STATUTORY INSTRUMENTS

1995 No. 2808

MEDICINES

The Medicines (Exemption from Licences) (Clinical Trials) Order 1995

Made - - - -	*27th October 1995*
Laid before Parliament	*6th November 1995*
Coming into force - -	*8th December 1995*

The Secretaries of State concerned with health in England, in Wales and in Scotland respectively and the Department of Health and Social Services for Northern Ireland, acting jointly in exercise of the powers conferred upon them by sections 15(1) and 129(4) of the Medicines Act 1968(**1**) or, as the case may be, those conferred by those provisions and now vested in them(**2**) 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 this Order(**3**), hereby make the following Order:

Citation and commencement

1. This Order may be cited as the Medicines (Exemption from Licences) (Clinical Trials) Order 1995 and shall come into force on 8th December 1995.

Interpretation

2.—(1) In this Order—

(a) "the Act" means the Medicines Act 1968;

"approved name" in relation to a constituent is either the name of the substance or article which appears in the current edition of the list prepared in accordance with section 100 of the Act (lists of names) and published by the Ministers or the international non-proprietary name recommended by the World Health Organisation;

(**1**) 1968 c. 67. The expressions "the Health Ministers" and "the appropriate Ministers" are defined in section 1 of that Act as amended by S.I. 1969/388, Schedule 1.

(**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 Department of Health and Social Services for Northern Ireland 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.

"medicinal product" includes any substance or article for human use specified in an order made under section 104 or 105(1)(b) of the Act (application of Act to certain articles and substances and to certain other substances which are not medicinal products) which is for the time being in force and which directs that sections 31 and 35(8) and (9) of the Act shall have effect in relation to that substance or article(**4**);

"monograph" means a monograph in the current edition of the European Pharmacopoeia, of any compendium published by the Health Ministers or the Agriculture Ministers under section 99 of the Act (new editions of British Pharmacopoeia and other compendia), of the British Pharmacopoeia or of the British Pharmaceutical Codex;

"monograph name" means, in relation to a constituent, the name which appears at the head of the relevant monograph;

"notice" means notice in writing;

"supplier" means a person selling or supplying, or procuring the sale, supply, manufacture or assembly of, a medicinal product for the purposes of a clinical trial;

"usage guideline" means the notice referred to in article 4(1)(a)(iii) of this Order;

(b) a reference to a numbered article is to the article of this Order bearing that number and a reference in an article to a numbered paragraph is to the paragraph of that article bearing that number.

(2) Section 127 of the Act (service of documents) applies to notices required or authorised to be given or sent by any provision of this Order as it applies to notices required or authorised to be given or sent by any provision of the Act.

(3) For the purposes of calculating any period of days referred to in this Order no account shall be taken of Christmas Day, Good Friday or a bank holiday in England under the Banking and Financial Dealings Act 1971(**5**).

Exemption from licences in respect of clinical trials

3. Subject to the conditions specified in article 4 and to the limitations specified in article 5, the restrictions imposed by section 7 of the Act(**6**) (which restricts dealings with medicinal products) shall not apply to anything done which consists of selling or supplying, or procuring the sale, supply, manufacture or assembly of, a medicinal product for the purposes of a clinical trial.

Conditions

4.—(1) The exemption conferred by article 3 is subject to the conditions that:

(a) the supplier has given or sent to the licensing authority a notice which states his intention to sell or supply, or procure the sale, supply, manufacture or assembly of, medicinal products of the description in question for the purposes of a clinical trial and which is accompanied by—

(i) the particulars and the summaries specified in Schedule 1 to this Order,

(**4**) *See* the Medicines (Surgical Materials) Order 1971 (S.I. 1971/1267), the Medicines (Dental Filling Substances) Order 1975 (S.I. 1975/533) and the Medicines (Specified Articles and Substances) Order 1976 (S.I. 1976/968), each amended by the Medical Devices (Consequential Amendments—Medicines) Regulations 1994 (S.I. 1994/3119).

(**5**) 1971 c. 80.

(**6**) Section 7 was amended by S.I. 1977/1050, regulation 2, (N.I.) S.R. 1077 No. 170, regulation 3, S.I. 1983/1724, regulation 2, S.I. 1992/604, regulation 2, S.I. 1994/276, regulation 3; it has effect in part, and with modifications, in relation to radiopharmaceutical-associated products (S.I. 1992/605); and is disapplied by S.I. 1994/3144, regulation 9(2), in relation to relevant medicinal products as defined in regulation 1 of those Regulations.

(ii) a certificate signed by a doctor which lists his medical and scientific qualifications and which states that he is a medical adviser in the employment of, or a consultant to, the supplier; that he has satisfied himself as to the accuracy of the summaries specified at paragraph 14 of Schedule 1 to this Order; and that, having regard to the contents of those summaries, he is of the opinion that it is reasonable for the proposed clinical trial to be undertaken, and

(iii) a notice containing the information specified in Schedule 2 to this Order;

(b) the licensing authority have not, before the end of the specified period, given or sent to the supplier a notice stating that the provisions of this Order shall not apply to the activities proposed to be carried out by him in relation to the medicinal product; and

(c) the supplier has given an undertaking to the licensing authority that he will inform them forthwith of—

(i) any adverse reactions associated with the administration of the medicinal product that are both serious and unexpected,

(ii) any other matter coming to his attention which might reasonably cause the licensing authority to think that the medicinal product could no longer be regarded as a product which could safely be administered for the purposes of the clinical trial or as a product which was of satisfactory quality for those purposes,

(iii) any change in respect of any matter specified in Schedule 3 to this Order, and

(iv) any refusal to approve the clinical trial by a committee established or recognised by a health authority constituted under the National Health Service Act 1977(**7**) or, as the case may be, by a Health Board or a Special Health Board constituted under the National Health Service (Scotland) Act 1978(**8**) or by a Health and Social Services Board constituted under the Health and Personal Social Services (Northern Ireland) Order 1972(**9**), to advise on the ethics of research investigations on human beings.

(2) In paragraph (1)(b) and article 5(1), "the specified period" means the period of thirty-five days from the date on which the licensing authority gives or sends the supplier notice that they have received the notice referred to in paragraph (1)(a), or such period extended by the licensing authority by not more than twenty-eight days; and if they so extend such period such licensing authority shall give or send to the supplier, within such period of thirty-five days, a notice stating the duration of the extension.

Coming into effect, duration and termination of exemption

5.—(1) The exemption conferred by article 3 shall take effect on the expiry of the specified period and shall continue, if the conditions specified in article 4 are fulfilled, for a period of three years unless it is terminated in accordance with paragraphs (2) and (3).

(2) The licensing authority may, by notice given or sent to the supplier, terminate the exemption conferred by article 3 in relation to any description of medicinal product if it appears to them that—

(a) medicinal products of that description can no longer be regarded as products which can safely be administered for the purposes of the clinical trial in question; or

(b) the specification or standards to which medicinal products of that description are manufactured can no longer be regarded as satisfactory; or

(**7**) 1977 c. 49. The definition of "health authority" in section 128(1) of that Act was substituted by the Health and Social Security Act 1984 (c. 48), paragraph 11 of Schedule 3. See also section 2 of the National Health Service and Community Care Act 1990 (c. 19).

(**8**) 1978 c. 29. Section 2, under which Health Boards are constituted, was amended to permit the creation of Special Health Boards by the National Health Service and Community Care Act 1990, section 28.

(**9**) S.I. 1972/1265 (N.I. 14).

(c) any changes which have been notified in respect of matters specified in Schedule 3 to this Order may adversely affect the safety of a patient taking part in the clinical trial; or

(d) the notice referred to in article 4(1)(a) or any document which accompanied it was false or incomplete in a material particular; or

(e) the supplier is in breach of any part of the undertaking referred to in article 4(1)(c).

(3) The date on which the termination referred to in paragraph (2) takes effect shall be such date as may be specified by the licensing authority in the notice referred to in that paragraph.

Amendment of Order

6. In article 3 (exemption from licences and certificates in respect of clinical trials) of the Medicines (Exemption from Licences) (Clinical Trials) Order 1981(**10**) the words "section 7 and" are omitted.

Tom Sackville
24th October 1995 — Secretary of State for Health

William Hague
27th October 1995 — Secretary of State for Wales

James Douglas-Hamilton
25th October 1995 — Minister of State, The Scottish Office

Sealed with the Official Seal of the Department of Health and Social Services for Northern Ireland on

L.S.

F. A. Elliott
25th October 1995. — Permanent Secretary

(**10**) S.I. 1981/164.

SCHEDULE 1

Article 4(1)(a)(i)

PARTICULARS AND SUMMARIES WHICH ARE TO ACCOMPANY A NOTICE GIVEN OR SENT UNDER ARTICLE 4(1)(a)

1. The name and address of the supplier and any other name under which he carries on business.

(a) (a) The name and address of any person taking part, in the course of a business carried on by him, in the manufacture or assembly of the medicinal product, and

(b) in the case of an imported product, the name and address of the manufacturer or assembler of the medicinal product in the form in which it is to be imported.

3. The name or proposed name of the medicinal product or, where it has not been given a name, the designation by which the supplier identifies that product.

4. The chemical structural formula for each active constituent or, where an active constituent is the subject of a monograph, the monograph name if preferred.

5. A description of the pharmaceutical form in which the medicinal product is to be administered.

6. The specification of the medicinal product including a statement of its qualitative and quantitative composition, giving the constituents whether active or not, and including all colouring matter, flavouring agents and perfumes.

7. In respect of each constituent, whether active or not—

(a) the approved name or the monograph name, or

(b) where there is no approved name or monograph name, a designation by which it can readily be identified.

8. A description of the containers used for the medicinal product and a statement of any special directions given by the manufacturer for storage and transport.

9. The proposed dosage and its duration, and the methods and routes of administration, of the medicinal product.

10. A description of the proposed clinical trial including the duration of the trial, the number of patients involved and a description of how safety will be monitored during the trial.

(a) (a) A summary of pharmaceutical data in respect of the method of synthesis or preparation of each active constituent and, where appropriate, the results of physico-chemical tests to substantiate the structure of the compound, or

(b) where the active constituent is the subject of a monograph, the monograph name, if preferred.

(a) (a) Where a specification has been established for a constituent—

(i) a summary of pharmaceutical data in respect of the specification of each such constituent (whether active or not) or, where a constituent is the subject of a monograph, the monograph name, if preferred,

(ii) in the case of each constituent (whether active or not), a summary of pharmaceutical data in respect of the quality control procedures and methods to be applied to ensure compliance with the specification of that constituent;

(b) where a specification has not been established for a constituent, a batch characterisation for each batch of that constituent to be used in the clinical trial.

13. A summary of pharmaceutical data in respect of—

(a) the method of manufacture or assembly of the medicinal product,

(b) the procedures and methods employed and specifications used in the process of manufacture or assembly to ensure the uniformity of each medicinal product (together with evidence of the stability of the medicinal product and of its bio-availability for the use intended), and

(c) the methods to be employed during manufacture for determining the identity, purity and potency of the medicinal product (together with the address of the premises where such processes are to be carried out).

14. Summaries of reports and evaluations of any experimental and biological studies and of other preclinical, clinical or laboratory studies carried out with each medicinal product or its constituents, which in the view of the supplier are relevant to the assessment of the safety, quality or efficacy of the medicinal product, together with references to relevant publications or other clinical trials.

SCHEDULE 2

Article 4(1) (a) (iii)

INFORMATION TO BE CONTAINED IN USAGE GUIDELINE

1. The name or proposed name of the medicinal product or, where it has not been given a name, the designation by which the supplier identifies that product.

2. A description of each clinical use to be investigated and, in respect of each such use,

(a) the nature and purpose of the clinical trial,

(b) a description of each pharmaceutical form in which the medicinal product is to be administered, and, in respect of each such form, the methods and routes by which the medicinal product is to be administered, the proposed maximum daily dosage and the proposed maximum duration of exposure to the product.

3. The minimum and maximum ages, and the maximum number, of patients to be involved in the clinical trial, and, where the clinical trial comprises a series of investigations, the maximum number of patients to be involved in each investigation in that series.

4. The criteria for the selection of patients for, and the exclusion and withdrawal of patients from, the clinical trial.

5. A description of how safety will be monitored during the clinical trial.

SCHEDULE 3

Article 4(1)(c)(iii)

MATTERS IN RESPECT OF WHICH THE LICENSING AUTHORITY SHALL FORTHWITH BE INFORMED OF CHANGES

(a) (a) The name and address of any person taking part, in the course of a business carried on by him, in the manufacture or assembly of the medicinal product, and

(b) in the case of an imported medicinal product, the name and address of the manufacturer or assembler of the medicinal product in the form in which it is imported.

2. The active or inactive constituents, or the method of manufacture or assembly, of the medicinal product, where such change will affect the bio-availability or the shelf life of that medicinal product or both.

3. The method of synthesis of any active constituent where such change will affect the range or level of impurities produced.

4. Information in the usage guideline.

EXPLANATORY NOTE

(This note is not part of the Order)

This Order and the Medicines (Exemption from Licences and Certificates) (Clinical Trials) Order 1995 (S.I.1995/2809), which comes into force immediately after this Order came into force, together effect the revocation and replacement of the Medicines (Exemption from Licences) (Clinical Trials) Order 1981 ("the 1981 Order"). The 1981 Order granted, in respect of medicinal products for use in clinical trials, exemption from restrictions imposed by Part II of the Medicines Act 1968 ("the Act") on certain dealings in medicinal products without product licences or clinical trial certificates. The 1981 Order specified conditions subject to which the exemption applied, and provided for the termination of the exemption in specified circumstances.

Article 3 of this Order exempts specified dealings in medicinal products, for the purposes of a clinical trial, from the restrictions in section 7 of the Act. By virtue of the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 (S.I.1994/3144), section 7 no longer applies in relation to medicinal products that are "relevant medicinal products" as defined in regulation 1. The exemption conferred by article 3 is subject to the conditions and provisions set out in articles 4 and 5 of, and Schedule 1 and 3 to, this Order.

The principal changes from the conditions imposed by the 1981 Order are that:

(1) in accordance with article 4(1)(a)(iii), the supplier must submit to the licensing authority, in addition to the particulars and summaries and the doctor's certificate referred to in article 4(1)(a)(i) and (ii), a usage guideline (article 2(1)(a) and Schedule 2);

(2) in accordance with article 4(1)(c)(i), the supplier must undertake to inform the licensing authority forthwith of any serious unexpected adverse reactions associated with the administration of the medicinal product; the 1981 Order required an undertaking to inform of any adverse reactions or effects;

(3) the number of matters in respect of changes in which article 4(1)(c)(iii) requires the supplier to undertake to inform the licensing authority is reduced, and the matters now include the usage guideline;

(4) there is no requirement to submit to the licensing authority the names and qualifications of investigators.

Article 6 amends the 1981 Order so as to replace the exemption it granted from the restrictions imposed by section 7 of the Act with the exemption in article 3 of this Order.