1952 No. 1933

The Diseases of Animals (Therapeutic Substances) Order, 1952

Made - - - - *6th November*, 1952

Coming into Operation *1st January*, 1954

The Minister of Agriculture and Fisheries, in pursuance of Sections 1 and 53 of the Diseases of Animals Act, 1950(a), and of all other powers enabling him in that behalf, hereby makes the following Order:—

PART I.—GENERAL

Short Title, Extent and Commencement

1. This Order, which may be cited as the Diseases of Animals (Therapeutic Substances) Order, 1952, and extends to England and Wales and Scotland, shall come into operation on the first day of January, nineteen hundred and fifty-four.

Interpretation

2.—(1) In this Order, unless the context otherwise requires, the following expressions have the meanings hereby respectively assigned to them:—

"Anaerobic vaccine" means a vaccine derived from or containing cultures of anaerobes.

"Antigen" means a suspension of an organism, or a solution or suspension of the special constituent or product of the organism, which is capable of inciting antibody production.

"Inspector" means a person appointed by the Minister to be an inspector for the purposes of the Diseases of Animals Act, 1950, and includes a veterinary inspector appointed by the Minister.

"Killed bacterial vaccine" means a sterile suspension of a killed culture of a micro-organism or micro-organisms.

"Living bacterial vaccine" means a vaccine containing micro-organisms which have not been treated by any method likely to kill them.

"Minister" and "Ministry" mean respectively the Minister and the Ministry of Agriculture and Fisheries.

"Registered" means in relation to a veterinary surgeon, registered in pursuance of the Veterinary Surgeons Act, 1881(b), in the Register of Veterinary Surgeons, and in relation to a veterinary practitioner, registered in pursuance of the Veterinary Surgeons Act, 1948(c), in the Supplementary Veterinary Register.

"Relative Schedule" in relation to a therapeutic substance means such part of the Second, Third or Fourth Schedules to this Order as applies to that substance either specially or to the group of substances to which the substance belongs.

(a) 14 Geo. 6. c. 36. (b) 44 & 45 Vict. c. 62. (c) 11 & 12 Geo. 6. c. 52.

"Sera and antitoxins" means the sera or solutions of the purified proteins of sera separated from the blood of normal animals or of animals which have been artificially immunised against cultures of one or more organisms or against a soluble toxin or toxins produced by the organism or organisms or against antigenic substances prepared from the organism or organisms.

"Therapeutic substance" means any of the following substances intended to be used solely for veterinary purposes—

(*a*) Sera and antitoxins, and antigens.

(*b*) Anaerobic vaccines.

(*c*) Killed bacterial vaccines.

(*d*) Viral vaccines.

(*e*) Living bacterial vaccines.

"Viral vaccine" means a vaccine containing either living or dead virus.

(2) For the purposes of this Order the cubic centimetre may be used wherever the millilitre is indicated.

(3) The Interpretation Act, 1889(**a**), shall apply to the interpretation of this Order as it applies to the interpretation of an Act of Parliament.

Saving as to Therapeutic Substances Act, 1925, *etc.*

3. The provisions of this Order shall be in addition to, and not in derogation of, the provisions of the Therapeutic Substances Act, 1925(**b**), of any Regulations made thereunder, and of the Foot-and-Mouth Disease (Sera and Glandular Products) Order of 1939(**c**).

Revocation

4. The Diseases of Animals (Importation of Therapeutic Substances) Order of 1936(**d**) is hereby revoked.

Prohibition of Manufacture or Importation of Therapeutic Substances

5. No person shall, except under the authority of a licence issued by the Minister and in accordance with any conditions subject to which the licence was issued, manufacture for sale, or land in Great Britain from any other country, any therapeutic substance:

Provided that no licence shall be issued under this Article for the manufacture or landing of any therapeutic substance the use of which in the opinion of the Minister may spread any disease which is a disease for all or any of the purposes of the Diseases of Animals Act, 1950.

6.—(1) Such of the forms set out in the First Schedule to this Order as may be applicable (or a form substantially to the like effect) shall be used whenever a licence under this Order is granted by the Minister or an application for such a licence or for the renewal of a licence previously granted is made to the Minister.

(2) Licences granted under this Order shall, unless sooner suspended or revoked, continue in force for a period of two years.

(**a**) 52 & 53 Vict. c. 63.
(**b**) 15 & 16 Geo. 5. c. 60.
(**c**) S.R. & O. 1939/707; Rev. II, p. 544; 1939 I, p. 158.
(**d**) S.R. & O. 1936/515; Rev. II, p. 413; 1936 I, p. 110

PART II.—LICENCES FOR MANUFACTURE OF THERAPEUTIC SUBSTANCES

7. A licence to manufacture a therapeutic substance for sale (hereinafter referred to as a "manufacturing licence") shall be issued subject to the special conditions, if any, set out in the relative Schedule and to the following general conditions:—

(*a*) manufacture shall be carried on only upon the premises specified in the licence;

(*b*) the licensee shall at all times provide an adequate staff and plant and maintain the premises aforesaid in a suitable condition for the proper manufacture of the substance in respect of which the licence is issued;

(*c*) without prejudice to the generality of the foregoing requirement, every holder of a licence to manufacture a therapeutic substance, who for any purpose engages in the culture or manipulation of pathogenic spore-bearing micro-organisms, shall provide to the satisfaction of the Minister separate laboratories and utensils and apparatus for the culture or manipulation of such micro-organisms, and the laboratories and utensils and apparatus so provided shall not be used for the manufacture of any other therapeutic substance:

Provided that in any particular case the Minister may, if he thinks fit, dispense with the requirements of this paragraph either wholly or in part;

(*d*) the licensee shall either—

(i) provide and maintain an adequate staff and adequate premises and plant for carrying out such tests of the substance as, pursuant to Part V of this Order, may be required to be carried out by him, including proper housing for animals used for the purpose of such tests, or

(ii) make arrangements approved by the Minister for such tests to be regularly carried out on behalf of the licensee;

(*e*) the licensee shall not sell or offer for sale a therapeutic substance manufactured by him unless it has been subjected by the manufacturer, or on the manufacturer's behalf in accordance with arrangements approved by the Minister for the purpose of carrying out tests, to the tests prescribed in Article 16 of this Order, and has attained the standard of purity prescribed in that Article:

Provided that the Minister may, in the case of any particular therapeutic substance, dispense with this condition either wholly or in part;

(*f*) when the therapeutic substance is intended for sale in liquid form in containers which are sealed in such a manner that portions of the contents can be withdrawn for use on different occasions, the liquid shall contain a sufficient proportion of a suitable bacteriostatic to prevent the growth of any organism which may be accidentally introduced in the process of removing a portion of the contents of the container:

Provided that the Minister may, in the case of any particular preparation of any therapeutic substance, dispense with this condition;

(*g*) the following particulars shall be printed or written in indelible ink either on the label borne by the container of any therapeutic substance or on a label or wrapper affixed to any package in which any such container is issued for sale:—

(i) the name and address of the manufacturer of the final product;

(ii) where a bacteriostatic has been added, the nature and percentage proportion of the bacteriostatic in the substance as prepared for use;

(iii) the precautions necessary for preserving the properties of the contents to the date referred to in sub-paragraph (*d*) of paragraph (1) of Article 13 of this Order as the date to which the substance, if kept under suitable conditions, may reasonably be expected to retain its potency.

No label or wrapper shall be used for the purposes of this paragraph unless the general form of such label or wrapper has been approved by the Minister;

(*h*) the licensee shall keep permanent records of the details of manufacture of each batch of the substance which is issued for sale and of the application of the tests thereto in such form as to be available for inspection and to be easily identified by reference to the number of the batch as shown on the label of each container;

(*i*) the licensee shall allow any inspector authorised by the Minister in that behalf to enter, at all reasonable times, any premises where the manufacture is carried on and to inspect the premises and plant and any animals on the premises and the process of manufacture and the means employed for testing the substance in accordance with the provisions of this Order and to take samples of the substance;

(*j*) the licensee shall report immediately to the Minister any changes in the expert staff responsible for the manufacture or testing of the substance and any material alterations in the premises or plant used for that purpose;

(*k*) the licensee shall on request furnish to the Minister from every batch of the substance or from such batch or batches as the Minister may from time to time specify a sample of such amount as the Minister may consider adequate for any examination required to be made; and the licensee shall, if so required, furnish full protocols of the tests which have been applied;

(*l*) if the Minister so directs, the licensee shall not sell or offer for sale any batch in respect of which a sample is or protocols are furnished under the last preceding sub-paragraph until a certificate authorising the sale of the batch has been issued to him by the Minister;

(*m*) the licensee shall, on being informed by the Minister that any part of any batch of the substance has been found by the Minister not to conform with the standards specified in this Order and on being directed so to do, withdraw the remainder of the batch from sale, and, so far as may in the particular circumstances of the case be practicable, recall all issues already made from that batch;

(*n*) the licensee shall comply with all the relevant provisions of Part II of the Diseases of Animals Act, 1950, and of this Order and with such further requirements, if any, as may be specified in any subsequent Act or Order relating to therapeutic substances.

PART III.—LICENCES FOR IMPORT OF THERAPEUTIC SUBSTANCES

8. An applicant for a licence to land in Great Britain from any other country a therapeutic substance for purposes other than those of scientific research (in this Part of this Order referred to as an "import licence") shall furnish to the Minister a written undertaking in a form approved by the Minister, signed by or on behalf of the person who manufactures the therapeutic substance to which the application relates (hereinafter referred to as the "manufacturer"), that for the duration of the licence—

(*a*) the applicant shall be the sole accredited agent of the manufacturer for the import of the substance;

(*b*) the manufacturer will comply with the conditions imposed on a licensee by paragraphs (*b*) to (*j*) inclusive of Article 7 of this Order ;

(*c*) the manufacturer will immediately report to the Minister any proposal to carry on the manufacture of the therapeutic substance in premises other than those in which it was carried on when the licence was issued and every such change of premises if and when effected and in a case in which the manufacture is carried on in more than one factory any proposal for redistributing functions between factories and every such redistribution if and when effected ;

(*d*) the manufacturer will comply with the provisions of Part IV of this Order ;

(*e*) every substance manufactured by the manufacturer for import under licence will conform with the provisions of Part V of this Order ;

(*f*) the manufacturer will comply with such further requirements, if any, applicable to manufacturers of therapeutic substances as may be specified in any subsequent Order relating to therapeutic substances.

9.—(1) An import licence shall be issued subject to the observance by the manufacturer of such undertaking as aforesaid, and for the purpose of the suspension or revocation of the licence any breach of such undertaking on the part of the manufacturer shall be deemed to be a non-compliance on the part of the licensee with the conditions of the licence.

(2) An import licence shall, in addition, be subject to the following conditions:—

(*a*) the licensee shall allow any inspector authorised by the Minister in that behalf to enter at all reasonable times any premises where the imported substance is stocked and to inspect the premises and the means (if any) employed for testing the substance and to take samples ;

(*b*) the licensee shall on request furnish to the Minister from every batch of the substance or from such batch or batches as the Minister may from time to time specify, a sample of such amount as the Minister may consider adequate for any examination required to be made ; and the licensee shall, if so required, furnish full protocols of the tests which have been applied ;

(*c*) if the Minister so directs, the licensee shall not sell or offer for sale any batch in respect of which a sample is or protocols are furnished under the last preceding sub-paragraph until a certificate authorising the sale of the batch has been issued to him by the Minister ;

(*d*) the licensee shall, on being informed by the Minister that any part of any batch of the substance has been found by the Minister not to conform with the standards specified in this Order and on being directed so to do, withdraw the remainder of that batch from sale and so far as may in the particular circumstances of the case be practicable, recall the issues already made from that batch ;

(*e*) the licensee shall comply with such further requirements, if any, applicable to the holders of import licences, as may be specified in any subsequent Act or Order relating to therapeutic substances.

10. Every licence to land in Great Britain from any other country a therapeutic substance for the purpose of scientific research (in this Part of this Order referred to as a " research licence ") shall be issued subject to the following conditions:—

(*a*) the licensee shall use the substance imported under the licence for purposes of scientific research exclusively, and shall carry on such research only upon the premises specified in the licence or in such other place as the Minister may from time to time authorise ;

(*b*) the licensee shall allow any inspector authorised by the Minister in that behalf to enter at all reasonable times the premises where the substance is kept and to inspect the premises and investigate the manner in which the substance is being used, and to take samples thereof ;

(*c*) the licensee shall keep a record showing, in respect of each quantity of the substance imported under the licence, the quantity imported, the date of importation and the name of the manufacturer ;

(*d*) the licensee shall comply with such further conditions, if any, as may be specified in the licence ;

(*e*) the licensee shall comply with such further requirements, if any, applicable to the holders of research licences, as may be specified in any subsequent Order.

11. The Minister may, at any time, if he is satisfied that it is in the public interest so to do, revoke or suspend any import or research licence, but, before revoking or suspending such a licence, he shall give to the licensee an opportunity to make representations against the proposed revocation or suspension.

PART IV.—PROVISIONS WITH REGARD TO CONTAINERS, LABELS, ETC.

12. No therapeutic substance shall be sold or offered for sale unless it is in a sealed container of a material inert towards the substance and the container, having been previously sterilised, has been sealed in such manner as will suffice to preclude the access of micro-organisms.

13.—(1) Any sealed container in which a therapeutic substance is to be sold or offered for sale shall have indelibly marked thereon by the manufacturer or on a label affixed to it by him the following description:—

(*a*) the name of the substance as entered in the licence under which the substance is manufactured or imported ;

(*b*) the number of every licence under which the substance or any of its constituents is manufactured or imported, preceded in the case of import licences by the words " Import Licence " ;

(*c*) a distinctive batch number, that is to say, the number by reference to which the prescribed tests and details of manufacture of the particular batch from which the substance in the container is taken are permanently recorded and available for inspection ;

(*d*) the date to which the substance, if kept under suitable conditions, may reasonably be expected to retain its potency:

Provided that in no case shall this date be a date later than two years from the date when the tests of the batch of the substance prescribed in Part V of this Order were completed ;

(*e*) in the case of a serum or anti-toxin, the name of the species of animal in which it has been prepared ;

(*f*) the words " to be used solely for veterinary purposes ".

(2) No label shall be used for the purposes of this Article unless the general form of such label has been approved by the Minister.

14. The date of manufacture of any therapeutic substance, that is to say the date on which the tests of the batch of the substance prescribed in Part V of this Order were completed, shall be printed or written in indelible ink either on the label borne by the sealed container or on a label or wrapper fixed to any package in which the substance is sold or offered for sale.

Prohibition of sale of substance after the prescribed date

15. No person shall sell a therapeutic substance after the expiration of whichever of the following periods from the date of manufacture expires first—

(*a*) a period of two years, or

(*b*) a period ending on any date stated on a label borne by the container, or on a label or wrapper fixed to any package in which the substance is sold or offered for sale, as the date to which the substance, if kept under suitable conditions, may reasonably be expected to retain its potency.

PART V.—STANDARD OF PURITY AND TESTS FOR DETERMINING WHETHER THAT STANDARD HAS BEEN ATTAINED

16. The prescribed tests to be used for determining whether the standard of purity of a therapeutic substance manufactured for sale has been attained shall be the tests specified in this Part of this Order and such other tests (if any) as are specified in the relative Schedule and the prescribed standard of purity shall be the standard required for passing the tests so specified.

Tests for Sterility

17. Tests for sterility shall be carried out in the manner provided in the six next following Articles:

Provided that (*a*) if the manufacturer satisfies the Minister that he has already in use tests for the presence of living aerobic or anaerobic micro-organisms in any therapeutic substance, and that these tests, as applied by him to the substance, will detect the presence of such micro-organisms in any batch thereof or in filled containers with a certainty at least equal to that afforded by the application of the tests prescribed by this Part of this Order, the Minister may approve the use of such tests in the place of the prescribed tests, but in such a case the Minister may at any time withdraw such approval and require the manufacturer to carry out the prescribed tests; and (*b*) in the case of any particular therapeutic substance the Minister may approve, as an alternative to the prescribed tests, such other tests as he may deem proper in the circumstances of the case.

18. The tests shall be applied—

(*a*) to samples taken from each batch of the substance before the operation of filling and sealing the containers in which it is to be issued has commenced; and

(*b*) to the contents of containers selected as samples from containers ready for issue for the purposes of sale, which selected containers are hereafter referred to as " sample containers ".

19. The samples required to be taken under the last preceding Article shall be taken in the following proportions:—

(*a*) in the case of samples taken from the batch, the quantity taken shall be not less than 0.1 per cent. of the total volume of the batch if the volume is not more than 10 litres, and not less than 10 millilitres if the volume is 10 litres or more, but shall in no case be less than 1 millilitre:

Provided that if, at the time when the test is made, the batch is contained in a number of bulk containers, samples in the foregoing proportions shall be taken from each of such bulk containers and be separately tested ;

(*b*) in the case of the contents of sample containers, the number of containers taken for test shall not be less than 1 per cent. of the total number filled from the batch if this number is not more than 1,000, and not less than 10 containers if the total number is more than 1,000.

20.—(1) Except where otherwise provided, the tests shall be made in fluid media. If a substance contains an added antiseptic or agent which inhibits the growth of micro-organisms there shall be added to the sample before it is tested—

(*a*) such volume of medium as will dilute the antiseptic or agent so that the growth of micro-organisms is not inhibited, or

(*b*) such a substance in such concentration as will prevent the antiseptic or agent from inhibiting the growth of micro-organisms but which will not itself inhibit such growth.

(2) In the case of a test for aerobic micro-organisms the medium shall, except where otherwise provided, consist either of a meat extract with the addition of 1 per cent. of peptone, or of such an equivalent as can be prepared by suitable digestion of muscle. After the final sterilisation the hydrogen-ion concentration of the medium shall be between the limits represented by pH=7·2 and pH=7·8.

(3) In the case of a test for anaerobic micro-organisms the medium shall consist of a nutrient broth similar to that used in testing for aerobic micro-organisms, with the addition of heat coagulated muscle of an amount sufficient to occupy a depth of not less than 1 centimetre at the bottom of the tube. After the final sterilisation the hydrogen-ion concentration of the medium shall be between the limits represented by pH=7·2 and pH=7·8. Before the test inoculation the medium shall be heated to 100° C. for a period sufficient to free it completely from dissolved oxygen, and then be cooled to 37° C. or lower.

(4) The Minister may, at the request of any licensee, authorise the use, for the test prescribed under either paragraph (2) or (3) of this Article, of any other specified medium or method of using a specified medium, on being satisfied that its use affords equal certainty in the detection of the presence of living aerobic or anaerobic micro-organisms, as the case may be.

21.—(1) In the case of samples taken from the batch each sample shall be inoculated into tubes or other vessels containing the media, one-half of the total volume of the sample being used for the aerobic and one-half for the anaerobic test.

(2) In the case of the contents of sample containers the contents of each container shall be subjected to the test for aerobic and the test for anaerobic micro-organisms. When the volume in the container is 2 millilitres or more, 1 millilitre shall be used for each test. When the volume in the container is less than 2 millilitres the contents shall be divided into two approximately equal parts, one part being used for the aerobic and the other for the anaerobic test.

(3) The inoculated tubes shall be incubated at 37° C. for five days and be examined after incubation, permanent records being kept of the examination of each tube:

Provided that in the case of the test for anaerobic micro-organisms in respect of an anaerobic vaccine the inoculated tubes shall be incubated at 37° C. for ten days.

22.—(1) If at this examination no growth of micro-organisms is found in any tube, the sample may be regarded as having passed the test.

(2) If at the examination a growth of micro-organisms is found, a second sample may be taken in the prescribed manner and the tests may be repeated on the second sample.

(3) If on examination of the second sample no growth of micro-organisms is found the sample may be regarded as having passed the test; but if the same organism is found as in the sample first tested the batch shall be treated as not sterile.

(4) If a growth of a different micro-organism is found in the test of the second sample, a third sample may be taken and the tests repeated. If on examination no growth of micro-organisms is found the sample shall be regarded as having passed the test. If a growth of micro-organisms is found the batch shall be treated as not sterile.

(5) The material contained in a batch which is to be treated as not sterile shall not be issued or used as part of a further batch until it has been re-sterilised or has been otherwise treated in a manner approved by the Minister and until it has passed the test.

(6) No container shall be issued unless—

(*a*) a sample from the batch from which it is filled has passed the test;

(*b*) the contents of the sample containers drawn from the same batch have passed the test.

(7) If samples have been drawn from bulk containers in accordance with the proviso to paragraph (*a*) of Article 19 of this Order references to a batch in this Article shall be construed as references to the contents of a bulk container.

23. Notwithstanding anything contained in the last preceding Article, in any case where—

(*a*) a substance is required in an emergency by a registered veterinary surgeon or practitioner, but the licensee has no filled containers in stock; or

(*b*) a substance is in the opinion of the Minister so unstable in solution that the delay occasioned by the completion of the sterility test on filled containers would render its issue in active form impossible,

the licensee may issue the substance from a batch which has already passed the tests for sterility and freedom from abnormal toxicity without completing the sterility test on the filled containers, provided that he complies with the following conditions:—

(i) the licensee shall before the issue take samples in the required proportions from the containers into which the batch is filled, and after issue shall carry out the required inoculation and incubation and shall examine the tubes every day for the number of days specified in paragraph (3) of Article 21 of this Order;

(ii) if at any examination any growth is visible in any of the tubes, he shall immediately notify the Minister;

(iii) he shall keep available for inspection a record of all issues made under this Article containing such particulars of the circumstances in which the issue is made as the Minister may require.

Tests for freedom from abnormal toxicity

24. Tests for freedom from abnormal toxicity, except where otherwise provided in the relative Schedule, shall be carried out on every batch of the substance in the following manner:—

(1) A dose of 0.5 millilitre of the substance shall be injected subcutaneously into each of two healthy mice, and the substance shall be treated as having passed the test for freedom from an excess of antiseptic if the injections do not produce death or serious symptoms in either mouse within five days.

(2) A dose of not less than 2 millilitres of the substance shall be injected intraperitoneally into each of two healthy guinea pigs and the substance shall be treated as having passed the test for freedom from other toxic constituents if the injections do not produce death or serious symptoms in either guinea pig within ten days:

Provided that if the manufacturer satisfies the Minister that he has already in use tests for freedom from abnormal toxicity and that these tests, as applied by him to the substance, will detect the presence of abnormal toxicity in any batch thereof, with a certainty at least equal to that afforded by the application of the tests prescribed in this Article, the Minister may approve the use of such tests in the place of the prescribed tests, but in such a case the Minister may at any time withdraw such approval and require the manufacturer to carry out the prescribed tests.

PART VI.—THERAPEUTIC SUBSTANCES MANUFACTURED OR IMPORTED FOR EXPORT ONLY

25. The Minister may in the case of any particular substance dispense with any of the requirements of this Order if he is satisfied that the substance is being manufactured exclusively for sale outside Great Britain or is being imported exclusively for re-export and that such dispensation is desirable, regard being had to the nature of any arrangements for regulating the manufacture and sale of the substance in operation in the country to which the substance is to be exported.

In witness whereof the Official Seal of the Minister of Agriculture and Fisheries is hereunto affixed this sixth day of November, nineteen hundred and fifty-two.

(L.S.) *Tom Dugdale,*
Minister of Agriculture and Fisheries.

FIRST SCHEDULE

FORM 1

FORM OF APPLICATION FOR * A LICENCE FOR MANUFACTURE OF THERAPEUTIC SUBSTANCES FOR SALE

Diseases of Animals (Therapeutic Substances) Order, 1952

To the Minister of Agriculture and Fisheries

I, / We, , of

hereby apply for a * licence to manufacture at the undermentioned therapeutic substances† for sale:—

and I / We undertake to allow any inspector authorised by the Minister to enter any premises where the manufacture of any of the above-mentioned substances is or is intended to be carried on and to inspect the premises and plant and process of manufacture and any animals on the premises for the purpose of enabling the Minister to be satisfied that the conditions upon which the licence may be issued are or will be complied with, and for the same purpose to take samples.

The names and qualifications of the expert staff responsible for the manufacture or testing of the above-mentioned substances are as follows:—

Names. Qualifications.

Signature.

Date.

FORM 2

FORM OF MANUFACTURING LICENCE

DISEASES OF ANIMALS ACT, 1950

Diseases of Animals (Therapeutic Substances) Order, 1952

The Minister of Agriculture and Fisheries hereby licences of to manufacture at the undermentioned therapeutic substances for sale:—

This licence is granted subject to the conditions and requirements pertaining to the manufacture of the above-named substances set out in the said Order and Act. The licence will, unless previously suspended or revoked, continue in force until the day of .

In witness whereof the Official Seal of the Minister of Agriculture and Fisheries is hereunto affixed this day of one thousand nine hundred and .

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* In the case of an application for renewal insert after "for" the words "the renewal of".

† Group the substances under the headings of sera, antitoxins, antigens, anaerobic vaccines, killed bacterial vaccines, viral vaccines, and living bacterial vaccines.

FORM 3

FORM OF APPLICATION FOR * A LICENCE TO IMPORT A THERAPEUTIC SUBSTANCE

Diseases of Animals (Therapeutic Substances) Order, 1952

To the Minister of Agriculture and Fisheries

I, / We, , of

hereby apply for a * licence to import from of the undermentioned therapeutic substance.†

I / We enclose with this application an undertaking signed by or on behalf of the said as required by Article 8 of the said Order.

Signature.

Date.

FORM 4

FORM OF IMPORT LICENCE

DISEASES OF ANIMALS ACT, 1950

Diseases of Animals (Therapeutic Substances) Order, 1952

The Minister of Agriculture and Fisheries hereby licences of to import from the under-mentioned therapeutic substance:—

This licence is granted subject to the conditions and requirements pertaining to the importation of the above-named substance set out in the said Order and for the time being in force. The licence will, unless previously suspended or revoked, continue in force until the day of .

In witness whereof the Official Seal of the Minister of Agriculture and Fisheries is hereunto affixed this day of one thousand nine hundred and .

FORM 5

FORM OF APPLICATION FOR A * LICENCE TO IMPORT THERAPEUTIC SUBSTANCES FOR THE PURPOSE OF SCIENTIFIC RESEARCH

Diseases of Animals (Therapeutic Substances) Order, 1952

To the Minister of Agriculture and Fisheries

I, , of

hereby apply for a licence to import the under-mentioned therapeutic substance(s) for the purpose of scientific research at :—

and I undertake to comply with the conditions applicable to this licence.

This application is supported by the recommendations appearing below.

Signature.

Date.

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* In the case of an application for renewal insert after "for" the words "the renewal of".

† State whether the substance is a serum, antitoxin, antigen, anaerobic vaccine, killed bacterial vaccine, viral vaccine, or living bacterial vaccine.

We / I *recommend that the above application be granted.

1
of
Chairman (President or Principal) of
2
of
Professor of

FORM 6

FORM OF RESEARCH LICENCE

DISEASES OF ANIMALS ACT, 1950

Diseases of Animals (Therapeutic Substances) Order, 1952

The Minister of Agriculture and Fisheries hereby licences of to import the under-mentioned therapeutic substance(s) for the purpose of scientific research at or in such other place as the Minister may from time to time authorise.

This licence is granted subject to the general conditions pertaining to the importation of the therapeutic substance(s) for the purpose of scientific research set out in the said Order and for the time being in force and to the following special conditions:—

The licence will, unless previously suspended or revoked, continue in force until the day of .

In witness whereof the Official Seal of the Minister of Agriculture and Fisheries is hereunto affixed this day of one thousand nine hundred and .

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* The recommendation must be signed by one of the persons named at (*a*) below and also (unless the applicant be such a person) by a person holding one of the offices named at (*b*) below:—

(*a*) The Chairman of the Agricultural Research Council;
The Chairman of the Medical Research Council;
The President of the Royal Society;
The President of the Royal Society, Edinburgh;
The President of the Royal Colleges of Physicians in London or Edinburgh;
The President of the Royal Colleges of Surgeons in London or Edinburgh;
The President of the General Medical Council;
The President of the Royal Faculty of Physicians and Surgeons of Glasgow;
The President of the Royal College of Veterinary Surgeons;
The Principal of a Veterinary College or School;
The President of the Royal Institute of Chemistry; or
The President of the Pharmaceutical Society of Great Britain.

(*b*) A professor of physiology, medicine, anatomy, medical jurisprudence, materia medica, surgery, pathology, bacteriology, pharmacology, therapeutics or biochemistry in a university in Great Britain, or in a college in Great Britain which is incorporated by royal charter, or a Director of a Research Institute authorised so to sign by the Minister.

SECOND SCHEDULE

SERA AND ANTITOXINS

PART I

SPECIAL PROVISIONS APPLICABLE TO THE PRODUCTION OF SERA AND ANTITOXINS

Condition and Housing of Animals

1.—(1) The animals used in the production of sera and antitoxins must be adequately and healthily housed.

(2) Only healthy animals may be used in the preparation of sera and antitoxins, and in particular the presence of glanders in horses or other equidae and of tuberculosis in cattle must be excluded by testing with mallein and tuberculin respectively.

(3) Every new equine and bovine animal intended to be used as a source of serum or antitoxin must be subjected to a period of observation in quarantine for at least seven days before being admitted to the premises in which the serum-yielding animals are housed.

(4) Every equine or bovine animal used as a source of serum or antitoxin must either be actively immunized against tetanus toxin or must be passively immunized against that toxin by injections of tetanus antitoxin in such doses as to ensure the constant presence of that antitoxin in the blood during the whole period of the use of the animal as a source of serum or antitoxin.

Precautions to be observed in preparation

2.—(1) Laboratories where sera or antitoxins are exposed to the air in the course of the process of preparation must be separated by a sufficient distance from stables and animal houses to avoid the risk of aerial contamination with micro-organisms from animal excreta, and must be rendered fly-proof to prevent such contaminations by insects. Such laboratories must have impervious walls and floors and must be capable of being readily disinfected when necessary.

(2) A special room with impervious walls and floor which can be washed and, when necessary, chemically disinfected must be provided for the collection of blood from the living animal.

(3) An efficient system of manure removal must be used, which will prevent its accumulation in the vicinity of any room where blood or serum is collected or handled.

(4) An adequate number of efficient sterilizers must be provided for the sterilization of all glass-ware or other apparatus with which the serum or antitoxin may come into contact in the course of its preparation.

(5) All processes to which the serum or antitoxin is subjected during and after the collection of serum from the animal, must be designed to preserve its sterility, but in the case of artificially concentrated sera or antitoxin, it shall suffice that the process of concentration is conducted with scrupulous cleanliness and in such a manner as to avoid unnecessary or dangerous contamination.

Unhealthy or infected animals

3. If an animal used in the production of sera or antitoxins is found to be suffering from an infection, except one produced by living organisms against which it is being immunized, or shows signs of serious or persistent ill health not reasonably attributable to the process of immunization, the licensee shall immediately report the matter to the Minister and shall, if the Minister orders an inspection and the inspector so directs, cause such animal to be killed and a post-mortem examination of it to be made, and take steps to prevent any serum or antitoxin produced from the animal being sold or offered for sale until permission is given by the Minister. If the result of the post-mortem examination is such as to bring under suspicion the health of any of the other animals used for the production of sera or antitoxins, the Minister may prohibit the use of

those animals for the production of sera and antitoxins or may take such other steps as may be necessary to prevent the issue of sera or antitoxins which may be dangerous to animal health:

Provided that in a case of emergency the person in charge of the establishment may order the destruction of an animal used in the production of sera or antitoxins and suspected of infection, and shall in that case give notice forthwith to the Minister and shall permit an inspector to be present at the post-mortem examination.

Part II

Special Provisions applicable to the Testing of Sera and Antitoxins for Freedom from Abnormal Toxicity

Tests for freedom from abnormal toxicity

Every batch of serum or antitoxin which has not been passed through a bacteria-proof filter shall be tested for abnormal toxicity in the manner provided by paragraph (1) of Article 24 of this Order and also in the following manner (instead of in the manner provided by paragraph (2) of the said Article 24):

Doses of 10 millilitres and 5 millilitres drawn from every batch of the substance shall be centrifuged for ten minutes at a speed of 3,000 r.p.m. and the deposits resuspended in 2 millilitres physiological saline. 1 millilitre of the fluid containing the deposit derived from the initial dose of 10 millilitres shall be injected intraperitoneally into each of two healthy guinea pigs and 0.5 millilitre of the fluid containing the deposit derived from the initial dose of 5 millilitres shall be injected subcutaneously into each of two healthy mice. The substance shall be treated as having passed the test for freedom from other abnormal toxic constituents if the injections do not produce death or serious symptoms in any of the animals within five days.

THIRD SCHEDULE

VIRAL VACCINES

Part I

Special Provision applicable to the Testing of Viral Vaccines containing Living Virus

Tests for freedom from abnormal toxicity

Every batch of vaccine containing or stated to contain living virus shall be tested in the following manner (instead of in the manner provided by Article 24 of this Order):

A dose of 1 millilitre of the vaccine shall be injected subcutaneously either into each of two healthy guinea pigs or into each of two other healthy animals not susceptible to the virus contained in the vaccine and the vaccine shall be treated as having passed the test if the injections do not produce death or serious symptoms in either guinea pig or either of the other animals, as the case may be, within ten days.

Part II

Additional Provisions applicable to particular Viral Vaccines

A.—Crystal Violet Swine Fever Vaccine

Definition

1. Crystal Violet Swine Fever vaccine is a mixture of defibrinated blood from pigs artificially infected with the specific virus, crystal violet and glycerol.

Preparation from sterile tissue

2. The tissue from which the vaccine is prepared shall be bacteriologically sterile.

Additional Test

3. The following additional test shall be applied to every batch of crystal violet swine fever vaccine:

A dose of 40 millilitres of the vaccine shall be injected subcutaneously into each of two normal pigs and the vaccine shall be treated as having passed the test if the injections do not produce serious symptoms in either pig within ten days.

B.—CANINE DISTEMPER VACCINE

Definition

1. Canine distemper vaccine is a suspension of the tissue of an infected dog or an infected ferret containing canine distemper virus which has been so treated that the virus has been killed or sufficiently inactivated to render it non-infective to susceptible dogs or ferrets.

Additional Test

2. The following additional test shall be applied to every batch of canine distemper vaccine:

Either a dose of 10 millilitres of the vaccine shall be injected into each of two healthy and susceptible dogs or a dose of 2 millilitres shall be injected subcutaneously into each of two healthy and susceptible ferrets; and the vaccine shall be treated as having passed the test if the injections do not produce death or serious symptoms in either animal within ten days.

FOURTH SCHEDULE

LIVING BACTERIAL VACCINES

PART I

SPECIAL PROVISION APPLICABLE TO THE TESTING OF LIVING BACTERIAL VACCINES

Tests for sterility

1.—(1) Subject as provided in sub-paragraph (2) of this paragraph, every living bacterial vaccine shall be tested for sterility in the manner provided by Articles 17 to 23 of this Order.

(2) For the purpose of the test for aerobic micro-organisms a medium prepared by adding 1.5 per cent. agar to the medium described in paragraph (2) of Article 20 of this Order shall be used instead of that medium, and the vaccine shall be treated as having passed the test if at the examination made in accordance with paragraph (3) of Article 21 of this Order there is found no growth of micro-organisms other than that from which the vaccine was prepared.

PART II

ADDITIONAL PROVISIONS APPLICABLE TO PARTICULAR LIVING BACTERIAL VACCINES

A.—ANTHRAX SPORE VACCINE

Definition

1. Anthrax spore vaccine consists of a suspension of living spores of an uncapsulated, avirulent strain of *Bacillus anthracis* in a mixture of glycerol and physiological saline solution containing saponin.

Seed material

2. The seed material to be used for the purpose of the preparation of anthrax spore vaccine shall be an uncapsulated avirulent strain of *Bacillus anthracis* obtained from the Veterinary Laboratory, Ministry of Agriculture and Fisheries, New Haw, Weybridge, Surrey.

Additional Test

3. The following additional test shall be applied to every batch of anthrax spore vaccine:

A dose of 2 millilitres of each batch of vaccine shall be injected subcutaneously into each of two healthy and susceptible sheep and the vaccine shall be treated as having passed the test if the injections do not produce death or serious symptoms in either sheep within ten days.

B.—BRUCELLA ABORTUS (STRAIN 19) VACCINE

Definition

1. *Brucella abortus* (Strain 19) vaccine is a living culture of *Brucella abortus* (Strain 19) organisms in the " S " (smooth) phase suspended in a buffered solution (pH = 6.3).

Seed material

2. The seed material to be used for the purpose of the preparation of *Brucella abortus* (Strain 19) vaccine shall be obtained from the Veterinary Laboratory, Ministry of Agriculture and Fisheries, New Haw, Weybridge, Surrey.

Additional Test

3. The following additional test shall be applied to every batch of *Brucella abortus* (Strain 19) vaccine:

A dose of 1 millilitre of each batch of vaccine shall be injected intramuscularly into each of two healthy guinea pigs and the vaccine shall be treated as having passed the test if the injections do not produce death or serious symptoms in either guinea pig within ten days.

EXPLANATORY NOTE

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

This Order prohibits, except under the authority of a licence issued by the Minister and in accordance with any conditions subject to which the licence is issued, the manufacture for sale, or the landing in Great Britain from any other country, of any therapeutic substance as defined therein. It prescribes the conditions subject to which such a licence will be issued, the standard of purity and the tests applicable to those substances and the form of licences and applications therefor.

The Order also (1) prohibits the sale or offering for sale of a therapeutic substance otherwise than in a container of a prescribed character and requires a prescribed label to be affixed to the container; and (2) requires that the date of manufacture of the substance shall be stated on containers and prohibits the sale of the substance after a prescribed period from that date.

The Diseases of Animals (Importation of Therapeutic Substances) Order of 1936 is revoked by this Order.