GOVERNMENT OF INDIA

MINISTRY OF HEALTH

AGENDA AND MINUTES OF THE EIGHTEENTH MEETING OF THE DRUGS TECHNICAL ADVISORY BOARD

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AGENDA FOR THE EIGHTEENTH MEETING OF THE DRUGS TECHNICAL ADVISORY BOARD HELD ON THE 23RD JULY 1957, AT NEW DELHI

1. Confirmation of the minutes of the seventeenth meeting.

2. Consideration of Government of India, Ministry of Health letter No. F. 1-2/56-D dated the 30th January, 1956 containing proposal for revision of Schedule F and amendment of Schedule K to the Drugs Rules. (Enclosure A).

3. Consideration of Government of India, Ministry of Health endorsement No. F. 1-11/56-D dated the 29th March, 1956 containing proposal for the amendment of rule 109(8) (b) and (d) to the Drugs Rules regarding labelling to drug with date of expiry (Enclosure B).

4. Consideration of Govt. of India, Ministry of Health letter No. F. 1-4/56-D dated the 19th/21st May, 1956 containing comments of various parties on the draft amendments to rules 65 and 97, Schedules E, G and H and the new Schedule L to the Drugs Rules and Uniform State Poisons List (Enclosure C).

5. Consideration of Govt. of India, Ministry of Health letter No. F. 1-19/55-D, dated the 26th June, 1956 containing proposal for inclusion of preparations of 'Rauwolfia Serpentina' in Schedule H to the Drugs Rules (Enclosure D).

6. Consideration of Govt. of India, Ministry of Health letter No. F. 1-25/56-D dated the 13th July, 1956 containing proposal for including fresh forms in the Drugs Rules for repacking of drugs (Enclosure E).

7. Consideration of Govt. of India, Ministry of Health letter No. F. 1-7/56-D dated the 25th August, 1956 containing proposal for insertion of additional rule under rule 52 of the Drugs Rules empowering Drugs Inspectors to seize records, registers etc. (Enclosure F).

8. Consideration of Govt. of India, Ministry of Health letter No. F. 3-7/56-D dated the 4th October, 1956 regarding storage of Poisons under Schedule E to the Drugs Rules (Enclosure G).

9. Consideration of Govt. of India, Ministry of Health letter No. F. 1-68/56-D dated the 5th January, 1957 containing proposal for the amendment of item 12 of Schedule C to the Drugs Rules, (Enclosure H).

10. Consideration of Govt. of India, Ministry of Health letter No. F. 1-12/57-D dated the 19th February, 1957 containing proposal for inclusion of Viomycin in Schedule C(1) to the Drugs Rules (Enclosure I).

11. Consideration of Govt. of India, Ministry of Health letter No. F. 1-30/56-D dated the 24th April 1957 containing proposal for the amendment of provisions laid down for Tetanus Antitoxin in Schedule F to the Drugs Rules (Enclosure J).

12. Consideration of Govt. of India, Ministry of Health letter No. F. 1-28/55-D dated the 20th June, 1957 regarding amendment of item 5 of Schedule K to the Drugs Rules granting exemption to Govt. hospitals, charitable institutions etc (Enclosure K).

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13. Consideration of Govt. of India, Ministry of Health letter No. F. 1-35/57-D dated the 24th June, 1957 containing proposal for amendment of Schedule K granting exemption to insecticides and their formulations in respect of sale licences (Enclosure L).

14. Consideration of Govt. of India, Ministry of Health letter No. F. 1-36/57-D dated the 24th June, 1957 containing proposal for granting restricted sale licences to only certain specified classes of household remedies. (Enclosure M).

15. Consideration of Govt. of India, Ministry of Health letter No. F. 1-34 /57-D dated the 24th June, 1957 containing proposal for introducing special licence forms for repacking of drugs (Enclosure N).

16. Consideration of Govt. of India, Ministry of Health letter No. F. 1-33/57-D dated the 21st June, 1957 containing proposal for including standards for Penicillin Aluminium Monostearate (PAM) in Schedule F to the Drugs Rules (Enclosure O).

17. Consideration of Govt. of India, Ministry of Health letter No. F. 1-52/56-D dated the 26th June, 1957 containing proposal for recognition of preparations covered by the earlier editions of the Pharmacopoeias and amendment of the Schedule to the Drugs Act, 1940 (Enclosure P).

18. Consideration of Govt. of India, Ministry of Health letter No. F. 1-38/57-D dated the 27th June, 1957 containing proposal for the amendment of rule 65(9) (Enclosure Q).

19. Consideration of Govt. of India Ministry of Health letter No. F. 1-37 /57-D dated the 27th June, 1957 containing proposal for the amendment of provisions for labelling in Part I of Schedule F in respect of Cholera Vaccine (Enclosure R.)

20. Consideration of Govt. of India, Ministry of Health letter No. F.1-39 /57-D, dated the 27th June, 1957 containing comments received on the draft standards for "Crude Liver Extract for parenteral administration" for inclusion in Schedule F. (Enclosure S).

21. Any other items with the approval of the Chair.

ENCLOSURE A

No. F. 1-2/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 30th January, 1956.

FROM

Shri P. N. Anand,
Under Secretary to the Government of India.

To

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services.
NEW DELHI.

SUBJECT :—*Drugs Rules,* 1945—*Revision of Schedule F and amendment of Schedule K Recommendations of the Drugs Consultative Committee.*

SIR,

I am directed to invite your attention to the minutes of the third meeting of the Drugs Consultative Committee in respect of item 8 of the agenda, and to request that the recommendations made by the Committee relating to the revision of Schedule F and amendment of Schedule K to the Drugs Rules, 1945 may kindly be placed before the Drugs Technical Advisory Board at its next meeting and the views of the Board communicated to this Ministry in due course.

Yours faithfully,
(Sd.) X X X
P. N. ANAND,
Under Secretary.

Item 8 of the Agenda—Examination of labelling provisions and the Schedules to the Drugs Rules in the light of experience so far gained :—

It was agreed by the Committee that the labelling provision of the Drugs Rules should be recast in simple language on the lines of the Canadian Foods and Drugs Act and Rules thereunder.

The question of keeping the poisons list and other Schedules of the Drugs Rules up-to-date was also examined and the Committee desired that the possibility of appointing a Poisons Board should be examined in consultation with the Government of India.

The question of revising Schedule 'F' and bringing it in conformity with the latest editions of the recognised Pharmacopoeias should be taken up and whatever provisions were considered superfluous in these Schedules should be deleted.

The Committee also recommended that the first item in Schedule K should be amended and brought in line with the corresponding entry in Schedule D of the Drugs Rules.

ENCLOSURE B.

No. F. 1-11/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 29th March, 1956.

FROM

Shri P. N. Anand,
Under Secretary to the Government of India.

To

All Parts State Governments. (except Madras and Jammu & Kashmir)

SUBJECT :—*Drugs Rules,* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule* 109(3) (*b*) *and* (*d*).

SIR,

COPY OF LETTER REF. NO. 90667-D/55, DATED 4TH JANUARY, 1956 FROM 4th January, 1956, from the Director of Medical Services and Drugs Controller, Madras, to the Government of Madras and to request that the views of the State Government in the matter may kindly be intimated to this Ministry by the 15th May, 1956.

Yours faithfully,
(Sd.) X X X
P. N. ANAND,
Under Secretary.

No. F. 1-11/56-D

Copy, with a copy of the enclosure, forwarded to the Secretary, Drugs Technical Advisory Board, Directorate General of Health Services, with a request that the matter may kindly be placed before the Drugs Technical Advisory Board at their next meeting and the views of the Board intimated to this Ministry. The views of the State Governments will be communicated to the Board as soon as received.

By Order,
(Sd.) X X X
P. N. ANAND,
Under Secretary.

COPY OF LETTER REF. NO. 90667- D/55, DATED 4TH JANUARY, 1956 FROM THE DIRECTOR OF MEDICAL SERVICES AND DRUGS CONTROLLER, MADRAS, TO THE SECRETARY TO GOVERNMENT, HEALTH, EDUCATION AND LOCAL ADMINISTRATION DEPARTMENT, MADRAS-9.

SUBJECT :—*Drugs Act* 1940—*Madras Drugs Rules* 1945—*Labelling of Date of expiry on the label of substances specified in Schedule C.*

The date of manufacture and the date of expiry (wherever required) should be furnished either on the label borne by the container of any substance specified in Schedule C or on a label or wrapper affixed to any package in which any such container is issued for sale *vide* Rule 109(3) (b) and (d).

Inasmuch as the above rule does not bind the manufacturer to put the date of expiry on the label of the container, if it has been indicated on the outer cartons, it is likely unscrupulous sellers can dispose of time-expired drugs without the cartons. In order to prevent the above fraud it is requested that the Government of India may kindly be addressed to suitably amend the above rule to make provision that the date of expiry should also be given on the vials or ampoules themselves as well as on the outer containers or cartoons.

(True Copy.)

(Sd.)X X X
Superintendent.

No. F. 1-11/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 29th June, 56.

FROM

Shri T. V. Anantanarayanan, M. A.,
Under Secretary to the Government of India.

To

The Secretary to the Drugs Technical Advisory Board,
C/o Director General of Health Services,
NEW DELHI.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule*—109 (3) (*b*) & (*d*).

SIR,

With reference to correspondence resting with your letter No. 8-14/56-DAB, dated the 21st April, 1956 and in continuation of this Ministry's endorsement No. F. 1-11/56-D, dated the 29th March, 1956, on the subject mentioned above, I am directed to forward herewith copies of the replies received from the State Governments in this connection.

Yours faithfully,
(Sd.) X X X
PRETAM SINGH,
For Under Secretary.

COPY OF LETTER NO. 2831/H, DATED THE 24TH APRIL, 1956, FROM THE GOVERNMENT OF ORISSA, HEALTH DEPARTMENT TO THE MINISTRY OF HEALTH, GOVERNMENT OF INDIA, NEW DELHI.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule*—109 (3) (*b*) & (*d*).

With reference to your letter No. F. 1-11/56-D dated the 29th March, 1956 on the subject noted above I am directed to say that the State Government agree to the proposed amendment to rule 109 (3) (b) and (d) of the Drugs Rules of 1945.

COPY OF LETTER NO. 28088 Q/56-2 HEALTH, DATED THE 30TH APRIL, 1956, FROM THE GOVERNMENT OF ANDHRA, HEALTH AND ADMINISTRATION DEPARTMENT KURNOOL, TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules*, 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule* 109 (3) (*b*) & (*d*).

REFERENCE :—*Shri P. N. Anand's letter No. F.* 1-11/56-*D, dated* 29*th March* 1956.

I am directed to say that this Government agree to rule 109(3) (b) and (d) of the Drugs Rules being amended as suggested by the Director of Medical Services and Drugs Controller, Madras.

COPY OF LETTER NO. DRG 1156/30607-H, DATED THE 9TH MAY, 1956 FROM THE GOVERNMENT OF BOMBAY, PUBLIC HEALTH DEPARTMENT, TO THE MINISTRY OF HEALTH, GOVERNMENT OF INDIA, NEW DELHI.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule*—109 (3) (*b*) & (*d*).

I am directed to refer to the Government of India Ministry of Health's letter No. F. 1-11/56-D, dated 29th March, 1956, on the subject mentioned above, and to state that the Government of Bombay agrees with the views expressed by the Director of Medical Services, and the Drugs Controller, Madras, in his letter No. 90667-D/55; dated the 4th January, 1956 in respect of Rule 109(3) (b) and (d) of the Drugs Rules, 1945. The above rule may be suitably amended.

COPY OF LETTER NO. IIIDI-1-169/56-15242/H, DATED THE 12TH MAY, 1956 FROM A. KARIM, ESQR., ADDL. DEPUTY SECRETARY TO THE GOVERNMENT OF BIHAR, HEALTH DEPARTMENT TO THE MINISTRY OF HEALTH, GOVERNMENT OF INDIA, NEW DELHI.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule 'C'—Amendment to Rule*—109 (3) (*b*) & (*d*).

I am directed to refer to your letter No. F. 1-11/56-D dated the 29th March, 1956, on the above subject and to say that this State Government agree to the amendment of the rule as proposed by the Director of Medical Services and Drugs Controller, Madras.

COPY OF LETTER NO. MMD. 203/55/100, DATED THE 28TH MAY, 1956, FROM THE GOVERNMENT OF ASSAM, MEDICAL DEPARTMENT, MEDICAL BRANCH, SHILLONG, TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule*—109 (3) (*b*) & (*d*).

REFERENCE.—*Shri P. N. Anand's letter No. F.* 1-11/56-*D, dated the* 29*th March* 1956.

I am directed to refer to the letter quoted above and to say that this Government agree with the views of the Madras Government in the matter.

COPY OF LETTER NO. 5185/XVI-804/1951, DATED THE NIL JUNE, 1956, FROM SRI B. D. SETH, DEPUTY SECRETARY TO GOVERNMENT OF UTTAR PRADESH, TO THE MINISTRY OF HEALTH, GOVERNMENT OF INDIA.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule* 109 (3) (*b*) & (*d*).

With reference to the Ministry of Health's letter No. F. 1-11/56-D, dated March 29, 1956, on the above subject, I am directed to say that this State Government have no objection to the proposed amendment to rule 109(3) (b) and (d) of the Drugs Rules 1945.

COPY OF LETTER NO. MEDL./3817/3D-24/56 DATED THE 11TH MAY, 1956, FROM THE GOVERNMENT OF WEST BENGAL MEDICAL AND PUBLIC HEALTH DEPARTMENT, MEDICAL BRANCH, TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule* 109 (3) (*b*) & (*d*).

With reference to Shri P. N. Anand's letter No. F. 1-11/56-D, dated 29th March, 1956 on the above subject, I am directed to state that the Government of West Bengal have no objection to the proposed amendment of the Drugs Rules, 1945 in the manner suggested in the letter No. 90667-D/55 dated the 4th January, 1956 of the Director of Medical Services and Drugs Controller, Madras. It has however been the experience of the Drugs Control Directorate of this State that manufacturers mention expiry of date of potency on the label of the container as well as on the carton.

COPY OF LETTER NO. 5998-S-2HB-56/19392 DATED THE 14/15TH MAY, 1956, FROM THE GOVERNMENT OF PUNJAB, HEALTH AND LOCAL GOVERNMENT DEPARTMENTS, CHANDIGARH, TO THE MINISTRY OF HEALTH, GOVERNMENT OF INDIA.

SUBJECT :—*Drugs Rules*, 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule* 109 (3) (*b*) & (*d*).

With reference to your letter No. F. 1-11/56-D, dated the 29th March, 1956, on the subject cited above, I am directed to say that the Punjab Government are in favour of the proposed amendment to rule 109(3) (b) & (d) of the Drugs Rules, 1945, as they consider that such a step would check fraudulent practices on the part of manufacturers in the matter of disposal of drugs whose efficacy and usefulness is limited for a certain period.

COPY OF LETTER NO. 5196/3021-XIV, DATED THE 6TH MAY, 1956, FROM THE GOVERNMENT OF MADHYA PRADESH, PUBLIC HEALTH DEPARTMENT, NAGPUR, TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs rules* 1945—*Labelling of drugs—Date of expiry on the label of substances specified in Schedule C—Amendment to Rule* 109 (3) (*b*) & (*d*).

I am directed to refer to your letter No. F. 1-11/56-D dated 29th March, 1956 and to say that rule 109 (3) of the Drugs Rules 1945 may please be suitably amended so that all the particulars required under Rule 109 (3) (a), (b), (c), (d), (e) and (f) should be required to be printed or written in indelible ink on the containers themselves and also on the labels affixed to any package in which such containers is issued for sale.

ENCLOSURE C

No. F. 1-4/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 19th/21st May, 1956.

FROM

Shri T. V. Anantanarayanan, M. A.
Under Secretary to the Government of India.

To

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT :—*Drugs Rules* 1945—*Amendment of Rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule L.*

SIR,

I am directed to refer to this Ministry's endorsement No. F. 1-48/55-D, dated the 23rd December, 1955, and to forward copies of the correspondence detailed given below which may kindly be placed before the next meeting of the Drugs Technical Advisory Board thereon communicated to this Ministry before the proposed amendments to the Drugs Rules, 1945 published in this Ministry's notification No. F. 1-48/55-D. dated the 15th December, 1955, are finalised.

(1) Letter No. HL 9-27576/55/DD, dated 19-3-56 from the Government of Travancore-Cochin.

(2) Letter No. DRG.1155/90399-H, dated 5-3-56 from the Govt. of Madras.

(3) Letter No. MS 870-Health, dated 5-3-56 from the Govt. of Bombay.

(4) Letter No. nil dated 26-3-56, from the Saurashtra Chemists' and Druggists' Association.

(5) Letter No. B.1955, dated 31-3-56 from the Retail & Dispensing Chemists' Association, Bombay.

(6) Letter No. A/7/56, dated 12-3-56 from the Barielly Chemists' Association.

(7) Letter No. DSCA/56/708, dated 26-4-56 from the Delhi State Chemists' Association.

(8) Letter No. DRG. 1155/25522-H, dated 1-5-56 from the Govt. of Bombay.

(9) Letter No. Medl/2628/3D-2/56, dated 9-4-56 from the Govt. of West Bengal.

Yours faithfully,
(Sd.) T. V. ANANTANARAYANAN,
Under Secretary.

COPY OF LETTER NO. HL 9-27576/55/DD, DATED THE 19TH MARCH, 1956, FROM THE GOVERNMENT OF TRAVANCORE-COCHIN TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH.

SUBJECT :—*Drugs Rules* 1945—*Amendment of Rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule.*

REFERENCE :—*Your letter No. F.* 1-48/55-*D, dated* 15-12-1955.

I am directed to invite a reference to the letter cited above and to inform you that the amendment proposed to the Drugs Rules by the Government of India is accepted by this Government subject to the modification suggested below :—

In the Schedules E, G & H the words "Registered Medical Practitioner" shall be amended to read "Registered Medical Practitioners in Modern Medicine".

COPY OF LETTER NO. DRG 1155/90399-H, DATED THE MARCH, 1956, FROM THE GOVERNMENT OF BOMBAY (LOCAL SELF-GOVERNMENT AND PUBLIC DEPARTMENT) TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH.

SUBJECT :—*Drugs Rules,* 1945—*Amendment to Rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule L.*

With reference to the Government of India, Ministry of Health's letter No. F. 1-48/55-D, dated 15th December 1955 on the subject mentioned above, forwarding to State Govts. for comments draft amendments to rules 65 and 97, Schedules E, G & H and the insertion of a new Schedule L to the Drugs Rules, 1945, I am directed to state as follows :—

1. The following substances should be added to the proposed new schedule 'E' :—

Apiol Morphine-N-oxide, its derivatives N-allyl-morphine and any other pentavalent morphine derivatives. Methanol (Methyl Alcohol) 'Hydroxypethidine' which is given at entry 65 is considered to be a dangerous drugs in Great Britain and hence it should also be marked with an (*) "asterisk" and brought within the purview of Dangerous Drugs Act, 1930. In item 47 after the words "di-nitrocresols" following should be inserted "their compounds with a metal or a base".

2. The following typographical mistakes should be corrected :—

Item 55 'butane' should read 'butene'.

Item 132 'Toxidine' should read 'Troxidone'.

'Di Sulfiram' in Schedule 'H' should read 'Disulfiram'.

3. (a) Physeptone, which is included in the proposed Schedule 'H' should be deleted therefrom, as it will be covered under Methadone at entry 76 in Schedule E. Physepton is a proprietory name for injection of Methadone and hence it will be included in Schedule 'H' under the general entry "Drugs coming under Dangerous Drugs Act and marked with an asterisk in Schedule E of the Drugs Rules, 1945".

(b) In Schedule 'H' *after* the words 'Dinitrocresols', *add* "their compounds with a metal or base".

4. "Pituitary gland, the active principles of", should be deleted from Schedule G, as it will now be covered by Schedule H and hence it will have to be labelled in accordance with Rule 97(c) as follows:—

> Schedules H Drug Warning—to be sold by retail on the prescription of a Registered Medical Practitioner only" and hence requirement of labelling it is Schedule G product becomes redundant.

5. Attention is invited to Government Resolution, Local Self Government and Public Health Department No. 7015/33, dated 5th September, 1952, and the preliminary Notification accompanying it, a copy of which was forwarded to the Government of India. The question of amendment of Schedule 'E' was then under consideration of the Government of India. The Drugs Controller for the State of Bombay in paragraph 3 of his letter No. DC(I)/4246 dated 21st May 1953 (a copy of which was forwarded to the Government of India under this Department Letter No. 7015/33-H, dated 23rd May, 1953), had suggested that the system of numbering the poisons in the Schedule should not be introduced as it will lead to unnecessary confusion while introducing a new poison in the Schedule or deleting one therefrom. It is observed that the system of numbering has been continued which should be deleted.

6. At the end of Schedules 'E', 'H' and 'L' the following general clauses should be added:—

> "Any substance or article which is sold under the name synonym, description, designation or label of any poison included in these Schedules shall be deemed to be a Schedule 'E', 'H' or 'L' drug as the case may be".

7. It would be desirable to add the following additional item in the Schedule 'L' under antibiotics so as not to modify it from time to time as soon as any new Antibiotic is introduced in the market:—

> "Any substance or article which purports or claims to have antibiotic properties".

8. The following general clause should be added as a foot-note to each of the Schedules 'E', 'H' and 'L' that—

> "Preparations containing above substances are also covered by the Schedule".

This clause is necessary because the Chief Justice, Bombay, High Court, has held in the case of State *versus* S. B. Nagarkar of India Chemical Works, Jalgaon, that preparations of vitamins will not include preparations containing small quantities of vitamin according to Schedule C(1).

In the proposed Schedule 'L' the words "their preparations" in the entry on Antibiotics' and 'Para-amino salicylic acid' will mean that only preparations of Antibiotics and para-amino salicylic acid will be included and preparations containing these will not be included.

Preparations of and containing 'Adrenocortico tropical hormone' and Isonicotinic acid hydrazide in Schedule 'L' should be deleted and a general clause as suggested above be added to all the three Schedules 'E', 'H' and 'L'.

9. I am to add that the Government of India has already been approached under this Department letter No. DRG. 1255/55247-H, dated 12th September, 1955 to amend Schedule C (1) so as give effect to the judgment of the High Court and unless a similar general entry is incorporated in all the Schedules under amendment, it is likely that the purpose of amending these Schedules so as to cover a wider range of substances will be frustrated.

COPY OF LETTER NO. MS. 870 HEALTH, DATED THE 5TH MARCH, 1956, FROM THE GOVERNMENT OF MADRAS (HEALTH EDUCATION AND LOCAL ADMINISTRATION DEPARTMENT) TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH.

SUBJECT :—*Drugs—Drugs Rules*, 1945—*Amendment of Rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule L—Views of this Government communicated.*

REFERENCE :—*Sri P. N. Anand's letter No. F.* 1-48/55-*D, dated* 15-12-55.

I am directed to forward a copy of the letter No. 1577-D/56, dated 16-2-56 of the Drugs Controller, Madras with the enclosure thereto, in the matter for necessary action.

(ENCLOSURE)

COPY OF LETTER REF. NO. 1577-D/56, DATED 16-2-56, FROM THE DRUGS CONTROLLER, MADRAS STATE, MADRAS-6, TO THE SECRETARY TO THE GOVERNMENT OF MADRAS, HEALTH, EDUCATION AND LOCAL ADMINISTRATION DEPARTMENT, MADRAS-9.

SUBJECT :—*Drugs—Drugs Rules* 1945—*Amendment of Rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule* L.

REFERENCE :—*Government Endt. No.* 129765/55-1-*H. II, dated* 3-1-56.

In enclosing herewith a copy of remarks of the Government Analyst (Foods and Drugs) King Institute, Guindy and of the Drugs Inspector Madras City, I am to state that I agree with their remarks.

(True copy.)

COPY OF LETTER NO. R. C. NO. 4976/D6/56 DATED 9-2-56, FROM THE GOVERNMENT ANALYST (FOOD AND DRUGS) KING INSTITUTE, GUINDY, ADDRESSED TO THE DRUGS CONTROLLER, MADRAS STATE, MADRAS-6.

SUBJECT :—*Drugs—Drugs Rules* 1945—*Amendment of Rules* 65 *and* 97—*Revision of schedules E. G and H—Insertion of a new Schedule.*

REFERENCE :—*Your letter No.* 1577-D-55 *dated* 6-1-56 *communicating Endt. No.* 129765-55-1-*H. II, dated* 3-1-56 *over the Govt. of India letter No. F.* 1-48-55-*D, dated* 15-12-55.

Item III of the draft amendments

The exemption from the Poisons Rules for substance containing less than a specified percentage of the poison does not appear to be justified in most cases. This is apparent from a study of the United Kingdom Poisons List.

In the U. K. all poisons are included in the Poisons List which is divided into Part I and II (This division does not concern us here, as it refer to the authority to sell Poisons). In addition to the Poisons List there are a few Schedules of which the First Schedule and the Third Schedule are relevant to the present discussion. These schedules do not contain any Poisons other than those listed in the Poisons List. But poisons in the First Schedule are subjected to special restrictions, in that they should be sold only to authorised persons and a record of the sale should be kept. Certain exemptions are provided in the first Schedule but the exempted drugs are free from the special restrictions only and not from the general rules common to poisons. The Third Schedule consists of some substances which are absolutely exempted from the Poisons Rules. On the other hand, in our Poisons List which is copied from the U. K. List, exempted substances in both the First and Third Schedules of the U. K. List have been clubbed together indiscriminately, and removed from the operation of the poisons Rules, which is wrong.

An example will make the position clear. In U.K. "Cocaine" is a poison included in the Poisons list and also in the first Schedule but substances containing less than 0·1 per cent of cocaine are only exempted from the special restrictions and not exempted from the general provisions in regard to 'Poisons'. In other words a substance containing less than 0·1 per cent of cocaine is a poison subject to the Poisons Rules, whereas in our Poisons List it is not a poison.

Only the exemptions copied from the Third Schedule of the U. K. Poisons Rules are in order and may remain. Thus although "Hydrochloride Acid" is a poison in Part II of the U.K. List substance containing less than 9 per cent of the Hydrochloride acid in the Third Schedule and are not therefore listed as being poisons.

The following is a list of the poisons in Schedule E which should be treated as poisons irrespective of the concentration. It is suggested that the words "except substances containing less than....." occurring in the following items of Schedule E may be deleted.

Item No. 3.—Alkaloid, the following, their salts, simple or complex :—

(3) Aconite
(4) Apomorphine
(5) Atropine
(7) Belladonna, alkaloids of
(12) Coca, alkaloids of
(13) Cocaine
(14) Codeine
(15) Colchicine

(16) Conicine
(17) Conarnine
(27) Ecgonine
(31) Ethylmorphine
(32) Gelsemium, alkaloids of
(33) Homatropine
(34) Hyoscine
(35) Hyoscyamine
(38) Morphine
(40) Papaverine
(43) Sabadilla alkaloids
(46) Strychnine
(47) Thebaine
(49) Veratrum, alkaloids of

10. Aminoalcohols
15. Antimonial Poisons
16. Arsenic
26. Cantharidine
40. Digitalis
62. Hydrocyanic acid
74. Mercury
83. Morpholinyl ethyl morphine
90. Nux Vomica
92. **Opium.**

The following substances may be deleted from the Schedule E as they are not classified as Poisons in U.K :—

3(6) Berberine
11. Aminoptarin
39. 4:4 Diamino diphenylsulphone
64. 3-hydroxy N methylmorphinan and its salts
89. Nitrophenols
100. Pentaquine
117. Quinacrine
133. Zinc Chloride.

Of the above drugs Aminopterin and Pentaquine have been already included in the draft Schedule G and 4 · 4—Diamino—diphenyl sulphone in draft Schedule H.

3. (39) Nicotine	Exemption should be given, Under this head to tobacco.
78. Methyl Alcohol	The unqualified categorisation of this as a poison is not desirable. Exemption may be granted to methylated spirit.
86. Nisentil (NU—1196)	The chemical name should be given instead of the trade name.
95. Oxalic Acid	The exemption given to Potassium quadroxalate should be omitted as all metalic oxalates are in the U. K. Poison List.

Item IV of the Draft Amendments

Amendments suggested in Schedule G:

Item No. 3(6) of the draft Poisons List, Berberine, and item No. 64.3-hydroxy-N-Methyl morphinan and its salts may be included in Schedule G.

Item V of the Draft Amendments

117. Quinacrine may be included in Schedule H.

COPY OF LETTER NO. REF. NO. 59-DI/56 DATED 27-1-56 FROM THE DRUGS INSPECTOR, MADRAS CITY ADDRESSED TO THE DRUGS CONTROLLER, MADRAS STATE, MADRAS-6.

SUBJECT :—*Drugs—Drugs Rules* 1945—*Amendment of Rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule L.*

REFERENCE :—*Your Memo. No.* 1577-D/55, *dated* 6-1-56.

The following remarks are submitted in respect of certain draft amendments:—

1. (b) *Rule* 65(9):—The period of six months specified for the retention of prescription for the sale of schedule H and L drugs is not considered adequate and it may be enhanced to 2 years as provided for the preservation of all registers and records maintained under Rule 65(7).

It is usually found during inspections that the sale of schedule H drugs without prescription are entered in the name of some R.M.P. or institution which is fictitious.

Therefore the proviso exempting the requirements of prescription for the supply of schedule H and L drugs to a Registered Medical Practitioner etc. may be modified so as to facilitate detection of sales which are not bonafide by making it incumbant on the licencee to preserve the requisition from the R.M.P. or institution.

1. (c) *Rule* 65(16).—As schedule L drugs are also required to be sold by retail on a prescription and schedule L includes schedule C and CI drugs also, the details of the purchase of schedule L may also be required to be entered in the proposed register. Schedule C may be exempted from the purview of this sub-rule by a proviso.

It is also necessary to furnish the Batch No. and name of manufacturer of the drugs.

II (*b*) *Rule* 97(5).—Since "Industrial Methylated spirit" contains Methyl alcohol (in the form of Woodnaphtha) which is specified in the proposed list of schedule E, the word "Poisons" may also be included on the label, in addition to the words "for External use only".

As Schedule L drugs are required to be sold by retail on a prescription, another sub-rule *viz.* *97(6) may be added, similar to the labelling requirement of schedule L drugs.

*97(6) the container of a medicine made up ready for the treatment of human ailments shall, if it contains a substance specified in schedule L, be labelled with the words: "Schedule L Drugs" Warning:— To be sold by retail on the prescription of a R.M.P.

VI "Cortisone" and similar preparations may also be included in Schedule L since the properties are similar to ACTH.

(True Copy.)

(Sd.) X X X

Superintendent.

COPY OF LETTER DATED THE 26TH MARCH, 1956, FROM THE SECRETARY, THE SAURASHTRA CHEMISTS' & DRUGGISTS' ASSOCIATION, RAJKOT TO THE MINISTRY OF HEALTH, GOVERNMENT OF INDIA. NEW DELHI.

With reference to the draft amendment to the Drugs Rules, 1945 notified on December 15, '55 and inviting objections and suggestions from interested parties by April 1, '56, my Association submits as follows:—

Amendment I(*a*).—The removal of Proviso to condition (a) to Rule 65 will remove the distinction between sales of Schedule E drugs in packings and loose. The sales in packings which are allowed by persons who are not "qualified persons" under the Drugs Rules, are intended to be disallowed. The underlying object is not very much disputed but until such time there are adequate "qualified persons", this amendment, it is requested, should be postponed. If permitted, we may further request that the Proviso should be so amended that sales of Schedule E drugs in loose form is permitted by persons who are not "qualified persons".

Amendment I(*b*).—The condition (9) to Rule 65 is intended to be replaced by another condition and as applying to Schedule H & L Drugs. The first para of the first paragraph of the new condition is not objected to but the second part thereof which requires retention of prescriptions for schedule H & L drugs for 6 months is objected to often the prescription is an important document for the patient and he would not like to part with it. The Doctors, often Consultants, who issue such prescriptions will not find it convenient to issue it in duplicate. The patient preparing a duplicate for retaining it for himself is not a good alternative. It is likely to lead to serious consequences sometimes. In future consultation too the original prescription would be indispensable and the duplicated prescription will not be acceptable. Under these circumstances, it is requested that the good faith of the "qualified persons" who alone will be able to dispense such prescriptions, be relied upon; if this is not possible it may be prescribed that where this is not possible, a duplicate of the prescription signed by the purchaser is retained.

Amendment I(c).—This requires maintenance of registers of Purchases for resale of Schedule E drugs just like purchases of Schedule C drugs are recorded in registers. This is strongly objected to because it will entail heavy clerical work. The Schedule E is proposed to be enlarged and this will bring in it many items which are at present outside Schedule E. In normal course of business purchases of all drugs are recorded in purchases vouchers and if there is no rule requiring retention of these vouchers, the proper measure would be to introduce such a rule requiring retention of such vouchers and the proposed rule may lay down the particulars such vouchers should contain. It would be a sheer waste of man—hours in a vital profession as this in ordering duplication of particulars relating to purchases from purchases registers. If permitted, we would submit that the above objection be considered in respect of the present rules requiring maintenance of purchase registers for Schedule C drugs.

Amendments II, III, IV, V & VI.—No objection or suggestion except that the manufacturers and importers should be required gradually to mark their respective preparations with letters "E", "G", "H" & "L" to denote that the particular preparation would fall below the respective Schedule.

Thanking you.

COPY OF LETTER NO. B. 1955, DATED THE 31ST MARCH, 1956 FROM THE RETAIL AND DISPENSING CHEMISTS ASSOCIATION, BOMBAY, TO THE UNDER SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT:—*Draft Notification in the Gazette dated* 15-12-1955 *making amendments to the Drugs Rules,* 1945.

With reference to the above Draft Notification, we beg to offer the following comments for the favour of your sympathetic consideration:—

Clause I (a) to the Draft Amendments

The dropping of the proviso to condition (2) of Rule 65 will mean that the retail sale of even a packed bottle of a preparation containing Schedule E drug cannot be made except by or under the personal supervision of a qualified person. Schedule E is comprised of vast range of drugs. Under the existing Rule a sale of a packed bottle of Schedule E drug does not require the supervision of a qualified person, whose maintenance is not within the easy reach of all. A majority of retail chemists has a business of hardly Rs. 75 to Rs. 100 a day. It will be appreciated that retail chemists having such a small turnover, cannot afford to employ a qualified person.

Under the circumstances the dropping of the above proviso will add to the already existing hardships of the Chemists and many of them will be deprived of their fundamental rights to continue in business which they have been doing since long. Moreover, Government is not unaware of the fact that sufficient qualified persons are not available in the country at present and, therefore, it will be conceded that it may not be possible to enforce this change without driving so many retailers out of trade. One is also at a loss to understand as to how the presence of a qualified person is going to help the Government in controlling the misuse of these drugs, if any, by the public. It is doubtful that a person would misuse the poisonous drug knowingly as everyone now-a-days is fairly conscious of the responsibility of oneself and nothing would stop a desparado.

It will not be out of place to mention here that most of the so called qualified persons are compounders only who have practically little knowledge of patent medicines. It is a fact that such compounders are of no use to a retail chemist so far as the sale of patent medicines is concerned. This statement sounds rather surprising, nevertheless it is true.

It is earnestly requested, therefore, that the change contemplated may not be carried out.

Clause I(b) to the Draft Amendments

The submitted condition (9) in Rule 65 makes major changes in the present conditions. The addition of Schedule L in condition (9) is not at all desirable as this Schedule includes very common antibiotics like Penicillin etc., which should be within easy reach of a consumer for treatment of such common ailments as cold, sore-throat etc. If such common things like Penicillin Lozenges are not available to the public without the prescription from the Medical Practitioner it is evident that it will definitely result in great hardships to all, consumers, dealers and the doctors. In our opinion, therefore, this is not a practical proposition at all.

The condition of retaining the prescription which is now being added is again an impractical proposition.

It is a well known fact that the Medical Practitioners and especially the consultants have no time to study the Drugs Act and Rules and, therefore, they are not normally aware of its various restrictions and the details of the Schedules. They prescribe all the medicines on one prescription. Even the case history of the patient and all directions and instructions meant for patient are also written on the same prescription. Under the circumstances, it is quite natural that the patient does not like to part with the prescription. Again the consultants invariably demand the original prescriptions on subsequent visit of the patient.

We humbly request the Government to take into consideration all these practical difficulties which are very real and important.

We wish to impress upon you, Sir, that if this new condition is enforced, the sale of very important and vital drugs will automatically pass into the hands of unauthorised dealers who may pass on sub-standard and spurious drugs to the needy persons not holding prescriptions. This menace to the public health will be very difficult to control.

It may be added here that even the prescriptions of Dangerous Drugs like Morphine and Cocaine are not required to be retailed by the Chemists under the Dangerous Drugs Act. The necessity of retaining the prescriptions was never felt as Chemists are faithfully observing all the restrictions, which may be proved from facts.

We beg to impress upon you that the enforcement of the condition of supplying common drugs only on prescriptions which are to be retained is simply impossible. It may be recalled that all offences under the Drugs Act and Rules have been made cognizable. It is submitted, therefore, that laying down of conditions which are impossible to observe will simply expose the poor Chemist to the extreme punishments. The logical result of all this would be favouritism, corruption and what not.

We are confident that the Government will seriously think over the matter before doing something which will let loose the very evils which they want to put an end to.

Clause I(c) to the Draft Amendments

The addition of condition (16) making provision for a Register of Purchases for Schedule E drugs will increase the clerical work of the retail Chemist enormously without any advantage to anyone. The Chemists at present are already overburdened with innumerable Records, Registers and odd jobs of the business. It will be observed that the Chemists' clerical job is increasing from year to year and the noble profession of a Pharmacist or a qualified person is being converted into a clerk's job. It is a fact that a major part of his time is being wasted in writing voluminous records, and Registers which are seldom of any use to anybody. With all humility, we feel that this unproductive labour is a collosal waste of National Energy, which cannot be justified in the present conditions of India. We regret to find that the technical skill of a Pharmacist is being gradually converted into the monotonous work of a clerk.

The hardships of a law abiding Chemist have increased to such an extent that he finds it difficult to continue with honesty. It can be proved from facts and figures that during the last 5 years real honest Pharmacists have changed their line of profession and unscrupulous persons have replaced them. This undesirable state of affairs is bound to continue unless something is done in the matter.

We are confident that the Government will seriously consider the above submissions.

Thanking you.

COPY OF LETTER NO. A/7/56, DATED THE 12TH MARCH, 1956 FROM THE BAREILLY CHEMISTS' ASSOCIATION TO THE HON. MINISTER FOR HEALTH, GOVERNMENT OF INDIAN UNION, NEW DELHI.

Please refer to the Government Notification dated 15th December 1955 regarding the draft of further amendments to the Drug Rules, 1945 proposed to be made under Section 33 of the Drugs Act, 1940 (XXIII of 1940).

We have the honour to lay down the following objection to the same.

In rule 65:—

(b) Re: the new condition (9).

The second sentence in the new condition (9) *viz.* "The Prescription shall be retained by the retail dealer dispensing the prescription for a period of six months" may please be deleted as it will not be practicable.

Hoping to receive due consideration.

COPY OF LETTER NO. DSCA/56/708 DT. 26TH APRIL, 1956 FROM THE DELHI STATE CHEMISTS ASSOCIATION TO THE SECRETARY, MINISTRY OF HEALTH, GOVERNMENT OF INDIA, NEW DELHI.

SUBJECT :—*Drugs Rules,* 1945.

REFERENCE :—*Notification No. S. R. O.* 3774, *dated* 15*th December* 1955, *of your Ministry, issued in the Gazette of India, dated* 31*st December,* 1955.

With reference to above, I am to submit that the Executive Committee of this Association considered the proposed amendments to the Drugs Rules, 1945, as notified in the above notification, in its meeting on 14th instant.

The Committee was of the unanimous opinion that the proposal requiring the Retail chemists to keep a record of the prescriptions of all the Drugs of Schedules H & L is neither practicable nor necessary. If prescribed, it will entail unnecessary trouble to all the chemists, as detailed below:—

I. That the chemists are already keeping record of the sales of Schedule H Drugs in the prescribed registers and this will only entail duplication.

II. The prescriptions as issued by the Medical practitioners are usually scribbled in haste and do not contain all the implied wants of the "Prescription" as defined in the Drugs Act. If the amendment under reference is enforced, the responsibility for incompleteness of the prescriptions will fall on the chemists. Moreover, the Chemists have no method of testifying the genuineness of the prescriptions and Signatures of the Doctores, though they would be called upon to accept liability on their behalf.

III. The Doctors issue only one copy of prescriptions, which the patient always desires to retain with himself. Whenever a patient is asked to give the prescription for record, he must smell insincerity on the part of the chemist. *Legally speaking, he is the owner of it and chemist has no right to demand it.*

IV. Usually the prescriptions contain details for more than one medicine and its retention by the chemist, providing the H or L Schedule Drug will compel the customer to buy all the medicines from the same shop, which may not suit the patients convenience.

V. All the hospitals, dispensaries, and charitable institutions and even certain private Medical Practitioners demand their patients to bring the same prescription chit on the following day, if they wish to be consulted. Consequently the patient would never be willing to part with the prescription.

In view of these we are to request you not to make retaining of the prescriptions as compulsory; when it serves no useful purpose. In the end, we would request you to consider these practical difficulties before arriving at final decision.

It appears that we have been little late in submitting our views but hope this delay will be ignored.

Thanking you.

COPY OF LETTER NO. DRG 1155/25,522-H, DATED THE 1ST MAY, '56 FROM THE GOVERNMENT OF BOMBAY TO THE UNDER SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules, 1945—Amendment of Rules 65 and 97—Revision of Schedules E, G & H—Insertion of a new Schedule L.*

With reference to the correspondence resting with this Department Letter No. DRG 1155/10339-H, dated 3rd March, 1956, on the subject mentioned above, I am directed to state that the Drugs Controller for the State of Bombay, has intimated to the State Government that he came across recent amendment to the Poison Schedule under the Poisons Act in Great Britain. He, therefore, considers that necessary amendments should also be made to Schedule E of the Drugs Rules amendments to which are under consideration of the Government of India at present. The State Government agrees with the views expressed by the Drugs Controller and requests that the Government of India, may kindly be moved to incorporate the following amendments while finalising amendment to Rule 65-97 and revisions of Schedules E, G & H and insertion of a new Schedule L :—

I. *Schedule E* :—

(1) Head of item No. 3 should read as follows :—

Alkaloids, the following; their salts, simple or complex; their quaternary compounds.

(2) In sub-item 39 at item 3 instead of 'Nicotine' the following should be added :—

"Nicotine, its salts".

(3) Item 63 should be amended as follows :—

"Hydrofluoric acid, potassium fluoride, sodium fluoride, sodium silicofluoride, and other alkali fluorides".

(4) After item 68, 'Ketobemidone', the following should be added :—
"Laudexium".

(5) After item 71 the following should be added :—

"Mannityl Hexanitrate"

(6) In item 110, namely, Phosphorus compounds, after 'Schradan' the following should be added :—

"Sulphotepp".

II. Since preparations of Schedule L are to be sold only on the prescription of a Registered Medical Practitioner, it is necessary that such preparations should also be labelled on the same lines as Schedule H preparations are required to be labelled, under clause (c) of sub-rule 1 of Rule 97, and following amendment to sub-rule 1 of the rule 97 is suggested :—

(d) If it contains a substance specified in Schedule L, it shall be labelled with the words :—

"SCHEDULE L DRUG

Warning—To be sold by retail on the prescription of a Registered Medical Practitioner only."

COPY OF LETTER NO. MEDL/2678/3D-2/56, DATED THE 9TH APRIL, 1956, FROM THE GOVERNMENT OF WEST BENGAL TO THE SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules, 1945—Amendment of rules 65 and 97—Revision of Schedules E, G and H—Insertion of a new Schedule L.*

With reference to Shri P. N. Anand's letter No. F. 1-48/55-D, dated the 15th December, 1955 on the above subject, I am directed to furnish below the comments of the Government of West Bengal on the different items of draft amendment published with the Ministry's Notification No. F. 1-48/55-D, dated the 15th December, 1955 :—

Item I(a) . .	We agree.
Item I(b) . .	We agree and further suggest that rule 65(11) of the Drugs Rules, 1945, which deals with the procedure of supplying schedule 'H' drugs more than once on old prescriptions, may be deleted. After the draft amendment is finalised, question of repetition of old prescription does not arise.
Item I(c) . .	We agree.
Item II(a) . .	We agree.
Item II(b) . .	We agree.
Item III . .	We agree.
Item IV . .	We agree.
Item V . . .	We agree.
Item VI . . .	We agree and further suggest that these drugs may be labelled like schedule 'H' drugs. For this purpose, after Rule 97 (1) (c), the following sub-rule may be inserted:— Rule 97(1)(d)—"if it contains a substance specified in schedule 'L' it should be labelled with the words 'Schedule L Drugs'."
Warning . .	To be sold by retail on prescription of Registered Medical Practitioners only.

COPY OF LETTER NO. DO-1, DATED 15-3-56 FROM M/S VOLTAS LIMITED, BOMBAY TO THE DRUGS CONTROLLER, INDIA, NEW DELHI.

With reference to the announcement in the Gazette of India, 31st December 1955, Ministry of Health, New Delhi-2, 15th December 1955, S.R.O.-3774, giving details of a further draft amendment to Schedule E of the Drug Rules, 1945 which will be taken into consideration on or after 1st April 1956, our Principals, Messrs. F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland, propose placing on the market in India a cough syrup styled "ROMILLAR" which has as its active ingredient the substance Dextromethorphan in a concentration of 0·2% Dextromethorphan base equivalent to 0·3% of Dextromethorphan Hydrobromide and, as such, they request that Dextromethorphan; its salts, may be deleted from the proposed draft. Should this step not be possible from the Government's view point, we would request you to consider amending the present wording in the draft Schedule so as to exclude those substances containing less than 1·5% of Dextromethorphan.

In this regard the United Kingdom has amended its Poison Law in respect of Dextromethorphan and the First Schedule is amended as follows:—

'(c) for the item "Dextromethorphan; its salts" substitute the item "Dextromethorphan; its salts, except substances containing less than 1·5 per cent of Dextromethorphan".'

For your ready reference, we enclose a photo copy of page 6 of the Pharmaceutical Journal dated 7th January 1956 on the subject of New Poisons Regulations, Amendments to the List and Rules, which came into operation on 20th January 1956, and would draw your attention to the bottom left hand corner, last item, which we have quoted above.

Should it not be possible for you to exclude Dextromethorphan and its salts from the provisions of Schedule E, we should be most grateful, on the basis of the above information, if you would kindly exclude from the provisions of Schedule E substances containing less than 1·5% of Dextromethorphan.

COPY OF LETTER NO. 339, DATED 29-3-1956 FROM THE PHARMACEUTICAL & ALLIED MANUFACTURERS' & DISTRIBUTORS' ASSOCIATION, LIMITED, BOMBAY-1 TO THE DRUGS CONTROLLER, INDIA, DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI.

We refer to the draft amendments to the Drugs Rules of the 15th of December 1955 and published in the Gazette of India, December 31st 1955. Several of our member firms have suggested alterations to the proposed amendment which we give in the following :—

Pituitary gland, the active principles of, are according to the new amendment included into Schedule E, into Schedule G and into Schedule H. In this case labelling requirements of both Schedule G and Schedule H would apply. It is, therefore, proposed that *pituitary gland, the active principles of,* should be deleted from the proposed Schedule H and be only retained in Schedules E and G.

Suprarenal gland, the active principles of; their salts.—With the new amendment, Adrenaline will come within the purview of Schedule H. Our member firms draw attention to the fact that Procaine Adrenaline combinations have been introduced in dental practice for many years as local anaesthetics. As Procaine Adrenaline will now fall under Schedule H, sale of this combination will only be possible on the presentation of a prescription by a registered medical practitioner. There are registered dentists in this country but a very large number of dentists are not registered medical practitioners. Thus it will not be possible to those un-registered dentists to prescribe this drug. If the proposed amendment would be implemented in its present form it would create considerable hardship for both the dental profession and for the public, particularly in rural areas. It is, therefore, suggested to omit *Suprarenal gland, the active principles of; their salts* from Schedule H.

Another of our member firms draws attention to the fact that preparations of corticosterone in the form of eye drops and eye ointments would as proposed in Schedule H preparations fall under prescription. It is suggested that these preparations are meant only for local application, hence the rate of absorption would be too small for systemic side-effects to occur.

Mepacrine Hydrochloride.—One of our members proposes that Mepacrine Hydrochloride which has been included into Schedule E in the draft amendment should be exempted again. Mepacrine is not designated as a poison in other countries and would, therefore, require special labelling in the Indian market. The member firm further comments that the inclusion of *Pethidine hydrochloride* into Schedule H would mean special labelling for the Indian market. Pethidine as a dangerous drug is so closely controlled that there is hardly any likelihood of the drug being sold to the general public except on prescription.

Finally attention is drawn to the newly created Schedule L in your draft amendment. So far no special labelling provisions seem to be proposed for this Schedule as the items falling under it do not come within the provision of Schedule E. It is proposed that an amendment be made to Rule 97 extending the same labelling provisions to Schedule L preparations as those at present applying to Schedule H drugs.

Altogether it may clarify matters if to every item mentioned in the different schedules letters are added indicating in which other schedules the drug is also included. It will materially help to avoid mistakes in labelling.

Hoping that our suggestions will have your consideration, we are,

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COPY OF LETTER NO. 367, DATED 1-5-1956, FROM THE PHARMACEUTICAL & ALLIED MANUFACTURERS' & DISTRIBUTORS' ASSOCIATION, LTD., BOMBAY TO THE DRUGS CONTROLLER, INDIA, DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI.

We beg to refer to our letter No. 339, dated 29th March, 1956, offering our suggestions in regard to the proposed amendments to the Drugs Rules, 1945.

At the moment preparations of Cortisone can only be made on the prescription of a registered medical practitioner which has been counter-signed by the Civil Surgeon. It is our feeling that the object of including Cortisone preparations under Schedule H was made with the object of dispensing with the necessity of a counter signature by the Civil Surgeon. We therefore suggest that the proposed amendment to the Drugs Rules under this heading should be amended to read "Cortisone/preparations of and their derivatives excluding those for external use".

COPY OF MEMO NO. MISC. 1/56/485, DATED 1ST MAY, 1956 FROM THE ASSISTANT DRUGS CONTROLLER, INDIA TO THE DRUGS CONTROLLER, INDIA, DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI.

SUBJECT :—*Draft amendment to Drugs Rules.*

REFERENCE :—*Notification in the Gazette of India, Part II—Sec. 3 of the Ministry of Health of* 15-12-1955.

(S.R.O. 3774)

It is observed that the words "or Propylenediamine" have been omitted to be included at the end of the entry "Antihistamine-substances the following etc..... of ethylene diamine" under the proposed draft of *Schedule H,* though they appear in the draft Schedule E at the corresponding entry as well as in the U.K. Poisons List. An amending notification may therefore be caused to be issued in this regard, if considered necessary or this may please be corrected at the time of issuing the final amendment.

No. F. 1-4/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 31st May, 1956.

FROM

Shri T. V. Anantanarayanan, M. A.,
Under Secretary to the Government of India.

To

The Secretary,
All India Chemists & Druggists Federation,
10, Bongfield Lane,
Calcutta-1.

SUBJECT :—*Drugs Rules,* 1945—*Amendment of rules* 65 *and* 97—*Revision of Schedules E, G and H—Insertion of a new Schedule L.*

SIR,

With reference to your letter No. 16/415, dated the 15th May, 1956, I am directed to say that the observations made therein in regard to the proposed amendments to the Drugs Rules, 1945 will be duly considered before the finalisation of the said amendments.

Yours faithfully,
(Sd.) T. V. ANANTANARAYANAN,
Under Secretary.

No. F. 1-4/56-D.

Copy, with a copy of the letter under reply, forwarded to the Secretary, Drugs Technical Advisory Board, C/o Directorate General of Health Services, New Delhi with reference to his u. o. No. 8-36/56-D, dated the 14th May, 1956. It is requested that the letter from the All India Chemists & Druggists Federation may kindly be placed before the next meeting of the Board and the views of the Board thereon communicated to this Ministry before the proposed amendments are finalised.

By Order,
(Sd.) T. V. ANANTANARAYANAN,
Under Secretary.

COPY OF LETTER NO. 170/56 DATED THE 13TH APRIL, 1956, FROM DR. B. P. MOORARKA, PRVL. SECRETARY, M. P. PRVL. BRANCH, ALL INDIA MEDICAL LICENTIATES' ASSOCIATION, BILASPUR, M. P. TO SHRI P. N. ANAND, UNDER SECRETARY TO THE GOVERNMENT OF INDIA, NEW DELHI.

SUBJECT :—*Drugs Rules,* 1945—*Amendment of.*

With reference to your letter No. F. 1-9/56-D, dated 10-4-56 I have pleasure to note that I am in receipt of your letter and have to note as follows :—

As the Government is unable to change the rules so as to enable the Schedule 'E' drugs to be sold under the prescription of regd. medical practitioner, it is requested that item No. 3, sub-item No. 30—*Ergot* and item No. 16—*Arsenicals esp. injectibles arsenicals* under schedule 'H' so as to make them saleable under the prescription of a regd. practitioner. The quackery depends on these products mainly, among other products and it is essential that these two products should be brought under schedule 'H' and it is sincerely hoped that due consideration will be given to our suggestion. As there is no check, the people in villages are using Ergot preparations indescriminately and so is the case with Arsenical injections and it is requested that these two items be removed from schedule 'E' and added to schedule 'H'. As regards the fixing of definition of 'registered medical practitioner' it is submitted that only those practitioners who have had training in allopathic medicines should only be allowed to prescribe. Persons who have undergone mixed training as for example Benares University A.M.S. may be allowed but certainly, all ayurvedic practitioners, Unani and Homoeopathic practitioners should not be included in this category. It may be noted that in Homoeopathic science injection therapy is not recommended even and as such only those who have training in these drugs should be included in the definition of registered medical practitioner.

It is sincerely hoped that above few facts will be given utmost consideration and an early reply is expected.

COPY OF LETTER NO. 16/415 DATED THE 15TH MAY, 1956, FROM THE ALL INDIA CHEMISTS & DRUGGISTS FEDERATION TO THE SECRETARY, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drug Rules,* 1945.

REFERENCE :—*Notification No. S. R. O.* 3774, *dated* 15*th December,* 1955, *of your Ministry issued in the Gazette of India, dated the* 31*st December,* 1955.

In continuation of our letter No. 15/363, dated the 9th May, 1956, addressed to the Drugs Controller (India), requesting an extension of time for submission of objections on the above proposed amendment I beg hereby to submit the following for your consideration. I hope, you will kindly consider our objections in all seriousness.

The Federation is of opinion that the proposal requiring chemists to maintain records of sale of all drugs of Schedules H & L and to preserve prescription of Doctors is something unpracticable and unnecessary. If this proposal is given effect to it will simply create complication, trouble and delay for the chemists and the public in the matter of service of prescriptions for the reasons given below :—

1. The Chemists are already overburdened with maintenance of various kinds of registers, records, etc., under the Drugs Act and other Government Acts and when records of sales and purchases are already kept by the chemists it is mere duplication of work to maintain registers again.

2. Prescriptions are generally written out by Doctors without giving their addresses and registration numbers and names are often not signed legibly. The addresses of patients are very seldom written by Doctors. If service of prescriptions are refused to patients for any of the above defects it will create a chaos and the people will suffer.

Besides it is not possible for a chemist to know the signature of all doctors and as such a chemist should not be made responsible if any unauthorised person signs the prescriptions and takes delivery of goods.

This Federation wonders at the proposal that a chemist should retain the prescriptions of a doctor, containing Schedule L drugs and preserve it for six months.

It is undoubtedly known to you that no Hospital or Charitable Dispensary will attend an old patient unless the prescriptions of the previous visits are brought in and these previous prescriptions are always consulted by all physicians before they examine and prescribe drugs for a patient on a subsequent date.

As such no patient will agree to leave his prescription to a chemist from whom he purchases a drug. Moreover it may not be convenient or possible for a patient to purchase all drugs of Schedule L from one chemists shop either in consideration of price or availability of stocks.

Considering all these points, I hope you will be good enough to drop the proposed amendment and save the chemists as well as the public from unnecessary trouble and harassment. This is the considered view of this Federation and I hope the Government will surely give it due consideration.

COPY OF LETTER NO. F. 1-17/56-D, DATED 31-5-1956 FROM THE UNDER SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI TO THE SECRETARY TO THE GOVERNMENT OF WEST BENGAL, MEDICAL & PUBLIC HEALTH DEPTT., CALCUTTA.

SUBJECT :—*Drugs Rules, 1945—Proposal for amendment—for restricting the retail sale of Schedules C and E drugs only on the prescriptions of medical practitioners.*

With reference to your letter No. Medl/2923/6P-30/56, dated the 17th April, 1956, I am directed to say that the question of restricting the sale of Schedule E drugs, as in the case of Schedule H drugs, only on the prescriptions of registered medical practitioners, was examined by the Poisons Sub-committee of the Drugs Technical Advisory Board. While observing that such an arrangement would be ideal, the Sub-committee, taking into consideration the hardships that would be caused to consumers, however, recommended that till such time as medical and ancillary personnel were adequate enough to run the medical services, it would not be advisable to give effect to the proposal. The recommendation of the Sub-Committee which was endorsed by the Drugs Technical Advisory Board, was accepted by the Government of India and it is considered that there is no need to make any change in this regard at present.

2. As regards the question of restricting the sale of Schedule C drugs only on the prescriptions of registered medical practitioners, it may be stated that the matter has been referred to the Drugs Technical Advisory Board, and will be further considered after the views of the Board have been received by the Government of India.

No. F. 1-17/56-D.

Copy, with a copy of the letter under reply, forwarded to the Secretary, Drugs Technical Advisory Board, C/o Directorate General of Health Services, New Delhi with reference to his u.o. No. 8-36/56-D, dated the 22nd May, 1956. It is requested that the question of restricting the retail sale of Schedule C drugs only on the prescription of medical practitioners may kindly be placed before the Board at its next meeting and the views of the Board communicated to this Ministry in due course.

COPY OF LETTER NO. MEDL./2923/6P-30/56, DATED THE 17TH APRIL, 1956, FROM SHRI S. C. ROY, ASSISTANT SECRETARY TO THE GOVERNMENT OF WEST BENGAL TO THE SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH.

SUBJECT :—*Stoppage of quackery and sale of medicines without prescriptions.*

I am directed to say that for some time past this Government have been noticing the baneful effects of quack practice in the medical profession and the sale of medicines without prescriptions, which accompanies such a practice and therefore, considering ways and means to see how far such undesirable practices can legitimately be restricted. While prohibition of quack practice is a desideratum in our existing regulation, this Government feel that it is not immediately feasible to rectify and consider that the only effective way is to gradually modify Drugs Rules in such a way that essential drugs will more and more be required to be sold in retail on the prescriptions of registered medical practitioners only. For this purpose, this Government suggest that provisions be made in the Drugs Rules, 1945 restricting sale in retail on prescriptions of medical practitioners only, of the following two classes of drugs :—

(a) Schedule 'C' drugs (Injections); and

(b) Schedule 'E' drugs (Poisons);

misuse of drugs will appreciably decrease if the above suggestion is stabilised into the rules on the subject.

2. I am to request that, in the circumstances, the Government of India may be moved for considering the suggestion of this Government as contained in the preceding paragraph and to take necessary action in this regard.

COPY OF LETTER NO. A/7/56 DATED THE 13TH MARCH, 1956, FROM BAREILLY CHEMISTS ASSOCIATION, BAREILLY, TO THE HON. MINISTER OF HEALTH, GOVERNMENT OF INDIA UNION, NEW DELHI.

Please refer to the Government Notification dated the 15th December, 1955 *re* : the draft of further amendments to the Drugs Rules, 1945 proposed to be made under Section 33 of the Drugs Act, 1940 (XXIII of 1940).

We have the honour to lay down the following objection to the same.

In Rule 65 :—

(b) *Re* : the new condition (9) :

The second sentence in the new condition (9) *viz.* "The Prescription shall be retained by the retail dealer dispensing the prescription for a period of six months." may please be deleted as it will not be practicable.

Hoping to receive due consideration.

We remain.

COPY OF LETTER NO. AGV/1210, DATED 14-3-1956 FROM M/S. MAY & BAKER (INDIA) LTD., BOMBAY TO THE DRUGS CONTROLLER, INDIA, NEW DELHI.

List of Poisons—Schedules E & H

Please refer to S. R. O. 3774 (Gazette of India, dated 31st December 1955), reproducing the drafts of new Schedules E and H. The following has been included in both these schedules:—

"Antihistamine substances, the following, their salts; their molecular compounds; ..... Promethazine; ....."

The new Schedules E and H, if introduced as they are, would also cover a product which we offer for the prevention and treatment of travel sickness. The product referred to by us is promethazine 8-chlorotheophyllinate which we sell under the trade name AVOMINE.

Motion sickness is largely a personal problem, occurring in the great majority of cases, in otherwise healthy individuals and, except in special cases, should not necessitate the expenditure of time and money involved in obtaining a doctor's prescription. Since its introduction, hundreds of thousands of tablets of AVOMINE have been sold throughout the world without any evidence of serious toxicity. Side effects, either as described in the literature [Harper, J. (1951) Lancet, *i*, 114], or reported to us by users or their physicians, have been very infrequent and of no practical significance and no instances of either intentional or accidental overdosage with AVOMINE have come to our notice.

AVOMINE is already specifically exempted from poisons legislation in a number of territories operated by May & Baker Ltd., Dagenham, such as New Zealand, Tasmania, certain States of Australia and Nigeria.

In the circumstances, we would like to suggest that consideration be given to excluding the 8-chlorotheophylline salt of promethazine from the proposed new schedules so that it may be released for the personal use of travellers in the same way as various hyoscine and other preparations.

COPY OF THE LETTER NO. AGV/1277 DATED THE 30TH MAY, 1956, FROM M/S. MAY & BAKER (INDIA) LTD., KARIMJEE HOUSE, SIR PHEROZSHAH MEHTA ROAD, BOMBAY, TO THE DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI.

List of Poisons—Schedules E & H

We regret the delay in replying to your communication No. 8-36/56-D of the 12th April, 1956.

As you probably know, antihistamine drugs as a class were brought within the scope of the Poisons Regulations in the United Kingdom some time ago, and Avomine, which is a derivative of the antihistamine Promethazine is, at present, covered by the regulations. An application has,

however, been made to the Secretary of the Poisons Board for the specific exemption on the grounds of prolonged and widespread clinical use as an anti-emetic and the absence of reports of toxicity. This application is still outstanding, but we are hopeful that it will be favourably considered because we believe that the Poisons Board is prepared to add and delete drugs from the Poisons List if they consider such action justified on the basis of evidence provided by interested parties.

We hope that you will consider adopting a similar policy. We have already provided information on the experimental and clinical use of Avomine, but if you wish to undertake an investigation yourself, we shall be very glad to supply, free of charge, quantities of Avomine itself for clinical use, or, if your prefer it, of Promethazine 8-chlorotheophyllinate for experimental use.

COPY OF THE LETTER NO. ATF/TC DATED THE 23RD MARCH 1956, FROM M/S. PARKE DAVIS & COMPANY, LIMITED, CANADA BUILDING, HORNBY ROAD, BOMBAY-1, TO THE DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES, GOVERNMENT OF INDIA, NEW DELHI.

Draft Amendments to Schedules E & H.

We should ask you to refer to the Draft Amendments to the Drugs Rules as published under S. R. O. 3774 in the Gazette of India dated December 31st 1955.

This letter is written with particular reference to the proposed addition of "Antihistamine substances, the following, their salts;....." to both Schedules E and H.

We had sent a copy of the draft Amendments to our Head Office and they have commented that if it is the intention to include all antihistamine substances within these two Schedules, the particular wording used for the proposed entry is not sufficiently all-inclusive.

It is pointed out that if a new antihistamine is introduced which is not covered by the description of the substances included in the proposed amendment (or it may be that the present suggested amendment does not cover all antihistamines which may already be on the market) such antihistamine preparations would enjoy a temporary advantage until the Government could take further appropriate action.

Would it not be advisable therefore to devise some other way of accomplishing the intended purpose which would not have this defect?

May we suggest that the above be given consideration when the draft amendment in question comes up for review?

COPY OF MEMO. NO. 9-A/140 DATED THE 10TH FEBRUARY, 1956 FROM SHRI S. H. MERCHANT, ASSISTANT DRUGS CONTROLLER (INDIA), MADRAS TO THE DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI-2 TOGETHER WITH THE COPY OF ANNEXURE.

SUBJECT :—*Amendments of Schedules E and H.*

Reference Government of India, Ministry of Health, Notification No. F-1-48/55-D, dated the 15th December, 1955, published as S.R.O. No. 3774, in Gazette of India, Part II-Sec. 3 dated the 31st December, 1955.

In connection with the above, this office desires consideration of certain additions and amendments to the list of Schedule E and H drugs published as a draft amendment, in the light of 'New Poisons Regulation and amendment to the List and Rules' in U.K., published on page 6 of the Pharmaceutical Journal dated January 7, 1956. Certain significant differences noted by this office are set out in the annexure for your information.

ANNEXURE

Additions :

I. Schedule E—

(a) After the item 'Dextrophan; its salts' (item 38) insertion of the item "Diacetyl-N-allylnormorphine; its salts";

(b) After the item 'Di-nitrocresols etc.' (item 47) insertion of the item "Dipipanone; its salts";

(c) After the item 'Mepacrine Hydrochloride' (item 73) insertion of the item "6-Mercaptopurine; its salts";

II. Schedule H—

(a) After the item beginning with the word 'Barbituric acid' insertion of the item "Beta-aminoprophylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts"; (transferred from seventh to fourth Schedule).

(b) After the item beginning with the word 'Gallamine' insertion of the item "6-Mercaptopurine"; (It is not clear why 'salts of this item' which have been included in the first schedule are omitted in the fourth schedule).

Amendments :

I. Schedule E—

(a) in the list of alkaloids, for the item (15) beginning with the word "Colchicine", substitution of the item "*Colchicum, alkaloids of,* except substances containing less than 0·5 per cent of the alkoloids of colchicum calculated as colchicine";

(b) for the item 'dextromethorphan; its salts' (item 38) substitution of the item "Dextromethorphan; its salts, *except substances containing less than* 1·5 *per cent* of dextromethorphan";

(c) for the items "6-methyl-6-desoxymorphine and its salts' (item 80) substitution of the item "Methyldesomorphine; its salts";

(d) for the item 'Tri-2(Chloroethyl) amine, its salts' (item 130) substitution of the item "Tri-(2-chloroethyl) amine; its salts; (It is felt that the figure '2' if shown within bracket as to qualify 'Choloroethyl would make significant difference).

II. Schedule H—

(a) for the item 'Diethylallylamine compounds; its salts' substitution of the item—"Dithienylallylamine compounds; their salts, except diethylthiambutene, dimethylthiambutene and ethylmethylthiambutene"; (If considered essential the exemption given to three salts may be omitted).

(b) for the item 'Tri-2-Chloroethyl) amine; its salts' substitution of the item "Tri-(2-chloroethyl) amine, its salts".

The item cortisone will have to be specifically given in Schedule L to the Drugs Rules *vide* Ministry of Health letter No. F. 20-5/56-D dated the 9th March, 1956.

COPY OF LETTER NO. D-01 DATED THE 12TH DECEMBER, 1956, FROM M/S VOLTAS LIMITED, PHARMACEUTICAL DEPARTMENT, BOMBAY-1, TO THE DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES.

Exemption for Dextromethorphan

Your letter No. 8-36/56-D dated the 13th September informed us that the question of exemption of substances containing less than 1·5% of Dextromethorphan from the proposed revised Schedule E is still under review. This was in reply to our letters requesting that we may be permitted to import Romilar Syrup on our regular Import Licence, which has as its active ingredient the substance Dextromethorphan in a concentration of 0·2% Dextromethorphan base equivalent to 0·3% of Dextromethorphan Hydrobromide.

Our principals, Messrs. F. Hoffmann-La Roche & Co. Ltd., Basle, Switzerland, now inform us that they are not interested at present in the introduction of Romilar Syrup in the Indian market, but would like to introduce Romilar tablets instead. Romilar sugar-coated tablets contain 15 mg of Dextromethorphan in the form of hydrobromide. One tablet weighs 100 mg so that the active ingredient amounts to 15 per cent.

We should be most grateful to your now giving consideration to the deletion of Dextromethorphan, its salts, from the proposed draft amendment so that the active ingredient amounts to 15%.

Thanking you in anticipation, we remain.

Control over the *sale* of Amphetamines can be exercised under the provisions of the Drugs Rules, 1945, Amphetamines are now included in Schedule E of the Drugs Rules, 1945 whereby these drugs can be dispensed only by a qualified person (registered pharmacist). This provision, is not sufficient to control its sale. Amphetamines may, therefore, be included in Schedule H of the Drugs Rules, 1945 whereby the drug could be made to be sold only against prescriptions from registered medical practitioners. This will make the controls stringent so far as sale is concerned.

As regards control over the manufacture of the drug it will be necessary to declare the drug as a "dangerous drug" under the Dangerous Drugs Act, so that its manufacture can be controlled under the Dangerous Drugs Rules. The Ministry of Finance (Revenue Division) may be asked to examine this question.

This Directorate may please be informed of Government's decision so that the drug may be included in Schedule H.

Extract from No. 20-19/56/6-D, dated the 19th October, 1956.

(*To be published in Part II, Section 3 of the Gazette of India.*)

No. F. 1-48/55-D.

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, dated the 15th December, 1955.

NOTIFICATION

The following draft of further amendments to the Drugs Rules, 1945, which it is proposed to make in exercise of the powers conferred by section 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said section for the information of all persons likely to be affected thereby and notice is hereby given that the draft will be taken into consideration on or after the 1st April 1956.

2. Any objection or suggestion which may be received from any person in respect of the said draft before the date specified will be considered by the Central Government.

Draft Amendments

In the said Rules—

I. In Rule 65—

(a) the proviso to condition (2) shall be omitted :

(b) for condition (9), the following condition shall be substituted, namely :—

"(9) Substances specified in Schedules H and L and preparations containing such substances shall not be sold by retail except on and in accordance with a prescription of a registered medical practitioner. The prescription shall be retained by the dealer dispensing the Prescription for a period of six months :

Provided that no prescription shall be required for sale or supply to a registered medical practitioner, hospital, infirmary or an institution approved by an order of a licensing authority".

(c) After condition (15) the following condition shall be added, namely :

"(16) The purchase for resale of a drug specified in Schedule E or preparation containing any such drug shall be recorded at the time of purchase in a register maintained for the purpose in which the following particulars shall be entered namely :—

(a) serial number of the entry.

(b) the date of purchase.

(c) the name and address of the supplier.

(d) the name of the drug or preparation and the quantity thereof".

II. In Rule 97—

(a) in sub-rule (2), the word 'liquid' occurring after the words "liquid anti-septic or other" shall be omitted;

(b) after sub-rule (4), the following sub-rule shall be inserted, namely :—

"(5) The container of medicine ready for treatment of human ailments shall, if the medicine contains industrial methylated spirit, indicate this fact on the label and be labelled with the words "For external use only".

II. For Schedule E, the following Schedule shall be substituted, namely :

"SCHEDULE E

(*See* Rules 65 and 97)

List of Poisons

1. Acetanilide; Alkyl acetanilides.

2. Aconite, roots of.

3. Alkaloids, the following; their salts, simple or complex :—

(1) "Acetyldihydrocodeine.

(2) Acetyldihydrocodeine—one; its esters.

(3) Aconite, alkaloids of, except substances containing less than 0·02 per cent of the alkaloids of aconite.

(4) Apomorphine, except substances containing less than 0·2 per cent of apomorphine.

(5) Atropine, except substances containing less than 0·15 per cent of atropine.

(6) Berberine and its preparations except substances containing less than 0·02 per cent of berberine.

(7) Belladonna, alkaloids of, except substances containing less than 0·15 per cent of the alkaloids of belladonna calculated as a hyoscyamine.

(8) *Benzoylmorphine.

(9) *Benzylmorphine.

(10) Brucine, except substances containing less than 0·2 per cent of brucine.

(11) Calabar bean, alkaloids of.

(12) *Coca, alkaloids of, except substances containing less than 0·1 per cent of the alkaloids of coca.

(13) *Cocaine, except substances containing less than 0·1 per cent of cocaine.

(14) *Codeine, except substances containing less than 1·5 per cent of codeine.

(15) Colchicine, except substances containing less than 0·5 per cent of colchicine.

(16) Coniine, except substances containing less than 0·1 per cent of coniine.

(17) Cotarnine, except substances containing less than 0·2 per cent of cotarnine.

(18) Curare, alkaloids of; curare bases.

(19) *Diacetylmorphine (hydrochloride).

(20) *Dihydrocodeine.

(21) *Dihydro-codeinone; its esters.

(22) *Dihydrodesoxymorphine; its salts.

(23) *Dihydrohydroxycodeinone; its esters.

(24) *Dihydromorphine; its esters.

(25) *Dihydromorphinone; its esters.

(26) *Diphemylmorpholinoheptanone; its salts.

(27) *Ecgonine; except substances containing less than 0·1 per cent of ecgonine; its esters.

(28) Emetine, except substances containing less than one per cent of emetine.

(29) Ephedra, alkaloids of, except substances containing less than one per cent of the alkaloids of ephedra.

(30) Ergot, alkaloids of.

(31) *Ethylmorphine, except substances containing less than 0·2 per cent of ethylmorphine.

(32) Gelsemium, alkaloids of, except substances containing less than 0·1 per cent of the alkaloids of gelsemium.

(33) Homatropine except substances containing less than 0·15 per cent of homatropine.

(34) Hyoscine, except substances containing less than 0·15 per cent of hyoscine.

(35) Hyoscyamine except substances containing less than 0·15 per cent of hyoscyamine.

(36) Jaborandi, alkaloids of, except substances containing less than 0·5 per cent of the alkaliods of jaborandi.

(37) Lobelia, alkaloids of, except substances containing less than 1·5 per cent of the alkaloids of lobelia.

(38) *Morphine, except substances containing less than 0·2 per cent of morphine calculated as anhydrous morphine.

(39) Nicotine.

(40) Papaverine, except substances containing less than one per cent of papaverine.

(41) Pomegranate, alkaloids of, except substances containing less than 0·5 per cent of the alkaloids of pomegranate.

(42) Quebracho, alkaloids of.

(43) Sabadilla, alkaloids of, except substances containing less than one per cent of the alkaloids of sabadilla.

(44) Solanaceous alkaloids, not otherwise included in the list, except substances containing less than 0·15 per cent of solanaceous alkaloids calculated as hyoscyamine.

(45) Stavesacre, alkaloids of, except ointments, lotions for external use and substances containing less than 0·2 per cent of the alkaloids.

(46) Strychnine, except substances containing less than 0·2 per cent of strychnine.

(47) *Thebaine, except substances containing less than one per cent of thebaine.

(48) Tropacocaine (Benzoyl Pseudo Tropine); its salts.

(49) Veratrum, alkaloids of, except substances containing less than one per cent of the alkaloids of veratrum.

(50) Yohimba, alkaloids of.

4. Allylisopropylacetylurea.

5. *Alpha-acetyl-methadol and its salts.

6. *Alpha-methadol and its salts.

7. Alpha-meprodine; its salts.

8. Alpha-prodine; its salts.

9. Amidopyrine; its salts; amidopyrine sulphonates, their salts.

10. Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenyl propionic acid, cinnamic acid or the derivatives of these acids, except in substances containing less than ten per cent of esterified aminoalcohols and except procaine when in a preparation containing Penicillin.

11. Aminopterin.

12. Ammonia, except substances containing less than five per cent, weight in weight, of ammonia

13. Amyl nitrite.

14. Antihistaminc substances, the following, their salts, their molecular compounds (excepting substances which are intended for external use). Antazoline; Bromazine; Chorcyclizine; Diphen hydramine; 3-Di-n-butyl-aminomethyl-4:5:6—trihydroxyphthalide; Phenindamine; Promethazine; substances being tetra substituted N—derivatives of ethylendiamine or propylenediamine.

15. Antimony, chlorides of; oxides of antimony; sulphides of antimony; antimonates; antimonites; organic compounds of antimony; antimonial poisons except substances containing less than the equivalent of one per cent of antimony trioxide.

16. Arsenic, halides of; oxides of arsenic; sulphides of arsenic; arsenates; arsinites; aceto-arsenites; this arsenates; organic compounds of arsenic; arsenical poisons; except substances, containing less than the equivalent of 0·01 per cent of arsenic trioxide.

17. Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid; its derivatives; their salts with any other substance.

18. Barium, salts of other than barium sulphate.

19. *Bemideon.

20. *Beta-acetyl methadol; its salts.

21. Beta-amino propyl benzene; its salts; its N-alkyl derivatives, their salts; beta-amino isopropyl benzene, its salts; its N-alkyl derivatives, their salts except when present in inhalers provided that the poison is absorbed in inert solid material within the inhalers.

22. Betameprodine; its salts.

23. Betaprodine; its salts.

24. Butylchloral hydrates.

25. *Cannabis (the dried flowering or fruiting tops and leaves of cannabis sativa Linn); the resin of cannabis, extracts of cannabis; tinctures of cannabis; cannabin tannate.

26. Cantharidates, except substances containing less than the equivalent of 0·01 per cent of cantharidin.

27. Cantharidin, except substances containing less than 0·01 per cent of cantharidin.

28. Carbachol.

29. Chloral formemide.

30. Chloral hydrate.

31. Chloroform except substances containing less than ten per cent of chloroform.

32. Chlor-promazine; it salts.

33. Chrysophanic acid.

34. Creosote from wood, except substances containing less than 50% of creosote.

35. Croton, oil and seeds of.

36. Datura, seeds and leaves of; preparations of datura, except substances containing less than 0·15 per cent of the alkaloids of datura calculated as hyoscyamine.

37. Dextromethorpha; its salts.

38. Dextrorphan; its salts.

39. Diaminodiphenylsulphone; its salts and derivatives, excluding their preparations and dressings for external use.

40. Digitalis, glycosides of, other active principles of digitalis except substances containing less than one unit of activity (as defined in the British Pharmacopoiea) in two grammes of the substance.

41. dimethylamino-4, 4-diphenyl-3-acetoxyheptane.

42. *6-dimethylamino-4, 4-diphenyl-3-heptanol.

43. *B-3-dimethyl-4-pheny-4-propionoxy piperidine and its salts.

44. Di-isopropyl fluorophosphate.

45. 1:4-dimethane sulphonoxybutane; its salts.

46. *3-dimethylamino-1; 1-di(2 thienyl-1-butane and its salts.

47. Di-nitrocresols; dinitronaphthols; dintrophenols; dinitrothymols.

48. Dinosam; its compounds with a metal or a base.

49. Dinoseb; its compounds with a metal or a base.

50. Disulfiram.

51. Dithienylallylamine componds; their salts.

52. Elaterin.

53. Ergot (the sclerotia of any species of Claviceps); extracts of ergot; tinctures of ergot.

54. Erythrityl tetranitrate.

55. *3-ethylmethyl amine-1, 1-di(2 thienyl)-1-butane and its salts.

56. Formaldehyde, except substances containing less than five per cent formaldehyde.

57. Gallamine; its salts; its quarternary compounds.

58. Glyceryl trinitrate (nitroglycerine).

59. Guanidines, the following: polymethylene diguanidines, dipara-anisylphentyl guanidine.

60. Hydantoin, its salts; its derivatives and their salts.

61. Hydrochloric acid, except substances containing less than nine per cent, weight in weight, of hydrochloric acid.

62. Hydrocyanic acid, except substances containing less than 0·1 per cent of hydrocyanic acid (HCN): cyanides; except substances containing less than the equivalent of 0·1 per cent, weight in weight, of hydrocyanic acid (HCN); double cyanides of mercury and zinc.

63. Hydrofluoric acid; potassium flouride; sodium fluoride; sodium silicofluoride.

64. *3-Hydroxy-N-Methyl morphinan and its salts.

65. Hydroxypethidine; its salts.

66. Insulin.

67. *Isomethadone (isoamidone); its salts.

68. *Ketobemidone; its salts.

69. Lead acetates; compounds of lead with acids from fixed oils.

70. Levomethorphan; its salts.

71. Levorthan; its salts.

72. Mannityl Hexanitrate.

73. Mepacrine Hydrochloride.

74. Mercuric chloride or mercuric ammonium chlorides; except substances containing less than one per cent of mercuric chloride; mercuric iodide except substances containing less than two per cent of mercuric iodide; nitrates of mercury, except substances containing less than the equivalent of three per cent, weight in weight, or mercury (Hg); potassiomercuric iodides, except substances containing less than the equivalent of one per cent of mercuric iodide; organic compounds of mercury, except substances containing less than the equivalent of 0·2 per cent, weight in weight, of mercury (Hg); mercuric oxycyanides; oxides of mercury, mercuric thiocyanate Phenyl mercuric salts except preparations containing less than 0·01% of phenyl mercuric salts as preservative.

75. Methadol, its salts.

76. *Methadone (amidone), its salts.

77. Methadyl acetate; its salts.

78. Methanol (Methyl alcohol).

79. *B-1-methyl-3-ethyl-4 phenyl-4-propionoxy piperidine and its salts.

80. *6-methyl-6-desoxymorphine and its salts.

81. *3-methoxy-N-methylmorphinan and its salts.

82. *Metopon; its salts (Methyldihydromorphinon I).

83. *Morpholinyl ethylmorphine; its salts, except substances containing less than 1·5 per cent of morpholinyl ethylmorphine.

84. Mustine.

85. Nalorphine; its salts.

86. *Nisentil. (NU-1196).

87. Nitric acid, except substances containing less than nine per cent weight in weight, of nitric acid.

88. Nitrobenzene

89. Nitrophenols, ortho, meta or para.

90. Nux Vomica, seeds of; preparations of nux vomica, except substances containing less than 0·2 per cent of the alkaloids of nux vomica.

91. Oil of Savin.

92. Opium, except substances containing less than 0·2 per cent of morphine calculated as anhydrous morphine.

93. Orthocaine; its salts.

94. Ouabain.

95. Oxalic acid; matallic oxalates other than potassium quadroxalate.

96. Oxazolidine; its derivatives.

97. Oxycinchoninic acid, derivatives of; their salts; their esters.

98. Para-amino-benzene-sulphonamide; its salts, derivatives of para-amino-benzene-sulphonamide having any of the hydrogen atoms of the para-amino group or the sulphamidé group substituted by another radical; their salts.

99. Paramethadione.

100. Pentaquine; its salts.

101. *Pethedine (Hydrochloride).

102. *Phenadoxone; its salts.

103. Phenetidylphenacetin.

104. Phenols, that is, any member of the series of phenols of which the first member is phenol and of which the molecular composition varies from member to member by one atom of carbon and two atoms of hydrogen and halogen derivatives of phenols except medicines with less than 1% of phenol, nasal sprays, mouth washes, pastiles, lozenges, capsules, pessaries, ointments, or suppositories, containing less than 2·5% phenol.

105. Phenylacetylurea.

106. Phenylbutazone; its salts.

107. Phenylcinchoninic acid, salicyl-cinchoninic acid; their salts; their esters.

108. Phenylene diamines; toluene diamines; other alkylated benzene diamines, their salts.

109. Phenylethylhydantoin; its salts; its acyl derivatives; their salts.

100. Pentaquine; its salts.

Diethyl thiophosphate of ethyl-mercapto-ethanol, dimefox, ethyl-para nitro-phenyl-benzene-thiophosphate; hexa ethyl tetraphosphate (HETP); 4-methyl-hydroxy coumarin-diethyl thiophosphate, mipafox, para nitrophenyl-diethyl phosphate, para-thion, schradan, tetra ethyl pyrophosphate (TEPP); triphosphoric penta-dimethylamide.

111. Phoshorus yellow.

112. Picric acid except substances containing less than nine per cent picric acid.

113. Picrotoxin.

114. Pituitary gland, the active principles of.

115. Polymethlenebistrimethylammonium salts.

116. Potassium hydroxide, except substances containing less than twelve per cent, weight in weight, of potassium hydroxide.

117. Quinacrine Hydrochloride.

118. Racemethorphan; its salts.

119. Racemorphan; its salts

120. Sodium hydroxide, except substances containing less than twelve per cent, weight in weight, of sodium hydroxide.

121. Sodium mono fluoracetate.

122. Sodium nitrite.

123. Sulphonal, alkyl sulphonals.

124. Sulphuric acid, except substances containing less than nine per cent, weight in weight, of sulphuric acid.

125. Strophanthus, glycosides of stropanthus.

126. Suprarenal gland, the active principles of; their salts.

127. Thallium, salts of.

128. Thyroid gland, the active principles of; their salts.

129. Tribromethyl alcohol.

130. Tri-2(chlorethyl) amine; its salts.

131. Triethanomelamine; its salts.

132. Troxidine (3:5:5 trimethyloxazolidine).

133. Zinc Chloride.

134. Zinc Phosphide."

IV. For Schedule G, the following Schedule shall be substituted, namely :—

"SCHEDULE G

(*See* Rule 97)

Aminopterin.

Amphetamine (Beta-aminopropyl benzene); its salts; its N-alkyl derivatives, their salts; beta-amino-isopropyl benzene, its salts; its N-alkyl derivatives, their salts, except when present in inhalers provided that it is absorbed in inert solid material within the inhaler.

Chrysophanic acid.

Insulin.

Phenylethylhydantoin; its salts; its acyl derivatives; their salts.

Pentaquin, its salts.

Pituitary gland, the active principles of.

Thyroid gland, the active principles of; their salts."

V. For Schedule H, the following Schedule shall be substituted namely :—

"SCHEDULE H

[*See* Rules 65(9) and 11).]

Allylisopropylacetylurea.

Acetyldihydrocodeine.

Methadone (amidone); its salts.

Amidopyrine; its salts.

Antihistamine substances, the following; their salts; their molecular compounds of, excepting preparations which are intended for external use :—

Antazoline; Bromozine; Chlorcyclizine; Diphenhydrazine; 3-di-n-butyl amino ethyl-4:5:6 trihydroxyphthalide; Pheninodamine; Promethazine; substances being tetra substituted N-derivatives of Ethylenediamine.

Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid; its salts; its derivatives; their salts with any other substance.

Chloral Hydrate; its preparations.

Chlorpromazine.

Diamino diphenyl sulphone excluding their preparations and dressings for external use.

Di-isopropyl flouro phosphorate.

1:4 dimethane sulphonoxybutane; its salts.

Dinitrocresols; dinitronaphthols; dinitrophenols; dinitrothymols.

Diethylallylamine compounds; its salts.

Di Sulfiram.

Do deca dimethyldiguanidine Hydrochloride (Synthelin).

Drugs coming under the Dangerous Drugs Act and marked with an asterisk (*) in Schedule E of the Drugs Rules, 1945.

Gallamine; its salts; its quarternary compounds.

Methyldiacetate; its salts.

Mustine; its salts.

Oxazilidine; its derivatives.

Paraaminobenzene sulphonamide; its salts; derivatives of Paraaminobenzene sulphonamide having any of the hydrogen atoms of paraamino group or the sulphonamide group substituted by another radical, their salts but excluding preparations and dressings containing these for external use.

Paramethadion.

Phenylacetylurea.

Phenylbutazone.

Phenylcinchoninic acid; Salicylcinchoninic acid; their salts; their esters.

Physeptone.

Polymethylene bistrimethyl ammonium salts.

Pituitary gland, the active principles of.

Sulphonal; alkyl sulphonals.

Suprarenal gland, the active principles of; their salts.

Tri-2-(Chlorethyl) amine; its salts.

Triethanomelamine; its salts.

Troxidine."

VI. After Schedule K, the following Schedule shall be inserted namely :—

"SCHEDULE L

[Rule 65 (9)]

Adreno cortico tropic hormone.

Antibiotics; the following; their preparations excluding those intended for topical, external or dental use :—

(1) Bacitracin.

(2) Chloramphenicol.

(3) Chlortetracycline.

(4) Erythromycin.

(5) Gramicidin.

(6) Magnamycin.

(7) Neomycin.

(8) Oxytetracycline

(9) Penicillin.

(10) Streptomycin.

(11) Tetracycline.

(12) Tyrothrecine.

(13) Viomycin.

Isonicotinic acid hydrazide and other hydrazine derivatives of Isonicotinic acid hydrazide; their derivatives; their salts.

Para amino salicylic acid; its salts and their preparations."

(Sd.) P. N. ANAND,
Under Secretary.

To

The Publisher,
Gazette of India,
New Delhi.

No. F. 1-52/55-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi, the 2nd November, 1955.

FROM

Shri P. N. Anand,
Under Secretary to the Government of India,

To

All Part A, Part B and Part C State Governments (except Jammu and Kashmir)

SUBJECT :—*Drugs Rules,* 1945—*Schedule E—State Poisons Rules.*

SIR,

I am directed to send herewith a copy of extracts from the minutes of the sixth meeting of the Poisons Sub-committee of the Drugs Technical Advisory Board. The recommendations of the Poisons Sub-committee have been accepted by the Drugs Technical Advisory Board. In accordance with recommendations of the Poisons Sub-committee, the Schedules to the State Poisons Rules have been examined *vis-a-vis* Schedule E to the Drugs Rules, 1945 and a uniform list of poisons (copy enclosed) has been drawn up for adoption under the State Poisons Rules. In preparing this uniform list, "purely drug items" have been eliminated from the present list of poisons of the various States but 'dual purpose' items have been retained in the list which also includes "non-drug" poisons. I am to request that, if there is no objection, the present Schedule to the State Poisons Rules may be replaced by the uniform list referred to above. This will ensure uniformity among all the States and also avoid overlapping with Schedule E to the Drugs Rules, 1945. This Ministry may kindly be informed of the action taken by the

State Government in the matter. Any suggestion which the State Government may have for making additions or deletions to the list may also be forwarded to this Ministry at an early date.

Yours faithfully,

(Sd.) P. N. ANAND,

Under Secretary.

F. 1-52/55-D.

Copy forwarded to the Director General of Health Services with reference to his U. O. No. 8-36/55/2-D, dated the 19-9-1955.

Copy with the enclosure forwarded to the Ministry of Home Affairs for information.

By order,

(Sd.) P. N. ANAND,

Under Secretary.

EXTRACTS FROM THE MINUTES OF THE SIXTH MEETING OF THE POISONS SUB-COMMITTEE.

(c) Item No. 3, Examination of Schedule 'E' to the Drugs Rules *vis-a-vis* the Poisons Rule framed by State Governments under the Poisons Act, 1940 with a view to finding out the extent of their overlapping.

6. A note on the State Poisons Rules under the Poisons Act, 1919 *vis-a-vis* Schedule E of the Drugs Rules was circulated by the Secretary (Appendix I). The various points mentioned in the note were discussed and the sub committee recommended that the following action should be taken :—

(i) All substances which will be covered by the definition of "Drug" in the Drugs Act and which are included in the State Poisons Lists under the Poisons Act should be removed from State Poison Rules and introduced in Schedule E of the Drugs Rules. The exemption limits at present provided for in Schedule E should apply to the items which are so transferred;

(ii) An additional provision should be introduced in the Drugs Rules providing for maintenance by dealers of registers showing quantities of Schedule E drugs purchased, stock in hand issues made;

(iii) The remaining items in the State Poisons Rules including those items such as Arsenic Salts, Corrossive sublimate, Cyandies etc. which are used for purposes other than medicinal will continue to be governed by the State Poisons Act; and

(iv) In order to prevent any overlapping of entries between the list of Poisons controlled under the State Poison Act and that controlled under Schedule E of the Drugs Rules it was suggested that a uniform list of Poisons should be adopted for the Poisons Rules by State Governments and that the Central Government should guide the States in this behalf. "Poisons" being

a subject falling within the purview of the "Concurrent List" under the Constitution of India, the Sub-committee considered that the Central Government was competent to legislate "Poisons" with a view to securing uniformity of administration in all the States. If required, the Sub-committee will be prepared to draw up a list of poisons for the purpose of the State Poisons Rules.

List of Poisons proposed for inclusion in the Poisons Rules of the State Governments.

Arsenic White; Arsenic Yellow; Arsenic Sulphide; Copper.

Arsenite (Scheels Green); Copper Accetoargenite (Paris Green).

Arsenic metal.

Abrus Precotorios (Gunj or Rati).

Barium, all salts of Barium.

Cyanide of Potash.

Cyanide of Sodium.

Hydrochloric Acid.

Lead in combination with oleic acid or other fatty acids.

Mercuric Perchloride.

Mercury Oxides (red, yellow or black); ammoniated mercury.

Mercuric Sulphocyanide; Mercuric Iodide; Liquor Hydrarg perchlor; Hydrargyri Sub-chloridum.

Marking Nuts.

Nitric Acid.

Oxalic acid, sodium oxalate; potassium oxalate; ammonium oxalate.

Prussic Acid.

Potassium Hydroxide.

Red Lead.

Strychnine; Strychnine Nitrate; Strychnine Sulphate; Strychnine Hydrochloride; Liquor Strychnine Hydrochloride and all other salts and solutions and preparations containing 0·2% or more of Strychnine.

Sulphuric Acid.

Sodium Hydroxide.

Tetra ethyl Lead.

Verdigris.

White lead.

COPY OF LETTER No. DC/1/18740 OF 1955 DATED THE 29TH NOVEMBER 1955 FROM THE DRUGS CONTROLLER FOR THE STATE OF BOMBAY TO THE DRUGS CONTROLLER, INDIA, NEW DELHI.

SUBJECT :—*Drugs Rules*, 1945—*Schedule E—State Poisons Rules.*

I invite a reference to Government of India, Ministry of Health, letter No. F. 1-52/55-D dated the 2nd November, 1955 and its accompaniments on the subject of the list of poisons proposed for inclusion in the Poisons Rules of the State Governments as per recommendations made by the Sub-committee at its sixth meeting which was forwarded to me by Government in the Local Self Government and Public Health Department, Bombay for remarks. On going through the Government of India's letter, I find that there is lacuna in the process suggested by the Government of India. It will be seen that Government of India propose to introduce in Schedule E of the Drugs Rules, 1945 all substances which will be covered by the definitions of the word 'drug' in the Drugs Act and which are at present included in the State Poisons Rules. While doing so one important factor appears to have been overlooked. It may be pointed out that while preparing a uniform list of poisons for adoption by the State Governments for the purposes of their Poisons Rules, the poisons drugs which are used in the Ayurvedic and Unani systems of medicine have not been taken into account. These drugs will therefore be free from the provisions of both the Drugs Act and the Poisons Act after removal from Poisons Rules. With a view to establishing proper control on these poisonous drugs are also included in the proposed uniform list of Poisons to be adopted for Poisons Rule whereby these drugs will be governed by the provisions of the Poisons Rules and will leave no scope for abuse.

Another point which deserves consideration is with regard to the Poisonous drugs that will be transferred from the existing Poisons Rules to Schedule E so far as their storage and security is concerned. The existing Rule 65 of the Drugs Rules, 1945 does not lay down that the poisonous drugs should be kept under lock and key while such a provision does exist in the Poisons Rules. It is therefore imperative that this security provision requiring the drugs to be kept under lock and key should be made applicable to all the drugs of Schedule E after inclusion of the Additional Poisonous Drugs in that schedule. In the 1st meeting of the Drugs Consultative Committee it was agreed to amend the Drugs Rules in this respect.

As these are my views, I request that you may consider and advise me in the matter to enable me to reply to the Bombay State Government.

This may please be treated as immediate.

COPY OF LETTER No. D.C./1/15 OF 1956 DATED THE 3RD JANUARY 1956 FROM THE DRUGS CONTROLLER FOR THE STATE OF BOMBAY TO THE GOVERNMENT OF BOMBAY AND COPY TO D.C.I.

REFERENCE :—*Government endorsement No. DRC 1155/78109-H. dated the 12th November*, 1955.

In continuation of this office letter No. DC 1/19973 dated the 17th December, 1955, I have the honour to state that at present the Poisons Act and Rules thereunder are applicable to all items included in the Schedule to the

Poisons Rules irrespective of the fact whether the substances are used in Ayurvedic. Unani or modern system of medicine. The acceptance of the proposal in the Government of India, Ministry of Health letter No. F. 1-52/55-D dated the 2nd November, 1955 will result in removing certain poisons from the Poisons Rules and the provisions of the Drugs Rules would be made applicable to the sale and distribution of poisons included in Schedule E of the Drugs Rules. According to the definition of the term "drug" under the Drugs Act, 1940 as amended by the Drugs (amendment) Act, 1955 substances exclusively used in Ayurvedic and Unani systems of medicine are excluded from the scope of the Act. This will mean that some poisonous indigenous crude drugs which are used in the Ayurvedic and Unani systems of medicine will go out of scope of both the Acts and will therefore have no control over their distribution and sale.

It is therefore suggested that in order that these drugs may still continue under control as far as their use in Ayurvedic and Unani Systems of medicine are concerned it would be necessary to incorporate the drugs listed below in the list of Poisons proposed for inclusion in the Poisons Rules of the State Governments sent along with the Government of India, Ministry of Health's letter quoted above:—

Aconite and their preparations.

Belladona; and all preparations or admixtures except substances containing less than 0·15 per cent of the alkaloids of belladona calculated as hyoscyamine.

Coca; and all preparations or admixtures, except substances containing less than 0·1 per cent of cocaine.

Croton—Oil and seeds of.

Datura seeds and leaves of; and all preparations and admixtures, except substances containing less than 0·15% of the alkaloids of datura calculated as hyoscyamine.

Nux vomica, seeds of : preparations or admixtures containing less than 0·2 per cent of the alkaloids of nux vomica.

Opium : All preparations and admixtures, except substances containing less than 0·2 per cent of morphine calculated as anhydrous morphine.

Poppies; all preparations of, except red poppy petails.

Stramonium; and all preparations containing it.

The Government of Bombay should therefore request the Government of India to incorporate the above drugs in the proposed list of poisons. The Government may also agree with the view expressed by the Poisons Sub-committee of the Drugs Technical Advisory Board for bringing all poisons used in the modern system of medicine within the scope of Schedule E to the Drugs Rules thereby avoiding the duplication of restriction under two legislations namely, the Drugs Act, 1940 and the Poisons Act, 1919.

COPY OF LETTER NO. 2495-S/2301-CH-2HB-55/17324, DATED THE 8TH MARCH, 1956, FROM SHRI S. R. MAINI, I.A.S., SECRETARY TO GOVERNMENT OF PUNJAB, HEALTH AND LOCAL GOVERNMENT DEPARTMENTS, CHANDIGARH, TO THE SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules*, 1945—*Schedule E—State Poisons Rules*.

With reference to Shri Anand's letter No. F. 1-52/55-D, dated the 2nd November, 1955, on the subject cited above, I am directed to say that the Punjab Government are of the view that all salts of Barium should not be included in the Poisons List. Barium Sulphate, which is an innocuous salt of Barium and used as Barium meal etc. should be excluded from the list. Against Barium in the list of poisons proposed by the Government of India, it may thus be substituted as under:—

"Barium; all salts of Barium, except Barium Sulphate."

COPY OF LETTER NO. 1250/4107/VIII/55, DATED 13-4-56, FROM THE UNDER SECRETARY TO GOVERNMENT OF MADHYA PRADESH, SEPARATE REVENUE, NAGPUR TO THE SECRETARY TO GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs Rules*, 1945—*Schedule E—State Poisons Rules*.

I am directed to refer to Shri Anand's letter No. 1-52/55-D, dated the 2nd November, 1955 on the above subject and to state that though Copper Sulphate and Cocculus Indicus are drugs they are not included in Schedule E of the Drugs Rules and though Teltra Ethyl Fluid is a poison it is not included in the list of poisons proposed for inclusion in the Poisons Rules of the State Governments enclosed with Shri Anand's letter referred to above.

2. Government of India are, therefore, requested to reconsider the question of inclusion of Copper Sulphate and Cocculus Indicus in Schedule E of the Drugs Rules and Teltra Ethyl Fluid in the list of poisons.

EXTRACT FROM DIRECTOR GENERAL OF HEALTH SERVICES NO. 20-1/55-D DATED THE 27TH JANUARY, 1956.

Methyl alcohol is not mentioned in Schedule E (List of Poisons) to the Drugs Rules 1945. However, Methanol (Methyl alcohol) has been included in Schedule E to the Drugs Rules in the "Draft Amendment to Rules 65 and 97 —revision of Schedules E, G and H—insertion of a new Schedule L" *vide* Ministry of Health No. F. 1-48/55-D, dated 15th December, 1955. After finalisation of this amendment the control over this item will be the same as for other poisons given in Schedule E to the Drugs Rules.

If, however, there is any misuse of Methyl alcohol in any State it would be possible to include Methyl alcohol in Schedule H to the Drugs Rules whereby its sale would be effected on the prescription of a doctor.

ENCLOSURE D

No. F. 1-19/55-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 26th June, 1956.

FROM

Shri T. V. Anantanarayanan, M. A.,
Under Secretary to the Government of India.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o The Directorate General of Health Services,
New Delhi

SUBJECT :—*Preparations of "Rauwolfia Serpentina"—Inclusion in Schedule 'H' to Drugs Rules*, 1945.

SIR,

I am directed to forward herewith a note containing the views of the members of the various Advisory Committees of the Indian Council of Medical Research on the subject mentioned above. Conflicting views have been expressed by the experts on the question whether Rauwolfia Serpentina preparations should be supplied only against prescription of registered medical practitioners. The majority of the experts desire that the use of the drug should be controlled but there is practical difficulty in enforcing any such restriction since the manufacturers can always claim that the preparation is an Ayurvedic one. Accordingly I am to request that the matter may kindly be placed before the Drugs Technical Advisory Board at its next meeting and the views of the Board intimated to this Ministry at an early date.

Yours faithfully,
(Sd.) T. V. ANANTANARAYANAN,
Under Secretary.

Note containing views of the members of the various Advisory Committee of the Indian Council of Medical Research.

Dr. B. Mukerji:

I wish to state that the number of cases recorded *cannot* be considered to be enough evidence to bring the preparation (Rauwolfia Serpentina) under Schedule 'H' to the Drugs Rules 1945. Ordinarily, Rauwolfia preparations are available for sale by retail only upon a prescription given by medical practitioners. However, in view of the widespread publicity that the drug has received in recent times, there has been considerable amount of its use by the lay public also. In the dosage generally recommended, crude Rauwolfia powder or preparations thereof are not toxic to any great extent. Purified alkaloids such as Reserpine, are, however, more toxic.

I am of the opinion that we should wait for further reports of toxic manifestations as a result of administration of this drug before taking a decisive step towards its inclusion in Schedule 'H' to the Drugs Rules 1945.

Dr. A. K. Basu :

Personally I think that this drug *should be* controlled under the provisions of the Drugs Act and should be included in Schedule 'H' to the Drugs Rules 1945.

Brigadier Sarup Narain :

No control trial on Rauwolfia Serpentina has been carried out in the Armed Forces, nor there have been any reports of Psychiatric reactions after its administration. Cases of Hypertension are uncommon in the Armed Forces. Those suffering from serious disease are invalided out of service.

In view of the reactions reported from U.S.A. on the basis of control trials, it is highly advisable that the Rauwolfia Serpentina may be controlled under the provisions of the Drug Act.

Dr. R. A. Lewis :

With regard to the occurrence of depressive reactions to rauwolfia therapy may I suggest that this is not surprising in view of the large number of patients receiving the drug, the relatively high doses which are possible due to purification of the crude powder, and the well known action of the drug upon hypothalamic centres. If manic patients can be restored to normal, then normal persons might be expected to have a tendency to get depressed on the drug.

In view of the small number of drugs listed under Schedule 'H' and their much greater toxicity, it would *not* seem appropriate to list R. Serpentina in this Schedule.

Dr. N. S. Vahia :

Depression following the administration of Rauwolfia has been fairly well recognised. It is also known that this depression at times might be very severe and might require special treatment like Elector Convulsive Treatment. At the same time it might be noted that in my opinion the incidence of severe depression after the administration of Rauwolfia is probably not common.

All the same in any given case it would be difficult for the patient or his relatives to recognise early symptoms of depression and its relation to the drug. Therefore it is certainly safer to supply this drug to the member of the public only when it is known that the patient would be under medical supervision.

Dr. M. V. Govindaswamy :

I strongly recommend that the preparation of Rauwolfia Serpentina be included amongst those drugs controlled under the provisions of Drugs Act and included in Schedule 'H' to the Drugs Rules 1945.

The experience of the Mental Hospital for the last two years with Rauwolfia and some of this proprietary preparations has convinced us that the drug should be prescribed only by physicians and the patient while under treatment should be under the constant observation of a competent physician.

Sudden fall in blood-pressure, confusion, giddiness and dis-orientated behaviours have all been noticed with this drug and in cases suffering from anaemia, the administration of this drug may be catastrophic.

Dr. K. L. Wig :

I personally think it is desirable to include Rauwolfia preparations under Schedule 'H' of Drugs Rules 1945, especially as we now know the drug's central action and some of its toxic effects.

ENCLOSURE E

No. F. 1-25/56-D.

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 13th July, 1956.

FROM

Shri T. V. Anantanarayanan, M. A.,
Under Secretary to the Government of India.

TO

The Secretary, Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT:—*Drugs Rules* 1945—*Licence forms* 25 *and* 28—*Suggestions to include fresh forms for issue of manufacturing licences for repacking Drugs.*

SIR,

I am directed to forward herewith a copy of letter No. 50373-D/56, dated the 2nd May, 1956 from the Drugs Controller, Madras to the Secretary to the Government of Madras in the Health, Education and Local Administration Department and to request that the matter may be placed before the next meeting of the Drugs Technical Advisory Board and their views communicated to this Ministry at an early date.

Yours faithfully,

(Sd.) T. V. ANANTANARAYANAN,
Under Secretary.

COPY OF LETTER REF. NO. 50373-D/56 DATED 2-5-56, FROM THE DRUGS CONTROLLER, MADRAS 6, TO THE SECRETARY TO THE GOVERNMENT, HEALTH, EDUCATION AND LOCAL ADMINISTRATION DEPARTMENT, MADRAS-9.

SUBJECTS :—*Drugs Act* 1940—*Drugs Rules* 1945—*Licence forms* 25 & 28—*Suggestion to include fresh forms for issue of manufacturing licences for repacking drugs.*

Drugs Licences in Forms 25 and 28 of the Drugs Act 1940 and the rules thereunder were being issued till now for manufacturers of drugs in the strict sense of the word 'manufacture'. After the implementation of the Drugs Amendment Act 1955, wherein repacking is also included in the 'Manufacture', there are several applicants in this State for 'manufacturing licences' for purposes of 'repacking only'. Recently the Chemists and Druggists Association, Madras waited on deputation on the Drugs Controller, Madras, explaining

the difficulty in applying for manufacturing licences in Form 25 or 28 as the case may be by dealers, who get ordinary drugs like Boric Acid, Magnesi Sulphate, Soda Bicarb, Eucalyptus Oil, etc., in bulk and repack them in small containers, for the retail sale and such dealers may not be able to satisfy all the conditions such as large premises, elaborate equipment and technical staff to obtain a manufacturing licence. It is considered that the conditions to be imposed before the issue of a 'Manufacturing licence' in Form 25 or 28 for repackers need not be so stringent as for real manufacturers in strict sense. For example a Graduate in Pharmacy or Pharmaceutical-Chemistry and elaborate equipment and an analytical laboratory are not necessary for the issue of 'manufacturing licences' for 'repackers'. All that would be required of them would be a set of clean and Hygienic premises and ordinary equipment necessary for carrying on repacking activity and a qualified compounder, provided that the applicant gives an undertaking that the samples from each Batch will be analysed in an approved laboratory for its standard quality before offering it for sale and he shall label the drugs as per Drugs Rules and will be solely responsible for the quality of drugs. In view of the Drugs Amendment Act 1955 there is bound to be a larger number of applicants for Manufacturing Licences for repacking purposes only and it would not be fair to refuse, provided they satisfy the above conditions. The net result will be the total number of Manufacturing licences in Forms 25 and 28 would show a very large number which is not really indicative of the state of 'real manufacture' in the strict sense. Therefore it is suggested that a separate licence as form '25-A' or '28-A' as the case may be, be considered on the analogy of sales licences in form 20-A and 21-A, to differentiate this type of manufacturers (Repackers) from real manufacturers. The conditions to be satisfied before the issue of these restricted licences may be less stringent.

Perhaps for the same reason it is also suggested that a different number may be given to the loan licences in form 25 and 28 licences in form 25-B or 28-B.

It is requested that the Government of India in the Ministry of Health may be addressed to place the matter before the Drugs Technical Advisory Board for consideration.

ENCLOSURE F

No. F. 1-7/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, dated the 25th August, 1956.

FROM

Shri T. V. Anantanarayanan, M.A.,
Under Secretary to the Government of India.

To

The Secretary,
Drugs Technical Advisory Board,
C/o The Directorate General of Health Services,
New Delhi.

SUBJECT :—*Addition to Rule 52 of the Drugs Rules.*

SIR,

I am directed to forward the letters noted below from the Government of Madras and the Government of Bombay with enclosures. The Government of India are advised that a rule can be framed giving power

to the Drugs Inspector to seize records, registers and articles other than drugs such as cartons, blocks, labels, instruments or any article used for the manufacture of spurious drugs. Accordingly I am to request that the matter may kindly be placed before the Drugs Technical Advisory Board at its next meeting for suggesting a suitable addition to Rule 52 of the Drugs Rules and the view of the Board intimated to this Ministry at an early date :

1. Letter No. F. 315/2180/H, dated the 2nd February, 1956, from the Govt. of Bombay with enclosure.
2. Letter No. MS 1053-Health, dated the 23rd March, 1956, from the Govt. of Madras with enclosure.

Yours faithfully,

(Sd.) T. V. ANANTANARAYANAN,

Under Secretary.

COPY OF LETTER NO. P. 315/2180/H, DATED THE 2ND FEBRUARY, 1956 FROM THE GOVERNMENT OF BOMBAY, LOCAL SELF-GOVERNMENT AND PUBLIC HEALTH DEPARTMENT, TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Enforcement of Drugs Act and Rules—Legal Powers to the Licensing Authority.*

I am directed to refer to Shri J. N. Saksena's letter No. F. 1-1/49-D, dated 27th June, 1949, on the subject mentioned above, and to forward herewith for the consideration of the Government of India a copy of letter No. DC 1/2378, dated the 5th April 1952 from the Drugs Controller for the State of Bombay addressed to the Surgeon General with the Government of Bombay.

2. I am to state that Section 22 of the Drugs Act, 1940, as amended by Section II of the Drugs (Amendment Act, 1955, No. II of 1955) does serve the purpose in view as there is no provision for seizure by the Drugs Inspector of articles other than drugs such as Books of Accounts, documents, cartons, blocks, labels, instruments or any other articles used for manufacture of spurious drugs which may be found in the place to be searched. The article other than drugs such as mentioned above play an important role in furnishing the clue to the information and for the purpose of proving the offence in prosecution under the Drugs Act, 1940. Any such article will prove to be of great value in collecting evidence. Therefore the additional proviso to clause (c) of Section 22 of the Drugs Act, 1940 proposed by the Drugs Controller in his accompanying letter is altogether necessary for the proper improvement of the Drugs Act, 1940, and rules thereunder. The State Government suggests that it may suitably be amended so as to authorise the Inspectors to seize all the incriminating articles and to seal the premises when the seizure cannot be effected immediately.

3. The action taken in the matter may kindly be communicated to the State Government in due course.

COPY OF LETTER NO. DC. 1/2378, DATED THE 5TH APRIL, 1952 FROM THE DRUGS CONTROLLER FOR THE STATE OF BOMBAY.

SUBJECT :—*Grant of Legal powers to the Drugs Controller for the State of Bombay*

With reference to the correspondence resting with this office letter No. D.C./1/18931, dated the 28th December 1950 on the subject mentioned above, I have the honour to state that at present under section 22 of the Drugs Act, 1940, the Drugs Inspector has power to enter premises where any drug is being manufactured, sold or stocked, inspect any premises where drugs are being manufactured, take samples of such drugs, and freeze or seize them if so authorised by the District Magistrate or the Chief Presidency Magistrate. Though the power of making a search is not specifically mentioned in the said section, power covered by clause (e) of that section are wide enough to include the power of search, as otherwise the other powers regarding inspection, taking samples etc. cannot be exercised unless the premises are searched.

2. As regards the power to seal the stocks believed to be spurious, misbranded or substandard, clause (c) of Section 22 provides that an order not to dispose of the stocks or to seize the stocks can only be made by the Inspector on being authorised by the District Magistrate or the Chief Presidency Magistrate. In view of this express provision in clause (c) of section 22 it cannot be argued that the Inspector has power to do so under his incidental powers under clause (e) of that section.

3. Under Rules 51 and 52 of the Drugs Rules, 1945, made applicable to this State under Rule 2 of the Bombay Drugs Rules, 1946, the duties of the Inspectors are prescribed but those rules also do not contain any provision under which the Inspector can seal the stocks on his own.

4. This being the present position as regards the powers of the Drugs Inspectors under the Drugs Act, 1940, the Inspectors have often to face a situation wherein they cannot take any action immediately, howsoever pressing it may be, and have to wait till the requisite authority from the District Magistrate or the Chief Presidency Magistrate to seize or seal the stocks is obtained. By the time the inspector is ready with the necessary authority the stocks in question disappear.

5. On the other hand, if a manufacturer or a dealer who has been served with a prohibitory order from this office requiring him to stop forthwith the manufacture or sale of his products without the drug licences, still persists in manufacturing or selling drugs in disregard to the orders; it becomes necessary to seal the premises to prevent the offender from disposing of surreptitiously the stocks so manufactured or possessed by him.

6. It is, therefore, suggested that in order to enable this office to make quick decisions and take prompt action against the offenders under the Drugs Act, 1940, the Drugs Controller (Licensing Authority) should also be invested with the discretionary powers and should be in a position to authorise the Drugs Inspectors to seal on the spot the stocks or even the premises where the offence is committed, where he has reason to believe that even the slightest delay would be ruinous.

7. In my opinion, unless some such discretionary powers are provided for in the Drugs Act whereby the Inspectors can take the orders for sealing the stocks or even the premises, straight from the Drugs Controller, the enforcement of the present Drugs Act, 1940 and the rules thereunder becomes

a 'meek affair' and the dealers being aware of this loophole, at times show a defiant attitude or act in a manner prejudicial to the Drugs Control Administration. The Drugs Controller being directly concerned with the administration of the Drugs Act, would be in a better position to use his discretionary powers with circumspection.

8. In the circumstances, and if the views expressed above are accepted, I suggest the following additional proviso to clause (c) of Section 22 of the Drugs Act, 1940, for the consideration of Government:—

"(2) Provided that the Inspector may take any action under this clause under the express orders of the Licensing Authority and if the Licensing Authority considers that such action is expedient in the interests of public health he may seal the premises where there is reason to believe that such contravention has been committed and the Inspector shall with all convenient despatch report the facts to the District Magistrate or the Chief Presidency Magistrate and take such measures as may be necessary according to law".

COPY OF LETTER NO. MS. 1053 HEALTH, DATED THE 23RD MARCH, 1956 FROM THE GOVERNMENT OF MADRAS, HEALTH, EDUCATION AND LOCAL ADMINISTRATION DEPARTMENT, TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI.

SUBJECT :—*Drugs—Drugs Rules* 1945—*Empowering the Drugs Inspectors to seize registers etc.—Amendment to rules.*

I am directed to enclose herewith copies of the letters noted below suggesting amendment to the Drugs Rules, 1945. I am to request that the matter may be placed before the Drugs Technical Advisory Board and necessary action taken in the matter.

From the Director of Medical Services Ref. No. 49771-D/55, dated the 27th February, 1956.

From the Public Prosecutor, Madras, letter No. Opn. 42/56, dated the 17th March, 1956.

COPY OF LETTER NO. 49771 D/55 DATED THE 27TH FEBRUARY, 1956 FROM THE DRUGS CONTROLLER, MADRAS TO THIS DEPARTMENT.

SUBJECT :—*Prosecution—Sambandar Medical Hall No. 22, Koviloor Road, Karaikudi—Contravention of Section* 18(a) (V) *the accused discharged—Opinion of the Public Prosecutor, Madras in this case —Necessary steps to amend the rules empowering the Drugs Inspector to seize registers etc.—Request of.*

Permission was accorded to the Drugs Inspector, Madurai to prosecute the above firm for contravening Section 18(a) (V) of Drugs Act 1940 read with rule 65(9) of Madras Drugs Rules 1945 by selling schedule H drugs without a prescription and making fictitious entries punishable under section 27 of the said act *vide* copy of proceedings enclosed.

A charge sheet was filed against the above firm by the Drugs Inspector, Madurai in the Court of the District Magistrate of Ramanathapuram at Devakottai in C. C. No. 325 of 1955. The registers and bill books of the above firm seized by the Drugs Inspector were filled as exhibits to prove the charges. The accused was discharged on 4-11-55 under Section 253(1) Cr. P. C. by the

learned Magistrate in view of the 'Lacuna' in the Act and rules by not providing necessary provisions for seizure of registers and documents to support the prosecution case by the Drugs Inspector and in view of Article 20(3) of the constitution and the rules thereunder being a bar to the court viewing the register as having been produced by the accused himself. The learned Magistrate has also observed in his judgment that there seems to be a 'Lacuna' in the Act, and it is for the Legislature to step in and remedy the defect, by clothing the Drugs Inspector with necessary authority, also to seize registers maintained under the Rules framed under the Drugs Act, 1940. A copy of the judgment in this case is herewith enclosed.

The opinions of the Assistant Public Prosecutor, Grade II Devakottai who conducted the case and Assistant public Prosecutor Grade I, Ramanathapuram at Madurai on the above point with reference to this case were obtained. The copies of their opinion are sent herewith. Assistant Public Prosecutor, Grade II is of opinion that a revision is not likely to succeed in this case. Assistant Public Prosecutor, Grade I has stated that he is unable to disagree from the finding of the District Magistrate. He has also stated that the opinion of the Public Prosecutor, Madras may be obtained as the same question is likely to arise throughout the State.

It is therefore requested that the Public Prosecutor, Madras may be consulted as to whether a revision may be filed in this case. It is also requested that necessary steps may kindly be taken to amend the rules suitably empowering the Drugs Inspector to seize registers, records and other material object from the dealers of drugs in order to prove the offences under Drugs Act 1940.

COPY OF THIS OFFICE PROCEEDINGS REF. No. 49771/D/55, DATED 1-8-55.

REFERENCE :—*Letter No.* 7244 D/55, *dated* 28-5-1955 *from the Drugs Inspector, Madurai.*

The Drugs Inspector, Madurai has reported that during a check of the registers of the above firm, he observed certain entries made therein to be suspicious with regard to the sale of Schedule H drugs (Sulphanilamide and suphadiazine). He had seized the registers and bill books and addressed. Dr. V. V. Rajan of Karaikudi on whose name two entries were made for the sale of sulpha drugs. The doctor has replied stating that he had not purchased any drugs from the above chemist. The dealer has therefore contravened Rule 65 (9) of the Drugs Rules 1945 read with Section 18(a) (v) of Drugs Act 1940 by selling drugs without a prescription and making fictitious entries punishable under Section 27 thereof. Permission is therefore accorded to prosecute the above firm.

(Copy of Judgment.)

IN THE COURT OF THE DISTRICT MAGISTRATE OF RAMANATHAPURAM AT DEVAKOTTAI

Present :—Sri R. Lakshmanan, M. A., B. L., District Magistrate, Friday the 4th day of November 1955 Calender case No. 325 of 1955.

State represented by the Drugs Inspector, Madurai ..... *Complaint*

Vs.

Sri R. Desigan. ..... *Accused.*

This case having been taken on file on 5-10-1955 and coming on for hearing on 19-10-1955, 2-11-55 and 3-11-55 before me in the presence of A. P. P. Grade II for the State and of K. Chandrasekara Iyer, Advocate for

the accused and having stood over to this day for consideration, the court made the following :—

ORDER

The Drugs Inspector Madurai has laid the complaint against the accused, one R. Desigan, Proprietor of Sambandar Medical Hall, No. 22, Koilur road, Karaikuddy, under section 18(a) (v) of the Drugs Act 1940 read with S. 27 thereof Rule 65(9) for sale of drugs in contravention of the Rules framed under the Act.

2. The prosecution case is, that on 22-2-1955 the accused made fictitious entries of sale, of 12 tablets of Sulphanilamide a 'H' schedule drugs to one Rangaswami, whose address is not given, in the registers maintained for the purpose, ostensibly made under the prescription of one P. Paramasivan (P. W. 2) who is not a registered Medical Practitioner. He also sold on 14-3-1955, 25 tablets of Sulphanamide, a 'H' schedule-drugs without prescription, from a Registered Medical Practitioner, but made entries in the register as if the sale of 25 tablets was made to Doctor V. V. Rajan, himself a registered medical practitioner. Again, on 1-4-1955, the accused had sold 6 tablets of Sulphadiazine, a 'H' schedule drug without prescription from a registered medical practitioner making entries in the register as if the sale was to V. V. Rajan himself.

3. The defence is two-fold : Firstly, the accused did not violate any rules, and only supplied to a Doctor, or as per a doctor's prescription. Secondly, no violation is proved, because the seizure of the registers, maintained by the accused, is illegal, the Drugs Inspector having no powers expressly conferred on him, by the Drugs Act for seizure of such documents, apart from the seizure of stocks of drugs. When once the seizure is illegal, the accounts cannot be directed to be produced, in view of Art. 20(3) of the Constitution Act, which says that no accused can be compelled to give evidence against himself, or to produce a document which may incriminate him. Therefore the alleged unauthorised sales in contravention of the Rules framed under the Drugs Act, are not proved.

4. The point for determination is : Whether, legally, there is a *prima facie* case against the accused.

5. The evidence of P. W. I., Dr. Rajan shows that he never purchased 25 tablets of Sulphanamide on 14-3-55 or 6 tablets of Sulphadiazine, on 1-4-55, for his chemist is one Selvanayaki stores, and the witness is not a customer of Sambandar Medical Hall. He wrote Ex. P.I., denying any purchase by himself in answer to a query of the Drugs Inspector. Therefore, if the entries in the register, seized and produced by P.W.S. are legal evidence, instance 2 and 3, mentioned in the complaint dated 5-10-55 may have to be accepted as true.

6. With regard to the 12 tablets of sulphanamide, a 'H' schedule drugs sold to one Rangaswami, that purchaser, Rangaswami is not a prosecution witness. Therefore, only if the register, seized and produced, is legal evidence against the accused, then as Dr. Paramasivan gave Ex. P 2. saying that he used only Ayurvedic medicines, and as he has deposed that he told the Drugs Inspector, that he used only Ayurvedic Drugs, and never English or Allopathic drugs, the first instance, mentioned in the complaint may also have to be considered as proved.

7. But, the difficulty, in this case, is : That the accused takes technical advantage of the fact, that unlike under the Sales Tax Act or the Madras Prohibition Act, for instance, under the Drugs Act, and inspecting officer is not clothed with the powers of a "Police-Officer" to seize registers. If the Drugs Inspector is "Police-Officer", a search and seizure by him will not be invalid, under Art. 20(3) of the Constitution [*Vide* SORNALINGAM CHETTIAR *vs.* State decided by Balakrishnaier J. and reported in 1955 Madras weekly Notes (Criminal (Page 151).] Rule 51(6) shows, that the Drugs Inspector should maintain a record of all inspections made, and actions taken by him in the performances of his duties, including the taking of samples and the seizure of stocks and to submit copies of such record to the controlling authority. Rule 51(7) shows, that the Drugs Inspector may make enquiries and inspections, as may be necessary, to detect the sale of drugs in contravention of the Act. The argument for the accused is, that there is no provision empowering the Drugs Inspector to seize the registers, bills and other records, maintained in a Medical shop. The absence, of such a provision in the Drugs Act, and the rules framed thereunder is contrasted, naturally with the presence of a provision for seizure of accounts by a Sales Tax or commercial tax officer, and seizure of contrabands by a prohibition officer making a search and seizing articles or implements, used for the manufacture, of illicit arrack, under a mahazar. It is also pointed out that Rule 51(6) refers to the seizure of stocks, but there is no reference to the seizure of registers or bills. A.P.P. II could not contend, that seizure of stocks or drugs would include seizure of registers but he argued, that seizure of registers may be construed to come within the purview of rule 51(7), which empowers the Drugs Inspector to make such enquiries and inspections, as may be necessary, to detect the sale of drugs in contravention of the Act. There seems to be a LACUNA in the Act; and it is for the Legislature to step in, and remedy the defect, by clothing the Drugs Inspector, with the necessary authority, also to seizure registers maintained under the Rules framed under the Act; for it is idle to contend that it is enough that the Drugs Inspector, makes an inspection and notes the points and initials the registers, when a seizure is very necessary, to prevent any possible tampering with the registers, after the Drugs Inspector leaves a medical hall after inspection. The only alternative, for the Drugs Inspector, is to have moved police, who can get a search-warrant from a competent magistrate search the premises, and seize the registers, in the absence of any express or specific power to seize which has been conferred by other enactments, but is absent in the Drugs Act and the rules framed thereunder. The defence counsel relies on a Bench Ruling of the Madras High Court in SWARNALINGAM CHETTIAR *vs.* ASSISTANT LABOUR INSPECTOR, Karaikudi, 1955 N.W.N. (Criminal 173, to show, that the learned Chief Justice on behalf of a Bench of the Madras High Court held that in view of Article 20(3) of the constitution, summons cannot be issued to an accused, to compel him to produce documents in his possession which may support the prosecution case, and, the Supreme Court has held in BEHRAM KHURSHED PESIKAKA *vs.* THE STATE OF BOMBAY reported in 1954 (N. W. N. Criminal) 289, that the fundamental right under Art. 20(3) of the Constitution is one, which is based on public Policy, and cannot be waived by an individual. If the Drugs Inspector, had after inspecting the registers, taken a confession-statement from the accused, that would admissible; and the prosecution-case would be then, strong as P.W. 3 is not a Police Officer. But no such statement was taken by P.W. 3 P.W. 3 was also rather slow to act, after April 55 till 5-10-55, the date of the complaint here.

8. The net result is that in view of a lacuna in the Act rules not providing from seizure of registers and documents support the prosecution case by the Drugs Inspector, and in view of non-production of the documents and

in view of Art. 20(3) of the Constitution and the rules thereunder being a bar to the court viewing the register as having been produced by the accused himself I am reluctantly technically constrained to discharge the accused; for, in the absence of proof of sales in contravention of the Drugs Act and the Rules thereunder the evidence of P.Ws. 1 and 2 cannot hold the prosecution to show, a case, with which would warrant a conviction, if unrebutted. The accused, is, accordingly, discharged under Section 253(1) Cr. P. C.

Dictated to the shorthand writer, transcribed by him corrected by me and pronounced in open court, this the 4th day of November, 1955.

(Sd.) R. LAKSHMANAN,

District Magistrate.

Prosecution Witnesses :—

3. 1. Shri V. V. Rajan (Dr.); 2. Shri Parameswarann (Native Dr.); 3. Shri C. V. Narasimhan (Drugs Inspector).

Prosecution exhibits :—

P-1; 27-4-55 : Letter to Drugs Inspector by P. W. 1

P-2; 17-9-55 : Statement of P. W. 2 to P. W. 3

P-3; 2-2-55 : Counterfoil in the bill book showing sale of 12 tablets of Sulphanilamide.

P-3a; 14-3-55 : Counterfoil in the bill (No. 371) for sale of 25 tablets of Sulphanamide.

P-4; 22-2-55 : Entry for prescription purported to have been given by P. W. 2.

P-4a; 14-3-55 : Entry in stock register for the sale of 25 tablets covered by Ex-P-3-a.

P-4b; 1-4-55 : Entry in stock register for sale of 6 tablets of Sulphadiazine.

P-5; 1-4-55 : Bill for sale of 6 tablets of Sulphadiazine covered by Ex-P-Ex-P-3-b (Counterfoil No. 402).

Defence Exhibits :—

D-1; Prescription Chit alleged to have been given by P. W. 1.

D-2; 5-5-55 : Notice sent by P. W. 3 to the accused.

D-3; 24-5-55; Reply of the accused to D-2.

Material objects :—Nil.

(Sd.) R. LAKSHMANAN,

District Magistrate.

COPY OF OPINION OF THE ASSISTANT PUBLIC PROSECUTOR, GRADE I, RAMNATHAPURAM AT MEDURAI ON THE DISCHARGE OF THE ACCUSED IN C.C.N. 325/55 ON THE FILE OF THE DISTRICT MAGISTRATE, DEVAKOTTAI A CASE UNDER THE DRUGS ACT.

The accused had been complained against by the Drugs Inspector for fictitious entries of sales of sulphanamide Tablets on three occasions, and not covered by the prescription of Registered Medical Practitioner *viz.* on 22-2-55, 14-3-55 and 1-4-55.

The main contention of accused is against the seizure of his accounts by the Drugs Inspector, as offending the provisions of Act 20(3) of constitution and that such a seizure would amount to compulsion of the accused to be a witness against himself. The District Magistrate has discharged the accused agreeing with the above contention.

Though the Drugs Inspector has been given wide powers in respect of the enforcement of the act and the detection of offences, there is no specific provision under the Act or the rules framed thereunder clothing him with the powers of seizure of the accounts of the accused. Section 22(e) authorises him to exercise such other powers as may be necessary for carrying out the purposes of that chapter or rules made thereunder. Whether this could be construed as a provision authorising him to seize records and accounts, is to vital question. In other Statutes as referred to in the Judgment of the District Magistrate, there is specific authorisation for the officers for such seizure. In the absence of any such specific provision in the Drugs Act, the construction could be against such powers of seizure of accounts, documents from the accused. In 1955 M.W.N. 173 (cr) it has been held by the High Court, that summoning documents even by the Court, from an accused would amount to a compulsion offending Art. 20(3). The seizure of the accounts by the Police during investigation, is authorised by statute. There being no specific on the Inspector : the seizure of the accounts or documents from the accused and furnishing it as evidence against him, appears to me to be offending Art. 20 (3).

The District Magistrate has even suggested the taking of suitable steps for amending the rules, providing for such seizure of account etc.

I am unable to disagree from the finding of the District Magistrate and I would advise the authorities to obtain the opinion of the Public Prosecutor, Madras, as the same question is likely to arise throughout the State.

COPY OF OPINION OF THE ASSISTANT PUBLIC PROSECUTOR, II, DEVAKOTTAI ON THE DISCHARGE ORDER IN C. C. 325/55 ON THE FILE OF THE DISTRICT MAGISTRATE, DEVAKOTTAI.

The accused in this case R. Desigan, Proprietor, Sambandar Medical Hall had been charged by the Drugs Inspector, Madurai under section 18(a) V of the Drugs Act 1940 read with S. 27 thereof Rule 65(9) for sale of drugs in contravention of the rules framed under the Act. After examining 3 witnesses on the side of prosecution, and after recording the statement of the accused, the District Magistrate, Devakottai has discharged him under S. 253(I) Cr. P. C. on 4-11-56. The Drugs Inspector now seeks my opinion whether this order can be taken up in Revision.

The entire case rests upon the evidence as disclosed on the records maintained by the accused and marked as Exhibits P3 to P5 which prove all the three instances of alleged sale without prescriptions of registered Medical

Practitioners. The trial court has based its finding on what is called a Lacuna in the Act. The taking away, or the production of the registers and bills from or by the accused by the Drugs Inspector has been found to be without any jurisdiction in the absence of specific provision in the Drugs Act and the rules made thereunder, empowering the Drugs Inspectors to seize the document with themselves upon an inspection of a Drugs Shop or even there produced by the parties themselves in the course of an inspection. It may also be mentioned here that some other Acts do really empower some persons to search and seize records in enforcing the provisions of the respective Acts. So much so, it can be said that the Legislature never intended that the officers enforcing the various provisions of the Drugs Act can search and seize the registers that were expected to be maintained by the licensee. It is on the same lines that the court has refused to give an interpretation to Rule 51(7) *viz.*, the seizure of the registers would come within the purview of "Enquiries" and "Inspection" which the Drugs Inspectors had empowered to do under the act.

A bench decision reported in 1955 M. W. M. Cr. 173 has also been relied upon by the Court to hold that the seizure of the documents by the Drugs Inspector either by himself or upon their being produced by the accused Voluntarily is hit by Art. 20(3) of the Constitution of India. There it was found that SUMMONS FROM EVEN COURT CANNOT BE ISSUED to an accused to produce a document. Here a Drug Inspector admittedly Not EMPOWERED TO SEIZURE is found to be barred by Art 20(3) as per the ruling cited above. When the seizure is found to be barred by Art. 20(3) then the records seized cannot be used, in evidence against the accused.

When once it is found that the seizure infringes the fundamental right of the accused under Art. 20(3), and the registers and records cannot be used in evidence against the accused, then we are left with absolutely no other documentary evidence to substantiate the charge against the accused, however, strong the oral evidence or P.W. I may be.

Even on facts, I feel, even if a charge is framed, ultimately the case is not likely to end in a conviction.

Under these circumstances, I am of the view that a Revision is not likely to succeed in his case.

COPY OF LETTER NO. OPN. 42/56, DATED THE 17TH MARCH, 1956 FROM PUBLIC PROSECUTOR, MADRAS TO THE ADDITIONAL SECRETARY TO GOVT. HILA. DEPT., MADRAS.

SUBJECT :—*Revision against discharge—C.C.—No.* 325 *of* 1955 *on the file of the district Magistrate, Ramanathapuram—Forwarding opinion.*

REFERENCE :—*Endorsement No.* 22235-HII/56, *Health, dated* 14-3-56.

With reference to the above endorsement I give below my opinion in the above matter.

2. The paper received for reference are returned herewith.

OPINION

The District Magistrate of Devacotta in C.C. No. 325 of 1955 has acquitted the accused R. Desikan for contravening section 18(a) V of the Drugs Act 1940 read with S. 27 thereof and Rules 65(9) of the Rules framed under the Act.

The question that arose in the case was whether the Drugs Inspector is empowered to seize the books of the accused. The lower court was of the opinion that Rule 51(6) and 51(7) does not refer to seizure of the registers or bills and as such the Drugs Inspector is not empowered to seize the books. He also finds that under Article 20 (3) of the Constitution of India the accused cannot be compelled to give evidence against himself. The Court ignored the registers and found that in the absence of the registers the prosecution case has not been proved.

No doubt Article 20(3) says that no person accused of any offence shall be compelled to be a witness against himself. Decisions have held that summons cannot be issued to the accused to compel him to produce the documents in his possession. In a recent decision His Lordship Mr. Justice Samasundaram has held in C.A. 552/55 that Article 20(3) of the Constitution does not apply to the police investigation. In this case it is possible to contend that the registers were produced by the Drugs Inspector and that the accused is not compelled to be a witness against himself. But in this case all this has become academic, the judgment was delivered on 4-11-55. The revision against the order of discharge ought to have been preferred within one month. Now as the time has expired and as no revision was preferred before the session judge the High Court cannot be moved in the matter. So this question may be taken up as and when it arises in future.

(True Copy.)

(Sd.)

Superintendent.

ENCLOSURE G

No. F. 3-7/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 4th October, 1956.

FROM

Shri T. V. Anantanarayanan, M. A.,
Under Secretary to the Government of India.

To

The Secretary,
Drugs Technical Advisory Board,
C/o Director General of Health Services,
New Delhi.

SUBJECT :—*Drugs Rules* 1945—*Schedule E—State Poisons Rules.*

SIR,

I am directed to forward a copy of letter No. 1321-Health, dated the 20th April, 1956 from the Government of Madras, Health Education and Local Administration Department with enclosure, on the subject mentioned above and to request that the matter may be placed before the next meeting of the Drugs Technical Advisory Board and their views communicated to this Ministry at an early date.

Yours faithfully,

(Sd.) T. V. ANANTANARAYANAN,

Under Secretary.

COPY OF LETTER NO. 1321-HEALTH, DATED THE 20TH APRIL, 1956, FROM THE GOVERNMENT OF MADRAS, EDUCATION, LOCAL ADMINISTRATION DEPARTMENT, ADDRESSED TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH.

SUBJECT :—*Drugs—Drugs Rules,* 1945—*Rule* 65(12)—*Amendment—Suggested to the Government of India.*

REFERENCE :—*From the Government of India, Ministry of Health Letter No.* F. 1-52/55-D, *dated* 2-11-55.

I am directed to enclose an extract from the letter of the Drugs Controller, Madras No. R. 122774/D/55, dated 12-12-55 suggesting certain amendments to Rules 65(12) of the Drugs Rules, 1945. I am to request that the matter may be placed before the Drugs Technical Advisory Board and necessary action taken in the matter.

AN EXTRACT FROM THE LETTER OF THE DRUGS CONTROLLER, MADRAS NO. R 122774/D/55 DATED 12-12-55.

2. It is also considered necessary to amend Rule 65(12) of the Drugs Rules, 1945, so as to provide for the manner of storage of poisons on similar lines to the provisions made under Rule 18 of the Poisons Rules framed by the Government of Madras under the Poisons Act, 1919 in view of the proposal to delete "Purely drug items" from the State Poisons Rules and include them in Schedule E of the Drugs Rules.

(True extract.)

Rule 18 of Madras Poisons Rules

18. CUSTODY OF POISONS KEPT FOR SALE AND LABELLING RECEPTACLES IN WHICH THEY ARE KEPT:—All poisons kept for sale under these rules by any licence holder shall be kept in a box almirah, room or building (according to the quantity maintained) which shall be secured by lock and key and in which no substance be placed other than poisons possessed in accordance with a licence granted under the Act; and each poison shall be kept within such box, almirah, room or building in a separate closed receptacle of glass, metal or earthenware. Every such box, almirah room or building and every such receptacle shall be marked with the word 'POISON' in red characters, both in English and in the vernacular of the district and in the case of receptacles containing separate poisons, with the name of such poison.

ENCLOSURE H

No. F. 1-68/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

FROM

The Under Secretary to the Government of India,
Ministry of Health,
New Delhi.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services.
New Delhi.

New Delhi-2, dated the 5th, January 1957.

SUBJECT:—*Amendment of item No.* 12 *in Schedule C to the Drugs Rules,* 1945.

SIR,

I am directed to say that the present entry at item No. 12 of Schedule C to the Drugs Rules, 1945, permits preparations to be classified as Schedule C items only when these are "in a form to be administered parenterally". In accordance with this definition there is room for doubt whether injectable preparations containing dry powder when packed with the solvent separately would be classifiable as Schedule C drugs. Certain firms have advanced the following argument against such classification:—

> "In such cases the preparation is not ir a form to be administered parenterally and that the preparation becomes ready only when mixed with the solvent."

2. The Government of India are of the view that such preparations should be controlled under the provisions applicable to Schedule C items.

In order to remove any ambiguity, the present entry at item No. 12 of Schedule C may be amended to read as follows:—

> "Any other preparation which is meant for parenteral administration either in the form in which it is marketed or after being made up with a suitable solvent or medium".

2. It is requested that the matter may kindly be placed before the next meeting of the Drugs Technical Advisory Board and the recommendations of the Board communicated to this Ministry in due course.

Yours faithfully,

(Sd.) X X X

Under Secretary.

ENCLOSURE I

No. F. 1-12/57-D.

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi 2, *the* 19*th February*, 1957.

FROM

Shri J. N. Saksena,
Under Secretary to the Government of India.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT:—*Drugs Rules,* 1945—*Amendment of Schedule C(I)—Inclusion of Viyomycin.*

SIR,

I am directed to forward a copy of letter No. Medl./5756/3D-29/56, dated the 27th July, 1956, on the subject mentioned above, from the Government of West Bengal and to request that the views of the Drugs Technical Advisory Board in the matter may be obtained and communicated to this Ministry in due course.

Yours faithfully,

(Sd.) J. N. SAKSANA,

Under Secretary.

GOVERNMENT OF WEST BENGAL

DEPARTMENT OF HEALTH

Medical Branch

No. Medl./5756/3*D*-29/56 *Calcutta, the* 27*th July*, 1956.

FROM

Shri S. C. Roy, M. A., W.B.C.S.,
Assistant Secretary to the Government of
West Bengal.

TO

The Secretary to the Government of India,
Ministry of Health.

SUBJECT:—*Drugs Rules,* 1945—*Amendment of Schedule C*(1)—*Inclusion of "Gramicidin".*

SIR,

I am directed to refer to Shri Anantanarayana's letter No. F. 1-51/55-D, dated the 22nd May, 1956 on the above subject and to say that the Government of West Bengal have no objection to the proposal of amendment circulated in the said letter.

2 I am, however, to point out that in the opinion of this Government the name of "Vivmycin" another new antibiotic should also be included in Schedule C(1) to the Drugs Rules.

Yours faithfully,
(Sd.) X X X,
Assistant Secretary.

ENCLOSURE J

No. F. 1-30/56-D

GOVERNMENT OF INDIA
MINISTRY OF HEALTH

New Delhi-2, the 24th April, 1957.

FROM

Shri J. N. Saksena,
Under Secretary to the Government of India.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT :—*Drugs—Drugs Act* 1940—*Drugs Rules,* 1945—*Provisions applicable to Antitoxins—Modification of.*

SIR,

I am directed to forward copies of the correspondence given below on the subject mentioned above and to request that the matter may kindly be placed before the Drugs Technical Advisory Board at their next meeting. The views of the Board may kindly be communicated to this Ministry in due course.

1. Letter No. 68321/H-2/56-1 Health. dated the 17-7-56 from the Govt. of Madras (with encl.).
2. Memo No. 2-7/56-SAV/23506, dated the 7-9-56. from C.R.I., Kasauli.
3. Letter No. 3937, dated the 16-10-1956 from the Haffkine Institute, Bombay.
4. Letter No. 1216-B4/57, dated the 18-2-1957 from the King Institute, Guindy.

Yours faithfully,
(Sd.) J. N. SAKSENA,
Under Secretary.

COPY OF LETTER No. 68321-H2/56-1 HEALTH DATED THE 17TH JULY, 1956 FROM SRI K. GHULAM MAHMOOD I.A.S., ADDITIONAL SECRETARY TO GOVERNMENT HEALTH, EDUCATION AND L.A. DEPARTMENT, MADRAS ADDRESSED TO THE SECRETARY TO THE GOVERNMENT OF INDIA, MINISTRY OF HEALTH, NEW DELHI (WITH ENCL.).

SUBJECT :—*Drugs—Drugs Act* 1940—*Drugs Rules,* 1945—*Provisions applicable to Anti-toxins-Modifications of.*

I am to enclose herewith a copy of letter No. 65747/D/56 dated 27th June 1956 from the Drugs Controller of this State with its enclosures, on the above subject and to request that necessary action may be taken as proposed in that letter, to amend the provisions applicable to Tetanus Anti-Toxins under section (1) of Part IV in Schedule F to the Drugs Rules 1945.

COPY OF LETTER R. No. 65747-D/56 DATED 27-6-1956 RECEIVED FROM THE DIRECTOR OF MEDICAL SERVICES, MADRAS.

SUBJECT :—*Drugs—Drugs Act* 1940—*Drugs Rules,* 1945—*Provisions applicable to Anti-toxins—Modification of.*

I forward herewith a copy of letter cited with a request that the Drugs Technical Advisory Board may be consulted in the matter with a view to modify the provisions applicable to Anti-Toxins under section D in Schedule F, to the Drugs Rules, 1945, as suggested by the Director, King Institute, Guindy.

COPY OF LETTER No. 13592/B4/56 FROM THE DIRECTOR, KING INSTITUTE, GUINDY, DATED 29-5-1956.

In the Drugs Rules, 1945, as enunciated under the Drugs Act, 1940 (As corrected up to 30th September 1953) Part IV, Section D lays down the provisions governing biological and other special products with particular reference to those applicable to Tetanus Anti-Toxin. (Please refer to page 111 Drugs Standard Control, the Drugs Act, 1940, and the Drugs Rules Government of India in 1954.)

Here item number 4(2) containing the provision relating to the presence of solid matter in liquid sera reads:— that a solution of the separated Anti-toxic globulins shall not contain more than 0·1 grm. of solid matter for each 300 Anti-toxic units (International Unit of 1950).

This is the same as the provisions contained in the Therapeutic Substances Act, London etc., (1935) relating to the presence of solid matter in Tetanus Anti-toxin.

The Madras Drugs Rules also contain the same provision regarding this.

In the British Pharmacopoeia, (1953), the British Pharmacopoeial codex and the United States Pharmacopoeia the provision relating to solid matter in Anti-toxic Sera with particular reference to Tetanus Anti-toxin states that the Total solids should not exceed 20%.

The provisions relating to this subject as laid down in the various standard publications are tabulated with appropriate reference in the annexed form.

According to the provision that the total solids in the Anti-toxin can be 0·1 grm. for each 300 units as anti-toxin with total solids as high as even 80% will pass the prescribed regulations. For example a curative anti-toxin contains 25,000 I.U. (1950). In accordance with the existing rules an anti-toxic solution containing 25,000 I.Us. can contain 8·3 gms. of solid matter. This 8·3 gms. is generally contained in 10 cc. hence this will work up to 83% total solids. I wish to point out that this is an anomaly.

Prescribing a limit for total solids is essential as this controls the nature, specificity and to a certain extent the colour of the Serum which factors contribute severally and individually towards the quality of the serum. The rule as it reads gives room for low quality sera to pass the regulations. Moreover, this leads to the possibility of low grade Sera with high content of non-specific Proteins being passed as satisfying the Drug Rules though the total solid content is far above the safe limit of 20%. Such Sera are unsuitable for human use.

Hence it is suggested, that the clause relating to the limiting the presence of solid matter in Tetanus Antitoxin be modified as follows:—

A solution of the separated Anti-toxic globulins shall not contain more than 20% of total solid matter.

In the Drugs Rules, 1945, as enunciated under the Drugs Act, 1940 as corrected up to 30-9-1953, Part IV, Section D which lays down the provision governing the strength of Tetanus Anti-toxin states that Tetanus Anti-toxin having a potency of less than 150 I.U./cc. shall not be used for prophylactic use and that Tetanus Anti-toxin having a potency of less than 800 I.U./cc. shall not be issued for the treatment of Tetanus. This is the same as the provision contained in the Therapeutic Substances Act, 1935. The Madras Drugs Rules also contain the same provision. The provisions relating to this subject as laid down in the various standard publications are tabulated with appropriate references in the annexed form. Since the minimum potency of the anti-toxin for Prophylactic and Therapeutic use is limited by this provision the maximum volume of Anti-toxin that can be issued is consequently limited. The maximum volume in which Tetanus Anti-toxin can be issued for Prophylactic use (1500 I. U.) and for Therapeutic use (25,000 I.U.) according to the various regulations are tabulated below.

Name of Publication	Maximum volume which a Prophylactic dose can be issued 1500 I. U. (1950)	Maximum volume in which the Therapeutic dose can be issued 25000 I. U. (1950)
Therapeutic Substances Act . . .	10 c. c.	31·25 c. c.
Drug Standard Control	10 c. c.	31·25 c. c.
Madras Drugs Rules	10 c. c.	31·25 c. c.
British Pharmacopoeia	1·5 c. c.	8·33 c. c.
U. S. Pharmacopoeia	3·75 c. c.	62·5 c. c.

It is essential to limit the maximum volume in which Tetanus Antitoxin can be dispensed for Prophylactic or Therapertic use as this will necessarily exclude to a considerable extent non-specific Proteins in the finished

products. Thus, it will contribute to the issue of a Serum which can be claimed to be free to a large extent from materials which may lead to allergic and other untoward reactions. Further, in the treatment of Tetanus where it is necessary to administer large doses of tetanus Anti-toxin at frequent intervals it is essential that the individual doses are dispensed in as small a volume as possible. Hence. it is suggested that the provision governing the strength of the Anti-toxin in liquid preparations be modified as follows :-

Strength : Tetanus Anti-toxin having a potency of less than 500 *I.U./cc. in the case of liquid preparations shall not be issued for prophylactic use. Tetanus Anti-toxin having a potency of less than* 1,500 *I.U./cc in the case of liquid preparations shall not be issued for the therapeutic treatment of tetanus.*

According to this requirement, one Prophylactic dose of Tetanus Anti-toxin (1,500 I.U. 1950) could not be issued in more than 3·0 cc. volume one Therapeutic dose of Tetanus Anti-toxin (25,000 I.U. 1950) cannot be issued in more than 16·6 cc. volume.

FORM I

No.	Name of Publication	Reference to page	The provision as it reads
1.	Drug Standard Control. The Drugs Act, 1940. The Drugs Rules, 1945 thereunder revised and corrected up to 30-9-53.	Page 111	A solution of the separate Anti-toxic globulin shall not contain more than 1·0 gramme of solid matter for each 300 anti-toxic units (I. U. 1950).
2.	Therapeutic Substance Act, London, 1935.	Page 32	A solution of the separated Anti-toxic globulins shall not contain more than 0·1 gramme of solid matter for each 600 anti-toxic unit (I. U. 1928).
3.	British Pharmacopoeia Official from 1-9-53.	Page 50	Preparations of anti-toxic globulins do not contain more than 20% of solid matter.
4.	The British Pharmaceutical Codex, 1949, Supplement 1952.	Page 82	Preparations of anti-toxic globulins do not contain more than 20% WV of solid matter.
5.	The Pharmacopoeia of the United States of America Official from 1-11-1950.	Page 611	And its total solids must not exceed 20%.

FORM II

No.	Name of Publication	Reference to page	The provision as it read
1.	Drugs Standard Control. The Drugs Act, 1940. The Drugs Rules, 1945, thereunder revised and corrected up to 30-9-53.	Page 111	Strength : Tetanus Anti-toxin having a potency of less than 150 units per c. c. in the case of liquid preparations or less in the case of dried preparations shall not be issued for prophylactic use. Tetanus Anti-toxin having a potency of less than 8000 units per gramme in the case of dried preparations shall not be issued for treatment of Tetanus.
2.	The Madras Drugs Rules, 1945, G. O. Ms. No. 3240, P. H., dated 14-12-45.	Page 31	Do.

No.	Name of Publication	Reference to page	The prevision as it read
3.	Therapeutic Substances Act, London Ltd., 1945.	Page 41	Tetanus Antitoxin having a potency of less than 300 I. U. per c. c. in the case of Liquid preparations or less than 3,000 units per gramme in the case of dried preparations shall not be issued for prophylactic use. Tetanus Anti-toxin having a potency of less than 1,600 units per c. c. in the case of liquid preparations or less than 16,000 units per gramme in the case of dried preparations shall not be issued for treatment of Tetanus.
4.	The British Pharmacopoeia Official from 1-9-1953.	Page 564	Potency : for prophylactic use Native anti-toxic Serum has a potency of not less than500 units per ml. Dried native Anti-toxic Serum has a potency of not less than 5,000 units per gramme. Preparations of anti-toxic Globulins have a potency of not less than 1000 units per ml. Dried preparations of Anti-toxic globulins have a potency of not less than 7,500 units per gram. for Therapeutic use; Preparations of Anti-toxic Globulins have a potency of not less than 3000 units per ml. Dried preparations of Anti-toxic Globulins have a potency of not less than 15,000 units per gram.
5.	U. S. Pharmacopoeia Official from 1-11-1950.	Page 10	Tetanus Anti toxin has a potency of not less than 400 Anti-toxic units per c.c

COPY OF LETTER NO. 39037 DATED 16TH OCTOBER, 1956, FROM THE DIRECTOR, HAFFKINE INSTITUTE, BOMBAY, 12 ADDRESSED TO THE DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI-2.

SUBJECT :—*Modification of provisions applicable to Tetanus Anti-toxin in the Drugs Standard Control (Sept.* 1953).

Your letter dated 28th August 1956 regarding the above matter along with a copy of letter from the Director, King Institute, Guindy, and your subsequent reminder of even number 8-65/56-D dated the 5th October, 1956 has been received. I have the following comments to make.

1. The letter from the Director, King Institute does not quote the provisions in the Indian Pharmacopoeia (1955) relating to Tetanus Antitoxin. It has quoted all the other authorities, *e.g.*, B.P., B.P.C., U.S.P., Drug Standard Control (1953), Therapeutic Substances Act (London, 1935) and the Madras Drugs Rules. Our recommendations as given below are more in conformity with I.P. (1955) requirements.

2. We agree with the Director, King Institute, that the provisions relating to the presence of solid matter in Drug Standard Control (1953) for Tetanus Anti-toxin *viz.*, the last sentence in Part IV-D, item 4, para 2 should be modified to read "A solution of the separated antitoxic globulins shall not contain more than 20% of total solid matter".

This will be in accordance with I.P., B.P., B.P.C. and U.S.P. The earlier part of the same para relating to total solids in natural serum in the Drug Standard Control (1953) may be left undisturbed.

3. About the provisions relating to strength of Tetanus antisera in prophylactic preparations, I feel that the strength should be stated as "Tetanus antitoxin having a potency of less than 500 I.U. (1950) per c.c. in case of liquid preparations and 5,000 I.U. per gram. in the case of dried preparations shall not be issued for prophylactic use",

The provision about dried preparations does not find a mention in the letter of the Director, King Institute. Our suggestion is in keeping with those of I.P., B.P., and B.P.C.

4. About the provisions relating to strength of therapeutic tetanus antitoxin, the strength suggested by the Director of King Institute is 1500 I.U. /c.c. The strength required by I.P. is 1000 I.U./cc and B.P.C., B.P., specify 3000 I.U./cc while U.S.P. prescribes 400 I.U./cc. It is to be expected that the manufacturers of tetanus antisera for therapeutic use will always strive to attain the highest purity possible. I therefore suggest that the following be adopted. "Tetanus Antitoxin having a potency of less than 1000 I.U./cc for liquid preparations and 5,000 I.U./gram. for dried preparations should not be issued for the therapeutic use". This is in conformity with I.P. specifications.

5. The provisions in the Drugs Standard Control (1953) relating to tetanus anti-toxin units per 0·1 gram. of solid matter will not arise in view of the amendments suggested for total solid matter and strength of antisera in liquid and solid form prophylactic and therapeutic use.

COPY OF MEMO. NO. 2-7/56-S&V/23506 DATED THE 7TH SEPTEMBER, 1956, FROM THE DIRECTOR, CENTRAL RESEARCH INSTITUTE, P.O. KASAULI ADDRESSED TO THE DRUGS CONTROLLER, INDIA, DIRECTORATE GENERAL of HEALTH SERVICES, NEW DELHI-2.

REFERENCE :—*Your letter No.* 8-65/56-*D, dated* 26-8-1956.

The tetanus and other antitoxins received for testing at this Institute are mostly of foreign manufacture and chiefly from countries such as U.K., U.S.A., Germany & Italy. These products usually fulfil the "total solids" specifications as laid down in the British Pharmacopoeia. In the Indian Pharmacopoeia similar specifications have been incorporated. It is expected that with the enforcement of its provisions, the specifications relating to vaccines, sera and other biological products laid under Schedule F of the Drugs Rules will have to be revised and amended to bring them in alignment with the recommendations of the Indian Pharmacopoeia.

The Schedule F may even be dispensed with after the Indian Pharmacopoeia becomes the Official Authority for the Drugs Act.

Your attention is also invited to D.O. No. 16994 dated 17-7-52 from Dr. D.C. Laheri, Asstt. Director, Haffkine Institute, Bombay addressed to the Secretary, Indian Pharmacopoeia Committee. At present we have no data regarding the relationship of the "total solids" and the corresponding "unitage contents", of tetanus and other antitoxins manufactured in India.

It is desirable to collect this data in order to assess how far these specifications compare with those laid down in the British Pharmacopoeia & Indian Pharmacopoeia.

The Director, King Institute, Guindy, is correct in pointing out the various anomalies in this respect as laid down in the Drugs Standard Control, the Madras Drugs Rules, Therapeutic Substances act, the British & U.S. Pharmacopoeias. As has already been pointed out, with the enforcement of the provisions of Indian Pharmacopoeia these anomalies would cease to exist.

ENCLOSURE K

No. F. 1-28/55-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 20th June, 1957.

FROM

Shri D. J. Balaraj, I.A.S.,
Deputy Secretary to the Government of India.

To

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services.
New Delhi.

SUBJECT :—*Drugs Rules* 1945—*Amendment of item* 5 *of Schedule K.*

SIR,

With reference to the correspondence ending with your letter No. 8-15/54/5-DAB, dated the 28th January, 1955, I am directed to say that the matter was considered by the Board at their meeting held on the 25th February, 1955, *vide* a copy of the minutes attached. The views of the Board were communicated to the then ten Part A State Governments. Seven State Governments *viz.*, Bihar, Madhya Pradesh, West Benegal, Assam, Madras, Orissa and Andhra replied that they were against the proposed amendment to item 5 of Schedule K. After further consideration the matter was placed before the Drugs Consulative Committee. The Committee held its meetings on the 7th and 8th March, 1957. A copy of the Committee's recommendations is attached. The Government of India propose to split the entry at item 5 of Schedule K into two entries *i.e.*, 5 and 5-A in the manner indicated in the attached statement. I am to request that the matter may kindly be placed before the Board and their views may be communicated to this Ministry in due course.

Yours faithfully.

(Sd.) D. J. BALRAJ,

Deputy Secretary.

Recommendations of the Drugs Consultative Committee

"The Committee decided to recommend to the Government that the extent of exemption provided for hospitals and dispensaries in item 5 of Schedule K should be revised so as to lay down that though such institutions may not secure sale licences under the Drugs Rules, they should comply with all other provisions of Chapter IV of the Drugs Act and the rules thereunder. Drugs Inspectors should be enabled to carry out inspection of the stocks of drugs stocked by hospitals and dispensaries, check storage conditions and take samples of drugs for test. The hospitals and dispensaries need not however be required to maintain registers and records as required by Rule 65 of the Drugs Rules".

Items 5 *and* 5-*A of Schedule K*

Class of Drugs	*Extent and Conditions of Exemption*
5. Drugs supplied by a registered medical practitioner to his own patient or any drug specified in Schedule C supplied by a registered medical practitioner at the request of another such practitioner if it is specially prepared with reference to the condition and for the use of an individual patient provided the registered medical practitioner is not (a) keeping an open shop, or (b) selling across the counter, or (c) engaged in the importation, manufacture, distribution or sale of drugs in India to a degree which render him liable to the provision of Chapter IV of the Act and the rules thereunder.	All the provisions of Chapter IV of the Act and the Rules thereunder, subject to the conditions that, in the case of a medicine containing a substance specified in Schedule E. (a) the medicine shall be labelled with the name and address of the registered medical-practitioner by whom it is supplied; (b) if the medicine is for external application, it shall be labelled with the words "Poison", "For external use only", or, if it is for internal use with the dose; (c) the name of the medicine or ingredients of the preparation and the quantities thereof, the dose prescribed, the name of the patient & the date of supply and the name of the person who gave the prescription shall be entered at the time of supply in a register to be maintained for the purpose; (d) the entry in the register shall be given a number and that number shall be entered on the lable of the container; (e) the register and the prescriptions, if any, on which the medicines are issued, shall be preserved for not less than two years from the date of the last entry in the register or the date of the prescription as the case may be.
5-A. Drugs supplied by a hospital or dispensary maintained or supported by Government or a local body or by charity or voluntary subscrition.	The provisions of Chapter IV of the Act and the Rules thereunder which require them to be covered by a sale licence subject to the following conditions:— (1) the dispensing and supply of drugs shall be carried out by or under the supervision of a qualified person;

Class of Drugs	*Extent and Conditions of Exemption*
	(2) the premises where drugs are supplied or stocked shall be open to inspection by an Inspector appointed under the Drugs Act who can, if necessary, take sample for test;
	(3) the drugs shall be stored under proper storage conditions;
	(4) condition 3 under Rule 65 shall be complied with.

ENCLOSURE L

No. F. 1-35/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 24th June, 1957.

FROM

Shri P. M. Nabar,
Officer on Special Duty,

To

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services.
New Delhi.

SUBJECT :—*Drugs Rules* 1945—*Amendment of Schedule K.*

SIR,

I am directed to say that the definition of the term 'drug' in the Drugs Act, 1940, was amplified by the Drugs (Amendment) Act, 1955, to cover such insecticides, as may be notified by the Central Government, Accordingly a Notification was issued on the 20th October, 1956 under No. F. 1-10/56-D, declaring Pyrethrum and its formulations and DDT and its formulations as 'Drug'. The result of this Notification has been that these insecticides being "drug" would be subject to the same conditions as are applicable to all other drugs *viz.*, they can be manufactured against a licence secured under the Drugs Act and sold only by those parties who have sale licences under the Drugs Act.

2. The trade represented that after the issue of the above Notification considerable hardship will be caused to the consumers. This matter was examined by the Drugs Consultative Committee at their meeting held on the 7th and 8th March, 1957. The Committee recommended *vide* para 16 of the minutes of their meeting (copy attached) that whereas the manufacture and standards of such insecticides should be controlled rigorously, their sale should be exempted from the requirement of sale licence under

the Drugs Rules. The Committee desired that suitable exemption may be provided in the Drugs Rules. It is accordingly proposed to amend Schedule K of the Drugs Rules as follows: —

11.	Insecticides and formulations of insecticides.	The provisions of Chapters IV of the Act and the Rules thereunder which require them to be covered by sale licence.

It is requested that the matter may kindly be placed before the Drugs Technical Advisory Board and the views may be communicated to this Ministry in due course.

Yours faithfully,
(Sd.) P. M. NABAR,
Officer on Special Duty.

Minutes of the Fourth Meeting of the Drugs Consultative Committee held on the 7th & 8th March 1957

16. The Committee recommended that insecticides and formulations of insecticides should be exempted from the necessity of being sold by only dealers who hold sale licences under the Drugs Act and that suitable exemption for this purpose should be provided in the Schedule to the Drugs Rules. The manufacture and standards of such insecticides should, however, be controlled rigorously.

ENCLOSURE M

No. F. 1-36/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 24th June, 1957.

FROM

Shri P. M. Nabar,
Officer on Special Duty.

To

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services.
New Delhi.

SUBJECT :—*Drugs Rules*, 1945—*Restricted Licences for sale of drugs—Proposal that such licences should be confined to only certain specified classes of household remedies.*

SIR,

At their meeting on the 7th and 8th March, 1957, the Drugs Consultative Committee among other things considered the question of grant of restricted licences under the Drugs Rules, 1945. In accordance with the

existing Drugs Rules restricted licences can be granted to those drugs sale of which do not require the supervision of a qualified person. Thus the range of items that could be sold against such restricted licences is wide enough to cover spirituous preparations etc., though the intention was that such licences should cover only common household remedies. For the purpose of rectifying this discrepancy, the Drugs Consultative Committee recommended *vide* para. 14 of their minutes of the meeting (copy enclosed) that suitable amendments may be made in the licence forms and in the Drugs Rules so as to restrict the scope of restricted licences to only household remedies.

2. It will, therefore, be necessary to amend the Drugs Rules, 1945, as indicated in the attached list. I am to request that the matter may kindly be placed before the Drugs Technical Advisory Board and their views may kindly be communicated to this Ministry in due course.

Yours faithfully,

(Sd.) P. M. NABAR,

Officer on Special Duty.

Minutes of the Fourth Meeting of the Drugs Consultative Committee held on 7th & 8th March, 1957

14. The Committee recommended that:—

(a) Restricted licences should be issued only to cover the sale of household remedies and not other drugs such as tinctures. antibiotics etc. Such licences can be granted to parties which do not normally deal in drugs alone,

(b) Itinerant vendor licences should be granted only in sparsely populated areas where normal channels of distribution of drugs are not operative,

(c) Distribution of drugs through mobile vans may be covered by intinerant vendor licences,

(d) Itinerant vendor licences should not be granted to individuals for hawking drugs from door to door, and

(e) The licences forms in respect of restricted licences should be changed so as to make it possible for the licensing authority to indicate the particular category of drugs which could be sold by the licensee.

Amendments in the Drugs Rules

(a) In rule 61, after sub-rule (1), the following proviso shall be added, *viz.* :—

"Provided that a licence in form 20-A shall be valid for only such drugs as are specified in the licence".

(b) In rule 61, after sub-rule (2), the following proviso shall be added, *viz.* :—

"Provided that a licence in form 21-A shall be valid for only such drugs as are specified in the licence".

(c) In form 19-A, para 3 may be substituted by :—

"3. Names or classes of drugs proposed to be sold".

(d) Para 1 of form 20-A may be substituted by the following:—

"1.....is hereby licensed to sell, stock or exhibit for sale or distribute on the premises situated at/as vendor in the area.....the following drugs, being drugs other than these specified in Schedules C and C(1) of the Drugs Rules 1945 subject to the conditions specified below and to the provisions of the Drugs Act, 1940 and the rules thereunder."

(e) Para 1 of form 21-A may be substituted by the following :—

"1.....is hereby licensed to sell, stock and exhibit for sale and distribute by retail on the premises situated at/as vendor in the area .....the following drugs, being drugs other than those specified in Schedules C&C(1) to the Drugs Rules, 1945, subject to the conditions specified below and to the provisions of the Drugs Act, 1940, and the rules thereunder."

ENCLOSURE N

No. F. 1-34/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 24th June, 1957.

FROM

Shri D. J. Balaraj, I.A.S.,
Deputy Secretary to the Government.

To

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT :—*Repacking of drugs—Special provisions of licences under the Drugs Rules.*

Sir,

I am directed to say that at the fourth meeting of the Drugs Consultative Committee held on the 7th and 8th March, 1957, the question arose whether the conditions for the grant of licences to simple repackers should be made the same as those now prescribed for regular manufacturers. The Committee decided that the pre-requisite conditions for the grant of licences to cover repacking activities need not be stringent in respect of competent technical personnel, accommodation, equipment etc., as in the case of manufacturers and the licence fees for such licences may be reduced suitably. Accordingly the Committee recommended that separate application and licence forms should be introduced for "repacking" licences and the consequential changes made in the Drugs Rules. In this connection para 32 of the minutes of the meeting of the Committee are attached.

2. After examining the matter the Government of India are of the view that the recommendations of the Drugs Consultative Committee may be accepted. It is, therefore, proposed to amend the Drugs Rules, 1945 in the manner indicated in the attached list. I am to request that the matter may kindly be placed before the Drugs Technical Advisory Board and their view may be communicated to this Ministry in due course.

Yours faithfully,
(Sd.) D. J. BALRAJ,
Deputy Secretary.

Minutes of the Fourth Meeting of the Drugs Consultative Committee held on 7th & 8th March, 1957

32. Consequent on the introduction of the definition for the term "manufacture" in the Drugs Act which includes within its scope repacking activities, the question arose whether the conditions for the grant of licences to simple repackers should be made the same as these now prescribed for regular manufacturers in the Drugs Rules. The Committee decided that the pre-requisite conditions for the grant of licences to cover repacking activities need not be strigent in respect of competent technical personnel, accommodation, equipment etc., as in the case of manufacturers and the licence fees for such licences may be reduced suitably. The Commitee recommended that separate application and licence forms should be introduced for "repacking" licences and the consequential changes made in the Drugs Rules.

Proposed Amendments to Drugs Rules

(A) A new Rule 69(B) reading as follows may be introduced :—

69(B) "Licences for repacking for sale or distribution of drugs".

1. Application for the grant or renewal of licences for repacking for sale or distribution of drugs shall be made to the Licensing Authority in Form 24-B and shall be accompanied by a fee of Rs. 40.

2. The Licensing Authority shall, before the grant of a licence for repacking, satisfy himself that the repacking operations will be carried out under sanitary conditions and under the supervision of a competent person, that adequate equipment is provided and that the licensee has arrangements to test the drugs for which the application is made either in his own premises or elsewhere.

(B) A new Rule 70(B) reading as follows may be introduced :—

70(B) "Form of licence to repack for sale or distribution of drugs".

A licence to repack for sale or distribution of drugs shall be issued in Form 25-B and shall apply only to these items which are specified in the licence.

(c) The following new forms may be introduced in Schedule A to the Drugs Rules:—

FORM 24-B

(*See* rule 69-B)

Application for grant or renewal of a licence to repack for sale or distribution of drugs.

1. I/We.....of.....hereby apply for grant/renewal of licence to repack the following drugs at the premises situated at.....

2. Name of drugs.....

3. Name, qualification and experience of competent staff.....

4. Details of arrangements for testing of drugs.

5. A fee of Rs. 40 has been credited to Government under the head of account.....

Signature of Applicant.

Date :

FORM 25-B

(*See* rule 70-B)

Licence to repack for sale or distribution of drugs.

1. Number of licence and date of issue.....

2. .....of.....is hereby granted a licence to repack the following drugs for sale or distribution on the premises situated at..... under the supervision of the following staff.

(a) Names of drugs.

(b) Details of competent staff.

3. The licence shall be in force for a period of 2 years from the date of issue.

4. The licence authorizes the sale by way of wholesale dealing by the licensee and storage for sale by the licensee of the drugs repacked under the licence subject to conditions applicable to licences for sale.

5. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs Act, 1940.

Signature.....

Designation.....

Date :

Conditions :—

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs Act, 1940.

2. Any change in the expert staff named in the licence shall be forthwith reported to the licensing Authority.

3. If the licensee wants to repack for sale additional drugs he should apply to the licensing Authority for the necessary endorsement to this licence. This licence will be deemed to extend to the categories of drugs so endorsed.

4. The drugs repacked under this licence shall bear on their label apart from other particulars required by these Rules, the name and address of the licensee who will be held responsible for the quality of the drugs.

ENCLOSURE O

No. F. 1-33/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, dated the 21st June, 1957.

FROM

Shri D. J. Balaraj I.A.S.,
Deputy Secretary to the Government of India.

TO

All State Governments and Union Territories.

SUBJECT :—*Drugs Rules, 1945—Standards for Pencillin Procaine Aluminium Monostearate.*

SIR,

I am directed to say that the standards for Penicillin Procaine with Aluminium Monostearate (P.A.M.) are available in U.S.P. XV. Since U.S.P. XV is a prescribed pharmacopoeia under the Drugs Act. 1940, this drug would be of 'standard quality' if it conforms to the standards laid down in U.S.P. The World Health Organisation has, however, approved of this drug as a drug of choice in the treatment of veneral diseases and has laid down additional standards for the quality and purity. A copy of the Organisation's Standards for P.A.M. is attached.

2. Since P.A.M. is used on a large scale in India in the mass V. D. Control campaign, it is essential that the P.A.M. available in the market whether imported or manufactured in the country, should conform to the standards laid down for it by the World Health Organisation. This will ensure success of the V. D. Control campaign.

3. In accordance with Rule 111 of Drugs Rules, 1945, every substance specified in Schedules C and C(1) intended for sale shall conform with the standards of strength, quality and purity specified in the said Rules and Schedule F. The Government of India, therefore, propose that additional standards for P.A.M. may be incorporated in Schedule F of the Drugs Rules, 1945. It is requested that your views in the matter may kindly be communicated to this Ministry at an early date.

Yours faithfully,
(Sd.) X X X,
Deputy Secretary.

No. 1-33/57-D

Copy, with a copy of the enclosures forwarded to the Secretary, D.T. A.B., C/o Directorate General of Health Services, New Delhi. It is requested that the matter may kindly be placed before the D.T.A.B. and the views of the Board may kindly be communicated to this Ministry in due course.

Copy forwarded for information to the Director General of Health Services with reference to his U.O. No. 8-14/57-D, dated the 10th June, 1957.

(By order),
(Sd.) X X X,
Section Officer.

COPY OF ANNEX. 5 OF THE W.H.O. TECHNICAL REPORT SERIES NO. 63.

Monograph on Oily Injection of Procaine Benzylpenicillin

Oily injection of procaine benzylpenicillin is a sterile suspension of procaine benzylpenicillin in a suitable oil containing 2% w/v of aluminium monostearate. It contains not less than 90% of the number of International Units of penicillin stated on the label.

Consistence.—Passes readily through a hypodermic needle of internal diameter 0·895—0·905 mm at 25°C.

Particle Size.—The diameter of not less than 65% of the particles does not exceed 5 u.

Stability.—When shaken by hand it forms a suspension which is stable for 48 hours at 37°C; if any separation takes place during this time, the thickness of the oily layer should not be greater than 3 mm.

Water.—Not more than 1·4%.

Sterility.—After the addition of a quantity of solution of penicillinase R or other suitable inactivating agent adequate to ensure complete inactivation of the penicillin present, complies with the tests for sterility.

Blood-Level Duration.—When determined as described in the Appendix, a quantity equivalent to 300,000 International Units of penicillin produces blood-serum levels at 72 hours of not less than 0·03 International Units per ml in not less than half the number of subjects used.

Other Requirements.—Complies with the requirements stated under "Injections".

Assay.—The potency is determined by the method required by the law of the country concerned; a suitable method is included in the Appendix.

Storage.—Oily injection of procaine benzylpenicillin should be stored in a cool place, but not in a refrigerator.

6—1 M of Health/58 (18th Meeting)

Labelling.—The label on the container must state; (1) the name of the injection, (2) the number of International Units in 1 ml; (3) "For intramuscular use only".

When oily injection of procaine benzylpenicillin is prescribed, no strength being stated, oily injection of procaine benzylpenicillin containing 300,000 International Units per ml. shall be dispensed.

APPENDIX

Blood-level Duration Test

1. **The Test.**—Ten or more persons in good health and weighing between 60 and 90 kg who have not taken penicillin or similar antibiotics in any form during the previous seven days are selected as test subjects. Each subject is injected with a quantity of the oily injection of procaine benzylpenicillin under the test equivalent to 300,000 International Units of penicillin. A 5 ml sample of venous blood is withdrawn 72 hours after the injection, and if desirable, at other times during the test period; the subject should receive no other antibiotic during this period. The blood is allowed to clot, and the serum is separated by centrifuging and transferred immediately to a sterile tube. If it is not to be tested on the same day, the serum is frozen at—20°C or below and stored frozen. The penicillin content of the samples of serum is determined as described below:

2. **The Blood Serum Assay (Sarcina Lutea Method).**—The antibiotic potency of a sample of serum presumed to contain penicillin is determined by comparing the volumes of it required to inhibit the growth of a standard strain of Sarcina Lutea with the quantities of a standard preparation of penicillin required to produce the same degrees of inhibition.

International Standard Preparation and Unit :

Working standard solution.—To about 0·015 g of the International Standard preparation of penicillin, accurately weighed in an atmosphere of 50% relative humidity or less, sterile 1% phosphate buffer, pH 6·0 is added to make a stock solution containing 0·6 mg per ml. (1,000 International Unit per ml). This solution is kept at a temperature of about 10°C and used for two days only. On the day of the assay, this stock solution is diluted to 1·0 International Unit per ml, using the above-mentioned buffer. Working dilutions of the latter solution are prepared using as the diluent boving albumin TS which, before use, has been filtered through a bacteria-proof filter and tested on plates for inhibition of Sarcina lutea under the conditions outlined below. Bovine albumin TS which shows inhibition under these conditions should not be used.

Preparations of serum samples.—Serum samples expected to contain not more than 0·4 International Unit per ml need not be diluted. Samples expected to have a potency greater than 0·4 International Unit per ml should be diluted to about 0·1 International Unit per ml with bovine albumin TS known to have not anti-biotic activity.

Suggested Method.—The geneal procedure described under "Biological Assay of Penicillin" is applied with the specific changes set forth below.

Media.—Nutrient agar for the base layer and for carrying the test organism is prepared as follows :—

Peptone	6·0 g.
Pancreatic casein digest	4·0 g.
Yeast extract	3·0 g.
Beef Extract	1·5 g.
Glucose R	1·0 g.
Agar R	15·0 g.
Water, sufficient to produce	1,000 ml.

The reaction is adjusted so that the pH is 6·9 to 7·0 after autoclaving. at 121° for 20 minutes.

Agar for the inoculated layer is prepared as above but omitting the pancreatic digest of casein and adjusting the reaction so that the pH is 6·5 to 6·6 after autoclaving.

Nutrient broth for preparing an inoculum of the test organism is prepared as follows:—

Peptone	5·0 g.
Yeast Extract	1·5 g.
Beef Extract	1·5 g.
Sodium chloride R	3·5 g.
Glucose R	1·0 g.
Dibasic potassium phosphate R	3·68 g.
Monobasic potassium phosphate R	1·32 g.
Water, sufficient to produce	1,000 ml.

The reaction is adjsted so that the pH is 6·9 to 7·0 after autoclaving

Instead of preparing the media from the individual ingredients specified, they may be prepared from a dehydrated mixture which, when reconstituted with water, has the specified composition. Minor modifications of the individual ingredients specified are permissible if the resulting media passes growth promoting properties at least equal to the media described.

Preparation of bulk culture suspension.—The test organism is Sarcina Lutea (P.C.I. 1001 and American Type Culture Collection 9341). The test organism is maintained on slants of nutrient agar as described for the base layer and transferred to a fresh agarslant once a week. A suspension of the test organism is prepared as follows : An agar plant is streaked heavily with the test organism and incubated for 24 hours at 26°C. The growth is washed off with 3·0 ml of nutrient broth. The suspension so obtained is used to inoculate the surface of a Roux bottle containing 300 ml. of this nutrient agar. The suspension is spread over the entire surface with the aid of sterile glass-beads. The bottle is incubated for 24 hours at 20°C. Growth is washed from the agar surface with 15 ml of nutrient broth prepared as described. The density of organisms in this bulk suspension is tested by diluting 1 part with 9 parts of nutrient broth, and measuring the light transmission at about 650 mu in a suitable photo electric colorimeter. If the light transmission is about 10% of that of sterile nutrient broth similarly

treated, the bulk suspension is satisfactory for use. Otherwise, the bulk suspension is adjusted by dilution so that a 10% dilution of the adjusted suspension gives about 10% light transmission. The bulk suspension, adjusted by dilution if necessary, may be used for at least two weeks.

Preparation of plates.—On the day of the assay, 10 ml of base layer agar medium is added to Petri Plates (20mm × 100mm). The agar is distributed evenly in the plates and allowed to harden.

0·4 ml of bulk culture suspension is added to 100 ml of the agar prepared for the inoculated layer, previously melted and cooled to 40°C. The culture and agar are thoroughly mixed and 4 ml are added to each of the plates containing the 10 ml of the hardened uninoculated agar. The inoculated agar is spread evenly over the surface by tilting the plates back and forth. The plates are covered with procelain covers, glazed on the outside.

Standard curve and assay procedure.—Six cylinders are placed on the inoculated agar surface so that they are at approximately 60° intervals on a 2·8 cm radius. One plate is used for each sample. Three cylinders on each plate are filled with the 0·1 ml International Unit per ml dilution of the International Standard Preparation, and three cylinders with the serum sample under test, alternating standard and sample. The plates are incubated for 16 to 18 hours at 26°C and the diameter of each zone of inhibition is measured. At the same time, a standard curve is prepared using concentrations of 0·03, 0·05, 0·10, 0·20, and 0·40 International Units per ml of the International Standard Preparation in bovine albumin TS. Three plates are used for the determination of each point on the curve, making a total of 15 plates. On each of three plates, three cylinders are filled with the 0·1 International Unit per ml dilution of the the International Standards Preparation, and the other three are filled with one of the five other diluted solutions of the International Standard Preparation. After the plates have been incubated the diameters of the zones of inhibition are read. Thus, three will be 45 determinations at 0·1 International Unit and nine determinations at each of the other points on the curve. The readings of 0·1 ml International Unit per ml. concentration and the readings of the point tested for each set of three plates are averaged and also all 45 readings of the 0·1 International Unit per ml concentration. The average of the 0·1 International Unit per ml concentration is the correction point for the curve. The average value obtained for each point is corrected to the figure it would be of the 0·1 International Unit per ml readings for that set of three plates were the same as the correction point. Thus, if the average of the 45 readings of the 0·1 International Unit concentration is 20·0 mm. and the average of the 0·1 International Unit concentration of a given set of three plates is 19·8 mm, the correction is + 0·2 mm. If the average reading of the 0·05 International Unit concentration of these same three plates is 17·0 mm, the corrected value becomes 17·2 mm. The corrected values, including the average of the 0·1 International Unit per ml concentration, are plotted on 2 cycle semi-logarithmic graph paper, using the concentration in International Units per ml as the ordinate (the logarithmic scale) and the diameter of the zone of inhibition as the abscissa. The standard curve is drawn through these points. To estimate the concentration of penicillin in the sample, the zone readings of the International Standard and the zone readings of the sample on the I plate used are averaged. If the sample gives a larger average zone—a size than the average of the International Standard, the difference between the two averages is added to the 0·1 International Unit zone on the standard curve. If the average sample value is lower than the

standard value, the difference between the average is substracted from the 0·1 International Unit value on the curve. From the curve are read the concentrations of penicillin, in International Units per ml. corresponding to these corrected average zone sizes.

The letter "TS" (test solution) and "R" (reagent) refer to the solutions and reagents listed in the Ph. I.

ENCLOSURE P

No. F. 1-52/56-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 26th June, 1957.

FROM

Shri P. M. Nabar,
Officer on Special Duty.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services
New Delhi.

SUBJECT :—*Drugs Rules,* 1945—*Recognition of preparations covered by earlier editions of Pharmacopoeias—Amendment of the Schedule to the Drugs Act,* 1940.

SIR,

I am directed to refer to this Ministry's endorsement No. F. 1-56/55-D, dated the 23rd December, 1955, on the subject mentioned above, and to say that the matter was placed before the Drugs Consultative Committee at their fourth meeting held on the 7th and 8th March, 1957 *vide* item 2 of the agenda (copy attached). The committee reiterated their previous recommendations that the earlier editions of the prescribed pharmacopoeias need not be recognised as "standards" under Rule 124 of the Drugs Rules and that the present provision in the Schedule to Drugs Act recognising the "Current edition" of the prescribed pharmacopoeias should continue and also made the following further recommendations:—

(a) The Schedule to the Drugs Act may be amended so as to permit Government Analysts to employ any tests to establish the identity, purity and strength of the items wherever adequate tests were not laid down for this purpose in the prescribed pharmacopoeias.

(b) A provision may be made in the Drugs Act for approval by Central Government of the formulae of patent and proprietary medicines before they are imported, manufactured or sold in order to obviate the manufacture and sale of preparations of doubtful medicinal value.

2. It is requested that the matter may please be placed before the Drugs Technical Advisory Board. The views of the Board may kindly be intimated to this Ministry in due course.

Yours faithfully,

(Sd.) P. M. NABAR,

Officer on Special Duty.

EXTRACT FROM THE MINUTES OF THE FOURTH MEETING OF THE DRUGS CONSULTATIVE COMMITTEE HELD ON 7TH AND 8TH MARCH 1957.

Item 2 of the Agenda

Examination of Rule 124 *of the Drugs Rules* vis-a-vis *the enforcement of the Drugs Act with particular reference to the recognition of earlier editions of the prescribed pharmacopoeias*

3. Some of the members were of the view that the standards for most of the preparations covered by the earlier editions of the pharmacopoeias, especially the tinctures, and spirituous preparations were not adequate and that as a result it was difficult to control such preparations from the quality point of view. The States where prohibition is in force were particularly faced with the problem of widespread sale of such tinctures which were misused as substitutes for alcohol and for which no standards other than alcohol content were specifically laid down in the earlier pharmacopoeias. If the earlier Pharmacopoeias were not recognised as "Standard", it would be possible to exercise over such spirituous preparation a greater measure of control as patent or proprietary medicine. As against this view, it was contended that several preparations in the latest edition of the pharmacopoeias, particularly the tinctures etc., did not have adequate standards and that consequently the whole question should be viewed *not* from the prohibition angle but from the point of view of laying down comprehensive standards for these items.

4. After detailed discussion the Committee reiterated its decision that the earlier editions of the prescribed pharmacopoeias need *not* be recognised as "Standards" under Rule 124 of the Drugs Rules and that the present provision in the Schedule to the Drugs Act recognising the "Current editions" of the prescribed pharmacopoeias should continue. It was at the same time considered by the Committee that several preparations covered by the B.P., B.P.C., etc. did not have adequate standards. In the interests of the Drugs Standard Control, the Committee felt that the Schedule to the Act should be amended so as to permit Government Analysts to employ and tests to establish the identity, purity and strength of the items wherever adequate standards were *not* laid down for this purpose in the prescribed pharmacopoeias. The Committee further recommended that provision should be made in the Drugs Act for approval by Central Government of the formulae of patent and proprietary medicines before they are imported, manufactured or sold in order to obviate the manufacture and sale of preparations of doubtful medicinal value. The Committee also recommended that the question whether the definition of the term "patent or proprietary medicine" in the Drugs Act requires to be amended should be examined.

ENCLOSURE Q

No. 1-38/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, dated the 27th June, 1957.

FROM

Shri D. J. Balaraj, I. A. S.,
Deputy Secretary to the Government of India.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT :—*Drugs Rules*, 1945—*Amendment of Rule* 65(9).

SIR,

I am directed to say that in accordance with the existing provisions of sub-rule (9) of Rule 65 of Drugs Rules, 1945, "substances specified in Schedule H and preparations containing such substances shall not be sold by retail except on and in accordance with a prescription of a registered medical practitioner". The State Drug Standard Control Authorities represented at the fourth meeting of the Drugs Consultative Committee held on the 7th and 8th March, 1957, that

(i) Before action can be taken for the contravention of sub-rule (9) of Rule 65, the Inspector has to prove that the drug was actually sold.

(ii) Often the seller gets off on the plea that he did not actually sell the drugs and in the absence of cash memo it is difficult to prove 'sale'.

2. The Drugs Consultative Committee recommended *vide* para 31 of the minutes of their meeting (copy enclosed) that the word "sold" in Rule 65(9) should be substituted by the word "supplied". The Government of India have examined the matter and it is proposed to amend the existing Rule 65(9) so as to read as follows :—

> "Substances specified in Schedule H and preparations containing such substances shall not be sold or supplied by retail except on and in accordance with a prescription of a registered medical practitioner."

3 It is requested that the matter may kindly be placed before the Drugs Technical Advisory Board and their views may be communicated to this Ministry in due course.

Yours faithfully,

(Sd.) D. J. BALARAJ,

Deputy Secretary.

EXTRACT FROM THE MINUTES OF THE 4TH MEETING OF THE DRUGS CONSULTATIVE COMMITTEE HELD ON THE 7TH AND 8TH MARCH, 1957.

It was represented that the wording of Rule 65(9) was such as to throw the onus of establishing the "sale" of Schedule H drugs on the inspector. The Committee recommended that the word "sold" in Rule 65(9) should be substituted by the word "supplied".

ENCLOSURE R

No. 1-37/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 27th June, 1957.

FROM

Shri D. J. Balaraj, I.A.S.,
Deputy Secretary to the Government of India.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services.
New Delhi.

SUBJECT :—*Drugs Rules, 1945—Proposal for the amendment of provisions for labelling in Part I of Schedule F in respect of Cholera Vaccine.*

SIR,

I am directed to say that the Director, Haffkine Institute has suggested that the provisions for labelling of Cholera Vaccine with the number of micro-organisms per c.c. as laid down in Part I of Schedule to the Drugs Rules should be amended suitably. The Haffkine Institute is at present manufacturing Cholera Vaccine in a liquid medium of Casein Hydrolysate where considerable autolysis occurs and it is not possible to count the number of micro-organisms per c.c. of the vaccine. Nevertheless the Cholera Vaccine made by the Haffkine Institute is as good as any other Cholera Vaccine made in the country as well as abroad. The Director, Haffkine Institute has proposed *vide* a copy of his letter attached that the provisions for labelling Cholera Vaccine with the number of micro-organisms as laid down in Part I of Schedule F may be amended so that the Cholera Vaccine made by them need not be labelled with the number of micro-organisms etc. The matter was referred to the Director, Central Research Institute, Kasauli and Director, Central Drugs Research Institute, Lucknow for their comments and copies of their replies are attached.

2. It is requested that the matter may kindly be placed before the Drugs Technical Advisory Board and their views may be communicated to this Ministry in due course.

Yours faithfully,

(Sd.) D. J. BALARAJ,
Deputy Secretary.

COPY OF OUR LETTER NO. 16936 DATED THE 30TH MAY, 1955 ADDRESSED TO THE SECRETARY, DRUGS TECHNICAL ADVISORY BOARD, OFFICE OF THE DIRECTOR GENERAL OF HEALTH SERVICES, GOVERNMENT OF INDIA, NEW DELHI.

We are at present preparing a new layout for our vaccine labels according to the Drugs Control Act and I would like to invite your attention to some difficulty met with in complying the provision of Rule No. 6 of Schedule F, Part I, Bombay Drug Rules, 1946.

According to the provisions of the rule the label on the container shall indicate the composition of the Vaccine by reference either (a) to the number of micro-organisms per cc. or (b) to the weight of the substance of the micro-organisms per cc or (c) to the number of micro-organisms or the dried substance of the micro-organisms used in preparing I cc of the finished product.

You may be aware of the fact that this Institute prepared two vaccines Anti-Plague Vaccine and Anti-Cholera Vaccine in a liquid medium namely casein hydrolysate. The incubation period for the growth of plague in this medium is 14 days and that for Cholera is 3 days. During such a long period of incubation considerable autolysis of the organisms takes place in the culture medium. Specially in the case of cholera though the incubation period is comparatively shorter the autolysis is very rapid and it is impossible to take an accurate count of the number of organisms present in a specifie volume of the culture at the end of this incubation period. A rough estimate by haemocytometer method shows this number to be between 3000-5000 millions per c.c. but this excludes the large number of organisms that undergone the lysis. Ordinarily the Anti-cholera agar vaccine contains 8.000 millions organism per cc.

Though no count of the organisms is made for liquid vaccines we test them by the mouse protection test.

This biological test has shown that our liquid medium vaccines is as good as, if not superior to, any other agar vaccine produced in this as well as in foreign countries. This also incidentally shows that the final count as obtained in the case of our liquid vaccine has no correlation with the efficacy of the vaccine.

For your information I may also state that this question was raised with reference to the International Sanitary Regulations, when some countries demanded the numerical content of cholera vaccine on inoculation certificates of International passengers and it has been accepted now by almost all countries that such a statement is not necessary. The W.H.O. expert committee on epidemeology and quarantine has made no such recommendations regarding the statement of the numerical strength of cholera vaccine.

I, therefore, feel that provisions of the Rule 5 mentioned above can be suitably modified in case of liquid vaccine and I have to request you therefore to move in the matter with a view to introduce the necessary amendments in Drugs Rules. Appropriate State Drug Control authorities may also be instructed not to enforce the rule until this question is finally settled.

I am confident that you will realise the technical difficulties involved in meeting these provisions of the Drug Rules in the case of liquid vaccine, and therefore initiate appropriate action in the matter as early as possible.

(Sd.) P. M. WAGLE,
M. D. D.P.H.
Director, Haffkine Institute.

COPY OF LETTER NO. SV/20993/A DATED THE 11TH AUGUST, 1956 FROM THE DIRECTOR, CENTRAL RESEARCH INSTITUTE, P. O. KASAULI, TO THE DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI.

SUBJECT :—*Showing the number of micro-organisms of Cholera Vaccine per c.c. on the label of the container as required under the provisions of Schedule F to the Drugs Rules*, 1945.

Please refer to your letter No. 8-40/56-D, dated 31-7-56.

Cholera Vaccine prepared at this Institute is a killed suspension of V. Cholerae grown on nutrient agar and is standardised to contain 8,000 million micro-organisms per c.c. We have no experience of the manufacture of the vaccine prepared in liquid medium such as Casein hydrolysate. The pleas put forward by the Director, Haffkine Institute, Bombay, that considerable autolysis occurs during the prolonged incubation of the growth in the liquid medium and that this does not permit the accurate estimation of bacterial count is valid to a certain extent. Under the provision of Rule 6 of Schedule F, Part I Bombay Drugs Rules, option has been given to the manufacturers either to state in numerical figures the bacterial count or weight of the bacterial substance per cc of the vaccine on the label. It should be feasible for the manufacturers to estimate the weight of the total bacterial contents per cc in the liquid vaccine and thus comply with the provisions of these Drugs Rule. If these provisions are laxed or omitted I am afraid there would be no check over the quality of the vaccine so far the total bacterial contents are concerned.

The mouse protection test has not been extended to any official recognition so far and the potency figures will not convey much significance to the medical practitioner and Public Health Administrater, who is accustomed to rely on the number of bacteria per cc contained in the vaccine.

COPY OF D. O. NO. DIR (3)/56-DC, DATED AUGUST 24, 1956 FROM DR. B. MUKERJI, DIRECTOR, CENTRAL DRUG RESEARCH INSTITUTE, CHATTAR MANZIL PALACE, LUCKNOW TO SHRI P. M. NAMBAR, DRUGS CONTROLLER (INDIA), DIRECTORATE GENERAL OF HEALTH SERVICES, NEW DELHI.

I am so sorry I could not reply to your D.O. letter No. 8-40/56-D, dated the 31st July, 1956 regarding anti-cholera vaccine earlier. No standard for this vaccine has yet been fixed by the W.H.O. In fact this question was discussed at length at two meetings and it was found difficult to lay down correct standard because of the variations in the medium used in the manufacture of cholera vaccine in different centres of the world. In India, however, cholera vaccine is such an important item that it was considered desirable to fix standards so that the materials prepared by different centres in India do not vary significantly from batch to batch. The figure regarding bacterial count that was given in the Indian Pharmacopoeia holds good for a vaccine grown in agar medium. The count, 8000 million organisms per cc. would naturally not be possible to get in a vaccine which is grown in Casein hydrolysate medium.

The Director, Haffkine Institute claims that the "Cholera Vaccine made in his institute with Casein hydrolysate vaccine medium is as good, if not superior, to any other agar grown vaccine...". This is probably based on comparative 'mouse protection test'. Though this may not have any correlation to human immunisation, there can be no objection to have this as one of

the standards for vaccine manufacture. The inability to express the vaccine in terms of total cellular count (inclusive of lysed calls) shall not be drawback if the manufacturer is able to state on the label that the vaccine is as good as any other agar grown vaccine with a organismal count of 8000 million per cc. Experimental protocols in support of this may be made available to the Drugs Controller whenever required.

If we have to recognise the Haffkine made vaccine in casein hydrolysate medium we have to alter the monograph in the Indian Pharmacopoeia. The Director, Haffkine Institute may kindly be asked to supply you with the standard protocols of mouse protection test made on their vaccine. We may consider this point carefully in an Expert Committee meeting and redraft the monograph on cholera vaccine so that both types of vaccine can be accepted as standard products.

If any further clarification is considered necessary, I shall be glad to discuss the matter with you when I am in Delhi next.

With kind regards.

ENCLOSURE S

No. F. 1-39/57-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 27th June, 1957.

FROM

Shri D. J. Balaraj, I.A.S.,
Deputy Secretary to the Government of India.

TO

The Secretary,
Drugs Technical Advisory Board,
C/o Directorate General of Health Services,
New Delhi.

SUBJECT :—*Drugs Rules* 1945—*Draft standards for "Crude Liver Extract for parenteral administration" for inclusion in Schedule F.*

SIR,

I am directed to refer to this Ministry's Notification No. F. 1-31/55-D, dated the 10th September, 1955 (copy enclosed) and to say that comments received from the various parties on the draft standards for "Crude Liver Extract for parenteral administration" to be included in Schedule F of Drugs Rules, 1945, are attached herewith. It is requested that the matter may kindly be placed before the Drugs Technical Advisory Board and their comments may kindly be communicated to this Ministry in due course.

Yours faithfully,

(Sd.) D. J. BALARAJ,

Deputy Secretary.

(To be published in Part II, Section A of the Gazette of India dated the 17th September, 1955.)

No. F. 1-31/55-D

GOVERNMENT OF INDIA

MINISTRY OF HEALTH

New Delhi-2, the 10th September, 1955.

NOTIFICATION

The following draft of a further amendment in the Drugs Rules, 1945 which it is proposed to make after consultation with the Drugs Technical Advisory Board in exercise of the powers conferred by Sections 12 and 33 of the Drugs Act, 1940 (XXIII of 1940), is published as required by the said sections, for the information of persons likely to be affected thereby and notice is given that the said draft will be taken into consideration after the 17th December, 1955.

2. Any objections or suggestions which may be received from any person with respect to the said draft, before the date so specified will be considered by the Central Government.

Draft Amendment

In Part IX of Schedule F to the said Rules after the entry "Any other preparation in form to be administered parenterally" the following shall be added namely :—

(A) LIVER EXTRACT CRUDE FOR PARENTERAL ADMINISTRATION.

CRUDE LIVER EXTRACT FOR PARENTERAL ADMINISTRATION

Introduction.—Crude liver extract for parenteral use is a sterile solution in water for injection containing that specific thermostable principle from mamalian livers which increases the number of red-blood-corpuscles in the blood of persons suffering from macrocytic anaemias.

The approximate antianaemia potency of Crude Liver extract for parenteral use is expressed in terms of its cyanocobalamine (vitamin B12.) content which should be determined by the microbiological method using L leichmanil 313 and should be less than 2 micrograms of cyanocobalamine (vitamin B_{12}) per ml. A suitable preservative shall be added.

2. **Proper name.**—The proper name of the preparation is "Injection of Crude Liver Extract".

3. **Description.**—A brownish liquid which at times may show slight turbidity or precipitate.

4. **Test.**—(a) *Reaction.*—As far as possible neutral and in no case should the acidity be higher than that corresponding to pH 5·0.

(b) *Total solids.*—Evaporate to dryness on a water bath, dry at 105° for 1 hour and then at 60° in a vacuum for 2 hours; cool in a desiccater and weight. The total solids should not be less than 15%(W/V).

(c) *Limits for proteins.*—The protein nitrogen should not exceed 0·08 per cent as determined by precipitating the proteins with an equal volume of 10 per cent trichlor acetic acid and by estimating the nitrogen content of the precipitate by the micro-kjeldhal method.

(d) *Absence of undue toxicity.*—The test should be performed on a batch of 5 healthy white mice weighing between 17 and 22 g. Interperitoneal injection of the sample in dosage of 0·25 ml per 20 g. of mouse should not cause death of any of the 5 mice tested within a period of 120 hours. If any of the 5 mice dies, the test should be repeated and if there is no mortality in the second batch of 5 mice within a period of 120 hours the sample passes the test.

(e) *Sterility and pyrogen test.*—Complies with sterility and pyrogen tests as laid down for parenteral products in the B. P.

(f) *Potency.*—By the microbiological method specified below:—

MICROBIOLOGICAL ASSAY OF VITAMIN B_{12} ACTIVITY

TITRIMETRIC METHOD

Reagents and Apparatus :

1. *Acid-hydrolysed Casein Solution.*—First prepare "Vitamin-free" casein in the following manner : Place in a flat bottomed flask or carboy 15 litres of distilled water and add with shaking 1Kc. of commercial casein (fat content less than 1%) preventing the formation of lumps. Add 10 ml. of I/N HCI. stir well and allow to stand one hour with occasional shaking. Siphon off the supernatant. Repeat these operations twice more. Wash one more with distilled water by sedimentation and siphoning. Add 15 litres of distilled water and add with stirring 300 ml or more of I/N ammonia till the mixture becomes a thin paste; decant off if any insoluble impurities settle to the Bottom. Add slowly with continuous stirring I/N HCI until the casein coagulates (approximately pH 4·7). Allow the casein to settle, siphon off the supernatant and wash once with distilled water. Strain the casein through a clean muslin. Suspend the wet casein in 7 litres of 95% alcohol stir well for 1 hour and filter through muslin. Suspend the casein in 7 litres of 95 per cent alcohol contained in a 15 litre round-bottomed flask and boil the mixture gently under reflux for 1 hour.

Filter through a wide buchner funnel, wash with 1 litre of hot alcohol and drain off all the alcohol. Spread the casein on a clean enamelled or stainless-steel tray and dry in a vacuum oven at a temperature not exceeding 50°. Alternatively dry the casein under a fan at room temperature and complete the drying in a vacuum desiccator.

Prepare the acid-hydrolyzed casein in the following manner : Mix 100 g. of "vitamin-free" casein and 500 ml of approximately 6 N hydrochloric acid (concentrated hydrochloric acid diluted with an equal volume of distilled water) in a litre flask and autoclave the mixture at 121° (15 lbs. per square inch steam pressure) for 5 hours. Remove most of the hydrochloric acid by distillation under reduced pressure until a thick paste is left behind. Dissolve the paste in 400 ml of distilled water and repeat distillation under reduced pressure until a thick paste remains.

1. Dissolve the paste in about 800 ml of distilled water and adjust the pH of the solution to 3·5 with 10 N sodium hydroxide. Make up the volume to 1 litre with distilled water. Decolorize the solution by stirring with 20 g of activated charcoal for 1 hour; filter through a large fluted

paper or by suction through a buchner funnel. Repeat the treatment with activated charcoal and filration. Place the clear, almost colourless, filtrate in flask stoppered bottle and store in a cool place with the addition of 5 ml of chloroform and a thin layer of toluene. On standing for some days, a precipitate of tyrosine may appear; shake up the solution before using.

2. *Cystine—Tryptophan Solution.*—Suspend 2·0 g of L-cystine and 100 g of L-trytophan (or 2·0 g of DL-tryptophan) in about 400 ml of distilled water. Heat the suspension to about 75° and add 20% hydrochloric acid (1 : 1) dropwise with stirring until the amino acids are completely dissolved. Cool and make up to 500 ml with distilled water. Store in a cool place with the addition of a layer of toluene.

3. *Tomato Juice Filtrate.*—Clarify 1000 ml of commercial canned tomato juice filtration through a wide buchner funnel with the help of 8·0 g of an analytical grade filter aid. Adjust the pH of the clear filtrate to 3·5 with dilute hydrochloric acid, mix it with 10 g of activated charcoal and stir the mixture for half an hour. Filter through a layer of 4 g of filter aid placed on a wide buchner funnel so that a clear, almost colourless, filtrate is obtained. Store the filtrate under a thin layer of toluene in a refrigerator.

4. *Asparagine Solution.*—Dissolve 1·0 of L-asparagine in water and make the volume to 100 ml. Store under toluene in a refrigerator.

5. *Adenine-Guanine-Uracil Solution.*—Suspend 100 mg each of adenine Sulphate (or adenine hydrochloride), guanine hydrochloride and uracial in 5 ml of N hydrochloric acid and dissolve by heating gently. Cool and add water to make the volume 100 ml. Store under a layer of toluene in a refrigerator.

6. *Xanthine Solution.*—Suspend 100 mg of xanthine in 20 ml water, heat the suspension to about 60° and add 3 ml of 10% (w/w) anmonia to dissolve the xanthine. Cool and add water to make the volume 100 ml. Store under a layer of toluene in a refrigerator.

7. *Biotin Stock Solution.*—Dissolve 10 mg. of D-biotin in 200 ml of 50 per cent alcohol and preserve in a refrigerator.

8. *Riboflavin-Thiamine-Biotin-Nicotinic Acid Solution.*—Dissolve in 150 ml of 0·02N acetic acid, 5 mg of riboflavin, mg of thiamine hydrochloride, and 10 mg of nicotinic acid; add 1 ml of biotin stock solution (Reagent No. 7) and make up to 200 ml with 0·02 N acetic acid. Store under a layer of toluene in a refrigerator for not more than two weeks.

9. *D-Aminobenzoic Acid-Pyridoxine-Pyridoxal-Pyridoxamine Solution.*—Dissolve in 200 ml of 25 per cent alcohol, 10 mg of p. aminobenzoic acid, 20 mg of pyridoxine hydrochloride, 20 mg of pyridoxal hydrochloride and 4 mg of pyridoxamine dihydrochloride. Store in refrigerator for not more than two weeks.

10. *Calcium Pantothenate-Folic Acid Solution.*—Dissolve 5 mg. of folic acid in the minimum volume of dilute ammonia and add it to a solution of 25 mg of calcium pantothenate in 500 ml of 25 per cent alcohol. Store in a refrigerator for not more than two weeks.

11. *Salt Solution A.*—Dissolve 5 g of K_2HPO_4 and 5 g of KH_2PO_4 in water and make volume of 100 ml. Add a drop of concentrated hydrochloric acid and store under a layer of toluene in a cool place.

12. *Salt Solution B.*—Dissolve 2·0 g of magnesium sulphate ($MgSO_4 7H_2O$) 0·1 g of sodium chloride, and 0·1 g of ferrous sulphate ($FeSO_4 7H_2O$) 0·1 g of manganese sulphate ($MgSO_4 H_2O$) in water and make up volume to 100 ml. Add a drop of concentrated hydrochloric acid and store under a layer of toluene in a cool place.

13. *Sorbitan Monooleate Derivative Solution.*—Dissolve 10 g of polyoxyethylene derivative of sorbitan monoleate in alcohol (95%) to make a volume of 100 ml store in a refrigerator.

14. *Culture Medium.*—Dissolve 0·75 g of dried yeast extract, 0·75 g of peptone. 1 g of anhydrous doxtrose and 0·2 g of KH_2PO_4 in 5·0 ml of water. Add 10 ml of tomato juice filtrate, prepared as described under 3 but omitting the treatment with activated charcoal, and 1 ml of sorbitan mono-oleate derivative solution. Adjust pH of solution to 6·8 with dilute sodium hydroxide and add water to make 100 ml. Place 10 ml portion of the solution in test tubes with lips, plug with cotton and sterilize the tubes by heating in an autoclave for 15 minutes at 121° (15 lbs. per square inch of steam pressure). Cool the tubes rapidly and store in a refrigerator for not more than one month.

15. *Stock culture of Lactobacillus Leichmanii* 313.—To 100 ml of culture medium (Reagent No. 14) add 1·5 to 2·0 g of agar and dissolve the agar by heating the mixture on a steam bath with stirring. While the solution is hot, transfer 10 ml portion of it to test tubes. Plug the tubes with cotton and sterilize by autoclaving at 15 lbs. steam pressure (121°) for 15 minutes. Cool the tubes rapidly and store in refrigerator for not more than one month.

Prepare stab cultures of *Lactobacillus Leichmanil* 313 in 2 or more tubes. Incubate at 37° for 16 to 24 hours and store in refrigerator. Set a side one tube as stock culture and use the others for transfer into inoculum medium. From the stock culture prepare fresh subcultures every 2 or 3 days and do not use it for preparing the inoculum if the culture is more than 4 days old.

16. *Basal Medium Stock Solution.*—

Reagent No.	Reagent	Quantity
1	Acid hydrolyzed casein solution	25 ml
2	Cystine-Tryptophan solution	25 ml
3	Tomato juice filtrate	50 ml
4	Asparagine solution	5 ml
5	Adenine-Guanine-Uracil solution	5 ml
6	Xanthine solution	5 ml
7	Riboflavin-Thiamine-Biotin-Nicotinic acid solution	10 ml
8	P-Aminobenazoic acid-Pyridoxine-Pyridoxal-Pyridoxamine solution	10 ml
9	Ca-pantothenate-Folic acid solution	5 ml
10	Salt Solution A	5 ml
11	Salt Solution B	5 ml
12	Sorbitan monooleate derivative solution	10 ml
13	Dextrose anhydrous	10 g
14	Sodium acetate anhydrous	5 g
	(or Sodium acetate Crystalline	8·3 g)
15	Ascorbic acid	1 g

Dissolve the dextrose, sodium acetate and ascorbic acid in tomato juice filtrate, add the remaining solutions and 50 ml of water adjust pH to 6·0 with 1 N sodium hydroxide and finally add water to make the solution 250 ml.

17. *Suspension Medium.*—Dilute 25 ml of basal medium stock solution (reagent No. 16) with an equal volume of water, place 10 ml of the diluted solution in each of 5 test tubes, plug the tubes and sterilize them as described for culture medium (Reagent No. 14). Cool the tubes rapidly and store in refrigerator for not more than 7 days.

18. *Inoculum.*—Make a transfer of a few cells of Lactobacillus leichanii 313 from a recent subculture into two sterilized tubes each containing 10 ml of culture medium (Reagent No. 14) and incubate for 16 to 24 hours at a temperature of 37°. Securely tie the plug to the tube by means of a rubber band or piece of thread and centrifuge the culture till the cells have settled to the bottom of the tube as a mat. Under aseptic conditions decant off the supernatant fluid and suspend the cells in 10 ml of sterile suspension medium (Reagent No. 17). Centrifuge again similarly, and decant off the supernatant. Repeat this treatment a third time. Finally suspend the cells uniformly in 10 ml of sterile suspension medium (Reagent No. 17) aseptically add a ml of the suspension to 10 ml of sterile suspension medium and mix well. The resulting cell suspension is the inoculum.

19. *Standard Cyanocobalamin Stock Solution.*—Accurately weight the Cyanocobalamin. Reference Standard and dissolve in 25 per cent alcohol to yield a solution containing 0·1 microgram of cyanocobalamin per ml. Store in a refrigerator for not more than two months.

20. *Standard Cyanocobalamin Solution.*—Dilute the Standard Cyanocobalamin Stock Solution with water so that the dilute solution contains 0·02 milli-microgram of cyanocobalamin per ml. Prepare a fresh Standard Solution for each assay.

21. *Test Solution of the Material to be Assayed.*—Weigh or measure accurately a suitable amount of the material to be assayed and dissolve it in water or dilute if necessary. Add dilute hydrochloric acid or dilute sodium hydroxide to adjust the pH to 6·0 and add water to make a suitable volume. If the solution contains insoluble matter, centrifuge and dilute the clear supernatant with water so that the final solution contains the vitamin B_{12} activity of approximately 0·02 milli-microgram of cyanocobalamin per ml.

22. *Test Tubes.*—Lipless hard glass test tubes 150 mm long and 19-20 mm in diameter are suitable.

The tubes may be arranged in metal racks each holding 6 × 6 tubes. The tubes may be plugged with cotton or preferably be covered with glass or aluminium caps. A single rust-free metal lid 35 to 80 mm deep covering all the tubes in the rack is also suitable.

Extreme care is necessary in cleaning the tubes since the growth of the test organism may be appreciably stimulated by traces of vitamin B12 activity remaining in the tubes or inhibited by small amounts of the cleaning agent.

Assay Procedure

To triplicate test tubes add 0·0 ml, 0·5 ml, 1·0 ml, 1·5 ml, 2·0 ml, 2·5 ml, 3·0 ml, 3·5 ml. 4·0 ml. 4·5 ml and 5·0 ml respectively of the Standard Cyanocobalamin Solution (Reagant No. 20). To each tube add 5·0 ml of the basal medium stock solution (Reagent No. 16) and sufficient water to make the solution 10 ml.

To similar triplicate test tubes add 1·0 ml., 2·0 ml., 3·0 ml., and 4·0 ml. respectively of the test solution to be assayed (Reagent No. 21). To each tube add 5·0 ml. of the basal medium stock solution (Reagent No. 16) and sufficient water to make the solution 10 ml.

Mix the contents well, cover the tubes suitably to prevent bacterial contamination and sterilize the tubes by heating for 5 minutes at 121° (15 lbs. pressure) in an autoclave that has been preheated to this temperature. Cool as rapidly as possible by carefully releasing the steam from the autoclave and placing the tubes in a shallow tray containing cold water. When all the tubes have come to the room temperature, aseptically inoculate each tube with one drop of the inoculim (Reagent No. 18). Incubate the tubes for 64 to 72 hours at any chosen temperature within the range 30°-37° but held constant and uniform to within 0·5°. Titrate the contents of each tube with 0·1 N sodium hydroxide to pH. 7·0 electrometrically or using 0·1 per cent bromothymol blue as internal indicator to a green colour.

Reject the whole assay if the tubes are obviously contaminated with another organism or if the blank tubes to which no Standard Cyanocobalamin Solution was added give titration values exceeding 3 ml. of 0·1 N sodium hydroxide.

Determine the average of the triplicate titration values for each level of Standard and test sample used, discarding any value that does not lie within the range 90 to 110 per cent of the mean of the remaining two values. On a graph paper plot the average titration values expressed in ml. of 0·1 N sodium hydroxide against the corresponding levels of Standard Cyanocobalamin Solution added. Draw a smooth curve to fit as many points as possible.

Making use of only that part of the standard curve corresponding to the range 0·5 to 4·5 ml. of the Standard Cyanocobalamin Solution, determine by interpolation the vitamin B_{12} activity per ml. of the test solution for each level used. Strike a provisional average of the values and discard any value that falls beyond the range 90 to 110 per cent of the provisional average. At least three of the four assay values should remain; calculate their mean value.

Turbidimetric Method

Reagent and Apparatus

With the exception of the following, all reagents and apparatus are the same as described under "Titrimetric Method".

20. *Standard Cyanocobalamin Solution.*—Dilute the Standard cyanocobalamin stock solution with water so that the dilute solution contains 0·04 millimicrogram of cyanocobalamin per ml. Prepare a fresh standard solution for each assay.

21. *Test Solution of the material to be assayed.*—Proceed as described for Reagent No. 21 under "Titrimetric Method" and prepare the final dilute solution to contain the vitamin B_{12} activity of approximately 0·04 millimicrogram of cyanocobalamin per ml.

Assay Procedure

Proceed as described under "Titrimetric Method" except for the following deviations.

Include also two tubes as "uninoculated blanks" *i.e.*, to which neither standard cyanocobalamin solution, nor test solution, nor inoculum is added.

Incubate all tubes for only 16 to 25 hours. Mix thoroughly the contents of the "uninoculated blank" tubes, transfer the contents to the photoelectric colorimeter tube and adjust the transmittance at 640 ml. to 100 per cent. Thoroughly mix the contents of each tube, transfer to the colorimeter tube and record the transmittance reading. Avoid too vigorous a shaking since this may entrap air bubbles and result in unduly high turbidity.

Calculation

Reject the whole assay if the tubes are obviously contaminated with another organism or if the blank tubes to which no standard cyanocobalamin solution was added give transmittance values less than 80 per cent.

On a graph paper plot the transmittance values against the corresponding levels of standard cyanocobalamin solution added. Draw a smooth curve to fit as many points as possible. Making use of only that part of the standard curve corresponding to the range 0·5 to 4·5 ml. of the standard cyanocobalamin solution, determine by interpolation the vitamin B_{12} activity per ml. of the test solution for each level used. Strike a provisional average of the values and discard any values falling beyond the range 90 to 110 per cent of the provisional average. At least 8 of the 12 assay values should remain; calculate the potency from the average of these remaining values.

5. **Container.**—The containers should either be glass ampoules properly sealed to exclude contaminants: or where multiple doses are issued, glass vials with proper type of rubber capping and seal. The containers should conform to the tests for limit of alkalinity.

6. **Storage.**—Crude Liver Extract for parenteral use shall be stored in a cool place protected from light.

7. **Labelling.**—The label of the container should contain the following in addition to any other particulars prescribed in these rules :—

(i) The amount of cyanocobolamine (Vitamin B_{12}) per ml. which should not be less than 2 mcgm. in a single recommended dose.

(ii) The amount of raw liver processed to produce 1 ml. of the extract.

(iii) The date of expiration of potency which should be not later than 18 months from the date of manufacture.

(iv) A note on the storage instruction "Keep in a cool place, and protected from light".

(v) The name and quantity of the preservative, if any, added.

(Sd.) P. N. ANAND,
Under Secretary.

To

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No. F. 1-3/55-D

Copy forwarded to the Director General of Health Services with reference to his U. O. No. 8-1/55/24-D, dated the 26th July, 1955.

Statement of comments received on the Draft Standards for Liver Extract, Crude, for parenteral administration to be included in Schedule F to the Drugs Rules.

Sl. No.	Reference to the Draft standards published in Govt. of India, Ministry of Health Notification No. F. 1-32/55-D., dated the 10th September, 1955.	Comments received.
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		(*From Shri B. V. Patel*).—The heading of the provisions has been given as "(A) Liver Extract, Crude, for parenteral administration". While in the subsequent page the description "Crude Liver Extract for parenteral administration" has been used. Therefore, wherever the words "Crude Liver Extract for parenteral administration" of the words "Crude Liver Extract" are used, they should be substituted by the words "*Liver Extract, Crude, for parenteral administration*" or by the words "Liver Extract, Crude" as the case may be.
1	Introduction . . .	(*From Dr. G. B. Ramasarma*).—There is lack of agreement between the following statements appearing under (1) Introduction and (7) Labelling:

Introduction	*Labelling*
A suitable preservative shall be added.	The name and quantity of the preservative added.
....should not be less than 2 micrograms of Cyanocobalamin per ml.	....should not be less than 2 mcgm. per ml.

Although it is not stated, the Central Drugs Laboratory will presumably maintain and supply the Cyanocobalamin Reference Standard Preparation.

(*From Messrs. Bengal Chemical & Pharmaceutical Works Ltd.*).—Whose observations are based on the activity of L. leichmanii and who are of the opinion that A.T.C.C. 7830. L. Leichmanii 313 and L. Leichmanii A.T.C.C. 7830 are virtually the same.

1. *The description.*—"Liver Extract, Crude, for parenteral administration" seems to be a more appropriate term than "Crude Liver Extract for parenteral administration".

The potency should be expressed in terms of vitamin B12 activity equivalent to micrgorams of cyanocobalamin per ml. in view of the fact that mammalian livers contain the vitamin predominantly in the hydroxy form.

2. 1 microgram and 2 micrograms per ml. of Liver Extract, Crude, is official in the U. S. P. and in view of the relative scarcity of pernicious anaemia in our country, 1 microgram per ml. strength may also be made official.

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		(*From Shri B. V. Patel*).—The potency of Liver Extract, Crude, for parenteral use, is expressed in terms of its cyanocobalamine (Vitamin B12) content. It is suggested that the potency should be expressed in terms of Vitamin B12 activity and not cyanocobalamine, since the liver extract also contains Hydroxycobalamine. Further, U.S.P. XV accepts the Liver Extract containing 1 or 2 microgram of Cyanocobalamine while the draft Notification requires the liver extract to contain not less than 2 microgram of cyanocobalamine. It is suggested that this point needs re-consideration because some papers have been published which indicate that the Vitamin B12 activity decreases on storage. Therefore, it may not be advisable to fix the standards on the B12 activity which may be present at the time of manufacture.
2	Proper name . . .	Nil.
3	Description . . .	Nil.
4	Tests	Nil.
4(a)	Reaction . . .	[*From M/s. Lederle Laboratories (India) Ltd.*].—We believe that the acidity as high as pH 4·5 could be allowed without any deterioration of the product.
4(b)	Total solids . . .	(*From PAMDAL*).—The minimum for total solids has been set too high. If the percentage of solids is higher than 10%, crude liver extract is likely to show appreciable reactions and toxicity, in which case it will be difficult to conform to the proposed tests for toxicity. The only authorities who at present list any standards for the liver extract are the U.S.P. and the Canadian Food and Drugs Regulations. Neither of these fix any figure for total solids. If it is considered necessary to fix a limit for solids, then this should not exceed 10% with possibly a lower limit of 5%. It is suggested that the appropriate portion of this Rule should read— "The total solids should be not more than 10% weight volume and not less than 5%". [*From M/s. Lederle Laboratories (India) Ltd.*].—As far as limits of total solids are concerned, we feel that lower potency liver extracts will be able to meet this requirement. However, we have our doubts as to whether it will be possible to meet 15% limits of total solids in case of high potency Crude Liver Extracts (*i.e.* 15 mcgm. and 20 mcgm. per cc. of B12).
4(c)	Limits for proteins . .	[*From M/s. Lederle Laboratories (India) Ltd.*].—Although protein test is a desirable test and we would suggest that it should be put in, we doubt if our Indian Liver Extracts will be able to meet this requirement. We agree that proteins must be completely removed, but from experience we find that it is not always the case in case of Indian Livers.
4(d)	Absence of undue toxicity	(*From PAMDAL*).—Albino rats weighing between 120 and 140 gms. should be included in the test for Absence for Undue Toxicity along with or in place of Mice Test and dosage described accordingly (0·6 cc. intravenously or 1·0 cc. intraperitoneally for 140 gms. body weight

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		may be selected). Mice are usually difficult to procure, breed and rear up and much more expensive than albino rats. One of our member firms have found that albino rats have been very satisfactory in determining toxicity of liver extracts. *Test for Undue Presence of Histamine.*—This specification should be included and the upper limit of Histamine should be given as 10 mcg. per cc. of crude liver extract, to be assayed biologically. (Ref. THE TESTING OF ANTIANAEMIC OPOTHERAPEUTIC EXTRACTS Jean Cheymol, and Pierrm Blonde, Ann. Phare. Franc., 6, 39, (1948), Chemical Abstracts, 42, 1948; 7492g.).
4(e)	Sterility and Pyrogen test .	(*From Army Headquarters, MGO Branch*).—In clause 4(e) of the specification it is stipulated that the B.P. method should be followed in respect of this test. B.P. and U.S.P. tests for freedom of pyrogen in parenteral injections differ. Recently lot of work has been done in U.K. on 'Pyrogens' which has been systematically published in the journal of Pharmacy & Pharmacology (Dare, J. Pharm. Pharmacol., 1953, 5. 528; and 1953, 5. 898 Symposium on Pyrogens Dare, J. Pharm. Pharmacol, 1954, 6, 303). On the basis of salient recommendations in these publications, we have collected a fair amount of data on the requirements of Pyrogen test. These requirements are briefly described below and it is felt that these should be laid down for routine examination of freedom of 'Pyrogens' in parenteral injections: (i) Selection of rabbits should be done prior to the test (B.P. does not specify this, while U.S.P. lays down a very rigorous drill which is not practicable during routine examination of samples). Rabbits not falling within the temperature range of 38·9 to 39·8 C should be discarded. (ii) At least two readings of rectal temperature at 45 mts. interval should be recorded before injection on the day of test. The mean of these readings should be regarded as the mean pre-injection temperature. Subsequent to injection, temperature, should be recorded at 45 mts. interval for 3 hours and the maximum recorded temperature should be compared with the mean pre-injection temperature for estimating a rise in temperature due to the injection. (iii) It is not necessary to subject the test animals to severe restrictions before and during the experiments. The rabbits in the colony should be allowed to have normal diet; on the days of selection and test, the animals should not be allowed to have access to food. There should, however, be plentiful supply of water in each case. During temperature recording, the animals need not be severely restricted, gentle holding on the bench with hands has been found to be satisfactory.

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		(iv) In case a sample fails to pass the test on the first three rabbits, the test should be repeated on another five rabbits (B.P. has not specified repetition, while U.S.P. has stipulated repetition); from our own data it would appear that repetition on a set of another five rabbits is necessary. (v) The quantity of liver extract to be injected per rabbit in terms of body weight and stipulation of a diluent if necessary, are considered essential in the specification. This will be in conformity with the pharmacopoeial procedure as well as the commonly adopted practice by the Pharmacologists. [*From M/s. British Drug Houses (India) Ltd.*].—What volume of liver extract should comply with the B.P. pyrogen tests. (*From the Director, King Institute, Guindy*).—Since crude liver extract is not administered by the intravenous route, I feel that the Pyrogen test should not be insisted on. Such a preparation should be marked "for intramuscular use only—not for intravenous use". (*From PAMDAL*).—The pyrogen tested proposed is that given in the B.P. One of our member firms opines that this test if applied to liver extract would be so stringent that only very few preparations would pass it. Amendment is suggested. (*From Shri B. V. Patel*).—The draft notification states that the product must comply for sterility and pyrogen tests as laid down for parenteral products in B.P. The British Pharmacopoeia 1953 lays down pyrogen test for 'Water for Injection' and the dose to be administered to each rabbit is a quantity equivalent to 10 mls. per kg. of the rabit's weight. Liver extract cannot be administered in such high doses to rabbits for the pyrogen test. It would, therefore, be necessary to lay down the dosage that should be administered for the pyrogen test.
4(f)		(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—The potency should be not less than 100% and not more than 150% of that stated on the label. Whether both the titrimetric and turbidimetric methods should be tried or any one will suffice should be mentioned. (*From Shri B. V. Patel*).—It is necessary to lay down the limits of potency. The limit of potency should be stated as not less than 100 per cent and not more than 150 per cent of that stated on the label.
		MICROBIOLOGICAL ASSAY OF VITAMIN B12 ACTIVITY **Titrimetric Method** *Reagents and Apparatus* (*From Army Headquarters, MGO Branch*).—The biological assay specified in the specification is based on the microbiological estimation of Vitamin B12 content of the Liver Extract; this gives only an approximate estimate of the antipernicious anaemia activity of the preparation. The method of choice would be the one

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		which estimates the haemopoietic activity of the test substance in comparision with a standard preparation. Based on the publication: 'Effect of crystalline vitamin B12 on experimental anaemia in mice (Vijayaraghavan, P. K. and Dunn, M. S., 1950 Proc., Soc., Expt., Biol. and Med., 75), we are making efforts to establish a method for the Bio-assay of Liver Extracts, in which the criterion for the antipernicious anaemia activity of the preparation will be haemopoietic response in Laboratory animals with experimental pernicious anaemia. (*From the Director, King Institute, Guindy*).—Vitamin B12 is relatively quite cheap and could be added to the Liver Extract to suit the requirements of International Regulations. The percentage of Vitamin B12 may decrease on storage under certain conditions. It is, therefore, felt that Liver Extract should not be certified as suitable for parenteral use by testing the same only for its Vitamin B12 contents, and without testing for its haemopoietic effect on patient. [*From M/s. Lederle Laboratories (India) Ltd.*].—As far as microbiological assay procedure for B12 is concerned, the proposed method gives titrimetric and turbidimetric procedures. Since the titrimetric procedure seems to be adopted from the turbidimetric procedure we are not sure that it will work out properly. We feel very strongly that from a control standpoint the turbidimetric procedure is the one that has to be used since it is very much faster and accurate. We also feel that the method of choice should be the one currently set forth in the new U.S.P. XV. In our opinion, this method will give considerably better results than the one outlined in the draft memorandum.
1	Acid Hydrolysed Casein Solution.	Nil.
2	Cystine—Tryptophan Solution.	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—Cystine—Tryptophan Solution: It is better to use cystine and tryptophan in solid form in preparing the Basal Medium. (*From Shri B. V. Patel*).—According to U.S.P. XV, cystine and tryptophan are weighed out and dissolved at the time of preparing the basal medium. It is, therefore, suggested that the method of preparation of the solution may be substituted by the following:— "Dissolve 100 mg. of L-cystine and 50 mg. of L-tryptophan (or 100 mg. of DL-tryptophan) in about 5 ml. of 1 N hydrochloric acid and use immediately."
3	Tomato Juice filtrate	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—Fresh tomato is equally good for this preparation; moreover it is easily available. Charcoal-treated tomato-juice is omitted in the preparation of Basal Medium in the U.S.P. But in view of the findings of Loyetal this may be retained as well.
4	Asparagine Solution	Nil.
5	Adenine-Guanine-Uracil Solution.	Nil.

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6	Xanthine solution	Nil.
7	Biotin Stock Solution	Nil.
8	Riboflavin-Thiamine-Biotin-Nicotinic Acid Solution.	Nil.
9	O-Aminobenzoic Acid-Pyridoxine.	Nil.
10	Calcium Pantothenate-Folic Acid Solution.	Nil.
11	Salt Solution A	Nil.
12	Salt Solution B	Nil.
13	Sorbitan Mono-oleate Derivative Solution.	Nil.
14	Culture Medium	Nil.
15	Stock Culture of Lactobacillus Leichmani 313.	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—"The activity of the micro-organism can be increased by daily or twice-daily transfer of the stab culture, and may be considered satisfactory when definite turbidity in the liquid inoculum can be observed 2 to 4 hours after inoculation. A slow-growing culture seldom gives a suitable response curve, and any give rise to erratic results." (3) This observation should be included. (*From Shri B. V. Patel*).—It is suggested that a note about the maintenance of an active culture may be included on the lines of U.S.P.
16	Basal Medium Stock Solution.	(*From Shri B. V. Patel*).—The procedure for making the Basal Medium may be substituted by the following procedure:— "Mix reagents 1 to 12 in the order indicated. Remove the last traces of toluene in the mixture with the help of a separating funnel. Add reagent 13, dissolve the dextrose, sodium acetate and ascorbic acid and add 50 ml. of water. Adjust the pH to 6·0 with 1 N sodium hydroxide and finally add to make the solume 250 ml."
17	Suspension Medium	Nil.
18	Inocculum	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—The depth of the inoculum definitely affects the final growth of the micro-organism in the assay medium (5). It is quite likely that some variations in the amount of cell-growth in the culture medium will be encountered during day to day work. 0·5 mg. to 0·75 mg. of dry cell weight per 10 ml. of the inoculum has been defined as the standard depth in the U.S.P. But the method of determining the dry cell weight is very lengthy as well as laborious and as such is not likely to be practicable during routine work. It is more convenient to use an inoculum which gives a transmittance of 40-50% at any wave-length between 540 mu. and 660 mu. To ascertain this depth the washed cell-suspension may be aseptically diluted in stages and the transmittancy checked in a photo-electirc colorimeter fitted with a test-tube adapter, till the required transmittance of 40-50% is attained.

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19	Standard Cyanocobalamin Stock Solution.	[*From M/s. British Drug Houses (India) Ltd.*].—We do not believe that weighing cyanocobalamin in the quantity to be used is sufficiently accurate. We would suggest that a solution should be made and standardised at 361 mu. spectrophotometrically. (*From M/s. Bengal Chemidal & Pharmaceutical Works Ltd.*).—U.S.P. reference standard cyanocobalamin or some other standard preparation, which is to be used should be specified. (*From Shri B. V. Patel*).—It is desirable to indicate the Institutions from where the Reference Standard will be available. It is suggested that they should be made available at least at the following institutions:— 1. Central Drugs Laboratory, Calcutta; 2. Haffkine Institute, Bombay; and 3. Central Drugs Research Institute, Lucknow.
20	Stardard Cyanocobalamin Solution.	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—The strenth is given as 0·02 mug./ml. but this may vary between 0·04 mug./ml. depending upon the vigour of the micro-organism.
21	Test Solution of the material to be Assayed.	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—There is no need of taking a weighed quantity of the sample. A measured quantity not less than 1 ml. is to be taken in view of the potency laid down in terms of microgram Cyanocobalamin per ml. basis. The sentence "Dissolve in water" is superfluous as liver extract crude is a water-soluble product, dilution with water to the requisite expected strength will suffice. Though both hydroxy-cobalamin and cyanocobalamin are equally stable and active in the Basal Medium under the condition of assay. U.S.P. method requires treatment of the Liver Extract with sodium metabisulphite in phosphate citric acid buffer. As a precautionary measure against loss of activity of hydroxy-cabalamin, bisulphite treatment may be retained as well. (*From Shri B. V. Patel*).—It is more convenient to accurately measure Liver Extract solution and, therefore, the words "Weigh or" should be deleted.
22	Test Tubes	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—Test tubes and other glass-wares used in vitamin B12 assay should be kept exculsively separated for the purpose and they should be washed as soon as work is finished. Dipping the glass-wares in 65% w/v sulphuric acid for 2 hours and finally rinsing several times which distilled water give satisfactory result. *Assay Procedures* (*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—Three more tubes containing no cyanocobalamin should also be included as un-inoculated blank. Rapid cooling of the assay tubes after autoclaving is necessary only to avoid any colour formation due to slight charring of Dextrose. This colour may present some difficulty in the turbidimetric measurement; but in the titrimetric procedure no such difficulty is likely to arise. Heating the assay tubes even for longer periods does not affect the nutritional value of the medium. So in titrimetric procedure rapid cooling is not essential.

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It is better to dilute Bromothymol blue indicator solution B.P. (0·04% w/v) to ten times its volume with water and adjust the pH to 7·0. The assay tubes may conveniently be rinsed out to the reaction flask with several small portions of this solution using 10 ml. in all.

(*From Shri B. V. Patel*).—U.S.P. XV permits the determination of the percentage transmittance at a specific wave length range between 540-660 mu. It is, therefore, suggested that in para 3, instead of 640 mu. the wave length range 540-640 mu. may be given. The last two sentences in the 3rd para may be substituted by the following:—

"Thoroughly mix the contents of each tube; allow the tubes to stand for 10 to 15 minutes so that the bubbles rise to the surface. Gently transfer the contents to the colorimeter tube and record the transmittance reading."

[*From M/s. British Drug Houses (India) Ltd.*].—We would suggest that E. Coli, although not suitable for very dilute materials, makes a more satisfactory material for the assay of liver extracts.

May we draw your attention to the fact that a committee in the United Kingdom has been considering the assay of materials containing vitamin B12 and that their recommendations will be published in the near future. We understand that the Committee will recommend the use of Ochramonas Melhamensis.

It would appear to be desirable for India and the U.K. to have uniform regulations if possible.*

(*From MAC Laboratories Ltd.*).—The Microbiological Method specified for determining B12 content in Liver Extract using Lactobacillus leichmanii 313 requires many ingredients for preparing the assay medium and also require exacting conditions for asepsis. Ordinary Laboratories which have no facilities for a separate microbiological department will find it very difficult to perform the assay. An equally accurate and much simpler method requiring very simple assay medium and no exacting conditions of asepsis is the cup and plate method with the help of Davis Mutant Koli 113/3. The only difficulty is in vetting the micro-organisms. The other point is, interference of choline and methionine when present in very large amounts. The quantities of choline and methionine usually present in Liver Extract does not interfere. Hence, once the facility for getting sub-culture of the test-organism is arranged at some Central Laboratory this method, in our opinion, will be better suited to all those interested in determining the B12 content in Liver Extract.

We have adopted this method successfully and the results compare very well with results obtained by other methods. We are obtaining culture from our Principals Messrs. Carlo Erba, S.P.A., under our contract for technical assistance.

In this connection, the following reference, will be of interest:

1. Harrison E., Lees K.A., Wood F., The Analyst, 67,696, 1951.

2. Davis B. D., Mingioli E.S., J. Bact., 60, 17. 1950.

* The standards referred to are given in the end.

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(*From the Government o Madhya Bharat, Health Department*).—With reference to your letter No. F. 1-31/55-D., dated September 12, 1955 on the above subject, I am directed to say that the inclusion of provisions in respect of standards for Crude Liver Extract for parenteral administration in the Drugs Rules was long felt and as this amendment seeks to fill up this gap the State Government have no objection. However for the determination of potency two micro-biological assay methods have been prescribed. Micro-biological methods for assay of Cyanocobalamin (Vitamin B12) are subject to severe qualifications and limitations and finality has not yet been reached. Organisms in use included Lactobacillus lactis Dorner, L. Leichmannii, a mutant of Escherichis Coli, and the protozoon Ochrommonas malhamensis. The use of protozoa is comparatively novel in this type of assay, and Ford (Brit. J. Nutr. 1953, 7, 299) has shown that o' malhamensis is specific for cyanocobalamin in assays on a number of diverse products. This method appears very hopeful and is the subject of investigation at the present time by a panel of the Society for Analytical chemistry. In the circumstances other methods of determining the potency, should not be precluded and if possible some method of finding the potency by measuring extinction at specified wave length should be evolved which would be less cumbersome than the micro-biological method.

Turbidimetric Method

Reagents and Apparatus

20	Standard Cyanocobalamin Solution.	Nil.
21	Test Solution of the Material to be Assayed.	Nil.

Assay Procedure

(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—A drop of a suitable antifoam agent, say caprylic alcohol, may be added to each tube before mixing the the contents.

Calculation

(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—The best response is in the range of 0·01 to 0·06 milli-microgram of cyanacobalamin per assay tube, and the transmittance varies between 11%-13% for each increment of 0·01 milli-microgram within this range; above this range the response is not very good and the curve gradually becomes flattened. The range prescribed in the Draft Monograph is 0·02 to 0·18 milli-microgram (0·5 to 4·5 ml.) per tube. Everything will depend on the vigour of the organism; with vigorous, rapidly growing organism the lower range will be more appropriate. The prescribed range in the U.S.P. is from 0·01 to 0·10 milli-microgram per tube. A limit of response in terms of per cent transmittance should be included.

The Basal medium is adjusted to pH 6·0 and the titration is carried to pH 7·0. The difference in pH (from 6·0 to 6·8) accounts for about 1·7 ml. of N/10 NaoH solution per assay tube; and the maximum quantity of N/10 NaoH solution required in titrating the inoculated blank is 2·5 ml. *i.e.*, 0·8 ml. over that required in the uninoculated blank. So an amount not exceeding 1·0 ml. of

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		N/10 NaoH solution per assay tube over that required in the un-inoculated blank may reasonably be taken as a guard against undue growth in the inoculated blank. The smooth curve drawn should be reasonably steep. A limit response in terms of ml. of N/10 NaoH solution required for each increment of 0·01 milli-microgram of cyanocobalamin per 10 ml. assay tube, within the range of (0·009 mug. to 0·09 mug. per tube) should also be laid down. In our opinion 1·0 ml. to 1·4 ml. of N/10 NaoH solution per 0·01 milli-microgram increment of cyanocobalamin per 10 c.c. assay tube will be a workable standard.
5	Containers	(*From M/s. Bengal Chemical & Pharmaceutical Works Ltd.*).—The container should be of light amber glass to protect the product from light and shall be so labelled that easy inspection of the content is possible. The test for alkalinity of the glass of the container should be done before it is filled with the substance because once some acidic substance is filled, no purpose will be served by testing the container for alkalinity. In that case the pH of the substance may give some indication as to the alkalinity of the glass. In fact, B.P. also intends the test for alkalinity of the glass of the container to be done before filling.
6		(*From Shri B. V. Patel*).—It is suggested that instead of stating that Liver Extract shall be stored in a cool place, it would be desirable to specify the temperature at which it should be stored. The multi-dose containers when removed from their carton solution do not protect the Liver Extract from the effect of light if they are filled in colourless glass vials. It is, therefore, suggested that multi-dose packings of Liver Extract should be filled in amber coloured glass vials. The storage conditions that are to be specified in the proposed amendment to Schedule F should be corrected so, as to be in accordance with requirements laid down in the Indian Pharmacopoeia. The temperature for storage should be laid down as not more than 20.°C as laid down in the Indian Pharmacopoeia
7	Labelling	[*From Army Headquarters, MGO Branch*].—Packing details have not been incorporated in the specification although technical requirements regarding container (ampoules, vials) as well as relevant lavelling details have been mentioned. It is suggested that details in respect of materials as well as manner of packing should be stipulated in the specification. [*From M/s. Chowgule & Co. (Hind) Ltd.*].—We refer to the draft amendment for the Drugs Rules, 1945, published in the Gazette of India, September 24, 1955, concerning crude liver extract for parenteral administration. Para 7, labelling (iii) of the said draft amendment reads as follows:— The label of the container should contain the following in addition to any other particulars prescribed in these rules— * * * * (iii) The date of expiration of potency which should be not later than 18 months from the date of manufacture.

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		In this connection we have to state that the period of life of a crude liver extract given in the above amendment seems considerably under-estimated. Our manufacturers, M/s. Farbenfabriken Bayer, Leverkusen, were the first to introduce an injectable liver extract into the world market under the name of "Compolon". Campolon has for many years served as a standard product for other manufacturers have thus accumulated experience of almost a quarter of a century in the manufacture of liver extract, its properties and its stability. We had passed on the proposed amendment to the Drugs Rules, 1945, to M/s. Bayers' research laboratories in Leverkusen and Elberfeld, inviting their opinion concerning the stability of their crude liver extract in tropical countries. We have in answer to our enquiry received the following signed statement— *Campolon stability—India* According to the assays carried out here, we confirm that the vitamin B12 contents of our Campolon will remain stable for at least 3 years. From the above it appears that crude liver extract manufactured on generally accepted lines will preserve their cyanocobalamin (vitamin B12) contents for a minimum period of 3 years if they are kept under reasonable storage conditions as provided for in the Drugs Rule. Under the circumstances, we venture to suggest to alter para 7, Labelling (iii) and allow 3 years for expiration of potency from the date of manufacturing. (*From M/s. Bengal Chemical & Pharmaceutical Work Ltd.*).—Date of manufacture, Batch No. and dose should also be included. (*From M/s. Pharmaceutical & Allied Manufacturers' Distributors' Association Ltd.*).—In view of the specification in Item No. 4(b) fixing limits for solids, a declaration on the label as "*the amount of raw liver processed to produce 1 ml. of the extract*" should not be made compulsory. When potency is expressed in terms of cyanocobalamin date of expiration of potency should be fixed as 24 months from the date of manufacture, as from experience of a member firm it was found that cyanocobalamin in the liver extract remains unaltered during this period. (*From M/s. Pharmaceutical & Allied Manufacturers' Distributors' Association Ltd.*).—One of our member firms suggests that the information required in 7(ii) would not serve any useful purpose, as the potency will depend not only upon the amount of raw liver used, but also on the manufacturing process employed. Our member firm therefore, considers the proposed statement on the label, as irrelevant, the more so as to the amount of cyanocobalamine contained in the liver extract has been selected to express the approximate antianaemic potency of the liver extract. The period of life according to the experience of our member firms is considerably longer than that proposed in the amendment. A good liver extract one of our

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member firms contents retains its potency for at least five years if it is stored in a cool place away from light. Another one of our member firms after consultation of their principals states that the cyanocobalamin contents of liver extract remains stable for a period of at least 3 years.

Under the circumstances, it is suggested to extend the proposed period of life to 3 years.

(*From Shri V. B. Patel*).—(i) The label should indicate the Vitamin B12 activity per ml. instead of the amount of cyanocobalamin.

(ii) In order to remove the difficulty that may be experienced by the manufacturers on account of the variation in the B12 activity of the Liver processed by them it would be desirable to add the word "average" before the word "amount".

(iii) Under storage instruction, the temperature at which the product should be stored should also be indicated.

APPENDIX I

Errata

Line	*For*	*Read*
19	mamalian	mammalian
23,25	cyanocobalamine	cyanocobalamin
24	leichmanii	leichmannii
26	per ml.	per single recommended dose
32	PH	pH
39	micro-Kjeldhal	micro-Kjeldahl
41	interperitioneal	intraperitoneal
54	KG	Kg.
55	IN HCI	1 N HCI
59	IN	1 N
2	IN HCI	1 N HCl
3	ph	pH
26	flask	glass
45	Adeninie	Adenine
47	N hydrochloric acid	6 N hydrochloric acid
57	of nicotinic acid	of nicotinic acid;
60	D-Aminobenzoic Acid	p-Aminobenzoic Acid
61	plaminobenzoic	p-aminobenzoic
4	volume of	volume to
4	hydrochloride acid	hydrochloric acid
7	sodium chloride, and 0·1 g. of ferrous sulphate (Fes04 7H20)	sodium chloride, 0·1 g. of ferrous sulphate (Fe So4. 7H2O) and
19	portion	portions
23	Leichmanii	Leichmannii
29	Leichmanii	leichmannii
41	5 m ml.	5 ml.
57	voelution	volume
63	inoculu	inoculum
63	leichannii	leichmannii
34	volution	volume

Line	For	Read
38	volution	volume
60	0·45	0·5
19	640 ml.	640 mu (mill-microns)
38	issue	issued
45	(vitamin B12 per ml)	(Vitamin B12 per ml.)
45	cyanocobalamine	cyanocobalamin
52	preservative, if any, added.	preservative added

APPENDIX II

February, 1956 *No.* 959

THE ANALYST

Analytical Methods Committee

Report prepared by the Vitamin B_{12} Panel

THE ESTIMATION OF VITAMIN B_{12}*

The Analytical Methods Committee has received the following report from its Vitamin B_{12} Panel. The Report has been approved by the Analytical Methods Committee and its publication has been authorised by the Council :—

REPORT

In March, 1953, the Sub-Committee on Vitamin Estimations of the Analytical Methods Committee appointed a Vitamin-B_{12} Advisory Panel "to survey the methods already proposed for the estimation of vitamin B_{12} and to report to the Sub-Committee on the work required to establish a standard method or methods". The Panel made its report in September, 1953, and in it stated that an organism and a technique should be selected which would overcome the non-specificity attaching to the techniques generally employed, *e.g.*, those using Bacterium colimutant and Lactobacillus leichmanii, and recommended for the purpose the use of Ochromonas malhamensis as described by Ford.

The Analytical Methods Committee implemented the recommendations of this report and in November, 1953, appointed a Vitamin-B_{12} Working Panel under the Chairmanship of Dr. A. J. Amos "to establish, if possible, an agreed method for the estimation of vitamin B_{12} in foods and feeding stuffs as suggested in the report of the Vitamin B_{12} Advisory Panel". The members of the Panel were Dr. W. F. J. Cuthbertson, Dr. J. E. Ford, Dr. F. W. Norris, Mr. S. A. Price, Mr. G. E. Shaw, Dr. R. E. Stuckey, Mr. G. Sykes and Dr. F. Wokes, who acted as Honorary Secretary.

*Although the results of the assays in this report are expressed in terms of cyanocobalamin, the Panel considers that in the light of present knowledge the therm "vitamin "B_{12}" should be retained.

Introduction

The ultimate goal of a working Panel appointed by the Analytical Methods Committee is the establishment of a reliable analytical method. When the test substance has biological activity it is not the function of the Panel to supplement its analytical recommendations by interpretations of that activity or to institute relevant researches in clinical medicine and animal nutrition. The Panel responsible for the present report has accordingly restricted its deliberations and experiments to the establishment for the determination of vitamin B_{12} of an analytical method which, in our present state of knowledge, is least affected by the known vitamin B_{12} like substances that may co-exist with vitamin B_{12} the correlation between concentrations of vitamin B_{12} so determined and haematopoietic activity in man on the one hand or growth-promoting activity in animals on the other is not the concern of this Panel.

Most of the methods available for the measurement of vitamin B_{12} are open to criticism on the grounds of insensitivity and non-specificity, and hence have a limited application. Several of the established microbiological assay techniques that employ bacteria as test organisms are highly susceptible to interference by vitamin-B_{12} like compounds and, in some instances, by other non-specific interfering substances. The protozoan Ochromonas malhamensis is believed to have animal like specificity for vitamin-B_{12} and may be used to measure the vitamin even when related compounds are present.

Experimental Work

Under its terms of reference the Panel was required to investigate the microbiological method of Ford, in which O. malhamensis is used as the test organism. In order to check the accuracy of this method the assay procedure was applied to a solution of vitamin B_{12} the concentration of which was unknown to members of the Panel. The results showed excellent agreement between all the laboratories and also were in satisfactory agreement with the figure furnished by a spectrophotometric determination of the potency. The method was then applied to a sample of dried-liver powder, but the figures returned for the vitamin B_{12} content showed too wide a spread. This suggested that the method of extraction was not sufficiently closely defined and a modified extraction procedure was, therefore, devised.

In the second and third series of collaborative tests the analytical procedure as published and the modified method of extraction were applied to two samples of liver powder and a sample of fish solubles. The vitamin-B_{12} contents reported for each of these test substances showed acceptable agreement, particularly as most members of the Panel were unfamiliar with this assay and satisfied the Panel that the modifications introduced into the extraction procedure had been successful. As a final test of the method collaborative assays were performed upon two substances that presented particular difficulties, one was a sample of chick mash having a very low vitamin B_{12} content and the other was a sample of desiccated cow manure, a substance very rich in vitamin-B-like compounds.

All the standard vitamin-B_{12} solutions used throughout this investigation were checked spectrometrically before and after use in the microbiological assay and no significant changes in concentration were detected.

Full details of the modified extraction procedure and of Ford's analytical technique, which are recommended by the Panel, are given in the Appendix.

RESULTS OF COLLABORATIVE TESTS—

Table I shows the individual results of the collaborative assays that followed modification of the extraction procedure.

TABLE I

Results for Vitamin-B_{12} in Collaborative Assay Samples

Sample	Laboratory							
	A, µg.g.	B, µg.g.	C, µg.g.	D, µg.g	E, µg.g	F, µg.g	G, µg.g	H, µg.g
Liver Powder A*	0·91	..	0·92	..	0·94	..	0·91	..
	0·87	..	0·97	..	0·84	..	0·94	..
	0·95	..	0·94	..	0·75	..	0·89	..
Mean	0·91	..	0·91	..	0·84	..	0·89	..
Liver powder B	0·98	0·99	1·39	0·18	1·43	0.88	09·6	1·36
	1·18	..	0·09	0·89	1·20	0.95	11·2	1·17
	1·06	..	1·27	0·95	1·20	..	10·5	0·99
	1·05	..	..	..	1·16	..	..	..
Mean	1·07	0·99	1·25	0·97	1·25	0·92	1·04	1·17
Fish solubles	0·20	0·24	0·29	0·18	0·28	0·20	0·27	...
	0·22	..	0·29	0·16	0·29	0·24	0·24	..
	0·19	..	0·26	0·13	0·27	..	0·25	..
	0·20	..	..	0·14	0·27	..	0·24	..
Mean	0·20	0·24	0.28	0·15	0·28	0·22	0·25	...
Chick mash	0·01	0·02	0·010	0·020	0·013	0·018	..	0·022
	0·01	0·03	0·010	0·027	0·013	0·011	..	0·015
	0·01	..	0·017	0·020	0·012	..	..	0·012
	0·01	..	0·009	0·018	0·012	..	..	0·014
	..	..	..	..	..	..	..	0·013
Mean	0·01	0·25	0·012	0·021	0·012	0·015	..	0·015
Manure	0·20	0·19	0·13	0·11	0·23	0·15	..	0·23
	0·11	0·37	0·12	0·12	0·23	0·15	..	0·17
	0·19	..	0·10	0·13	0·18	..	..	0·121
	0·21	..	0·13	0·11	0·20	..	..	0·11
	..	..	..	..	..	..	..	0·11
Mean	0·18	..	0·12	0·12	0·21	0·15	0·20	0·15

*In this first collaborative trial, four of the laboratories encountered practical difficulties in establishing the assay and for this reason no results are reported

Summary

The Panel accepted published evidence of the non-specificity of microbiological assays of vitamin-B_{12} employing B coli, L leichmanii or Euglena as test organisms and a more specific technique using the protozoan Ochromonas malhamensis was selected for study.

In view of inherent difficulties encountered in microbiological assays and the low level of vitamin B_{12} in some of the samples examined the results provided by these collaborative trials were considered to be satisfactory.

APPENDIX

Recommended Procedure for the Microbiological Determination of vitamin B_{12} Preparation or Test Extracts—

Vitamin B_{12} may occur naturally in complex-bound forms that may escape detection because of non-quantitative extraction, or because of their unavailability to the test organism. A further problem is that the vitamin may be present as hydroxycobalamin, which is relatively unstable to heat and may thus be lost in the processes of measurement. Both problems can be largely resolved by the use of cyanide in the preparation of the test extract. The effect of cyanide is two fold. Firstly, it appears to facilitate extraction by displacing protein or polypeptide groups originally linked to the vitamin. Secondly, it converts the cobalamin to the stable cyano-form.

In general it is sufficient to add from 0·5 to 5·0 mg of sodium cyanide (as a 1 per cent. aqueous solution) to each gram of test sample, the amount depending upon the nature and potency of the test substance. It is most important, however, that the amount of sodium cyanide used should not be sufficient, even if no cyanide is lost during the extraction and sterilisation processes, to give a concentration of sodium cyanide in the final growth medium greater than 10 ug per ml. Hence, the lower the potency of the material the smaller should be the amount of cyanide used. The extraction procedure recommended is—

To 1 g of the test material in 125 ml conical flask add 30 ml of water and from 0·05 to 0·5 ml of freshly prepared 1 per cent, aqueous sodium cyanide, mix well and adjust the pH to between 4-6 and 5-0 with N hydrochloric acid. Allow the mixture to stand for 30 minutes at room temperature with occasional shaking and re-adjust the pH if necessary. Place the flask in a boiling-water bath and leave it for 30 minutes after the extract has reached 90°C. Cool, transfer the liquid to a 100-ml calibrated flask and dilute to 100 ml. with distilled water. Clarify by centrifuging; then take a 50 ml. aliquot of the cleared liquid and dilute it until the concentration of vitamin B_{12} is of the order of 0.0002 ug per ml.

Starcy samples may yield turbid extracts but they can be cleared by treatment with takadiastase.

Some materials, notably preparations of gut mucosa, have the property of "binding" vitamin B_{12} and rendering it unavailable to the test microrganism. The foregoing simple extraction method may not liberate the vitamin from such materials and a more elaborate procedure involving digestion with cyanide-activated papain should be used, as described by Gregory. Very few natural materials call for this enzymic extraction procedure, however, and in the main simple method recommended will prove adequate.

Maintenance of Stock Cultures

To 400 ml of an aqueous solution containing 0·00025 ug of vitamin B_{12} per ml add 100 ml of basal medium. Dispense 10 ml portions of this diluted and enriched basal medium into 50 ml contical flasks, plug the flasks, plug the flasks and sterilise by autoclaving for 15 minutes at 10 lb. pressure, covering the plugs with grease-proof paper during the autoclaving. Inoculate one of the flasks with a culture of Ochromonas malhamensis (Pringsheim strain)* and incubate.

*Obtainable from the Curator, Culture Collection of Algae and Protozoa, Downing Street, Cambridge, at 27° to 30° C one foot below a 60 watt "striplite tungsten filament lamp. Having established the culture, prepare sub-cultures at intervals, usually every 4 to 5 days, by transferring 0·5 ml of the current growth to a flask of sterile medium. When the organism is sub-cultured, the culture should be dense and yellow-brown in colour.

Preparation of Basal Medium

To 150 ml of distilled water add the following ingredients—

"vitamin-free" casein hydrolysate	5·0 g
Glucose	10·0 g
Di-ammonium hydrogen citrate	0·8 g
Potassium di-hydrogen phosphate	0·3 g
Magnesium sulphate	0·2 g
Calcium chloride (annydrous)	0·15 g
Sodium molybdate ($Na_2MoO_4,2H_2O$)	0·05 g
DL-Tryptophane	0·1 g
Dl-Methionine	0·2 g
Tween 80, T.B. culture grade†	1·0 ml
"Metals" solution	10·0 ml
Vitamins solution	2·0 ml
Sodium cyanide solution	0·2 ml

†Obtainable from Messrs. Honeywill and Stein Ltd., Devonshire House, Mayfair Place, Piccadilly, London, W. 1.

Stir 0·1 g of L-cystine into 15 ml of hot water and add 6 N hydrochloric acid dropwise until the amino acid is dissolved. Add the liquid to the foregoing solution, adjust the pH to 5·5 with 4N aqueous potassium hydroxide and dilute to 200 ml.

This basal medium should be stored frozen in screw-crapped polythene containers.

The solutions listed as ingredients of the bassal medium are prepared as follows :—

"Metals" solution-Dissolve 5 g. of ethylenediamine tetraacetic acid in 900 ml of hot water. Then in the solution dissolve the following—

Manganese sulphate, $MnSO_4\ H_2O$	6·0 g
Zinc sulphate, $ZnSO_4\ 7H_2O$	11·0 g
Ferrous sulphate, $FeSO_4\ 7H_2O$	1·0 g
Cobalt sulphate, $CoSO_4\ 7H_2O$	0·3 g
Copper sulphate, $CuSO_4\ 7H_2O$	0·04 g
Boric acid, $H_2\ BO_3$	0·06 g
Potassium iodide, KI	0·001 g

Make up the solution to I litre with water.

Vitamins solution—Weigh out 1 g of of inositol, 200 mg of choline chloride, 100 mg of p-aminobenzoic acid, 200 mg of thiamine hydrochloride and I mg of biotin and transfer to 200 ml calibrated flask. Dilute to the mark with 20 per cent v/v aqueous ethanol. Store in a refrigerator.

Sodium cyanide solution-Dissolve 1 g of sodium cyanide in water and dilute to 100 ml. The solution should be renewed at fortnightly intervals.

Setting up the Assay

Dispense each of the quantities 0·5, 1, 2 and 4 ml of a standard vitamin-B_{12} solution (0.0002 ug of cyanocobalamin per ml*) into each of four bacteriological test tubes

*Prepared by diluting a 5 ug per ml stock solution of cyanocobalamin. which must have been standardised spectrophotometrically, with 20 per cent. v/v aqueous ethanol. The stock solution will keep indefiniety if stored in the dark in a refrigerator. The dilutions should be prepared from 1 ml of the stock solution to which 1 drop of sodium cyanide solution has been added.

(19 × 15mm) and similarly put up in quadruplicate the same volumes of the test extract. To each of these 32 tubes and to each of 5 empty tubes add sufficient distilled water to give a total volume of 4 ml in each tube. To each of the 37 tubes now add 1 ml of the basal medium. Cap or plug the tubes, place them in suitable racks or baskets and autoclave for 10 minutes at 10 lb pressure. Cool the tubes to about 30°C by standing them in cold water and then inoculate all the tubes except one of the five containing only water with one drop of a five-day culture of Ochromonas malhamensis. This step should be performed as speedily and as uniformly as possible. Place the racks or baskets of tubes in a shaking machine installed in a dark incubator maintained at 29° to 30°C and keep the shaker in motion for 72 hours.

Measurement of Response

At the end of the incubation period remove the tubes and steam them for 5 to 10 minutes. Cool, mix the contents thoroughly and measure instrumentally with a suitable filter the turbidity of the contents of each

tube using, where necessary, the uninoculated tube as a 'blank'. A suitable procedure is to make the measurements in ½-cm cells in a Spekker absorptiometer, using Ilford H.508. filters.

Calculation of Results

A "standard" curve can be plotted from the dose response relationship provided by the tubes containing 0, 0·5, 1, 2 and 4 ml of standard vitamin-B_{12} solution and from this curve can be read the quantities of vitamin B_{12} corresponding to the turbidities found in the tubes containing test extracts.

References :

1. Ford, J. E., Brit. J. Nutr., 1953, 7, 299.
2. Coates, M.E. and Ford, J.E., in the press.
3. Gregory, M.E., Brit, J. Nutr. 1955, 8, 340

MINUTES OF THE EIGHTEENTH MEETING OF THE DRUGS TECHNICAL ADVISORY BOARD HELD ON THE 23RD JULY, 1957 AT NEW DELHI

PRESENT :

1. Lt. Col. C. K. Lakshmanan, Director General of Health Services, New Delhi, *Chairman*.
2. Dr. A. C. Chatterji, Government Analyst, Government of U. P.
3. Dr. P. K. Ghosh, 22, Nilmoni, Mitter Street, Calcutta.
4. Dr. M. L. Gujral, Professor of Pharmacology, Medical College, Lucknow.
5. Dr. G. K. Karandikar, Professor of Pharmacology, Medical College, Baroda.
6. Shri P. S. Krishnan, Chief Chemist, Central Revenues Control Laboratories, Post : Agricultural Research Institute, New Delhi.
7. Dr. H. R. Nanji, Managing Director, "Italab" Ltd., Bombay.
8. Shri B. V. Patel, Drugs Controller for the State of Bombay.
9. Dr. J. N. Ray, Bombay.
10. Prof. G. P. Srivastava, Professor of Pharmaceutical Chemistry, Banaras Hindu University, Banaras.
11. Dr. Sheo Vihari Lal, Govt. Analyst of Bihar.
12. Shri S. K. Borkar, Drugs Controller, India, *Member and Secretary*.

1. Apologies for absence were received from Doctors B. N. Ghosh, K. K. Sen Gupta, C. V. D'Silva and B. D. Kehar. Dr. G. K. Karandikar, who arrived late, participated in the deliberations of the liver extract subcommittee meeting held in the afternoon.

2. Dr. A. C. Chatterji and Shri S. K. Borkar, who were new members, were introduced.

3. The Chairman made a reference to the work done by Shri P. M. Nabar who was Secretary and Member of the Board for many years and suggested that a note of appreciation of his services be recorded. The Board agreed and passed the following resolution :—

"The Board places on record its deep appreciation of the services rendered by Shri P. M. Nabar both as Member and Secretary of the Drugs Technical Advisory Board".

4. It was decided that a copy of the resolution be communicated to Shri P. M. Nabar.

Item 1 of the Agenda—Confirmation of the minutes of the seventeenth meeting.

5. The comments received from Shri S. P. Sen and Dr. P. K. Ghosh on the minutes of the previous meeting were considered and the Board decided not to make any changes in the minutes, which were then confirmed.

Item 2 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-2/56-D dated the 30th January, 1956 containing proposal for revision of Schedule F and amendment of Schedule K to the Drugs Rules.

6. The Board agreed that Schedule F be brought in conformity with the latest editions of the recognised Pharmacopoeias and appointed a sub-committee consisting of the following persons for the purpose :—

1. Dr. M. L. Gujral.
2. The Director, Central Research Institute, Kasauli.
3. Shri B. V. Patel.
4. Dr. A. K. Hazra.
5. Shri S. K. Borkar, Member and Secretary.

7. The Board desired that the sub-committee should finalize its recommendations within a period of three months and that recommendation of the sub-committee should be circulated to the members of the Board.

8. The suggestion that the first entry in Schedule 'K' of the Drugs Rules should be amended and brought in line with the corresponding entry in Schedule 'D' was also agreed to.

The Board recommended that the entry in Schedule 'K' should be amended to read as follows :—

Class of Drugs	*Extent and conditions of exemption*
1. Substances not intended for medicinal use.	All the provisions of Chapter IV of the Act and the Rules thereunder, subject to the conditions that the drug is not sold for medicinal use or for use in the manufacture of medicines and is labelled conspicuously with the words "NOT FOR MEDICINAL USE".

Item 3 of the Agenda—Consideration of Government of India, Ministry of Health endorsement No. F. 1-11/56-D dated 29th March, 1956 containing proposal for the amendment of Rule 109(3) (b) and (d) and to the Drugs Rules regarding labelling of drugs with date of expiry.

9. The Board agreed that the date of the expiry of potency should be given not only on the label of the carton or packing in which the containers of Schedule C drugs are packed, but also on the label of the ampoule, vial etc., containing the drug.

Items 4 & 18 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-4/56-D dated the 19/21st May, 1956 containing comments of various parties on the draft amendments to rules 65 and 97, Schedules E, G, and H and the new Schedule L to the Drugs Rules and Uniform State Poisons List & Consideration of Government of India, Ministry of Health letter No. F. 1-38/57-D dated the 27th June, 1957 containing proposal for the amendment of Rule 65(9).

10. These items were considered together. The Board constituted the following Sub-Committee to examine the various comments received on Schedules E, G, H and L.

1. Shri B. V. Patel.
2. Dr. G. K. Karandikar.
3. Dr. M. L. Gujral.
4. Dr. A. C. Chatterji.
5. Shri P. S. Krishnan.
6. Shri P. S. Ramachandran, *Member and Secretary*.

11. The comments received on the amendments to Rule 65 were then examined. The Board agreed that the proviso to sub-rule (2) of Rules 65 should be deleted.

12. As regards Rule 65(9) the Board discussed the comments received from the trade pointing out the impracticability of retaining prescriptions of registered medical practitioners for Schedule H drugs and recommended that the proposed provision requiring the retention of such prescriptions need not be introduced.

13. The new Rule 65(16) proposed to be introduced was agreed to by the Board.

14. The deletion of the word "Liquid" occurring in the sub-rule 2 of Rule 97 was also agreed to.

15. The Board agreed that the language of existing Rule 65(9) should be amended in the manner suggested in Government of India, Ministry of Health letter No. F. 1-38/57-D, dated 27th June, 1957.

Item 5 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-19/55-D dated the 26th June, 1956, containing proposal for inclusion of preparations of Rauwolfia Serpentina in Schedule H to the Drugs Rules.

16. The views of experts on the question of including Rauwolfia Serpentina and its preparations in Schedule 'H' of the Drugs Rules were examined by the Board. It was felt that since Rauwolfia Serpentina was also used in the indigenous systems of medicines, it will not be possible

to enforce the provision in a satisfactory manner even if it was agreed to include the item in Schedule H. After discussion it was decided that the question of including Rauwolfia Serpentina and its preparations in Schedule H of the Drugs Rules should be postponed till further data on the toxicity of the drug was available.

Items 6 and 15 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-25/56-D, dated the 13th July, 1956, containing proposal for including fresh forms in the Drugs Rules for repacking of drugs and Consideration of Government of India, Ministry of Health letter No. F. 1-34/57-D dated the 24th June, 1957 containing proposal for introducing special licence form for repacking of drugs.

17. These items were considered together. The Board agreed that separate forms for the grant of manufacturing licences for re-packers of drugs should be included in the Drugs Rules and recommended the inclusion of the application forms, licence fees etc. suggested in Enclosure 'N' to the agenda, with minor alterations.

Item 7 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-7/56-D, dated the 25th August, 1956 containing proposal for insertion of additional rule under Rule 52 of the Drugs Rules empowering Drugs Inspectors to seize records, registers etc.

18. The Board considered Government of India, Ministry of Health letter No. F. 1-7/56-D, dated the 25th August, 1956, and agreed that Drugs Rules 51 and 52 should be amended on the following lines :—

(1) Amend sub-rule (7) of Rule 51 to read :—"To make such enquiries and inspections as may be necessary to detect the sale of drugs in contravention of the Act and to seize records, registers and other documents to establish such contravention".

(2) A new sub-rule 4(A) to be added to Rule 52 :—"(4-A). To make such enquiries and inspection as may be necessary to detect the manufacture of drugs in contravention of the Act and to seize records, registers, cartons, blocks, and any other material object required to establish such contravention".

Item 8 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 3-7/56-D, dated the 4th October, 1956 regarding storage of Poisons under Schedule E to the Drugs Rules

19. The Board agreed that the provisions relating to storage of poisons in the Drugs Rules should be brought in conformity with the State Poisons Rules and recommended that sub-rule 12 of rule 65 be amended to read:—

"(12) Substances specified in Schedule E kept in a retail shop or premises used in connection therewith shall be stored and secured by lock and key in :—

(a) a cupboard or a drawer reserved solely for the storage of poisons, or

(b) a part of the premises separated from the remainder of the premises and to which customers are not permitted to have access."

Item 9 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-68/D, dated the 5th January, 1957 containing proposal for inclusion of Viomycin in Schedule C(1) to the Drugs Rules.

20. The suggestion contained in Government of India, Ministry of Health letter No. F. 1-68/56-D dated 5-1-1957 that preparations containing dry powder for parenteral administration should be brought within the purview of Schedule C and the amendment for the purpose proposed in Rule 65(9) was agreed to by the Board.

Item 10 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-12/57-D, dated the 19th February, 1957 containing proposal for inclusion of Viomycin in Schedule C(1) to the Drugs Rules.

21. The Board recommended that Viomycin be included in Schedule C(1) of the Drugs Rules.

Items 11 and 19 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-30/56-D dated the 24th April 1957, containing proposal for the amendment of provisions laid down for Tetanus Antitoxin in Schedule F to the Drugs Rules. Consideration of Government of India, Ministry of Health letter No. F. 1-37/57-D dated 27th June, 1957 containing proposal for the amendment of provisions for labelling in Part I of Schedule F in respect of Cholera Vaccine.

22. It was explained to the Board that the question raised in items 11 and 19 of the agenda was proposed to be examined in detail by the Biological sub-committee of the Indian Pharmacopoeia Committee. The Board agreed to postpone consideration of these items till the views of the sub-committee of the Indian Pharmacopoeia Committee were known. It was decided that the views of the sub-committee should be circulated to the members of the Board.

Item 12 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-28/55-D dated the 20th June, 1957 regarding amendment of item 5 of the Schedule K to the Drugs Rules granting exemption to Government hospitals, charitable institutions etc.

23. The Board considered the recommendations of the Drugs Consultative Committee in regard to the exemption provided for hospitals and dispensaries in item 5 of Schedule K to the Drugs Rules and agreed to the amendments proposed by the Government of India in their letter No. F. 1-28/55-D dated 20-6-1957.

24. It, however, decided that condition (4) under "Extent and conditions of Exemption" against the proposed entry at item 5-A in Schedule K to the Drugs Rules be deleted.

Item 13 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-35/57-D, dated the 24th June, 1957 containing proposal for amendment of Schedule K granting exemption to insecticides and their formulations in respect of sale licences.

25. The Board agreed to the amendment proposed in Government of India, Ministry of Health letter No. F. 1-35/57-D, dated 24-6-57.

Item 14 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-36/57-D dated the 14th June, 1957 containing proposal for granting restricted sale licences to only certain specific classes of household remedies.

26. The proposed amendments to the Drugs Rules suggested by the Government of India, Ministry of Health in their letter No. F. 1-36/57-D, dated 24th June, 1957 were agreed to by the Board.

Item 16 of the Agenda—Consideration of Government of India, Ministry of Health letter No. 1-33/57-D dated the 21st June, 1957 containing proposal for including standards for Penicillin Aluminium Monostearate (PAM) in Schedule F to the Drugs Rules.

27. The Board agreed that the W. H. O. specifications for Procaine Penicillin with Aluminium Monostearate (PAM) should be adopted for the purpose of the Drugs Rules and incorporated in Schedule F.

Item 17 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-52/56-D dated the 26th June, 1957 containing proposal for recognition of preparations covered by the earlier editions of the Pharmacopoeias and amendment of the Drugs Act, 1940.

28. The Board discussed the recommendations made by the Drugs Consultative Committee regarding recognition of the earlier editions of pharmacopoeias and agreed that :—

(1) The earlier editions of the prescribed pharmacopoeias need *not* be recognized as "standards" under Rule 124 of the Drugs Rules and that the present provision in the Schedule of the Drugs Act recognising the current editions of the prescribed pharmacopoeias should be continued.

(2) Necessary amendments should be made so as to permit Government Analysts to employ any tests to establish the identity, purity and the strength of the items wherever adequate tests were not laid down for this purpose in the prescribed pharmacopoeias.

The Board, however, felt that the recommendation of the Drugs Consultative Committee that the formula of patent and proprietary medicines should be approved by the Central Government was *not* capable of being implemented in practice at this stage.

Item 20 of the Agenda—Consideration of Government of India, Ministry of Health letter No. F. 1-39/57-D, dated the 27th June, 1957 containing comments received on the draft standards for "Crude Liver Extract for parenteral administration" for inclusion in Schedule F.

29. The Board appointed the following sub-committee to examine the comments received from various sources on the provisions for Injection of Liver Extract Crude :—

1. Dr. J. N. Ray.
2. Shri B. V. Patel
3. Dr. M. L. Gujral.
4. Dr. P. K. Ghosh, and
5. Shri P. S. Ramachandran.

The following resolution, which was moved by Dr. A. C. Chatterji and seconded by Dr. G. P. Srivastava, was passed :—

> "Resolved that the sub-committee's report to be submitted to the Chairman who is authorized to finalize it and forward it to Government for necessary action."

Item 21 of the Agenda—Any other items with the approval of the Chair

30. The Chairman read out the letter (Appendix I) received from Dr. P. K. Ghosh and Dr. K. K. Sen Gupta in which notice had been given of a resolution proposed to be moved by them. The members discussed the question as to what would be the status and functions of the Central Drugs Laboratory and State Government laboratories should the proposal to expand and adopt the Customs Laboratories for the purpose of preliminary testing work under the Drugs Rules be accepted by Government. Drs. P. K. Ghosh and A. C. Chatterji raised certain points for clarification and the Chairman suggested that they should send a note containing their views on the subject for further examination.

31. The meeting terminated with a vote of thanks to the Chair.

APPENDIX I

To

The Secretary,
Drugs Technical Advisory Board,
Directorate General of Health Services,
Secretariat, New Delhi.

Dear Sir,

We want to place the following resolutions at the meeting of the D.T.A.B. to be held on 23-7-57 at New Delhi :—

I. "We the undersigned view with grave concern a recent proposal to bye-pass the Central Drugs Laboratory for analysis of drugs and to entrust its work to different Customs Laboratories increasingly. The new industrial policy of the Government of India is aiming at restricting the import of drugs to a very considerable extent. It will not therefore be proper to start newer laboratories under the aegis of Customs authorities, involving a very considerable outlay in foreign exchange especially when import of drugs will dwindle in the near future".

II. "We view with grave concern reports on manufacture of spurious drugs by unscrupulous persons. To prevent this we recommend that—

(1) Steps be taken to immediately increase the number of Drug Inspectors in the different States.

(2) The Drug Rules be so modified as to enable the Drug Inspectors have the power like Police Officers to seal the suspected goods immediately. This simple power will prevent at once the removal or replacement of spurious or adulterated drugs by the offender concerned.

Lastly, we do not know how the amendments to Drug Rules, 1945 have been modified after the Conference at New Delhi on 24-1-1957. May we please have some information on this subject, if they are not already being circulated for this meeting.

Yours faithfully,

(Sd.) P. K. GHOSH,

AND

K. K. SEN GUPTA.

GIPN—S5—1 M. of Health/58—18th (M...) 1-3-60—[illegible]