p.13.

(6) OJ No.L142, 25.5.89, p.14.

(7) OJNo.L181, 28.6.89, p.44.

(8) [1972 c. 68](#).

(9) The principal relevant Directives are Directive [65/65/EEC](#) (OJ No.22, 9.2.65, p.369/65 (OJ/SE1965–66, p.20) as amended, the Directives included in the definition of “the Directives” in regulation 1(2) above and Directive [89/343/EEC](#) (OJ No. L142, 25.5.89, p. 16). For present purposes, the relevant Directives amending Directive [65/65/EEC](#) are: [75/319/EEC](#) (OJ No.L147, 9.6.75, p.13), [83/570/EEC](#) (OJNo.L332, 28.11.83, p.1), [87/21/EEC](#) (OJ No.L15, 17.1.87, p.36) and [89/343/EEC](#), amending and supplementing Article 4; and [83/570/EEC](#), inserting Article 4a, and [89/341/EEC](#) (OJ No.L142, 25.5.89, p.11), [89/342/EEC](#) (OJ No.L142, 25.5.89, p.14) and [89/343/EEC](#), amending and supplementing that Article.

- (a) in respect of two or more products which have the same pharmaceutical form and either consist of the same single active constituent in different strengths, or consist of a mixture in different strengths of the same two or more active constituents in the same proportion;
- (b) in respect of two or more substances or two or more articles having the same physical form and either having the same single active constituent in different strengths or being a mixture in different strengths of the same two or more active constituents in the same proportion;
- (c) in the case of homoeopathic products and products using similar attenuations, in respect of—
  - (i) two or more attenuations of the same mother tincture or other solution of the same trituration, or
  - (ii) two or more attenuations of any mother tincture or other solution or trituration having the same specification and pharmaceutical form apart from the tincture, solution or trituration;
- (d) in the case of products being preparations of allergen extracts for the treatment of allergies, in respect of two or more attenuations of the same allergen extract or of the same mixture of allergen extracts; or
- (e) in the case of products for testing for allergic responses to specific substances in respect of two or more allergen extracts manufactured by one and the same method, provided that the application states the substances from which the extracts are prepared.

#### **Material to be contained in or accompany an application**

4.—(1) Subject to paragraphs (4), (5), (6) and (7) below, an application which relates to any product to which Chapters II to V of the 1965 Directive apply shall, in respect of each such product, contain or be accompanied by such of the information, documents, samples and other material specified in Schedule 1 as relate to the product, prepared and presented in accordance with the applicable requirements of the Directives.

(2) Subject to paragraphs (4) and (7) below, an application which relates to any product which is not a product to which Chapters II to V of the 1965 Directive apply shall, in respect of each such product, contain or be accompanied by such of the information, documents, samples and other material specified in Schedule 1 as relate to the product, prepared and presented in accordance with such of the requirements of the Directives as would be applicable to the product if it were a product to which those Chapters applied.

(3) Schedule 2 (which sets out exceptions to the requirements to provide the particulars of various tests and trials) shall have effect for the purposes of paragraph 8 of Schedule 1.

(4) Schedule 3 (under which certain particulars may, in certain circumstances, be provided otherwise than by the applicant) shall have effect.

(5) Insofar as an application relates to a product which has been, or is to be, imported into the United Kingdom and in respect of which a marketing or equivalent authorisation is in force elsewhere than in the United Kingdom, it need not contain or be accompanied by any material which, in accordance with Community obligations, may not be required by the competent authorities of a member State as a condition of granting a marketing authorisation.

(6) Where paragraph (5) above has effect in relation to any product, the application shall, in addition to any other material required by these Regulations, contain or be accompanied by information sufficient to identify the relevant marketing or equivalent authorisation and any relevant United Kingdom product licence, and shall be accompanied by a sample of the product complete with the outer packaging, immediate packaging and labels all in the form as marketed in the member or other State where the relevant marketing or equivalent authorisation is in force.

(7) The requirements of Part 2, paragraph A, point 3.3 of the Annex to Directive [75/318/EEC](#)(10) shall not apply in relation to an application made before 1st January 1995.

**Amendment of the Medicines (Applications for Product Licences and Clinical Trial and Animal Test Certificates) Regulations 1971**

5. In regulation 2(1) (interpretation) of the Medicines (Applications for Product Licences and Clinical Trial and Animal Test Certificates) Regulations 1971(11), at the end of the definition of “application”, there shall be inserted the words “or a request for the grant of a product licence, being a request which is an application to which the Medicines (Applications for Grant of Product Licences—Products for Human Use) Regulations 1993 apply”.

Signed by authority of the Secretary of State for Health

15th October 1993

*Tom Sackville*  
Parliamentary Under Secretary of State  
Department of Health

19th October 1993

*John Redwood*  
Secretary of State for Wales

15th October 1993

*Fraser of Carmyllie*  
Minister of State, Scottish Office

In witness whereof the Official Seal of the Minister of Agriculture, Fisheries and Food is hereunto affixed on 18th October 1993.

L.S.

*Gillian Shephard*  
Minister of Agriculture, Fisheries and Food

Sealed with the Official Seal of the Department of Health and Social Services for Northern Ireland on 21st October 1993.

L.S.

*F. A. Elliott*  
Permanent Secretary

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(10) OJ No.L147, 9.6.75, p.1. A new Annex was substituted by Directive [91/507/EEC](#) (OJ No.L270, 26.9.91, p.32).

(11) S.I.[1971/973](#).

Sealed with the Official Seal of the Department of Agriculture for Northern Ireland on 18th October 1993.

L.S.

*W. J. Hodges*  
Permanent Secretary

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## SCHEDULE 1

Regulation 4(1) and (2)

### INFORMATION, DOCUMENTS, SAMPLES AND OTHER MATERIAL REQUIRED IN RESPECT OF APPLICATIONS

- (a) (a) The name or corporate name of and the permanent address of—
    - (i) the person responsible for placing the product on the market in the United Kingdom,
    - (ii) the manufacturers and the sites involved in the different stages of the manufacture (including the manufacturer of the finished product and the manufacturers of the active ingredients), and
    - (iii) where relevant, the importer;
  - (b) where the licence applied for is required solely for the purpose of exporting a product, the name or corporate name of and the permanent address of the exporter; and
  - (c) in relation to any product in respect of which section 7(2) of the Act applies by virtue of section 43 of the Act, a description of the circumstances in which the relevant seller, supplier or exporter will sell, supply or export the product if he is not named under subparagraph (a) above.
2. The name of the product, that is to say, the brand name, or common name together with a trade mark, or name of the manufacturer, or scientific name together with a trade mark or name of the manufacturer.
  3. The qualitative and quantitative particulars of all the constituents of the product together with details of any relevant data concerning the container and, where appropriate, its manner of closure, and details of devices with which the medicinal product will be used or administered and which will be delivered with the product.
  4. A brief description of the method of preparation.
  5. Particulars of the therapeutic indications, contra-indications and side-effects.
  6. Particulars of the posology, pharmaceutical form, method and route of administration and expected shelf-life.
  7. A description, drawn up and signed by experts, of the control methods employed by the manufacturer (indicating the qualitative and quantitative analysis of the constituents and of the finished product, special tests, for example sterility tests, tests for the presence of pyrogenic substances and for the presence of heavy metals, stability tests, biological and toxicity tests, and controls carried out at an intermediate stage of the manufacturing process).
  8. Subject to Schedule 2, particulars, drawn up and signed by experts, of the results of:
    - (a) physico-chemical, biological or microbiological tests;
    - (b) pharmacological and toxicological tests;
    - (c) clinical trials;
- including all relevant details of any incomplete or abandoned pharmacotoxicological or clinical test or trial.
9. A summary of the product characteristics which shall contain the following information:
    - (a) the name of the product;
    - (b) its qualitative and quantitative composition in terms of the active ingredients, knowledge of which is essential for proper administration of the product, using international non-proprietary names or, where there is no such name, the usual common name or chemical description;

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- (c) its pharmaceutical form;
- (d) clinical particulars covering—
  - (i) therapeutic indications,
  - (ii) posology and method of administration for adults and, where necessary, for children,
  - (iii) contra-indications,
  - (iv) special warnings,
  - (v) special precautions for use and, in relation to any immunological medicinal product to which Directive [89/342/EEC](#)(**12**) applies, information regarding any special precautions to be taken by persons handling the product and persons administering it to patients, together with any precautions to be taken by the patient,
  - (vi) interaction with other medicaments and other forms of interaction,
  - (vii) use during pregnancy and lactation,
  - (viii) effects on ability to drive and to use machines,
  - (ix) undesirable effects (including their frequency and seriousness),
  - (x) overdose (covering symptoms, emergency procedures and antidotes);
- (e) its pharmacological properties and, insofar as this information is useful for therapeutic purposes, pharmacokinetic particulars;
- (f) pharmaceutical particulars covering—
  - (i) qualitative composition in terms of the excipients used,
  - (ii) major incompatibilities,
  - (iii) shelf-life, when necessary after reconstitution of the product or when the container is opened for the first time,
  - (iv) special precautions for storage,
  - (v) nature and composition of the container,
  - (vi) special precautions for disposal of unused products or waste materials derived from such products, if appropriate,
  - (vii) name or style and permanent address or registered place of business of the holder of the licence;
- (g) in relation to any radiopharmaceutical to which Directive [89/343/EEC](#)(**13**) applies—
  - (i) full details of internal radiation dosimetry, and
  - (ii) 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; and
- (h) in relation to any indications to which sub-paragraphs (a) and (b) of paragraph 22 below apply, a statement drawing the attention of persons qualified to prescribe or supply the product to the fact that the particulars available concerning the product are as yet inadequate in certain specified respects.

**10.** A copy of the manufacturing authorisation as defined in Article 16 of Directive [75/319/EEC](#)(**14**), and any other relevant document showing that the manufacturer is authorised in his own country to produce products.

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(12) OJ No.L142, 25.5.89, p.14.

(13) OJ No.L142, 25.5.89, p.16.

(14) OJ No.L147, 9.6.75, p.13.

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**11.** A copy of any authorisation obtained in a member State other than the United Kingdom or in a third country to place the relevant product on the market and of all the summaries of product characteristics in accordance with Article 4a of the 1965 Directive as approved by member States, and a list of countries in which an application has been submitted.

**12.** An expert's report (stating, where applicable, the grounds for using published references which the applicant claims to be entitled to use in accordance with paragraphs 1 to 4 of Schedule 2), signed and dated by the expert, on—

- (a) the chemical, pharmaceutical and biological documentation;
- (b) the pharmacotoxicological documentation;
- (c) the clinical documentation;

respectively.

**13.** Brief information about the educational background, training and occupational experience of each expert, and a declaration as to his professional relationship to the applicant.

**14.** One or more samples or mock-ups of the sales presentation, the outer packaging, the immediate packaging, the labels, and the package leaflet (or draft package leaflet) where one is to be enclosed.

**15.** A statement of the number of volumes of documentation submitted in support of the application.

**16.** A statement as to any samples provided.

**17.** Where the applicant is, by virtue of paragraph 8 above, required to provide particulars of the results of any safety test falling within Part 3, paragraph 1.1, second sub-paragraph of the Annex to Directive [75/318/EEC\(15\)](#), a copy of any certificate issued by the laboratory which carried out the test to the effect that the test was carried out in conformity with the principles of good laboratory practice referred to in that sub-paragraph.

**18.** Where the applicant is, by virtue of paragraph 8 above, required to provide particulars of the results of any clinical trial, a summary of the arrangements proposed to be made for the archiving of documentation of the trial in accordance with Part 4, paragraph B.2 of the Annex to Directive [75/318/EEC](#), including (in particular) the arrangements proposed for ensuring that any change of ownership in the relevant data is documented and that all relevant data and documents will be made available to the licensing authority if required.

**19.** A statement indicating—

- (a) which of the following should apply to the product, that is to say that the product should be available:
  - (i) on prescription only (that is to say, that it should be subject to restrictions imposed by section 58(2)(a) or 60(1)(b) of the Act);
  - (ii) only from a pharmacy (that is to say, that it should be subject to a restriction under section 52 or section 53 of the Act to the effect that it may be sold only at a registered pharmacy, but not subject to the restrictions imposed by section 58(2)(a) or 60(1)(b) of the Act); or
  - (iii) on general sale (that is to say, that it should not be subject to any of the restrictions referred to in paragraphs (i) and (ii) above); and
- (b) what, if any, provisions of the licence are proposed concerning the method of sale or supply of the product (including, in particular, any proposed restrictions affecting the circumstances of the use or promotion of the product).

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(15) OJ No.L147, 9.6.75, p.1. A new Annex was substituted by Directive [91/507/EEC](#) (OJ No.L270, 26.9.91, p.32).



- 20.** If the product is already authorised in other countries—
- (a) information in respect of adverse drug reactions to the product and products containing the same active ingredient (in relation to the usage rates if possible) and information from worldwide studies relevant to the safety of the product;
  - (b) in the case of vaccines, information on the monitoring of vaccinated subjects to evaluate the prevalence of the disease in question as compared to non-vaccinated subjects, when such information is available; and
  - (c) for allergen products, details of response in periods of increased antigen exposure.
- 21.** In relation to any generator to which Article 3 of Directive 89/343/EEC(16) applies—
- (a) a general description of the system together with a detailed description of the components of the system which may affect the composition or quality of the daughter nuclide preparation; and
  - (b) qualitative and quantitative particulars of the eluate or the sublimate.
- 22.** Where the applicant, in relation to all or any particular therapeutic indications, omits any information by virtue of paragraph 5 of Schedule 2—
- (a) detailed proposals for the programme of studies referred to in that paragraph (including a proposed period for carrying them out) for the purposes of a reassessment of the benefit/risk profile in relation to those indications; and
  - (b) a statement as to any proposal that the product in question should be administered for those indications only under strict medical supervision, possibly in a hospital, and, for a radiopharmaceutical to which Directive 89/343/EEC applies, by an authorized person.
- 23.** Where the licence applied for is required solely for the purpose of exporting a product, a statement to that effect.
- 24.** A statement indicating that the applicant agrees that the licence applied for is to be subject to the relevant standard provisions prescribed by the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971(17) or indicating which, if any, of those provisions it is desired shall be excluded from the licence, and what, if any, modifications it is desired should be made to any of those provisions.
- 25.** All other information which is relevant to the evaluation of the product, whether favourable or unfavourable to it.

## SCHEDULE 2

Regulation 4(3)

### EXCEPTIONS TO THE REQUIREMENT TO PROVIDE PARTICULARS OF THE RESULTS OF TESTS AND TRIALS REFERRED TO IN PARAGRAPH 8 OF SCHEDULE 1

- 1.** Subject to paragraphs 2 to 4 below, the applicant shall not be required, under paragraph 8 of Schedule 1, to provide particulars of the results of pharmacological and toxicological tests or of the results of clinical trials if he can demonstrate:
- (a) that the product is essentially similar to a product to which an existing product licence (not being one which relates solely to importation) applies and that the person responsible for placing that product on the market in the United Kingdom has consented to the

(16) OJ No.L142, 25.5.89, p.16.

(17) S.I.1971/972; the relevant amending regulations are S.I.1972/1226, 1974/1523, 1977/675, 1977/1039, 1977/1053, 1983/1730, 1992/2846, 1992/3272, 1993/833 and 1993/2539.

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pharmacological, toxicological or clinical references contained in the file on the original medicinal product being used for the purpose of examining the product in question;

- (b) by detailed references to published scientific literature presented in accordance with the second paragraph of Article 1 of Directive [75/318/EEC](#)(18) that the constituent or constituents of the medicinal product have a well established medical use, with recognised efficacy and an acceptable level of safety; or
- (c) that the product is essentially similar to a product which has been authorized within the European Economic Community in accordance with Community provisions in force, for not less than ten years and is marketed in the United Kingdom.

2. Notwithstanding paragraph 1 above, the applicant shall provide particulars of the results of appropriate pharmacological and toxicological tests and of clinical trials where the product is intended for a different therapeutic use from that of the other medicinal products marketed or is to be administered by different routes or in different doses.

3. Where the product is a new medicinal product containing known constituents not hitherto used in combination for therapeutic purposes, the applicant shall, notwithstanding paragraph 1 above, provide particulars of the results of appropriate pharmacological and toxicological tests and of clinical trials in relation to that combination but it shall not be necessary to provide references relating to each individual constituent.

4. The applicant shall not be entitled by virtue of the preceding provisions of this Schedule to omit to provide any particulars or results if proper consideration of the application without them could not be carried out without prejudicing any rights which arise under any law relating to the protection of industrial and commercial property and which are enforceable in the United Kingdom.

5. Subject to compliance with paragraphs 19(a) and 22 of Schedule 1, the applicant shall not be required, under paragraph 8 of that Schedule, to provide, in relation to particular therapeutic indications, the results of any tests or trials where, in respect of those indications, he can show that he is unable to provide comprehensive information on the quality, efficacy and safety under normal conditions of use because:

- (a) the indications for which the product is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence;
- (b) in the present state of scientific knowledge comprehensive information cannot be provided; or
- (c) it would be contrary to generally accepted principles of medical ethics to collect such information;

and where the applicant wishes the licensing authority to consider granting the licence on the basis that he would be required to carry out a programme of studies for the purposes of reassessing the benefit/risk profile, that the product would be supplied on medical prescription only (and subject to any other relevant restrictions) and that he would be required to provide relevant information in the package leaflet and medical information.

6. The applicant shall not be required under paragraph 8 of Schedule 1 to provide any material which—

- (a) has been or is provided in connection with another application (whether or not one to which these Regulations apply) made by the applicant previously or at the same time;
- (b) is identified in the application or in any document accompanying it, by reference to that other application, as so provided; and

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(18) OJ No.L147, 9.6.75, p.1. The Directive was amended by Directive [89/341/EEC](#) (OJ No.L142, 25.5.89, p.11), and the Annex to it was substituted by Directive [91/507/EEC](#) (OJ No.L270, 26.9.91, p.32).

- (c) would, if provided in connection with the application, meet the requirements of these Regulations.

### SCHEDULE 3

Regulation 4(4)

#### CIRCUMSTANCES IN WHICH CERTAIN PARTICULARS MAY BE PROVIDED BY A MANUFACTURER (OTHER THAN THE APPLICANT) OF CERTAIN ACTIVE INGREDIENTS

1. In the case of—

- (a) an active ingredient not described in the European Pharmacopoeia or in the pharmacopoeia of a member State; or
- (b) an active ingredient described in the European Pharmacopoeia or in the pharmacopoeia of a member State when prepared by a method liable to leave impurities not mentioned in the pharmacopoeial monograph and for which the monograph is inappropriate adequately to control its quality;

which is manufactured by a person other than the applicant, the latter may (subject to paragraph 2 below) arrange for the detailed description of the manufacturing method, quality control during manufacture and process validation to be supplied directly to the licensing authority by the manufacturer of the active ingredient.

2. Paragraph 1 of this Schedule shall not apply unless the manufacturer—

- (a) provides the applicant with all the data which may be necessary for the latter to take responsibility for the medicinal product; and
- (b) confirms in writing to the applicant that he shall ensure batch to batch consistency and not modify the manufacturing process or specifications without informing the applicant;

and the application is accompanied by—

- (i) such documents and other material as may be reasonably necessary to satisfy the licensing authority that the manufacturer has complied with sub-paragraph (a) above;
- (ii) a copy of the written confirmation referred to in sub-paragraph (b) above; and
- (iii) such other documents and material as may be reasonably necessary to satisfy the licensing authority that the applicant has made adequate arrangements with the manufacturer for the provision to the licensing authority of appropriate documents and particulars supporting any application to make any modification referred to in that sub-paragraph.

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## EXPLANATORY NOTE

*(This note is not part of the Regulations)*

These Regulations prescribe the information, documents, samples and other material to be provided in or with an application, made after the coming into force of the Regulations, for a product licence under Part II of the Medicines Act 1968 (“the Act”) in relation to medicinal products for human use. They replace, in relation to such applications, the requirements of the Medicines (Applications for Product Licences and Clinical Trial and Animal Test Certificates) Regulations 1971 (S.I.1971/973) which are amended in consequence.

The Regulations set out the requirements laid down in—

Article 4 (particulars and documents to accompany an application) of Council Directive [65/65/EEC](#) (OJNo. 22, 9.2.65, p.369/65 (OJ/SE 1965–66, p.20)) as amended and supplemented by Article 35 of Directive [75/319/EEC](#) (OJ No. L147, 9.6.75, p.13), Articles 1.1(a) and (c) of Council Directive [83/570/EEC](#) (OJ No. L332, 28.11.83, p.1), Article 1.1 of Council Directive [87/21/EEC](#) (OJ No. L15, 17.1.87, p.36) and Article 3 of Council Directive [89/343/EEC](#) (OJ No. L142, 25.5.89, p.16), and

Article 4a (information to be contained in the summary of product characteristics) of Directive [65/65/EEC](#) as inserted by Article 1.2 of Council Directive [83/570/EEC](#) and as amended and supplemented by Article 1.4 of Council Directive [89/341/EEC](#) (OJ No. L142, 25.5.89, p.11), Article 3 of Council Directive [89/342/EEC](#) (OJ No. L142, 25.5.89, p.14) and Article 4 of Directive [89/343/EEC](#),

(regulation 4(1) and Schedule 1) subject to minor adaptations to take account of the existing framework of the Act and relevant subordinate legislation made under it, and to modified ordering of the summary of product characteristics.

The Regulations also incorporate from other relevant Directives various additional specific items and other provisions of major substance required by those Directives, most notably the provisions concerning experts' reports laid down in Articles 1 and 2 of Council Directive [75/319/EEC](#) (see the definition of “expert” in regulation 1(2), and paragraphs 12 and 13 of Schedule 1). They incorporate by reference (see regulation 4(1) and the definition of “the Directives” in regulation 1(2)) the more detailed requirements of those Directives as to the preparation and presentation of the material (in particular those set out in the new Annex to Council Directive [75/318/EEC](#) (OJ No. L147, 9.6.75, p.1) as substituted by Commission Directive [91/507/EEC](#) (OJ No. L270, 26.9.91, p.32).

Schedule 2 to the Regulations sets out special circumstances in which the results of pharmacological and toxicological tests or clinical trials need not be provided. Paragraphs 1 to 4 reflect the provisions of Article 4.8(a) of Directive [65/65/EEC](#), dealing with circumstances where the product for which a licence is sought is essentially similar to an existing licensed product, or where the relevant information is available from published scientific literature. Paragraph 5 deals with the special exceptions set out in Part 4, paragraph G of the new Annex to Council Directive [75/318/EEC](#) concerning circumstances where comprehensive evidence cannot be provided because of the rarity of the relevant medical conditions, deficiencies in the state of scientific knowledge or ethical objections to carrying out tests.

Schedule 3 sets out the “drug master file” provisions laid down in Part 2, paragraph C.1 of the new Annex to Directive [75/318/EEC](#), under which the details of active ingredients manufactured by someone other than the applicant may, in certain circumstances, be supplied by the manufacturer instead of by the applicant.

The Regulations also provide that the same requirements as to the material to be provided in or with applications apply in relation to products which are not covered by the Directives as apply in relation to those which are (regulation 4(2)).

The Medicines (Standard Provisions for Licences and Certificates) Amendment (No. 2) Regulations 1993 (S.I. [1993/2539](#)) amongst other things make related provision to deal with, in particular, the provision to the licensing authority of new information and, in special circumstances (see paragraph 22 of Schedule 1 to these Regulations), the carrying out of a specified programme of studies, after the grant of a licence.