STATUTORY INSTRUMENTS

1963 No. 1456

THERAPEUTIC SUBSTANCES

The Therapeutic Substances (Manufacture of Preparations of Human Blood) Regulations 1963

Made - - - -	23*rd August* 1963
Laid before Parliament	2*nd September* 1963
Coming into Operation	16*th September* 1963

The Joint Committee constituted 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

1. These regulations may be cited as the Therapeutic Substances (Manufacture of Preparations of Human Blood) Regulations 1963 and shall come into operation on 16th September 1963.

Interpretation

2.—(1) 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(b);

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

"preparations of human blood" includes any serum or plasma made from human blood, any protein or other substance separated from human blood and any dried product prepared from any such serum, plasma, protein or other substance.

(2) 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.

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

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

Inclusion in schedule to Act

3. Notwithstanding the revocation by the general regulations of the Therapeutic Substances Regulations 1952(d), preparations of human blood shall continue to be included in schedule 1 to the Act.

(a) 4 & 5 Eliz. 2. c. 25.
(b) S.I. 1963/1450 (1963 II, p. 2483).
(c) 52 & 53 Vict. c. 63.
(d) S.I. 1952/1937 (1952 III, p. 3420).

PART II

GENERAL PROVISIONS RELATING TO PREPARATIONS OF HUMAN BLOOD

Provisions as to donors of blood

4. Except with the consent of the licensing authority preparations of human blood shall be prepared from blood taken from a person—

(*a*) who is known not to be suffering or not to have suffered from syphilis; or whose blood has been tested, with negative results, by a method approved by the licensing authority for evidence of syphilitic infection; and

(*b*) the haemoglobin content of whose blood, as ascertained by a method approved by the licensing authority, is not less than the equivalent of 85 per cent. as estimated against the National Physical Laboratory Haldane Haemoglobinometer Colour Standard (British Standard 1079: 1952); and

(*c*) who is, so far as can be ascertained by a registered medical practitioner after inspection or simple clinical examination and consideration of his medical history, free from disease transmissible by blood transfusion.

Withdrawal of blood

5. The operation of withdrawal of blood intended for the manufacture of a preparation of human blood shall be performed—

(*a*) as respects the insertion of the needle, by a registered medical practitioner and, as respects any other part of the operation, by or under the supervision of such a practitioner;

(*b*) by a method approved by the licensing authority and in conformity with the accepted standards of asepsis; and

(*c*) in premises suitable for the purpose approved by the licensing authority.

Method of preparation

6.—(1) Preparations of human blood shall be prepared by methods approved by the licensing authority.

(2) All apparatus used for the manufacture of preparations of human blood shall be cleaned and sterilised by methods approved by the licensing authority.

Tests for sterility

7. Preparations of human blood shall be tested for sterility by methods approved for the particular type of preparation by the licensing authority.

Records

8. A person licensed to manufacture preparations of human blood shall keep records, in such form and for such period as the licensing authority may require, of all information received by him, being information material for the purposes of regulation 4 of these regulations, and of the distribution by him of every batch of any such preparation, and shall allow any inspector authorised by the licensing authority in that behalf to inspect any such records.

Labelling

9.—(1) The particulars specified in regulation 6(1)(*a*)(*b*) and (*c*) of the general regulations shall be borne by the container of a preparation of human blood.

(2) The particulars specified in sub-paragraphs (*e*) and (*i*) of the said regulation 6(1) shall be borne either by the container of a preparation of human blood or by the package in which it is offered for sale.

(3) Paragraphs (1) and (2) of this regulation shall not apply to the substances to which part VII of these regulations applies.

PART III

SPECIAL PROVISIONS RELATING TO WHOLE HUMAN BLOOD

Definition and proper name

10. For the purposes of these regulations " whole human blood " means blood withdrawn from a human being for the purpose of transfusion and mixed with an anti-coagulant. Its proper name is " whole human blood ".

Method of preparation

11.—(1) The quantity of blood drawn on one occasion shall not exceed 420 millilitres.

(2) The anti-coagulant used shall be made with materials of a quality approved by the licensing authority, and shall be inserted in the container before the container is sterilised.

Quality

12. No container of whole human blood shall be issued for the purpose of transfusion unless—

(*a*) there is a clear line of demarcation between sedimented cells and supernatant plasma, and the plasma is free from visible products of haemolysis ; and

(*b*) the blood group into which the blood falls under the ABO system has been determined by the examination of both cells and serum, the blood group into which the blood falls under the Rhesus system has been determined by the examination of the cells ; and

(*c*) the volume of the blood contained in it is not less than 75 per cent. of the total volume of the contents.

Storage

13. The container shall, immediately after the insertion of the whole blood, be sealed and cooled to a temperature of 4°C. to 6°C., and shall thereafter be maintained at this temperature (except during any such period as may be necessary for examination and transfer, provided that such a period shall not exceed 30 minutes after which the blood shall immediately be cooled again to 4°C. to 6°C.).

Labelling

14.—(1) In addition to the particulars mentioned in regulation 9(1) and (2) of these regulations, the following further particulars shall be borne by the container of whole human blood:—

(*a*) the ABO group of the blood, as determined by a method approved by the licensing authority ;

(*b*) the Rhesus group of the blood, as determined by a method approved by the licensing authority ;

(*c*) the total volume of fluid, the proportion of blood and the nature and proportion of the anti-coagulant and of any other material introduced ;

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

(*e*) the date, calculated by reference to the period approved by the licensing authority as being the period during which whole human blood is suitable for use for transfusion, after which the preparation is not suitable for use for that purpose;

(*f*) the conditions of storage under which the preparation may be expected to maintain its quality until the date specified under the last foregoing sub-paragraph;

(*g*) a statement that the contents should not be used if there is any visible evidence of deterioration.

(2) For the purposes of the said sub-paragraph (*f*) the date on which the manufacture of a container of whole human blood is completed shall be the date on which the operation of withdrawing the blood was performed.

(3) Paragraph (4) of the said regulation 6 shall not apply in relation to whole human blood.

PART IV

SPECIAL PROVISIONS RELATING TO LIQUID HUMAN PLASMA AND LIQUID HUMAN SERUM

Definitions and proper names

15.—(1) Liquid human plasma is the fluid which is separated, by centrifuging or by standing, from whole human blood. Its proper name is "liquid human plasma".

(2) Liquid human serum is fluid which is separated from human blood which has been allowed to clot in the absence of an anti-coagulant. Its proper name is "liquid human serum".

Quality

16. No liquid human plasma or liquid human serum shall be issued for purposes of transfusion unless—

(*a*) it contains in the case of plasma not less than 4·5 per cent. and in the case of serum not less than 6·5 per cent. of protein as determined by a method approved by the licensing authority; and

(*b*) on inspection by the naked eye it is free from red blood corpuscles and colouration from haemoglobin.

Storage

17. Liquid human plasma and liquid human serum shall be stored at a temperature not higher than 20°C. in a place shaded from direct sunlight.

Labelling

18. In addition to the particulars required by regulation 9(1) and (2) of these regulations, the following further particulars shall be borne by the container of liquid human plasma or liquid human serum:—

(*a*) the protein content of the plasma or serum;

(*b*) in the case of plasma, the nature and proportion of the anti-coagulant and of any other material introduced;

(*c*) the date, calculated by reference to the period approved by the licensing authority, as being the period during which liquid human plasma or liquid human serum is suitable for use for transfusion, after which the preparation is not suitable for use for that purpose;

(*d*) the conditions of storage under which the preparation may be expected to maintain its quality until the date specified under the last foregoing paragraph;

(*e*) a statement that the plasma or serum should not be used if it is cloudy or there is a deposit.

PART V

SPECIAL PROVISIONS RELATING TO DRIED HUMAN PLASMA AND DRIED HUMAN SERUM

Definitions and proper names

19.—(1) Dried human plasma is liquid human plasma which has been dried by a method approved by the licensing authority. Its proper name is "dried human plasma".

(2) Dried human serum is liquid human serum which has been dried by a method approved by the licensing authority. Its proper name is "dried human serum".

Quality

20. The dried human plasma or dried human serum—

(*a*) shall not lose more than 0·5 per cent. by weight after exposure for 24 hours over phosphorus pentoxide at a pressure not exceeding 0·02 millimetre of mercury;

(*b*) shall dissolve completely in not more than 10 minutes when a volume of water for injection equal to the original volume of plasma or serum is added.

Storage

21. Dried human plasma and dried human serum shall be stored at a temperature not higher than 20°C. in a place shaded from direct sunlight. The atmosphere in the container shall consist of nitrogen.

Labelling

22. In addition to the particulars required by regulation 9 (1) and (2) of these regulations, the following further particulars shall be borne by the container of dried human plasma or dried human serum:—

(*a*) in the case of plasma, the nature and proportion of the anti-coagulant and of any other material introduced;

(*b*) the amount of diluent necessary to reconstitute the original volume of the plasma or serum;

(*c*) the protein content of the plasma or serum when reconstituted to the original volume of the plasma or serum;

(*d*) the date, calculated by reference to the period approved by the licensing authority as being the period during which dried human plasma or dried human serum is suitable for use for transfusion, after which the preparation is not suitable for use for that purpose;

(*e*) the conditions of storage under which the preparation may be expected to maintain its quality until the date specified under the last foregoing paragraph;

(*f*) a statement that the reconstituted plasma or serum must be used immediately after reconstitution.

PART VI

SPECIAL PROVISIONS RELATING TO CONCENTRATED HUMAN RED BLOOD CORPUSCLES

Definition and proper name

23. Concentrated human red blood corpuscles is the product resulting from the removal from whole human blood, not later than 14 days after the date of its manufacture, of a quantity of plasma and anti-coagulant solution amounting to not less than 40 per cent. by volume of the whole human blood. The proper name of the product is " concentrated human red blood corpuscles ".

Method of preparation

24. Concentrated human red blood corpuscles shall be prepared by a method approved by the licensing authority.

Quality

25. Concentrated human red blood corpuscles shall contain not less than 5·5 million red blood cells per cubic millimetre.

Storage

26. Concentrated human red blood corpuscles shall be stored at a temperature not higher than 6°C. or lower than 4°C.

Labelling

27. In addition to the particulars required by regulation 9 (1) and (2) of these regulations, the following further particulars shall be borne by the container of concentrated human red blood corpuscles:—

(*a*) the reference numbers of the containers of the whole human blood from which the preparation is made;

(*b*) the ABO group, as determined by a method approved by the licensing authority, of the whole human blood from which the preparation is made;

(*c*) the Rhesus group, as determined by a method approved by the licensing authority, of the whole human blood from which the preparation is made;

(*d*) the time, being not more than 12 hours after the completion of the removal of the plasma and anti-coagulant solution or more than 14 days after the date of the manufacture of the whole human blood from which the preparation is made, up to which the preparation is suitable for use for transfusion;

(*e*) the conditions of storage under which the preparation may be expected to maintain its quality until the date specified under the last foregoing paragraph;

(*f*) a statement that the contents should not be used if there is any visible evidence of deterioration.

PART VII

SPECIAL PROVISIONS RELATING TO HUMAN FIBRIN, FIBRINOGEN, THROMBIN AND GAMMA GLOBULIN

Definitions and proper names

28.—(1) Human fibrin is the insoluble protein which forms the matrix of a clot of human blood. Its proper name is " human fibrin ".

(2) Human fibrinogen is the soluble protein constituent of liquid human plasma which, on the addition of human thrombin, is transformed into human fibrin. Its proper name is " human fibrinogen ".

(3) Human thrombin is the enzyme which transforms human fibrinogen into human fibrin. Its proper name is " human thrombin ".

(4) Human gamma globulin is soluble protein which is derived from human plasma or serum and has specific antibacterial, antiviral, or antitoxic activity. Its proper name is " human gamma globulin ".

Quality, storage and labelling

29. Human fibrin, fibrinogen, thrombin and gamma globulin, and preparations thereof, shall be of a quality, and shall be stored and labelled in a manner, approved by the licensing authority.

PART VIII

SPECIAL PROVISIONS RELATING TO HUMAN SERUM ALBUMIN AND PREPARATIONS THEREOF

Definition and proper name

30. Human serum albumin is that fraction of the water soluble protein derived from human plasma or serum of which the mean molecular weight is 70,000. Its proper name is " human serum albumin ".

Preparation

31. During preparation, human serum albumin shall be heated at an attained temperature of 60°C.±0·5°C. for not less than 10 hours.

Quality

32.—(1) Human serum albumin, when in solution in an aqueous phosphate buffer at a pH value of 8·0 and at an ionic strength of 0·2, shall not contain more than 5 per cent. of globulins, as determined by electrophoretic analysis.

(2) In the case of a liquid preparation the pH value of the liquid shall be between 6·5 and 7·0 and the albumin shall be dissolved in a solvent approved by the licensing authority.

(3) Human serum albumin in the dry form—

(*a*) shall not lose more than 0·5 per cent. by weight after exposure for 24 hours to phosphorus pentoxide at a pressure not exceeding 0·02 millimetre of mercury;

(*b*) shall, when water for injection is added to give a concentration of 6 grammes per 100 millilitres, dissolve completely in not more than 10 minutes.

Storage and labelling

33.—(1) Human serum albumin and preparations thereof shall be stored in a manner approved by the licensing authority.

(2) In addition to the particulars required by regulation 9 (1) and (2) of these regulations, the following further particulars shall be borne by the container of human serum albumin or of a preparation thereof, namely, the total amount of human serum albumin in the container and the nature of any other substances which may have been added, and in particular, in the case of a liquid preparation, the nature and volume of the solvent.

PART IX

SPECIAL PROVISIONS RELATING TO 131-RADIOIODINATED HUMAN SERUM ALBUMIN

Definition and proper name

34. 131–Radioiodinated human serum albumin is a watery solution of the organic compound formed by the union of radioactive iodine (^{131}I) with human serum albumin. Its proper name is " 131–radioiodinated human serum albumin ".

Test for absence of denatured albumin

35. 131–Radioiodinated human serum albumin shall be tested for the absence of denatured albumin by a method approved by the licensing authority.

Test for free iodide

36. 131–Radioiodinated human serum albumin shall not contain more than 5 per cent. of its total iodine as free iodide, as determined by a method approved by the licensing authority.

Freedom from pyrogenic substances

37.—(1) 131–Radioiodinated human serum albumin shall, if so required by the licensing authority, be tested for freedom from pyrogenic substances in accordance with the general regulations, and shall in any event be free from such substances to such an extent that, if so tested, it would pass the test.

(2) The quantity of 131–radioiodinated human serum albumin for the purpose of the said test shall be such a quantity thereof as to contain a total radioactivity of not less than 10 microcuries per kilogram of the rabbit's weight.

Labelling

38. In addition to the particulars required by regulation 9(1) and (2) of these regulations, the following further particulars shall be borne by the container of 131–radioiodinated human serum albumin:—

(*a*) the nature and volume of the contents;

(*b*) the total radioactivity in microcuries or millicuries of the contents, and the date to which the measurement refers;

(*c*) the total weight of 131–radioiodinated human serum albumin in the container;

(*d*) the nature and concentration of the salts present; and

(*e*) the date after which the contents should not be used.

These regulations were made by the aforesaid Joint Committee on 23rd August 1963.

J. Enoch Powell,
Michael Noble,
Wm. J. Morgan,
Members of the Joint Committee.

B. H. Betts,
Clerk to the Joint Committee.

EXPLANATORY NOTE

(This Note is not part of the Regulations, but is intended to indicate their general purport.)

These regulations, made under part I of the Therapeutic Substances Act 1956 form part of a comprehensive code relating to the manufacture and importation of therapeutic substances and are to be read in conjunction with the Therapeutic Substances (Manufacture and Importation) General Regulations 1963.

These regulations consolidate with minor amendments those requirements of the Therapeutic Substances Regulations 1952 to 1957 which apply to preparations of human blood and in particular prescribe requirements as to:—

(*a*) donors of blood;

(*b*) withdrawal of human blood;

(*c*) method of preparation of human blood;

(*d*) tests for sterility;

(*e*) records; and

(*f*) labelling.