STATUTORY INSTRUMENTS

1966 No. 502

THERAPEUTIC SUBSTANCES

The Therapeutic Substances (Manufacture of Hormone Products) Regulations 1966

Made - - -	*27th April* 1966
Laid before Parliament	*5th May* 1966
Coming into Operation	*1st June* 1966

The Joint Committee constitued by section 4(1) of the Therapeutic Substances Act 1956(a), in exercise of the powers conferred on them by sections 1 and 5 of the said Act, after consultation with the Advisory Committee constituted under section 4(2) of the said Act, hereby make the following regulations:—

PART I

PRELIMINARY

Citation, Commencement and Interpretation

1.—(1) These regulations may be cited as the Therapeutic Substances (Manufacture of Hormone Products) Regulations 1966 and shall come into operation on 1st June 1966.

(2) In these regulations, unless the context otherwise requires—

" the Act " means the Therapeutic Substances Act 1956;

" the general regulations " means the Therapeutic Substances (Manufacture and Importation) General Regulations 1963, as amended(b);

" the licensing authority " has the same meaning as in the general regulations;

" parenteral injection " in relation to any substance includes any administration of the substance by insertion into the body by any route other than that of the gastro-intestinal tract but does not include any application of the substance to the skin.

(3) Any reference in these regulations to any provision of the general regulations shall be construed as a reference to that provision as amended, extended or re-enacted by any subsequent regulations made under Part I of the Act.

(4) For the purposes of these regulations the cubic centimetre may be used wherever the millilitre is indicated.

(5) The Interpretation Act 1889(c) shall apply to the interpretation of these regulations as it applies to the interpretation of an Act of Parliament.

(a) 4 & 5 Eliz. 2. c. 25. (b) S.I. 1963/1450, 1964/1076 (1963 II, p. 2483; 1964 II, p. 2380).
(c) 52 & 53 Vict. c. 63.

Revocation of existing regulations

2. The Therapeutic Substances (Manufacture of Hormone Products) Regulations 1963(a) and the Therapeutic Substances (Manufacture of Hormone Products) Amendment Regulations 1964(b) are hereby revoked.

Inclusion of substances in schedule to Act

3. Notwithstanding the revocation by these regulations of the Therapeutic Substances (Manufacture of Hormone Products) Regulations 1963 and the Therapeutic Substances (Manufacture of Hormone Products) Amendment Regulations 1964, the following shall continue to be included in schedule 1 to the Act:—

(a) corticotrophin and preparations thereof;

(b) preparations of pituitary (posterior lobe) or of the active principles thereof (whether obtained by fractionation of the gland or by synthesis) or of derivatives of those principles with the same specific biological action, which are intended for use by parenteral injection;

(c) chorionic gonadotrophin and preparations thereof.

PART II

GENERAL PROVISIONS

Labelling

4.—(1) Subject to the provisions of paragraph (2) of this regulation and of regulation 73 of these regulations—

(a) the particulars specified in regulation 6(1)*(a)*, *(b)* and *(c)* of the general regulations shall be borne by the container of any substance to which these regulations relate;

(b) the particulars specified in sub-paragraph *(g)* of the said regulation 6(1) shall be borne both by the container of any such substance and by the package in which it is offered for sale;

(c) the particulars specified in sub-paragraphs *(e)*, *(f)*, *(h)* and *(i)* of the the said regulation 6(1) shall be borne either by the container of any such substance or by the package in which it is offered for sale.

(2) Where by any provision of these regulations any particulars are required to be borne by the container of any substance to which these regulations relate and such container is of a capacity of less than 2·5 millilitres, such particulars may, with the consent of the licensing authority, be borne instead by the package in which the container is offered for sale.

PART III

GENERAL PROVISIONS RELATING TO INSULIN

Definition and proper name

5. Insulin is a preparation of the specific antidiabetic principle of the pancreas. Its proper name is " insulin ".

(a) S.I. 1963/1455 (1963 II, p. 2529). (b) S.I. 1964/1432 (1964 III, p. 3314).

Standard preparation

6. The standard preparation of insulin is one kept at the National Institute for Medical Research, London.

Unit of standardisation

7. The unit of insulin for the purposes of these regulations is the specific activity contained in such an amount of the standard preparation of insulin as is for the time being indicated by the licensing authority, on the advice of the Medical Research Council, as the quantity exactly equivalent to the unit accepted for international use.

Tests for sterility

8. Insulin and preparations thereof shall be tested for sterility in accordance with the general regulations:

Provided that in the case of any dry preparation of insulin the tests shall be applied with such modifications as the licensing authority consider appropriate for that preparation.

Potency and Quality

9.—(1) Insulin shall have a potency of not less than 23 units per milligram calculated with reference to the dried substance. For the purpose of this regulation the dried substance shall be such insulin as loses not more than 0·5 per cent. of its original weight when dried for a period of 24 hours at a temperature of 20°C to 25°C over phosphorus pentoxide at a pressure not exceeding 5 millimetres of mercury.

(2) Insulin which is issued as a watery solution shall have a pH value lying either between 3·0 and 3·5 or between 6·5 and 7·5.

(3) Insulin shall contain not more than 0·04 milligram of zinc per 100 units of insulin.

Test for Potency

10. Insulin shall be tested biologically for potency by comparison with the standard preparation, and the potency and the fiducial limits of error (P=0·95) of the potency shall be calculated from the results of the test. The estimated potency of the substance shall not be greater than 111 per cent. and not less than 90 per cent. of the potency stated by the manufacturer. The fiducial limits of error (P=0·95) of the estimated potency shall lie between 80 and 125 per cent. of the potency stated by the manufacturer:

Provided that this regulation shall not apply to insulin used in the manufacture of a preparation which is to be tested for potency in pursuance of regulation 13 of these regulations.

Method of issue

11. No mixture containing insulin with any other substance shall be issued unless the licensing authority are satisfied that such mixture is capable of passing the tests for purity and potency as provided in these regulations for insulin.

PART IV

PROVISIONS RELATING TO ALL PREPARATIONS OF INSULIN

Definition and proper names

12. The proper name of a preparation of insulin, or of a mixture of insulin with another therapeutic substance, for which a proper name is not expressly

provided in these regulations is " insulin " together with such words or abbreviations as may be approved by the licensing authority as descriptive of that preparation or mixture.

Test for potency

13. Preparations of insulin shall, if the licensing authority so require, be tested biologically by comparison with the standard preparation of insulin in the manner provided by regulation 10 of these regulations.

Method of Issue

14. No mixture containing preparations of insulin with any other substance shall be issued unless the licensing authority are satisfied that such mixture is capable of passing the tests for purity and potency as provided in these regulations for insulin.

Labelling

15. In addition to the particulars required by paragraph 1*(a)* and *(b)* of regulation 4 of these regulations, particulars of the strength of a preparation of insulin shall, except as provided in paragraph (2) of the said regulation 4, be borne by the container thereof, stated—

(a) if it is a liquid preparation, as the number of international units of insulin per millilitre;

(b) if it is a solid preparation in tablet form, as the number of international units of insulin in each tablet.

PART V

GENERAL PROVISIONS RELATING TO LONG-ACTING INSULIN AND PREPARATIONS OF LONG-ACTING INSULIN

Definition

16. Long-acting insulin consists of insulin prepared in such a way or combined with such a substance or substances that its hypoglycaemic action after parenteral injection is prolonged.

Test for prolongation of action

17. Long-acting insulin shall, if the licensing authority so require, be tested by comparison with the standard preparation of insulin, by a method approved by the licensing authority, for its power of prolonging insulin hypoglycaemia.

PART VI

SPECIAL PROVISIONS RELATING TO GLOBIN ZINC INSULIN

Definition and proper name

18. Globin zinc insulin is a preparation of the zinc salt of insulin combined with globin. Its proper name is " globin zinc insulin ".

Quality

19.—(1) The preparation shall not contain less than 1·45 nor more than 1·75 per cent. w/v of glycerin.

(2) The preparation shall not contain less than 0·25 nor more than 0·35 milligram of zinc for each 100 units of insulin.

PART VII

SPECIAL PROVISIONS RELATING TO PROTAMINE ZINC INSULIN

Definition and proper name

20. Protamine zinc insulin is the complex produced by the interaction of insulin with a suitable protamine and zinc chloride. Its proper name is " protamine zinc insulin ".

Quality

21.—(1) The quantity of protamine used in the preparation of protamine zinc insulin shall not be less than 1·0 milligram nor more than 1·7 milligrams of protamine sulphate for each 100 units of insulin.

(2) The liquor from which the precipitate of protamine zinc insulin has been removed shall not contain more than 4·0 per cent. of the stated activity of the original protamine zinc insulin.

(3) The suspension shall have a pH value lying between 6·9 and 7·3.

(4) The preparation shall not contain less than 0·2 nor more than 0·25 milligram of zinc for each 100 units of insulin.

(5) The preparation shall not contain less than 1·45 nor more than 1·75 per cent. w/v of glycerin.

Labelling

22. In addition to the particulars required by paragraph (1)*(a)* and *(b)* of regulation 4 of these regulations, a statement to the effect that the contents should be gently shaken immediately before use shall, except as provided in paragraph (2) of the said regulation 4, be borne by the container of a substance to which this part of these regulations relates.

PART VIII

SPECIAL PROVISIONS RELATING TO ISOPHANE INSULIN

Definition and proper name

23. Isophane insulin consists substantially of a crystalline complex of insulin, protamine and zinc suspended in a buffered medium. Its proper name is " isophane insulin ".

Quality

24.—(1) The quantity of protamine used in the preparation of isophane insulin shall not be less than 0·3 milligram nor more than 0·6 milligram of protamine sulphate for each 100 units of insulin.

(2) The suspension shall have a pH value lying between 7·1 and 7·4.

(3) The preparation shall contain not less than 1·4 nor more than 1·8 per cent. w/v of glycerin.

(4) The liquor from which the precipitate of isophane insulin has been removed shall not contain more than 4·0 per cent. of the stated activity of the original isophane insulin.

Test for freedom from protaminase

25.—(1) Isophane insulin shall be tested in accordance with this regulation to ensure its freedom from contamination with protaminase.

(2) A sample of 40 millilitres of isophane insulin shall be divided into two equal portions. One portion shall be centrifuged and the deposit washed with alcohol, dried and weighed. The other portion shall be placed in an incubator at 37°C and left for 30 days. It shall then be removed from the incubator and centrifuged, and the deposit similarly washed with alcohol, dried and weighed. The loss in weight after 30 days' incubation at 37°C shall not exceed 10 per cent. of the initial weight.

Labelling

26. In addition to the particulars required by paragraph (1)*(a)* and *(b)* of regulation 4 of these regulations, a statement to the effect that the contents should be gently shaken immediately before use shall, except as provided in paragraph (2) of the said regulation 4, be borne by the container of a substance to which this part of these regulations relates.

PART IX

SPECIAL PROVISIONS RELATING TO INSULIN ZINC SUSPENSIONS

Definition and proper names

27.—(1) Insulin zinc suspensions are preparations of insulin with zinc in a suitable buffer such that the insulin is in a form insoluble in water. The proper name of any such preparation is " insulin zinc suspension " followed in parenthesis by the word " crystalline " if the insulin is almost wholly in crystalline form or by the word " amorphous " if the insulin is almost wholly in amorphous form and, when not followed by a word in parenthesis, the term " insulin zinc suspension " shall denote a buffered suspension of seven parts of insulin zinc suspension (crystalline) with three parts of insulin zinc suspension (amorphous).

(2) Insulin zinc suspension (crystalline) is a buffered suspension of insulin with zinc chloride in the form of crystals insoluble in water.

(3) Insulin zinc suspension (amorphous) is a buffered suspension of insulin with zinc chloride in the amorphous form insoluble in water.

Quality

28.—(1) Insulin zinc suspensions shall have a pH value lying between 7·2 and 7·5.

(2) The liquor from which the precipitate of any of the insulin zinc suspensions mentioned in regulation 27 of these regulations has been removed shall not contain more than 4·0 per cent. of the stated activity of the original zinc suspension.

(3) The liquor from which the precipitate of any of the insulin zinc suspensions mentioned in regulation 27 of these regulations has been removed shall not contain more than 0·0055 per cent. w/v of zinc in preparations containing 40 units of insulin per millilitre nor more than 0·007 per cent. w/v of zinc in preparations containing 80 or more units of insulin per millilitre.

(4) The amount of insulin extractable with a suitably buffered acetone solution from any centrifuged precipitate of insulin zinc suspension (crystalline) shall be not greater than 15 per cent. of the total insulin present.

(5) The amount of insulin extractable with a suitably buffered acetone solution from any centrifuged deposit of insulin zinc suspension shall be between 27 and 40 per cent. of the total insulin present.

Labelling

29. In addition to the particulars required by paragraph 1*(a)* and *(b)* of regulation 4 of these regulations, a statement to the effect that the contents should be gently shaken immediately before use shall, except as provided in paragraph (2) of the said regulation 4, be borne by the container of a substance to which this part of these regulations relates.

PART X

GENERAL PROVISIONS RELATING TO PITUITARY (POSTERIOR LOBE)

Scope of this Part

30. This part of these regulations relates to preparations of pituitary (posterior lobe) which are intended for use by injection and to preparations of the active principles of pituitary (posterior lobe) intended for use by parenteral injection.

Standard Preparation

31. The standard preparation of oxytocic, vasopressor or antidiuretic substances is an acetone-dried powder of pituitary (posterior lobe) kept at the National Institute for Medical Research, London.

Unit of Standardisation

32. The unit for the purpose of this part of these regulations is the specific oxytocic, vasopressor or antidiuretic activity, as the case may be, contained in such an amount of the standard preparation of oxytocic, vasopressor or antidiuretic substances as is for the time being indicated by the licensing authority, on the advice of the Medical Research Council, as the quantity exactly equivalent to the unit accepted for international use.

Quality

33. Preparations of pituitary (posterior lobe), or of the active principles thereof, shall have a pH value lying between 3·0 and 4·5.

Test for Sterility

34. Preparations of pituitary (posterior lobe), or of the active principles thereof, shall be tested for sterility in accordance with the general regulations.

Labelling

35. In addition to the particulars required by paragraph 1*(a)* and *(b)* of regulation 4 of these regulations, particulars of the strength of a substance to which this part of these regulations relates shall, except as provided in paragraph (2) of the said regulation 4, be borne by the container thereof, stated—

(a) in the case of preparations of pituitary (posterior lobe) and preparations of the active principles of pituitary (posterior lobe), other than preparations of vasopressin, as the number of units (oxytocic) per millilitre of the preparation;

(b) in the case of preparations of vasopressin, as the number of units (vasopressor) per millilitre of the preparation.

PART XI

SPECIAL PROVISIONS RELATING TO PITUITARY (POSTERIOR LOBE) INJECTION

Definition and proper name

36. Pituitary (posterior lobe) injection is a watery extract of pituitary (posterior lobe). Its proper name is " pituitary (posterior lobe) injection ".

Method of preparation

37. The method used for preparing pituitary (posterior lobe) injection shall be such as the licensing authority may approve.

PART XII

SPECIAL PROVISIONS RELATING TO PREPARATIONS OF OXYTOCIN

Definition and proper name

38. This part of these regulations relates to preparations containing the oxytocic principle of pituitary (posterior lobe), whether obtained by fractionation from the glands of oxen or other mammals or by synthesis. The proper name of such a preparation is " oxytocin " qualified by a word or words approved by the licensing authority as indicating the nature of the preparation.

Test for freedom from vasopressor activity

39. Preparations of oxytocin, other than those obtained by synthesis, shall be tested biologically for freedom from vasopressor activity by comparison with the standard preparation defined in regulation 31 of these regulations, and shall pass the test if they contain less than one unit of vasopressor activity per 20 units of oxytocin.

PART XIII

SPECIAL PROVISIONS RELATING TO PREPARATIONS OF VASOPRESSIN

Definition and proper name

40. This part of these regulations relates to injectable preparations containing the vasopressor and antidiuretic principles of pituitary (posterior lobe), whether obtained by fractionation from the glands of oxen or other mammals or by synthesis. The proper name of such a preparation is " vasopressin " qualified by a word or words approved by the licensing authority as indicating the nature of the preparation.

Test for freedom from oxytocic activity

41. Preparations of vasopressin shall be tested biologically for freedom from oxytocic activity by comparison with the standard preparation defined in regulation 31 of these regulations, and shall pass the test if they contain less than 2 units of oxytocic activity per 20 units of vasopressin.

Labelling

42. Where the antidiuretic activity of a preparation of vasopressin has been determined by a method approved by the licensing authority, the number of units (antidiuretic) per millilitre may be stated on the container, in addition to the particulars required by regulation 35*(b)* of these regulations.

PART XIV

GENERAL PROVISIONS APPLICABLE TO CORTICOTROPHIN AND PREPARATIONS OF CORTICOTROPHIN

Definition and proper names

43.—(1) Corticotrophin is a substance which may be obtained from the anterior lobe of the pituitary gland and which contains the peptide hormone that increases the rate at which corticoid hormones are secreted by the adrenal gland.

(2) The proper name of corticotrophin is " corticotrophin ".

Method of preparation

44. The method used for preparing corticotrophin shall be such as the licensing authority may approve.

Standard preparations

45. The standard preparation of corticotrophin is one of dried corticotrophin kept at the National Institute for Medical Research, London.

Unit of standardisation

46. The unit of corticotrophin for the purpose of these regulations is the specific activity contained in such an amount of the standard preparation as is for the time being indicated by the licensing authority, on the advice of the Medical Research Council, as the quantity exactly equivalent to the unit accepted for international use.

Tests for sterility

47. Corticotrophin and preparations thereof shall be tested for sterility in accordance with the general regulations.

Labelling

48. In addition to the particulars required by paragraph 1*(a)* and *(b)* of regulation 4 of these regulations, the following particulars shall, except as provided in paragraph (2) of the said regulation 4, be borne by a container of corticotrophin or a preparation of corticotrophin:—

(a) the particulars specified in regulation 6(1)*(f)* of the general regulations;

(b) a statement of the species of animal from which the substance is derived;

(c) in the case of a solid preparation, the total number of units in the container and the volume to be added of the vehicle which is recommended for mixture with the preparation;

(d) in the case of a liquid preparation, the total number of units of the solution, the total volume in the container and the nature of the vehicle.

PART XV

SPECIAL PROVISIONS RELATING TO CORTICOTROPHIN

Quality

49.—(1) Corticotrophin shall not be issued with a potency of less than 24 units per milligram where the ox or the sheep gland is used as the source of the

substance, or less than 45 units per milligram where the pig gland is used as the source.

(2) Corticotrophin when dissolved according to the manufacturer's directions, or, if there are no such directions, in water, shall have a pH value lying between 3·0 and 5·0.

Test for potency

50.—(1) Corticotrophin shall, if the licensing authority so require, be tested for minimum potency by a method approved by such authority and shall comply with the requirements set out in paragraph (2) of this regulation.

(2) Corticotrophin shall be assayed in terms of the units defined in regulation 46 of these regulations by injection into hypophysectomised or otherwise specially prepared rats, by a method approved by the licensing authority, and the potency and fiducial limits of error of the potency shall be calculated from the results of the test. The estimated potency shall lie between 80 per cent. and 125 per cent. of the potency stated by the manufacturer. The fiducial limits of error (P=0·95) shall lie between 64 per cent. and 156 per cent. of the potency stated by the manufacturer.

Test for freedom from abnormal toxicity

51.—(1) Corticotrophin shall be free from abnormal toxicity and, if so required by the licensing authority, shall be tested for freedom from abnormal toxicity in accordance with this regulation.

(2) A solution containing 9·0 units of corticotrophin in not more than 0·3 millilitre of physiological saline shall be injected intravenously into each of 5 healthy mice, each weighing between 17 and 22 grams. The preparation shall pass the test either if none of the injected mice dies within 48 hours after the injection, or if only one of the mice dies within that period and, after similar injections have been made into 5 other such mice, none of these mice dies within 48 hours after the injection.

Test for freedom from pressor activity

52. Corticotrophin shall, if so required by the licensing authority, be tested biologically for freedom from pressor activity by comparison with the standard preparation of oxytocic, vasopressor and antidiuretic substances by a method approved by the licensing authority, and shall pass the test if it contains less than 5 units of vasopressor principle per 100 units of corticotrophin.

Labelling

53. In addition to the particulars required by paragraph (1)*(a)* and *(b)* of regulation 4, and regulation 48 of these regulations, a statement of the route of injection used in determining the potency of the substance shall, except as provided in paragraph (2) of the said regulation 4, be borne by the container of corticotrophin.

PART XVI

SPECIAL PROVISIONS RELATING TO PREPARATIONS OF CORTICOTROPHIN INTENDED FOR INTRAVENOUS USE

Method of Preparation

54. Preparations of corticotrophin intended for intravenous use shall be prepared from corticotrophin complying with part XIV of these regulations. They shall be sterilised by a method approved by the licensing authority.

Potency

55. Preparations of corticotrophin intended for intravenous use shall be assayed in their final form in terms of the units defined in regulation 46 of these regulations by intravenous injection into hypophysectomised or otherwise specially prepared rats, by a method approved by the licensing authority, and the potency and the fiducial limits of error of the potency shall be calculated from the results of the test. The estimated potency shall lie between 80 per cent. and 125 per cent. of the potency stated by the manufacturer. The fiducial limits of error (P=0·95) shall lie between 64 per cent. and 156 per cent. of the potency stated by the manufacturer.

Labelling

56. In addition to the particulars required by paragraph (1)*(a)* and *(b)* of regulation 4, and regulation 48 of these regulations, the container of a substance to which this part of these regulations applies shall, except as provided in paragraph (2) of the said regulation 4, bear a statement that the preparation is intended for intravenous use only.

PART XVII

SPECIAL PROVISIONS RELATING TO PREPARATIONS OF CORTICOTROPHIN INTENDED FOR OTHER THAN INTRAVENOUS USE

Method of Preparation

57. Preparations of corticotrophin intended for injection by other than the intravenous route shall be prepared from corticotrophin complying with part XIV of these regulations. They shall be sterilised by a method approved by the licensing authority.

Potency

58. Preparations of corticotrophin intended for injection by other than the intravenous route shall be assayed in their final form in terms of the units defined in regulation 46 of these regulations by subcutaneous injection into hypophysectomised or otherwise specially prepared rats, by a method approved by the licensing authority, and the fiducial limits of error of the potency shall be calculated from the results of the test. The estimated potency shall lie between 80 per cent. and 125 per cent. of the potency stated by the manufacturer. The fiducial limits of error (P=0·95) shall lie between 64 per cent. and 156 per cent. of the potency stated by the manufacturer.

Labelling

59. In addition to the particulars required by paragraph (1)*(a)* and *(b)* of regulation 4, and regulation 48 of these regulations, the container of a substance to which this part of these regulations applies shall, except as provided in paragraph (2) of the said regulation 4, bear a statement that the preparation is for subcutaneous or intramuscular use only.

PART XVIII

SPECIAL PROVISIONS APPLICABLE TO LONG-ACTING CORTICOTROPHIN

Definition

60. Long-acting corticotrophin is a sterile preparation of corticotrophin complying with part XIV of these regulations which is combined with or dissolved in a substance or substances which prolongs or prolong the period of its activity in the body.

Quality

61.—(1) Long-acting corticotrophin as a preparation of corticotrophin with gelatin shall have a pH value lying between 4·5 and 7·0.

(2) Long-acting corticotrophin as a preparation of corticotrophin with zinc hydroxide shall have a pH value lying between 7·6 and 8·1.

(3) Long-acting corticotrophin as a preparation of corticotrophin with zinc hydroxide shall not contain more than 3·0 milligrams of zinc per millilitre.

(4) The liquor obtained by centrifugation of long-acting corticotrophin as a preparation of corticotrophin with zinc hydroxide shall not contain more than 0·1 milligram of zinc per millilitre.

Potency

62. Long-acting corticotrophin shall be assayed in terms of the units defined in part XIV of these regulations by a method which shall involve subcutaneous injection and which shall be approved by the licensing authority.

Test for prolongation

63. Long-acting corticotrophin shall, if the licensing authority so require, be tested biologically to determine its power of prolonging the specific effects of the corticotrophin contained therein, and the nature of the test shall be such as the licensing authority may specify.

Labelling

64. In addition to the particulars required by paragraph (1)*(a)* and *(b)* of regulation 4, and regulation 48 of these regulations, the container of a substance to which this part of these regulations applies shall, except as provided in paragraph (2) of the said regulation 4, bear a statement that the preparation is for subcutaneous or intramuscular use only.

PART XIX

GENERAL PROVISIONS APPLICABLE TO CHORIONIC GONADOTROPHIN AND PREPARATIONS OF CHORIONIC GONADOTROPHIN

Definition and proper name

65.—(1) Chorionic gonadotrophin is a dry sterile preparation of the gonad-stimulating substance obtained from the urine of pregnant women.

(2) The proper name of chorionic gonadotrophin is " chorionic gonadotrophin ".

Methods of preparation and of sterilisation

66. Chorionic gonadotrophin shall be prepared from the urine of pregnant women and shall be sterilised by filtration.

Standard preparation

67. The standard preparation of chorionic gonadotrophin is one of dried chorionic gonadotrophin kept at the National Institute for Medical Research, London.

Unit of standardisation

68. The unit of chorionic gonadotrophin for the purpose of these regulations is the specific activity contained in such an amount of the standard preparation as is for the time being indicated by the licensing authority, on the advice of the Medical Research Council, as the quantity exactly equivalent to the unit accepted for international use.

Strength

69. Chorionic gonadotrophin in solid form shall have a potency not less than 1,500 units per milligram.

Tests for sterility

70. Chorionic gonadotrophin and preparations thereof shall be tested for sterility in accordance with the general regulations.

Test for freedom from oestrogens

71.—(1) Chorionic gonadotrophin shall be tested for freedom from oestrogens in accordance with this regulation.

(2) A solution containing not less than 100 units of chorionic gonadotrophin in not more than 0·5 millilitre of physiological saline shall be injected subcutaneously into each of 3 rats or 3 mice which have been prepared by ovariectomy not less than 14 days prior to the injection. The preparation shall pass the test if vaginal smears taken from all the rats or mice on each of the third, fourth and fifth days following the injection show no signs of positive oestrus response.

Test for freedom from abnormal toxicity

72.—(1) Chorionic gonadotrophin shall be tested for freedom from abnormal toxicity in accordance with this regulation.

(2) A solution containing not less than 1,000 units of chorionic gonadotrophin in not more than 0·5 millilitre of physiological saline shall be injected intravenously over a period of time not exceeding one minute into each of 5 healthy mice, each weighing between 17 and 22 grams. The preparation shall pass the test either if none of the injected mice dies within 48 hours after the injection, or if only one of the mice dies within that period and, after similar injections have been made into 5 other such mice, none of these mice dies within 48 hours after the injection.

Labelling

73. The labelling requirements of paragraph (1) of regulation 4 of these regulations shall not apply in respect of chorionic gonadotrophin or preparations of chorionic gonadotrophin, but instead the following requirements shall, subject to the provisions of paragraph (2) of the said regulation 4 and of regulation 78 of these regulations, apply:—

(a) the particulars specified in regulation 6(1)*(a)*, *(b)*, *(c)* and *(d)* of the general regulations shall be borne by the container thereof;

(b) the particulars specified in sub-paragraph *(f)* of the said regulation 6(1), together with a statement regarding the precautions necessary for best preserving the properties of the contents, shall be borne both by the said container and by the package in which it is offered for sale;

(c) the particulars specified in sub-paragraph *(e)* of the said regulation 6(1) shall be borne either by the said container or by the said package.

PART XX

SPECIAL PROVISIONS RELATING TO CHORIONIC GONADOTROPHIN AND PREPARATIONS THEREOF INTENDED FOR PARENTERAL INJECTION

Method of preparation

74. Preparations of chorionic gonadotrophin intended for parenteral injection shall be prepared from chorionic gonadotrophin complying with the preceding part of these regulations. They shall be sterilised by filtration.

Potency

75. Preparations of chorionic gonadotrophin intended for parenteral injection shall be assayed in their final form, in terms of units defined in regulation 68 of these regulations, by a method approved by the licensing authority, and the potency and the fiducial limits of error of the potency shall be calculated from the results of the test. The estimated potency shall lie between 80 per cent. and 125 per cent. of the potency stated by the manufacturer. The fiducial limits of error (P=0·95) shall lie between 64 per cent. and 156 per cent. of the potency stated by the manufacturer.

Freedom from pyrogenic substances

76.—(1) Chorionic gonadotrophin intended for parenteral injection shall, if the licensing authority so require, be tested for freedom from pyrogenic substances in accordance with the general regulations, and in any event shall be free from such substances to such an extent that, if so tested, it would pass the test.

(2) The number of units of chorionic gonadotrophin for the purpose of the test for freedom from pyrogenic substances shall be not less than 1,500 per kilogram of the weight of each rabbit used in the test.

Method of issue

77. No mixture containing chorionic gonadotrophin or preparations thereof intended for parenteral injection with any other substance shall be issued unless the licensing authority are satisfied that such mixture is capable of passing the tests for purity and potency as provided in these regulations for chorionic gonadotrophin or preparations thereof.

Labelling

78. The labelling requirements of regulation 73 of these regulations shall not apply in respect of chorionic gonadotrophin or preparations of chorionic gonadotrophin intended for parenteral injection, but instead the following requirements shall, subject to the provisions of regulation 4(2) of these regulations, apply:—

(a) the particulars specified in regulation 6(1)*(a)*, *(b)* and *(c)* of the general regulations shall be borne by the container thereof, and, in addition—

(i) in the case of a solid preparation, the total number of units in the container, the nature of the vehicle for mixing with the preparation and the volume to be added; or

(ii) in the case of a liquid preparation, the total number of units in the solution, the total volume in the container and the nature of the vehicle included in the mixture

shall be shown on the container;

(b) the particulars specified in regulation 6(1)*(e)*, *(f)*, *(g)* and *(h)* of the general regulations, together with the details of any substances which have been added, shall be borne either by the said container or by the package in which it is offered for sale.

These regulations were made by the aforesaid Joint Committee on 27th April 1966.

Kenneth Robinson,
William Ross,
W. J. Morgan,
Members of the Joint Committee

Wilfred Turner,
Clerk to the Joint Committee

EXPLANATORY NOTE

(*This Note is not part of the Regulations.*)

These regulations, made under Part I of the Therapeutic Substances Act 1956 consolidate, with amendments, the Therapeutic Substances (Manufacture of Hormone Products) Regulations 1963 and 1964.

The regulations apply to:—

(a) insulin and preparations thereof;

(b) pituitary (posterior lobe) and preparations thereof;

(c) corticotrophin and preparations thereof; and

(d) chorionic gonadotrophin and preparations thereof,

in respect of all of which they provide for:—

(a) standards of quality;

(b) tests for sterility, potency and other tests appropriate to the particular substance; and

(c) requirements as to labelling.