# 1966 No. 506

# THERAPEUTIC SUBSTANCES

## The Therapeutic Substances (Manufacture of Dextran Injections) Regulations 1966

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

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, Commencement and Interpretation*

**1.**—(1) These regulations may be cited as the Therapeutic Substances (Manufacture of Dextran Injections) 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.

(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.

*Revocation of existing regulations and inclusion of substances in schedule to Act*

**2.**—(1) The Therapeutic Substances (Manufacture of Dextran Solution) Regulations 1963(d) are hereby revoked.

(2) Dextran injections as defined in regulation 4 of these regulations are hereby added to schedule 1 to the Therapeutic Substances Act 1956 as being substances the purity or potency of which cannot be adequately tested by chemical means.

(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. (d) S.I. 1963/1453 (1963 II, p.2517).

## PART II

### PROVISIONS RELATING TO DEXTRAN INJECTIONS

*Definitions and proper names*

**4.**—(1) Dextran injections are solutions in physiological saline, or other vehicle suitable for intravenous injection, of dextrans derived from the dextrans produced by the fermentation of sucrose by means of a certain strain of *Leuconostoc mesenteroides* (National Collection of Industrial Bacteria, No. 8710), or, if the licensing authority so approve, by means of certain other strains of *Leuconostoc mesenteroides* or by means of purified enzymes derived from such strains. The dextrans are polymers of glucose in which the linkages between the glucose units are almost entirely of the $\alpha$ 1 : 6 type.

(2) The proper name of any one of the solutions referred to in paragraph (1) of this regulation is "dextran injection", qualified by a number which indicates the average molecular weight of the material in the solution and further qualified by a word or words approved by the licensing authority as indicating the nature of the vehicle.

*Method of preparation*

**5.** Dextran injections shall be prepared by a method approved by the licensing authority. The strains of *Leuconostoc mesenteroides* used during such preparation shall be ones which have been approved by the licensing authority.

*Strength*

**6.** The proportions (being not less than 5·5 grams nor more than 11·0 grams in a quantity of 100 millilitres) of dextran in dextran injections; and the methods to be used for determining such proportions shall be such as the licensing authority may approve.

*Quality*

**7.**—(1) Dextran injections shall:—

(*a*) be clear and almost colourless;

(*b*) have—

(i) where the vehicle is physiological saline, a pH value lying between 4·0 and 7·0;

(ii) where the vehicle is a solution of dextrose, a pH value lying between 3·5 and 6·5;

(*c*) where the vehicle is physiological saline, contain not less than 0·85 grams nor more than 0·95 grams of sodium chloride in a quantity of 100 millilitres;

(*d*) where the vehicle is a solution of dextrose, contain not less than 4·5 grams nor more than 5·5 grams of dextrose in a quantity of 100 millilitres.

(2) Dextran injections shall not contain any bacteriostatic and shall not contain in a quantity of 100 millilitres:—

(*a*) more than such quantity of sulphated ash, exclusive of that due to added sodium chloride, as the licensing authority may approve;

(*b*) more than 0·5 milligram of heavy metals, calculated as lead;

(*c*) more than 200 milligrams of reducing sugars, inclusive of sugars added in the vehicle, except when dextrose solution is the vehicle;

(*d*) more than 1·0 milligram of total nitrogen;

(*e*) more than 0·02 millilitre of acetone;

(*f*) more than 0·06 millilitre of alcohols.

*Test for sterility*

**8.** Dextran injections shall be tested for sterility in accordance with the general regulations.

*Test for freedom from pyrogenic substances and for freedom from abnormal toxicity*

**9.**—(1) Dextran injections shall be tested for freedom from pyrogenic substances in accordance with the general regulations, and the test shall be used also as a test for freedom from abnormal toxicity.

(2) The quantity of any dextran injection for the purpose of the said test shall be for each rabbit used in that test not less than 10 millilitres per kilogram of the weight of that rabbit.

(3) The substance shall be regarded as free from abnormal toxicity if none of the animals exhibits signs of distress during the period of the said test.

*Test for freedom from abnormal antigenicity*

**10.**—(1) Dextran injections shall be tested for freedom from abnormal antigenicity in accordance with this regulation.

(2) Into the peritoneal cavity of each of 6 healthy adult guinea pigs, each of which weighs not less than 250 grams and has not previously been treated with any material which will interfere with the test, 0·5 millilitre of dextran injection shall be injected on 3 occasions at intervals of 2 days. A further 0·2 millilitre shall be injected intravenously into each of 3 of the guinea pigs 14 days after the first intraperitoneal injection, and into each of the other guinea pigs 21 days after the first intraperitoneal injection. The guinea pigs shall be observed for 30 minutes after each intravenous injection and 24 hours later. The sample shall pass the test if the guinea pigs show no signs of anaphylaxis such as coughing, bristling or respiratory distress.

*Molecular size of dextrans*

**11.** The range of molecular size of the dextrans contained in dextran injections shall be such that when tested by methods approved by the licensing authority, the following requirements are satisfied:—

(*a*) the intrinsic viscosity of the dextrans shall be within a range approved by the licensing authority;

(*b*) the intrinsic viscosity of a fraction which contains as nearly as possible 10 per cent. of the dextrans, but not more than that quantity, and which has been prepared in such a way that it contains the largest molecules, shall be not more than a value approved by the licensing authority;

(*c*) the mean dextran content of all the urine samples collected within 48 hours after the intravenous injection into each of 2 rabbits shall be such as the licensing authority may approve having regard to the molecular size of the dextran injected.

*Labelling*

**12.**—(1) The particulars specified in regulation 6(1) (*g*) of the general regulations shall be borne both by the container of a dextran injection and by the package in which it is offered for sale.

(2) The particulars specified in sub-paragraphs (*a*), (*b*) and (*c*) of the said regulation 6(1) shall be borne by the container of a dextran injection.

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

(4) The following further particulars shall be borne by the container of a dextran injection:—

(*a*) the volume of the contents;

(*b*) the percentage concentration w/v of the dextrans and the nature of the vehicle;

(*c*) a statement that the contents should not be used if they are cloudy or if there is a deposit.

(5) Neither the container of a dextran injection nor the package in which it is offered for sale shall state that dextran injection is a substitute for whole human blood.

(6) For the purposes of sub-paragraph (*f*) of the said regulation 6(1), the date on which the manufacture of a dextran injection in any container is completed shall be such date as the licensing authority may approve.

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

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

*Wilfred Turner,*
Clerk to the Joint Committee.

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## EXPLANATORY NOTE

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

These regulations, made under Part I of the Therapeutic Substances Act 1956 replace the Therapeutic Substances (Manufacture of Dextran Solution) Regulations 1963.

The regulations encompass a wider range of dextran injections, in relation to which they provide for:—

(*a*) standards of strength and quality;

(*b*) tests for sterility and for freedom from pyrogenic substances, abnormal toxicity and abnormal antigenicity; and

(*c*) requirements as to labelling.