133 Molesworth Street
PO Box 5013
Wellington 6145, New Zealand
T +64 4 496 2000

09 JUN 2017

[redacted]

Ref: H201701896

Dear [redacted]

Response to your request for official information

Thank you for your request of 23 May 2017 under the Official Information Act 1982 (the Act) for

"…copies of the following: documents, emails, hand-written notes, minutes, texts and telephone conversations regarding:

1. *Requests from the Medicines and Healthcare Products Regulatory Agency (MHRA) to provide New Zealand information to them and/or the Expert Working Group (EWG) Inquiry into HPT products, including but not limited to Primodos.*
2. *Reports or other information from the MHRA regarding HPTs including but not limited to Primodos.*
3. *Correspondence to and from Schering/Bayer regarding the withdrawal of Primodos from the market.*
4. *Actions recorded and correspondence with Schering/Bayer to ensure compliance with the withdrawal of the drug under existing statutory regulations in addition to any other requirements made by the Department of Health.*
5. *Evidence to demonstrate how the NZ Department of Health "....removed stock from pharmacies", Medsafe Publications, 20th March, 2017.*
6. *All notifications to General Practitioners and/or their regulatory body regarding the withdrawal of HPTs including but not limited to Primodos.*
7. *All notifications to The Chemist Service Guild, Wholesalers and Retailers regarding the withdrawal of HPTs including but not limited to Primodos.*
8. *Documentation to show the process implemented to ensure that no stock remained in the possession of General Practitioners or Pharmacies.*
9. *Notices for publication in the NZ Gazette regarding the introduction and revocation of HPTs including but not limited to Primodos.*
10. *Notices for publication in the NZ Gazette regarding the introduction and revocation of intramuscular HPTs including but not limited to Duogynon and Primodos.*

11. *Minutes of meetings or other correspondence that shows what (if any) actions were considered by the Department of Health to research the histories of, or contact women (or their General Practitioners) who were prescribed HPTs, including but not limited to Primodos."*

The information relating to this request is itemised below, with copies of documents attached.

I have decided under section 9(2)(a) of the Act to withhold information to protect the privacy of natural persons. I have also decided to withhold information that is outside the scope of your request. Specific grounds are noted in each document where information has been withheld.

Request	Response
1. Requests from the Medicines and Healthcare Products Regulatory Agency (MHRA) to provide New Zealand information to them and/or the Expert Working Group (EWG) Inquiry into HPT products, including but not limited to Primodos.	This request is refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist.
2. Reports or other information from the MHRA regarding HPTs including but not limited to Primodos.	This request is refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist.
3. Correspondence to and from Schering/Bayer regarding the withdrawal of Primodos from the market. 4. Actions recorded and correspondence with Schering/Bayer to ensure compliance with the withdrawal of the drug under existing statutory regulations in addition to any other requirements made by the Department of Health.	Attached are: 1. Letter dated 4 June 1975 2. Letter dated 30 May 1975 with recall letter 3. Handwritten note dated 27 May 1975 4. Letter dated 26 May 1975 5. Letter dated 19 May 1975 6. Handwritten note dated 21 May 1975 7. Letter dated 1 May 1975 8. Handwritten note dated 29 April 9. Handwritten note dated 14 April 1975 10. Letter dated 10 April 1975 with Australian permit to import 11. Document with information from the World Health Organization 12. Document with a handwritten note 'DAAC' 13. Letter dated 2 April 1975

	14. Handwritten note dated 24 March 15. Letter dated 18 March 1975 16. Handwritten note dated 11 March 17. Letter dated 6 March 1975 18. Information from the Medical Journal of Australia 19. Letter dated 18 February 1975 with information from the World Health Organization and the Medical Journal of Australia
5. Evidence to demonstrate how the NZ Department of Health "....removed stock from pharmacies", Medsafe Publications, 20th March, 2017.	Attached are documents regarding Amenorone Forte: 1. Letter dated 26 June 1975. 2. Letter dated 19 June 1975. 3. Letter dated 13 June 1975. 4. Letter dated 9 June 1975. 5. Letter dated 18 June 1975. 6. Letter dated 26 May 1975. 7. Letter dated 9 May 1975. 8. Letter dated 1 May 1975 with information from the World Health Organization. 9. Letter dated 4 April 1975. 10. Letter dated 21 March 1975. 11. Handwritten note. 12. Document dated 19 March 1975. 13. Letter dated 13 March 1975 with information from the Medical Journal of Australia and the World Health Organization. Please also refer to documents regarding Primodos provided in response to questions 3 and 4.
6. All notifications to General Practitioners and/or their regulatory body regarding the withdrawal of HPTs including but not limited to Primodos.	This request is refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist.
7. All notifications to The Chemist Service Guild, Wholesalers and Retailers regarding the withdrawal of HPTs including but not limited to Primodos.	Please refer to documents regarding Amenorone Forte provided in response to question 5 (points 2 and 4).
8. Documentation to show the process implemented to ensure that no stock	Please refer to documents regarding Primodos provided in response to questions 3 and 4.

remained in the possession of General Practitioners or Pharmacies.	Please refer to documents regarding Amenorone Forte provided in response to question 5.
9. Notices for publication in the NZ Gazette regarding the introduction and revocation of HPTs including but not limited to Primodos.	This request is refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist.
10. Notices for publication in the NZ Gazette regarding the introduction and revocation of intramuscular HPTs including but not limited to Duogynon and Primodos.	This request is refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist.
11. Minutes of meetings or other correspondence that shows what (if any) actions were considered by the Department of Health to research the histories of, or contact women (or their General Practitioners) who were prescribed HPTs, including but not limited to Primodos.	This request is refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist.

I trust this information fulfils your request. You have the right, under section 28 of the Act, to ask the Ombudsman to review my decision to withhold information under this request.

Yours sincerely

[redacted]

Group Manager
Medsafe

142/70/2539

4 June 1975

Section 9(2)(a)
Marketing Manager,
Schering (N.Z.) Ltd,
P.O. Box 66011,
AUCKLAND 10

Dear Section 9(2)(a)

PRIMODOS ORAL

The Department is pleased to note the action taken by your Company to withdraw stocks of Primodos Oral from the retail pharmacy level from 9 June 1975.

An increasing number of articles from the world literature on the association between hormonal steroids and limb defects are coming to our notice. I feel sure that your Company has made a most appropriate decision.

Yours sincerely,

D.C.A

(D.A. Andrews)
Director,
Division of Clinical Services

Dr [illegible] JM
Dr. Bremner B
Dr [illegible] JMW.
Dr Griffiths RJ.
Dr Cook Klug
File M

Copy placed on 141/24 drug recall file MJB

SCHERING (N.Z.) LIMITED

Representatives for
Schering AG
Berlin/Bergkamen
Germany

Telegrams & Cables: Schering, Auckland
Telephone 437-159, 437-158
P.O. Box 66011, Auckland 10, N.Z.
Office & Warehouse:
Kahika Road, Birkdale, Auckland 10

The Director,
Division of Clinical Services,
Department of Health,
P.O. Box 5013,
WELLINGTON

30 May 1975

Attention: Dr D. A. Andrews

Dear Sir,

PRIMODOS ORAL

Further to your letter dated 26 May regarding the abovementioned subject, enclosed please find a copy of our Primodos Oral Recall letter which is being despatched to all wholesalers, and retail chemists, public and private hospitals by the Pharmaceutical Manufacturers' Association using the procedure laid down by yourselves.

You will note from this that we hope to have withdrawn all Primodos Oral from the New Zealand market by Monday 9 June 1975.

Yours faithfully,
SCHERING (N.Z.) LIMITED

Section 9(2)(a)

MARKETING MANAGER

ENCL:

SCHERING (N.Z.) LIMITED

Representatives for
Schering AG
Berlin/Bergkamen
Germany

Telegrams & Cables: Schering, Auckland
Telephone 437-159, 437-158
P.O. Box 66011, Auckland 10, N.Z.
Office & Warehouse:
Kahika Road, Birkdale, Auckland 10

CIRCULAR LETTER TO:

ALL WHOLESALERS AND RETAIL CHEMISTS, PUBLIC AND PRIVATE HOSPITALS

30 May 1975

Dear Sirs,

PRIMODOS ORAL RECALL

The New Zealand Health Department have requested that Primodos Oral should be withdrawn from the New Zealand market as a direct result of certain adverse comments which have appeared in the medical press overseas.

Therefore, Primodos Oral will be withdrawn from the New Zealand market by Monday 9 June 1975. We request that all stocks held by you should be returned as follows:

(1) Retail Chemists: Return via your wholesaler.

(2) Wholesalers: Return directly to Schering (N.Z.) Ltd, P.O. Box 66-011, Auckland 10.

(3) Public and private hospitals: Return directly to Schering (N.Z.) Ltd, address as above.

Enclosed with this letter is a short form which indicates the wholesaler or hospital name, the quantity returned and to whom the goods are to be credited, and we would request that these are filled out and returned with the goods. As Primodos Oral is a fairly light product we would suggest that it is returned by mail.

We look forward to your early co-operation in this matter.

Yours faithfully,
SCHERING (N.Z.) LIMITED

Section 9(2)(a)

MARKETING MANAGER

ENCL:

PRIMODOS ORAL RECALL

WHOLESALER/HOSPITAL NAME .....

QUANTITY .....

CREDIT TO: .....

142/70/2539 21-5-75

Schering (N.Z) Limited

Noted. ~~DHS~~.

(Primodos oral unavailable from 1-6-75)

142/70/2539

26 May 1975

The Managing Director,
Schering (N.Z.) Ltd,
P.O. Box 66011,
AUCKLAND 10

Dear [redacted]

PRIMODOS ORAL

Thank you for your letter. The Department is impressed with the responsible manner with which you have dealt with this problem.

The Department does not consider, however, that continued availability at retail level until stocks in the "pipe-line" are cleared is sufficient. Risk of foetal abnormality may be exceedingly small, but even one case that could have been prevented would be one too many.

It is considered that stock withdrawal from retail level should be implemented and all sales stopped. The agent for the other oral pregnancy test available in New Zealand has been asked to act likewise and has already notified the Department that his product will be officially withdrawn from sale from 1 June 1975.

Yours faithfully,

D.A.A

(D.A. Andrews)
for Director,
Division of Clinical Services

1 ~~Dr Chetwin~~ JW
2 ~~Dr Benson~~ RB
3 ~~Dr Wilson~~ Dave
4 ~~Dr Griffiths~~ BG
5 F. VK

B/u for Dr Andrews VK 17/6/75 Dog 17/6

SCHERING (N.Z.) LIMITED

Representatives for
Schering AG
Berlin/Bergkamen
Germany

Telegrams & Cables: Schering, Auckland
Telephone 437-159, 437-158
P.O. Box 66011, Auckland 10, N.Z.
Office & Warehouse:
Kahika Road, Birkdale, Auckland 10

The Division of Clinical Services,
Department of Health,
P.O. Box 5013,
WELLINGTON

19 May 1975

Attention: Dr D. A. Andrews

Dear Dr Andrews,

PRIMODOS ORAL

Thank you for your letter dated 1 May 1975 regarding our product, Primodos Oral. May we say straight away that we are very surprised that you still request withdrawal of this product, particularly when the decision of the Australian Drug Evaluation Committee is considered and when available evidence on the subject seems to be somewhat inconclusive.

We will however comply with your request which appears under No. 5 in the abovementioned letter, and to this end we are going to inform all wholesalers that Primodos Oral will no longer be available to them from 1 June 1975. We assume that you are quite happy for any Primodos Oral which is at present in the distribution pipeline with wholesalers and retail chemists to be sold in the normal manner. We will then discontinue any further supplies from 1 June.

Yours faithfully,
SCHERING (N.Z.) LIMITED

Section 9(2)(a)

MARKETING MANAGER

MINUTE SHEET

Subject: PRIMODOS ORAL

Department:

File No. 142/70/2539

Date: 2/[illegible]/7[illegible]

To— [illegible]

Ian is to discuss this with Jon as well as the Roussel product.

I think that we cannot condone sale of drugs 'in the pipeline'. Stocks could just be such that supplies are available for months to come if demand is not great.

I suggest that the two firms should adopt a consistent approach that withdrawal of the product to retail level is warranted until further evidence of safety becomes available.

[illegible signature]

Item 504

36096J—22,000pads/10/73D

IW:ZH

142/70/2539

1 May 1975

The Managing Director,
Schering (N.Z.) Limited,
P.O. Box 66011,
AUCKLAND,10.

Dear [redacted]

I again refer to your product Primodos Oral and thank you for your letter of 10 April which was jointly signed by yourself and [redacted]

The entire subject has again been reviewed and the following comments outline this Department's decision:-

1. Products such as these are still being used as pregnancy tests. Such use is frequently instigated by medical practitioners (laboratory facilities are not readily available to all) but also suggested by patients.

2. Alteration of advertising material would appear to achieve very little change to prescribing patterns; package inserts for example are rarely read by the medical practitioners. The Australian requirements therefore appear to this Department to be unsound since there is no guarantee that the patient will not receive such therapy.

3. There are various suitable alternative forms of therapy for treating secondary amenorrhea.

4. The question has been considered recently by the Committee on Adverse Drug Re-actions who have recommended that products of this type be withdrawn from the market. Further, The United States Food and Drug Administration have recently ruled that drugs of this type are not known to be safe and that shipment in inter-state commerce are unlawful.

5. The Department must repeat its request for the withdrawl of this product from the market and would like an early reply.

6. In a future Clinical Services letter the association of use of products of this type and foetal abnormality is to be mentioned.

Yours faithfully,

(Ian A. Witty)
for Director
Division of Clinical Services

MINUTE SHEET

Department:

Subject:

File No.

Primodos [illegible]

Date:

To—

v. [illegible], [illegible]

[illegible] our reply to company. [illegible] CADR recommendation; [illegible] ... a similar [illegible]

1. Products such as these are still being used as pregnancy tests. Such use is frequently instigated by doctors (laboratory facilities are not readily available to all) but also suggested by patients.

2. Alteration to advertising material would achieve very little change to prescribing patterns; package inserts for example are rarely read by doctors. The Australian requirements therefore appear to this Dept. to be unsound since there is no guarantee that the patient will not receive such therapy.

3. There are various suitable alternative forms of therapy for treating secondary amenorrhoea.

4. The question has been considered recently by CADR who have recommended that products of this type be withdrawn from the market. Further, the U.S. F & D Administration have stated recently that drugs of this type are not known to be safe & that shipment in interstate commerce are unlawful.

5. The Dept. must repeat its request for the withdrawal of this product from the market & would like an early reply.

6. In a future CSL the association of use of products of this type & foetal abnormality is to be mentioned.

[illegible signature]

29/4

MINUTE SHEET

Subject: Primodos Oral

Department:

File No. 142/70/2539

Date: 14/4/75

To— 1

Dr Andrews ~~DCH~~

~~Phillips DDS~~

28/4/75

~~Cochrane~~

Mr Whitting

GOW

4

For your comments and recommendations for action please.

[initials]

1. I should be interested in your opinion on this subject. In view of recent well documented reports of foetal deformity & use of systemic hormonal pregnancy tests in early pregnancy both our Drug Assessment Advisory Committee & the C.A.D.R. have recommended that the two local products be removed from the market.

2. We are aware that both formulations are being prescribed as pregnancy tests. Alteration of package insert (rarely read by doctor & not often given to patient) would not alter prescribing pattern.

3. How important is the treatment of 2° amenorrhoea with such products? Are there not sufficient alternatives that are not normally also used as pregnancy tests?

4. The other firm concerned (Roussel) has indicated its willingness to remove its product from the market.

D. A. Andrews
18/4

28/4/75 Would agree with the remarks on pregnancy testing. I feel no real indication for retaining the proper secondary Amenorrhoea - there is a place

hormones by oestrogen and progesterone in but many ways it is true that they should be specifically prescribed according to the pharmacopeia and not as a proprietary preparation. In this respect there is not a great need for drugs in combination such as this - probably better to prescribe individual drugs specifically. I think that this is the indispensible solution also. There is no need to retain the preparation because of its possible use in secondary amenorrhoea.

H. Cardwell

SCHERING (N.Z.) LIMITED

Representatives for
Schering AG
Berlin/Bergkamen
Germany

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Office & Warehouse:
Kahika Road, Birkdale, Auckland 10

The Director,
Division of Clinical Services,
Department of Health,
P.O. Box 5013,
WELLINGTON

10 April 1975

Dear Sir,

PRIMODOS ORAL - YOUR REFERENCE 142/70/2539

We were very surprised to receive your letter dated 2 April 1975 under the above reference requesting us to withdraw Primodos Oral from the New Zealand market. If we may we would like to discuss some of the points included in your letter as follows:

(1) Our understanding of the treatment of functional secondary amenorrhoea of short duration (under one year) is that, once any pathological reason for the amenorrhoea has been excluded and should the woman once again wish to become pregnant, then the administration of synthetic ovarian hormones is necessary to induce a withdrawal bleed resembling her normal menstruation. To achieve this, both oestrogen and progestogen are required. Ethinyl Oestradiol is considered preferable to Stilbestrol because the latter causes severe gastro-intestinal effects in many women. As well as Ethinyl Oestradiol a progestogen must be given and the one most commonly used for gynaecological purposes is Norethisterone (the acetate of which is included in Primodos Oral). With Primodos Oral both of these hormones are conveniently available for the patient in a two-tablet presentation and each tablet contains the hormones in their most widely-used dosage levels.

(2) As far as point No. 1 in your letter is concerned we would agree that previously Primodos Oral was used fairly widely for the diagnosis of pregnancy but at the present moment this product is not widely used for this indication as in the meantime adequate reliable in vitro methods of pregnancy testing have been developed which have the added advantage of enabling a doctor to test a woman's urine in her presence and tell her immediately whether she is pregnant or not. These tests have been widely advertised by the manufacturer concerned. Added to this, as we have already mentioned in our letter dated 18 March 1975, our promotion of Primodos Oral on a worldwide basis specifically excludes pregnancy testing as an indication.

(3) We understand that this matter has also been considered by the Australian Department of Health in Canberra through ADEC (Australian Drug Evaluation Committee) who also suggest "withdrawal of hormonal pregnancy tests from the market owing to questionable safety and availability of adequate and reliable in vitro methods". The Australian Health Department then cancelled our Australian subsidiary's permit (TS6) to import Duogynon

..2

(Primodos Oral), indicating that a new permit would be issued stating that the drug may not be promoted for pregnancy testing and also that all product literature must be amended as follows:

(a) The deletion of pregnancy testing as an indication.

(b) The addition of a warning box, prominently displayed, stating that the product is not to be used as a test for pregnancy or where pregnancy is suspected.

(c) Where amenorrhoea is included as an indication in any literature the term "amenorrhoea" must be qualified by the words "Proven not due to pregnancy".

All of the above requirements of the Australian Department of Health are being carried out by our Australian subsidiary and in the meantime the amended TS6 permit to import Duogynon (Primodos Oral) has been issued, allowing continued marketing of the product within these parameters.

Considering all the above points we feel we should be able to continue marketing Primodos Oral in New Zealand as it offers the doctor a convenient and reliable method of administering the ovarian hormones required in functional secondary amenorrhoea of short duration (under one year), but we would suggest that in future our packing leaflets could carry the following warning:

"Primodos Oral should not be used for pregnancy testing as there are adequate and reliable in vitro methods available"

or that we specify under the indication "amenorrhoea" -

"Treatment of secondary amenorrhoea of short duration proven not due to pregnancy".

We await the pleasure of your reply.

Yours sincerely,
SCHERING (N.Z.) LIMITED

Section 9(2)(a)

MARKETING MANAGER

Section 9(2)(a)

MANAGING DIRECTOR

P.S. Enclosed for your information is a copy of the TS6 mentioned in this letter. This has been included since this letter was dictated as it has just arrived today from our Australian subsidiary.

ENCL:

AUSTRALIAN GOVERNMENT
DEPARTMENT OF HEALTH

PERMIT TO IMPORT THERAPEUTIC SUBSTANCES UNDER REGULATION 5A OF THE CUSTOMS (PROHIBITED IMPORTS) REGULATIONS

PERMIT No. P 13939

To SCHERING PTY. LTD.
WEED ST
TEMPE
N.S.W. 2044

PLEASE NOTE
This Permit to be presented to the Collector of Customs at
SYDNEY

Permission is hereby granted for the importation into Australia of the following therapeutic substance(s) under Regulation 5A (1.) and/or Regulation 5A (3.) (a) of the Customs (Prohibited Imports) Regulations:
DUOGYNON INJECTION (CONTAINING 20mg PROGESTERONE and 2mg of OESTRADIOL BENZOATE); DUOGYNON SIMPLEX INJECTION (CONTAINING 50mg PROGESTERONE and 5mg of OESTRADIOL BENZOATE); DUOGYNON ORAL TABLETS (CONTAINING 10mg NORETHISTERONE ACETATE and 20mg ETHINYL OESTRADIOL); manuf. & supp. by SCHERING AG, GERMANY.

This permission is subject to the following requirements or prohibitions:
Permit valid until 30 June 1975.
Products not to be promoted for use in pregnancy testing.

4.3.75
Director-General of Health

R 73/2403

(PRIMODOS ORAL IS DUOGYNON ORAL IN AUSTRALIA)

142/70/2539

DAAC

(f) Hormonal Pregnancy Tests and Birth Defects

Two hormonal pregnancy tests are currently available on the New Zealand market. Reports have been received from overseas that birth defects have occurred when hormonal pregnancy tests have been taken in early pregnancy.

The Committee were of the opinion that these preparations should be withdrawn from the market.

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

CLINICAL AND PHARMACOLOGICAL EVALUATION OF DRUGS/QUALITY, SAFETY AND EFFICACY OF DRUGS

DRUG INFORMATION NO 150

6 April 1975

Resolutions WHA16.36/WHA26.31

ORIGINAL : ENGLISH

The United States Food and Drug Administration has informed the World Health Organization of a notice of withdrawal of approval of a new drug application with regard to a combination drug containing norethisterone[1] acetate and ethinylestradiol[2] as published in the Federal Register[3] dated 11 February 1975. These two drugs are contained in Gestest tablets used for pregnancy testing.[4] The Commissioner of Food and Drugs concluded, inter alia, as follows:

"Although the drug is effective as a presumptive test for pregnancy, there is a lack of proof of safety for that use in view of the potential danger in the presence of pregnancy and the availability of a number of very accurate chemical tests to detect pregnancy. The holder of the new drug application has waived its opportunity for a hearing, and no other interested person has requested a hearing."

"All identical, related, and similar drug products, as defined in 21 CFR 310.6, not the subject of an approved new drug application, are covered by the application reviewed and are subject to this notice."

"Shipment in interstate commerce of the above-listed product or of any identical, related, or similar product, not the subject of an approved new drug application, will then be unlawful."

---

[1] norethisterone is the International Nonproprietary Name (INN) proposed by WHO for 17α-ethynyl-17β-hydroxyestr-4-en-3-one.

[2] ethinylestradiol is the International Nonproprietary Name (INN) proposed by WHO for 17-ethynyl-estra-1,3,5(10)-triene-3,17β-diol.

[3] Copies of the relevant paper issued by the FDA can be obtained from WHO on request.

[4] Please see Drug Information Circular No. 144 dated 11 February 1975 on a similar subject.

142/70/2539

IW:
SG

2 April 1975

The Manager,
Schering (N.Z.) Ltd,
P.O. Box 66011,
Beachhaven,
AUCKLAND 10.

Dear [redacted]

Thank you for your letter dated 18 March 1975 concerning the marketing of Primodos Oral.

Your letter has been carefully considered and the following comments set out the conclusions reached:-

1. This product is frequently used for pregnancy testing. It is not thought that amendment of the package insert or recommendations for usage are likely to lessen its use for this purpose.

2. Recent literature now leaves little doubt of an association between use in early pregnancy and foetal abnormalities.

3. There are many alternative methods of treating secondary amenorrhoea.

4. This subject has been considered by the Drug Assessment Advisory Committee who have recommended the withdrawal of such products from the New Zealand market.

5. The Department therefore seeks the co-operation of your company in the withdrawal of Primodos Oral. An early reply to this request would be appreciated.

Yours faithfully,

(Ian A. Witty)
for Director
Division of Clinical Services

Dr Pharm

Blue for Dr. Witty, 15/4/75

(This recommendation now also supported by CADR)

Doc

142/70/2539

~~Dr Andrews~~ Dexi

1. Attached is a reply from Schering concerning Premodos Oral.

2. There letter is somewhat contradictory. While there is a special note re pregnancy testing there is no indication that Premodos Oral should not be used for this purpose.

3. I would suggest that all such references should be removed and a statement "Not to be used as a pregnancy test" be inserted.

4. Are you happy to let this product be distributed for secondary amenorrhoea.

Jaw

~~Dr Phill~~, JRV agree
Mr Witt,

1. The product is used often as a pregnancy test; altering the package insert (which doctors don't see anyway) or the recommendations for usage are unlikely to change its use for this purpose

2. Recent literature leaves little doubt of an association between use in early pregnancy & foetal abnormalities

3. DAAC have recommended the withdrawal from the market of both products & Australia has already acted similarly

4. The firm should be told, in addition to the above, that the other firm involved has been asked to withdraw its product

5. There are many alternative methods of treating 2° amenorrhoea

6. Schering should be told we would like a reply as soon as possible, & a B/U for 2/52

Dom 24/3

SCHERING (N.Z.) LIMITED

102

70/2530

Representatives for
Schering AG
Berlin/Bergkamen
Germany

Telegrams & Cables: Schering, Auckland
Telephone 437-159, 437-158
P.O. Box 66011, Auckland 10, N.Z.
Office & Warehouse:
Kahika Road, Birkdale, Auckland 10

The Director,
Division of Clinical Services,
Department of Health,
P.O. Box 5013,
WELLINGTON

18 March 1975

Attention: Dr D. A. Andrews

Dear Sir,

PRIMODOS ORAL

Further to our letter dated 6 March 1975 we have now taken up this matter with our Head Office in Berlin and received their reply. We would therefore like to answer your letter dated 18 February as follows:

Our packing leaflet for Primodos Oral - a copy of which is enclosed herewith - states the following under

Indication: Secondary amenorrhoea of short duration (under one year).

Special Note: If Primodos Oral is used for the diagnosis of early pregnancy the possibility of virilisation of female foetuses cannot be excluded with certainty.

To expand on this it is clear that Primodos Oral is not recommended as a pregnancy test since the possibility of virilisation of the female foetus cannot be excluded with certainty. For some time now the medical scientific promotion of Primodos Oral has been for the indication of treatment of secondary amenorrhoea only, on a worldwide basis.

It is a matter of policy of Schering AG Berlin and Schering (N.Z.) Ltd that when information is given to the medical profession on Primodos Oral, the only indication which is mentioned is secondary amenorrhoea of short duration (under one year). We feel therefore that Primodos Oral should continue to be available on the market for this particular indication, and we will be very interested to hear your further comments on this matter.

Yours faithfully,
SCHERING (N.Z.) LIMITED

Section 9(2)(a)

MARKETING MANAGER

Section 9(2)(a)

MANAGING DIRECTOR

ENCL:

restricted drug

Primodos oral
Progestogen-oestrogen combination

SCHERING AG
BERLIN/BERGKAMEN
GERMANY

Composition
1 tablet contains 10 mg. norethisterone acetate and 0.02 mg. ethinyl oestradiol.

Indication
Secondary amenorrhoea of short duration (under one year).

Dosage
One tablet daily for two days. A menstruation-like bleeding usually follows within 3-6 days or, in ex-

SCHERING (N.Z.) LIMITED

14.270/2539

Representatives for
Schering AG
Berlin/Bergkamen
Germany

Telegrams & Cables: Schering, Auckland
Telephone 437-159, 437-158
P.O. Box 66011, Auckland 10, N.Z.
Office & Warehouse:
Kahika Road, Birkdale, Auckland 10

The Director,
Division of Clinical Services,
Department of Health,
P.O. Box 5013,
WELLINGTON

6 March 1975

Attention: Dr D. A. Andrews

Dear Sir,

PRIMODOS ORAL

Thank you for your letter dated 18 February 1975 regarding the use of Primodos Oral as a hormonal pregnancy test in early pregnancy. As this is a somewhat technical matter we have decided to refer it to our head office in Berlin for their comments as we feel by this means we will be able to give you a more precise and correct answer. We therefore ask your patience in this matter and we will write to you once again when we have received the necessary information from Berlin.

Yours faithfully,
SCHERING (N.Z.) LIMITED

Section 9(2)(a)

MARKETING MANAGER

CORRESPONDENCE

Letters must be kept to a reasonable length. Otherwise it may not be possible to find space for them.

CLEFT LIP AND PALATE AND PREGNANCY TESTS

SIR: In the course of our investigations into the aetiology of cleft lip and palate (CLP) in Western Australia, a surprisingly high number of mothers had had an oral or parenteral pregnancy test in the first trimester of pregnancy. After a survey of the incidence of CLP in Western Australia (Journal, July 6), a retrospective study of cases occurring in the years 1963 to 1974 has been undertaken to investigate maternal histories during the first trimester of pregnancy and parental histories before conception. The number of cases studied was 222, and in 22 cases (10%) mothers received oral or parenteral pregnancy tests between the fifth and eighth week of gestation (Table 1). Eight patients were given

TABLE 1
Mothers of Children with Cleft Lip or Palate

Deformity	Number of Cases			
	With Parenteral or Oral Pregnancy Test		Total Studied	
	Males	Females	Males	Females
Cleft lip	3 (14%)	2 (9%)	40 (18%)	15 (7%)
Cleft lip and palate	6 (27%)	5 (23%)	67 (30%)	23 (10%)
Cleft palate	4 (18%)	2 (9%)	38 (17%)	39 (18%)
Total	13	9	145	77
	22		222	

Duogynon or Duogynon Simplex; in the remaining cases the preparations used were unknown; other preparations available for pregnancy testing by attempting to produce withdrawal bleeding in non-pregnant patients are Amenerone forte (Roussel), Menstrogen (Organon) and Secrodyl Tab (A & H), and all are progestogen-oestrogen combinations.

It is currently considered that CLP may be caused by many aetiological factors including single mutant genes, chromosomal aberrations and specific environmental agents; but the great majority are thought to be due to the interaction of heredity and environment.[1] It is, therefore, important to identify any environmental factors which may contribute to the production of these abnormalities which occurred in 1·73 per 1,000 births in Western Australia in the 10-year period 1963 to 1972.

As in our cases, oral pregnancy tests are usually administered at the most sensitive stage of embryogenesis and we consider that their use in an unwarranted risk. In investigations of neural tube malformations Gal[2] found a significantly higher number of mothers in the study than control mothers had received hormone test tablets during pregnancy. Further control and statistical studies taking other possible factors into account are under way in our series, but in the meantime, we wish to bring to notice that these preparations were used in 10% of mothers of CLP patients, yet alternative tests are available which do not require the administration of any drugs.

In only four cases (18%) was pregnancy desired; here oral pregnancy tests may have hastened the diagnosis, but are not essential. In the other 18 cases (82%) pregnancy was not wanted and abortion was requested several times. In the total group 54% of pregnancies were planned. Oral parenteral pregnancy tests may have been carried out in the hope of producing a miscarriage. This is obviously a misuse of the drug. If an early diagnosis is required to arrange termination of pregnancy some non-potentially teratogenic test should be used in case the patient decides to proceed to full term.

We wish to emphasize that the possible danger has only just been revealed in our study, and we know of no previous report which has been available to the medical profession in Australia.

Princess Margaret Hospital for Children, Box D 184, G.P.O., Perth, W.A. 6001. W. F. BROGAN.

[1] Frazer, F. C., *Amer. J. hum. Genet.*, 1970, 22: 336.
[2] Gal, I., *Advanc. Teratology*, 1972, 5: 7.

[The possible association between exposure to sex hormone therapy and some birth defects was discussed in the editorial columns (page 861) of our issue of December 14, 1974.—EDITOR.]

SKIN RASH, CONJUNCTIVITIS AND PLASTIC PERITONITIS WITH PRACTOLOL THERAPY

SIR: We would like to briefly report a patient who developed pustular psoriasis, conjunctivitis sicca and plastic peritonitis whilst on treatment with practolol for angina pectoris. The patient was a man aged 49 who had been taking practolol from March, 1972, until this drug was ceased in July, 1974. The dosage over most of this time was 600 to 800 mg/day. In May, 1973, a rash developed on the left foot, which over the succeeding months progressively spread. In September, 1973, it covered 90% of his whole body surface. He was seen by a consultant dermatologist who considered the rash to be psoriasis, and because of its severity, in December, 1973, commenced him on methotrexate, which was continued until July, 1974. The dose over most of this time was 15 mg taken orally each week. However, there was very little improvement. In December, 1973, the patient also developed a crusty irritation about the eyes. He was subsequently seen by an eye specialist, but despite regular treatment, there was little improvement. In June, 1974, the patient complained of attacks of colicky abdominal pains and vomiting. These symptoms progressed and subsequently, about six weeks later, definite evidence of a subacute bowel obstruction had developed with a large mass being found in the lower abdomen. At laparotomy a thin avascular membrane wrapping up the entire small bowel into three large lobules was found. The avascular membrane could be completely separated off the bowel and mesentery leaving normal bowel serosa.

At this time it was recognized that the psoriasis, conjunctivitis and plastic peritonitis could have been related to his medication and both practolol and methotrexate were withdrawn. Adverse drug reaction reports would indicate that practolol was the responsible agent. Subsequently the skin rash, conjunctivitis and abdominal

142/70/2539

18 February 1975

The Manager,
Schering (N.Z.) Ltd,
P.O. Box 66011,
Beachhaven,
AUCKLAND 10

Dear Sir,

PRIMODOS ORAL

The Department is aware of recent evidence associating the use of hormonal pregnancy tests in early pregnancy with birth defects.

Despite the rarity of this association concern is felt at the continued availability of your product on the New Zealand market.

Your comments on recent references in the literature to this association and your proposals for the continued marketing of this product will be examined with interest by the Department.

Yours faithfully,

D.C.A

(D.A. Andrews)
for Director,
Division of Clinical Services

142/20/2539

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

CLINICAL AND PHARMACOLOGICAL EVALUATION OF DRUGS/QUALITY, SAFETY AND EFFICACY OF DRUGS

DRUG INFORMATION NO 144

11 February 1975

Resolutions WHA16.36/WHA26.31

ORIGINAL : ENGLISH

The Australian Department of Health has informed the World Health Organization about the withdrawal from the market of a number of hormonal pregnancy testing preparations. The preparations[1] are Duogynon[2], Duogynon Simplex[3], Duogynon Oral[4], Amenorone Forte[5], and Secrodyl[5].

The Minister of Health[6] stated that the Australian Drug Evaluation Committee had recommended that systemic hormonal formulations for pregnancy testing be withdrawn from the Australian market on the basis of their questionable safety and the fact that there were adequate and reliable methods available which do not involve the administration of hormones. Such methods relied on the testing of body fluids by immunoassay methods.

The action of the Australian Drug Evaluation Committee and the Australian Department of Health was based on evidence from the United States which draws attention to the risk of unnecessary drug exposure in early pregnancy. This evidence was put forward in papers in 'Nature'[7,8,9] on the risks and benefits of the use of hormonal pregnancy test tablets.

The Department of Health had been made aware of four reports of congenital abnormalities occurring in Australia since 1968 which were possibly associated with hormonal pregnancy tests.

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[1] Contains 20 mg/ml of progesterone (INN)* and 2 mg/ml of estradiol benzoate (INN)

[2] Contains 50 mg/ml of progesterone (INN) and 3 mg/ml of estradiol benzoate (INN)

[3] Contains 10 mg of norethisterone (INN) acetate and 0.02 mg of ethinylestradiol (INN) per tablet

[4] Contains 50 mg of ethisterone (INN) and 0.05 mg of ethinylestradiol (INN) per tablet

[5] Contains 10 mg of dimethisterone (INN) and 0.05 mg of ethinylestradiol (INN) per tablet

[6] A copy of the statement can be obtained from the World Health Organization on request

[7] Laurence, M. et al., Hormonal Pregnancy Tests and Neural Tube Malformations, Nature, Vol. 233, October 15 1971, pp 495-496

[8] Gal, I., Risks and Benefits of the Use of Hormonal Pregnancy Test Tablets, Nature, Vol. 240, November 24 1972, pp 241-242

[9] Sever, L. E., Hormonal Pregnancy Tests and Spina Bifida, Nature, Vol. 242, April 6 1973, pp 410-411

* INN stands for International Nonproprietary Name proposed by WHO.

The Minister of Health also stated that apart from the pregnancy-testing products mentioned, there were a number of other hormonal preparations available in Australia for medical uses such as the treatment of breast cancer, which could also be used for pregnancy testing. The Department would require that product literature for those preparations contain a specific warning that they not be used for pregnancy testing, and the manufacturers and importers are being advised accordingly.

Although a number of contraceptive pills contain similar types of substances, they are used in much lower doses and are administered to prevent pregnancy. Thus, women on the pill had no cause for worry if they complied with recommended instructions. However, the practice of taking multiple doses of the pill on a few occasions in the event of doses being missed should be avoided. Similarly increased doses of the contraceptive pill should not be taken as a pregnancy test.

accumulations and depressed very low density lipoprotein. These studies, together with various sophisticated biochemical analyses with studies of enzymatic involvement, which have recently been attempted, give hope that at least some of the obscurities may be removed in the not too distant future and perhaps pave the way for a more rational and less empiric line of therapy.

INFECTIOUS MONONUCLEOSIS

INFECTIOUS MONONUCLEOSIS is a disease which, because of its various clinical manifestations in adolescence and young adults, may imitate a number of other infections. Conversely, there is always a temptation to label a febrile disease with otherwise undiagnostic features with the title of infectious mononucleosis.

The Paul-Bunnell test for heterophil antibody remains an important test in the diagnosis of infectious mononucleosis. Unfortunately, in childhood infections it often fails to become positive and this is also occasionally the case in classical disease in young adults. With the relatively recent discovery of the EB (Epstein-Barr) virus, a further marker has become available to study the epidemiology of this disease. A number of excellent prospective studies have shed light on childhood infections with the EB virus. In the Cleveland family study, it was found that EB virus infections in childhood were rarely associated with obvious symptoms and signs which would suggest a clinical diagnosis of infectious mononucleosis.[1] Most cases of non-bacterial tonsillitis or pharyngitis were found to be due to other viruses, often adenoviruses. In the Alaskan islands survey, 100% of primary infections were found to occur in children under the age of three years, but no distinctive clinical illness was observed.[2] It is possible, therefore, that some of the children with clinical infectious mononucleosis described by Hubble and his co-authors in this issue (page 863) were suffering from infections with viruses other than the EB virus.

Hubble *et alii*, in their retrospective study in Perth, have confirmed many of the well known features of this illness. Two peaks of infection, one in the under ten years age group and another between the ages of 15 and 24 years have been well documented, the first perhaps representing early childhood infections acquired from the patient's mother. The earlier peak amongst adolescent females is also well described and perhaps attributable to earlier sexual maturity.

Estimates of the crude annual incidence of heterophil antibody-positive infectious mononucleosis in general populations have ranged widely, and are clearly dependent upon the type of patients studied and the method of reporting.[3]

It is of interest that the Western Australia group have been unable to confirm the seasonal incidence of the disease reported by other workers. Such differences, if present, might have been revealed by the study of a more precisely defined population over a longer period of time; on the other hand, they may reflect the generally milder climate of the Australian temperate zone, compared with that of the countries in which the classical studies of infectious mononucleosis have been carried out. A study by C. R. Boughton of a hospital series of "glandular fever" cases in Sydney also found no significant seasonal variation in the admission rate.[4] Studies of the epidemiology of infectious mononucleosis which are performed retrospectively and without adequate virological confirmation must necessarily be limited in value. Undoubtedly, many of the patients described did have infectious mononucleosis, but it is probable that some others were suffering from infections with agents such as cytomegalovirus and toxoplasmosis. More conclusive results will only be obtained from prospective studies using the EB virus as a marker for this disease.

[1] Henle, G., and Henle, W., *J. Infect. Dis.*, 1970, 121: 303.
[2] Tischendorf, F., Shramek, G. J., Balagtas, R. C., *et alii*, *J. Infect. Dis.*, 1970, 122: 491.
[3] Heath, C. W., Brodsky, A. L., and Potolsky, A. I., *Amer. J. Epidemiol.*, 1972, 97: 46-52.
[4] Boughton, C. R., *Med. J. Aust.*, 1970, 2: 529.

BIRTH DEFECTS AND ORAL CONTRACEPTIVES

SINCE the first suspicions that some birth defects may be associated with exposure to sex hormone therapy,[1] oral contraceptives,[2,3] or hormonal pregnancy tests[4] during embryogenesis, more data have accumulated.[5] It appears that some infants, whose mothers have been administered progestogen/oestrogen hormones during the earliest part of pregnancy, may have an increased incidence of vertebral, anal, cardiac, tracheal, oesophageal, renal or limb anomalies (acronym: VACTERL).[6]

In a recent controlled study from New York, reported in *The New England Journal of Medicine*,[7] it was found that 15 (14%) of 108 mothers of malformed children were exposed to hormonal pregnancy tests, or supportive hormone therapy, or had "breakthrough" pregnancies while on oral contraceptives, while only four (4%) of 108 control mothers of normal children were thus exposed. In the survey, the malformed children all had limb-reduction defects which are defined as loss of an arm or leg or part thereof. There was a slight increase in the rate of twins among the affected infants, but only one of any pair was malformed. Of these mothers who became pregnant while taking oral contraceptives one was using a sequential type, and others used combination-type preparations. It was significant that affected children with histories of exposure to orally administered hormones were all male. This seems to imply that oral hormones have some type of sex-specific effect on the developing fetus. Of less certain significance is the finding that the rate of limb-reduction defects has increased by 33% since 1963, while the rate of malformations of all types has decreased about 6%. It is conjectured that this change has been apparent only since the introduction of oral

[1] Levy, E. P., Cohen, A., and Fraser, F. C., *Lancet*, 1973, 1: 611.
[2] Nora, J. J., and Nora, A. H., *Lancet*, 1973, 1: 941.
[3] Kaufman, J. L., *Lancet*, 1973, 1: 1396.
[4] Oakley, G. P., Flynt, J. W., Falek, A., *Lancet*, 1973, 2: 256.
[5] Balci, S., Say, B., Pirnc., T., and Ilkesamez, A., *Lancet*, 1973, 2: 1098.
[6] Nora, J. J., and Nora, A. H., *New Engl. J. Med.*, 1974, 291: 731 (October 3).
[7] Janerich, D. T., Piper, J. M., and Glebatis, D. M., *New Engl. J. Med.*, 1974, 291: 697 (October 3).

contraceptives, but this view awaits confirmation, and is expressed cautiously.

One conclusion of the study is that endogenous hormonal insufficiency may be present in those mothers who exhibit a breakthrough pregnancy while taking an oral contraceptive, or need supportive hormone therapy during pregnancy, and who then subsequently have a malformed child.

It is obvious that the great majority of pregnancies in which these drugs are used do not give rise to malformed infants. If progestogen/oestrogen hormones do produce malformations, it is at a low frequency rate, and probably operating in a predisposed mother. However, recommendations have been voiced that it would be wise to discontinue hormonal pregnancy tests, and to demonstrate that there is no pregnancy present before initiating oral contraceptive administration.[6,7]

RELAXATION OF REQUIREMENTS ON SMALLPOX VACCINATION

AUSTRALIANS long had a strict policy on smallpox vaccination requirements for arriving travellers. This has caused irritation from time to time on the part of people from overseas who are accustomed to the casual policy in some countries, and it has, within the bounds of prudence and commonsense, been modified a little in recent years. Nevertheless, a strict policy has been only too easy to justify and may well have saved us from serious outbreaks of the disease.

With the success of the World Health Organization's campaign to control smallpox, the ultimate goal of eradicating the disease now seems not too much to hope for. This had led to a more relaxed attitude overseas, even in places like the United Kingdom and the United States. However, as we pointed out when commenting on these changes some years ago, Australia, because of its geographical nearness to areas where smallpox is still epidemic, is scarcely in a position to take a lead in relaxing its guard against the disease.

Now, however, there is to be some further relaxation for travellers arriving in Australia, but still within the bounds of prudence and commonsense. An announcement made by the Commonwealth Minister for Health, Dr D. N. Everingham, on November 12, 1974, states that as from that date travellers who cannot be vaccinated because of a medical condition will no longer be compelled to enter quarantine on arrival, provided they have not come from, or stopped over at, countries infected with smallpox. Previously, all travellers without valid vaccination certificates were obliged to spend 14 days in quarantine unless they had spent the 14 days prior to arrival in the United States or Canada, or in those Pacific islands on the direct air route to Australia.

Dr Everingham said that the relaxation had been decided on after careful weighing up of the potential risks to the Australian community. However, certain essential safeguards were still necessary and would be rigorously enforced. Travellers seeking exemption must have a medical certificate, issued within the 12 months before embarkation and signed by a registered medical practitioner, stating that vaccination against smallpox was inadvisable because of a medical condition. The condition must be specified. The exemption did not extend to travellers from countries where smallpox was still endemic, or where the disease had been recorded in the previous 12 months.

At the present time, according to the Minister's statement, only four countries have endemic smallpox—Ethiopia, Pakistan, India and Bangladesh. To determine which countries are included, the Health Department will use as its guide the *Weekly Epidemiological Record*, in which the World Health Organization lists countries infected within the previous year. It is emphasized that travellers who simply land in these countries *en route*, as transit passengers, will be exempted, but not people who stop over.

The medical conditions which will qualify travellers for exemption are (i) pregnancy; (ii) history or presence of eczema or other skin diseases considered by the traveller's doctor to be a contraindication to smallpox vaccination; (iii) states of immunological deficiency which are (*a*) subsequent to treatment which depresses immunity (for example, deep X-ray therapy, administration of corticosteroids, alkylating and cytotoxic drugs) or (*b*) hypogammaglobulinaemic conditions; (iv) nephrosis; (v) organ transplants; (vi) general malignant disease. In addition, travellers accompanied by a doctor or nurse, for whom hospital care is likely for 14 or more days after arrival, will be exempted. There is no change in the rule regarding infants under 12 months of age; they will continue to be automatically exempt.

All travellers admitted in this way without vaccination will be given a form advising them to seek immediate medical attention if they become ill during the first six weeks after arrival. It is emphasized that the relaxation applies only to travellers with the medical conditions specified. Any other travellers arriving without valid vaccination certificates, or entering from smallpox-infected countries, will still have to go into quarantine.

In a concluding comment, Dr Everingham said that the World Health Organization was confident that smallpox would be totally eradicated from the world within a few years. However, in the meantime, Australia was determined to maintain its smallpox-free record and—with the exception of the present relaxation—would continue to take strict precautions with incoming travellers.

[6] Med. J. Aust., 1971, 2: 456 (August 28).

IW:ZH

142/70/1441

47-053

26 June 1975

The Manager,
Roussel (N.Z.) Limited,
P.O. Box 37111,
AUCKLAND.

Dear [redacted]

Thank you for your letter of 19 June concerning the withdrawal of Amenorone Forte.

The information supplied is most helpful and we would assure you that the Department is completely satisfied with the action taken.

Yours faithfully,

(Ian A. Witty)
for Director
Division of Clinical Services

Dr Andrews

Copy attached. It was unfortunate that my earlier letter was posted. You may recall this matter was discussed with you and that I was requested to write. Typing was in arrears about 8 working days and during this interim period Roussel wrote and you replied without my knowledge

Ian.

F

ROUSSEL

Roussel (N.Z.) Limited
280-288 Parnell Road
Auckland 1

19 June 1975

The Director-General
of Health,
Department of Health,
P.O. Box 5013,
WELLINGTON.

Ref: 142/70/1441
Attn: Mr. I. Witty.

Dear Sir,

Thank you for your letter under the above reference.

I wish to confirm that as previously mentioned in my letter of the 9th June, the Chemist Guild has been notified of our decision to withdraw Amenorone Forte from the market W.E.F. 1st June 1975, and that their members should return stocks to respective wholesalers for credit.

It would appear that this action plus the information which appeared in your Clinical Services letter No. 150, will ensure that all retail pharmacies have cleared their Amenorone Forte stocks before the 9th July.

For your information our average monthly sales during 1974 was 252 units for the whole of New Zealand. To date we have received back for credit over 400 packs, which would suggest that there are very few packs still left in circulation.

I trust this satifies the Departments requirements.

Yours faithfully,
ROUSSEL (N.Z.) LIMITED.

Section 9(2)(a)

MANAGER FOR NEW ZEALAND.

Phone: 370-636
P.O. Box 37-111
Cables: Rousselab - Auckland

142/70/1441

13 June 1975

[redacted]
Manager,
Roussel (N.Z.) Ltd,
280-288 Parnell Road,
AUCKLAND 1

Dear Sir,

I am pleased to note your assurances in your letter of 9 June that stocks of Amenerone Forte have been recalled from retail pharmacies. The Department is convinced that this decision has been the correct one even though it goes beyond steps taken in some overseas countries.

As you know, the newsmedia have been most interested in the subject recently and the point was strongly made to them by the Department that the manufacturers concerned had cooperated very fully and promptly in taking action.

Yours faithfully,

D.A. Andrews

(D.A. Andrews)
Director,
Division of Clinical Services

ROUSSEL

Roussel (N.Z.) Limited
280-288 Parnell Road
Auckland 1

9 June 1975

The Director-General
of Health,
Department of Health,
P.O. Box 5013,
WELLINGTON.

Ref: 142/70/1441
Attn: Dr. D.A. Andrews

Dear Sir,

I refer to your letter under the above reference, and would wish to clarify the whole matter for you.

In addition to mailing wholesalers throughout New Zealand a letter has been sent to The Chemists Guild, advising that their members may return stocks of Amenorone Forte to their respective wholesalers for credit purposes.

As this product had a very low volume turnover within New Zealand, it is not envisaged that many retail pharmacies will in fact have saleable stock; which also illustrates the true size of this issue.

It is however, pleasing to note the Departments reaction to our decision, and we trust that further fears held regarding the sale of Amenorone Forte after the 1st June, might now be dispelled.

Yours faithfully,
ROUSSEL (N.Z.) LIMITED.

Section 9(2)(a)

MANAGER FOR NEW ZEALAND.

Phone: 370-636
P.O. Box 37-111
Cables: Rousselab - Auckland

47-053

18 June 1975

Section 9(2)(a)
Roussel (N.Z.) Limited,
P.O. Box 37111,
AUCKLAND.

Dear Section 9(2)(a)

Further to our letter of 26 May, concerning the withdrawl of Amenorone Forte, we wish to advise that the distributor of a similar product has withdrawn all existing stocks from all distributors including retail pharmacies by 9 July.

An indication whether your company has withdrawn retail stocks would be appreciated at your earliest convenience.

Yours faithfully,

Ian

(Ian A. Witty)
for Director
Division of Clinical Services

142/70/1441

26 May 1975

[redacted] Section 9(2)(a)
Roussel (N.Z.) Ltd,
P.O. Box 37111,
AUCKLAND

Dear [redacted] Section 9(2)(a)

Thank you for your letter of 9 May. The Department is impressed with the responsible manner with which you have dealt with this problem.

It is not clear from your letter whether sales of Amenorone Forte will no longer be possible after 1 June, or whether existing stocks at retail level will continue to be available.

The Department is of the opinion that continued sales are unacceptable and would hope that retail pharmacists will also be requested to return stocks.

Yours faithfully,

D. A. A.

(D.A. Andrews)
for Director,
Division of Clinical Services

1. [illegible]
2. [illegible]
3. [illegible]
4. Dr Griffith [illegible]
5. [illegible]

ROUSSEL

Roussel (N.Z.) Limited
280-288 Parnell Road
Auckland 1

9 May 1975

The Director General
of Health,
Department of Health,
P.O. Box 5013,
WELLINGTON.

Ref: 142/70/1441

Dear Sir,

Your recommendations stated in your letter under the above reference have been noted, and the following action taken:

(1) All company stock frozen.

(2) Amenorone Forte to be officially withdrawn from sale within New Zealand - Effective 1 June 1975.

(3) Wholesalers notified of this decision and asked to return their stock to Roussel.

We trust that this action meets with your approval.

Yours faithfully,
ROUSSEL (N.Z.) LIMITED.

Section 9(2)(a)

MANAGER FOR NEW ZEALAND.

Phone: 370-636
P.O. Box 37-111
Cables: Rousselab - Auckland

IW:2H

142/70/1441

1 May 1975

The Managing Director,
Roussel (N.Z.) Limited,
P.O. Box 37111,
AUCKLAND.

Dear Section 9(2)(a)

Further to our letter of 4 April concerning Amenerone Forte we wish to advise that the question has been considered by the Committee on Adverse Drug Re-actions who have recommended that products of this type be withdrawn from the market. Further the United States Food and Drug Administration have recently ruled that drugs of this type are not known to be safe and that shipment in inter state commerce are unlawful.

The Department therefore confirms that it desires the withdrawl of Amenerone Forte and advises that other companies marketing these products have been advised similarly. A reply to this letter would be appreciated at your earliest convenience.

Yours faithfully,

Ian A Witty

(Ian A. Witty)
for Director
Division of Clinical Services

1) Dr Andrews Do-o

F

2) BU 18/5/75 JAW.

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

CLINICAL AND PHARMACOLOGICAL EVALUATION OF DRUGS/QUALITY, SAFETY AND EFFICACY OF DRUGS

DRUG INFORMATION NO 150

6 April 1975

Resolutions WHA16.36/WHA26.31

ORIGINAL : ENGLISH

The United States Food and Drug Administration has informed the World Health Organization of a notice of withdrawal of approval of a new drug application with regard to a combination drug containing norethisterone[1] acetate and ethinylestradiol[2] as published in the Federal Register[3] dated 11 February 1975. These two drugs are contained in Cestest tablets used for pregnancy testing.[4] The Commissioner of Food and Drugs concluded, inter alia, as follows:

"Although the drug is effective as a presumptive test for pregnancy, there is a lack of proof of safety for that use in view of the potential danger in the presence of pregnancy and the availability of a number of very accurate chemical tests to detect pregnancy. The holder of the new drug application has waived its opportunity for a hearing, and no other interested person has requested a hearing."

"All identical, related, and similar drug products, as defined in 21 CFR 310.6, not the subject of an approved new drug application, are covered by the application reviewed and are subject to this notice."

"Shipments in interstate commerce of the above-listed product or of any identical, related, or similar product, not the subject of an approved new drug application, will then be unlawful."

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[1] norethisterone is the International Nonproprietary Name (INN) proposed by WHO for 17α-ethynyl-17β-hydroxyestr-4-en-3-one.

[2] ethinylestradiol is the International Nonproprietary Name (INN) proposed by WHO for 17-ethynyl-estra-1,3,5(10)-triene-3,17β-diol.

[3] Copies of the relevant paper issued by the FDA can be obtained from WHO on request.

[4] Please see Drug Information Circular No. 144 dated 11 February 1975 on a similar subject.

EM:ZH
142/70/1441

4 April 1975

The Managing Director,
Roussel (N.Z.) Limited,
P.O. Box 37111,
AUCKLAND.

Dear Section 9(2)(a)

Thank you for your letter dated 21 March 1975 concerning the marketing of Amenerone Forte.

Your letter has been carefully considered and the following comments set out the conclusions reached:-

1. This product is frequently used for pregnancy testing. It is not thought that amendment of the package insert or recommendations for usages are likely to restrict its use to the treatment of secondary amenorrhoea only.

2. Recent literature now leaves little doubt of an association between use in early pregnancy and foetal abnormalities.

3. There are many alternative methods of treating secondary amenorrhoea.

4. This subject has been considered by the Drug Assessment Advisory Committee who have recommended the withdrawl of such products from the New Zealand market.

5. The Department therefore seeks the co-operation of your company in the withdrawl of Amenorone Forte. An early reply to this request would be appreciated.

Yours faithfully,

(Ian A. Witty)
for Director
Division of Clinical Services

ROUSSEL

Roussel (N.Z.) Limited
280-288 Parnell Road
Auckland 1

DAP:CS

21st March 1975

The Director
Division of Clinical Services
Department of Health,
P.O. Box 5013,
WELLINGTON, N.Z.

Your Ref: 142/70/1441

Dear Sir:

Amenorone Forte

We refer to your letter of the 13th March 1975 and regret that there has been some misunderstanding regarding your earlier letter of the 18th February 1975 which has not been received by us.

Following your second letter, Section 9(2)(a) has spoken to you regarding the policy of this Company in connection with hormonal pregnancy tests and this letter is intended to confirm the points made by him.

Various scientific work has been carried out which suggests a relationship between the use of oral pregnancy tests and the incidence of cleft palate. It is the view of this Company that from the evidence so far put forward there is no definitive link and further studies need to be carried out. However, a number of in vitro pregnancy tests have been developed in recent years and the need to use an oral form has decreased, therefore this Company is quite willing to delete pregnancy testing as an indication for the product. It is felt that Amenorone Forte can have a useful therapeutic effect in cases of Secondary Amenorrhea and we suggest that the product be retained for this purpose.

We will be interested to receive your comments on our proposals in due course.

Yours faithfully,

Section 9(2)(a)

Managing Director

Phone: 370-636
P.O. Box 37-111
Cables: Rousselab - Auckland

Dr Phillips JRV

142/70/1441

Amenerone Forte.

A telephone call was received on the 19th of March by Mr Rea.

This conveyed that Rousell did not know of any direct relationship between their product and resultant Foetal abnormalities. They wished to continue marketing the product but would abide by the departmental rulings.

Another phone call was received on the 20th. seeking information. I advised that as other forms of pregnancy testing were available which did not carry any risk to the Mother or Foetus it was considered that such products should not be used for pregnancy testing.

Rousell then asked if marketing of Amenerone Forte could be continued for secondary amenorrhoea. I advised that the company would be advised in writing and need take no further action until a letter is received.

What is your opinion concerning continued use for this purpose.

Jaw

Jaw This product must receive the same treatment as Primodos oral & following the prior DAAC recommendation we should seek removal from the market

JRV

F 12

142/70/144/

D.H.A.C. 19 MAR 1975

(f) Hormonal Pregnancy Tests and Birth Defects

Two hormonal pregnancy tests are currently available on the New Zealand market. Reports have been received from overseas that birth defects have occurred when hormonal pregnancy tests have been taken in early pregnancy.

The Committee were of the opinion that these preparations should be withdrawn from the market.

142/70/1441

IAW
CJB

13 March 1975

The Manager,
Roussell (NZ) Ltd,
P.O. Box 37111,
AUCKLAND.

Dear Sir,

AMENERONE FORTE

This Department wrote to you on the 18 February 1975 seeking your comments on recent references in the literature and your proposals for the continued marketing of this product.

As hormonal pregnancy tests of this nature will be discussed by the Drug Assessment Advisory Committee on the 19 March an early reply would be appreciated.

Yours faithfully,

Ian.

(Ian A. Witty)
for Director
Division of Clinical Services

Dr Andrews Doc B/u to Mr. Witty, 27/3/75

F M

CORRESPONDENCE

Letters must be kept to a reasonable length. Otherwise it may not be possible to find space for them.

CLEFT LIP AND PALATE AND PREGNANCY TESTS

SIR: In the course of our investigations into the aetiology of cleft lip and palate (CLP) in Western Australia, a surprisingly high number of mothers had had an oral or parenteral pregnancy test in the first trimester of pregnancy. After a survey of the incidence of CLP in Western Australia (Journal, July 6), a retrospective study of cases occurring in the years 1963 to 1971 has been undertaken to investigate maternal histories during the first trimester of pregnancy and parental histories before conception. The number of cases studied was 222, and in 22 cases (10%) mothers received oral or parenteral pregnancy tests between the fifth and eighth week of gestation (Table 1). Eight patients were given

TABLE 1

Mothers of Children with Cleft Lip or Palate

Deformity	Number of Cases			
	With Parenteral or Oral Pregnancy Test		Total Studied	
	Males	Females	Males	Females
Cleft lip	3 (14%)	2 (9%)	40 (18%)	15 (7%)
Cleft lip and palate	6 (27%)	5 (23%)	67 (30%)	23 (10%)
Cleft palate	4 (18%)	2 (9%)	38 (17%)	39 (18%)
Total	13	9	145	77
	22		222	

Duogynon or Duogynon Simplex; in the remaining cases the preparations used were unknown; other preparations available for pregnancy testing by attempting to produce withdrawal bleeding in non-pregnant patients are Amenerone forte (Roussel), Menstrogen (Organon) and Secrodyl Tab (A & H), and all are progestogen-oestrogen combinations.

It is currently considered that CLP may be caused by many aetiological factors including single mutant genes, chromosomal aberrations and specific environmental agents; but the great majority are thought to be due to the interaction of heredity and environment.[1] It is, therefore, important to identify any environmental factors which may contribute to the production of these abnormalities which occurred in 1·73 per 1,000 births in Western Australia in the 10-year period 1963 to 1972.

As in our cases, oral pregnancy tests are usually administered at the most sensitive stage of embryogenesis and we consider that their use is an unwarranted risk. In investigations of neural tube malformations Gal[2] found a significantly higher number of mothers in the study than control mothers had received hormone test tablets during pregnancy. Further control and statistical studies taking other possible factors into account are under way in our series, but in the meantime, we wish to bring to notice that these preparations were used in 10% of mothers of CLP patients, yet alternative tests are available which do not require the administration of any drugs.

In only four cases (18%) was pregnancy desired: here oral pregnancy tests may have hastened the diagnosis, but are not essential. In the other 18 cases (82%) pregnancy was not wanted and abortion was requested several times. In the total group 54% of pregnancies were planned. Oral parenteral pregnancy tests may have been carried out in the hope of producing a miscarriage. This is obviously a misuse of the drug. If an early diagnosis is required to arrange termination of pregnancy some non-potentially teratogenic test should be used in case the patient decides to proceed to full term.

We wish to emphasize that the possible danger has only just been revealed in our study, and we know of no previous report which has been available to the medical profession in Australia.

Princess Margaret Hospital for Children, Box D 184, G.P.O., Perth, W.A. 6001. W. F. BROGAN.

[1] Frazer, F. C., *Amer. J. hum. Genet.*, 1970, 22: 336.
[2] Gal, I., *Advanc. Teratology*, 1972, 5: 7.

[The possible association between exposure to sex hormone therapy and some birth defects was discussed in the editorial columns (page 861) of our issue of December 14, 1974.—EDITOR.]

SKIN RASH, CONJUNCTIVITIS AND PLASTIC PERITONITIS WITH PRACTOLOL THERAPY

SIR: We would like to briefly report a patient who developed pustular psoriasis, conjunctivitis sicca and plastic peritonitis whilst on treatment with practolol for angina pectoris. The patient was a man aged 49 who had been taking practolol from March, 1972, until this drug was ceased in July, 1974. The dosage over most of this time was 600 to 800 mg/day. In May, 1973, a rash developed on the left foot, which over the succeeding months progressively spread. In September, 1973, it covered 90% of his whole body surface. He was seen by a consultant dermatologist who considered the rash to be psoriasis, and because of its severity, in December, 1973, commenced him on methotrexate, which was continued until July, 1974. The dose over most of this time was 15 mg taken orally each week. However, there was very little improvement. In December, 1973, the patient also developed a crusty irritation about the eyes. He was subsequently seen by an eye specialist, but despite regular treatment, there was little improvement. In June, 1974, the patient complained of attacks of colicky abdominal pains and vomiting. These symptoms progressed and subsequently, about six weeks later, definite evidence of a subacute bowel obstruction had developed with a large mass being found in the lower abdomen. At laparotomy a thin avascular membrane wrapping up the entire small bowel into three large lobules was found. The avascular membrane could be completely separated off the bowel and mesentery leaving normal bowel serosa.

At this time it was recognized that the psoriasis, conjunctivitis and plastic peritonitis could have been related to his medication and both practolol and methotrexate were withdrawn. Adverse drug reaction reports would indicate that practolol was the responsible agent. Subsequently the skin rash, conjunctivitis and abdominal

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WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTE

CLINICAL AND PHARMACOLOGICAL EVALUATION OF DRUGS/QUALITY, SAFETY AND EFFICACY OF DRUGS

DRUG INFORMATION NO 144

11 February 1975

Resolutions WHA16.36/WHA26.31

ORIGINAL : ENGLISH

The Australian Department of Health has informed the World Health Organization about the withdrawal from the market of a number of hormonal pregnancy testing preparations. The preparations are Duogynon[1], Duogynon Simplex[2], Duogynon Oral[3], Amenorone Forte[4], and Secrodyl[5].

The Minister of Health[6] stated that the Australian Drug Evaluation Committee had recommended that systemic hormonal formulations for pregnancy testing be withdrawn from the Australian market on the basis of their questionable safety and the fact that there were adequate and reliable methods available which do not involve the administration of hormones. Such methods relied on the testing of body fluids by immunoassay methods.

The action of the Australian Drug Evaluation Committee and the Australian Department of Health was based on evidence from the United States which draws attention to the risk of unnecessary drug exposure in early pregnancy. This evidence was put forward in papers in 'Nature'[7,8,9] on the risks and benefits of the use of hormonal pregnancy test tablets.

The Department of Health had been made aware of four reports of congenital abnormalities occurring in Australia since 1968 which were possibly associated with hormonal pregnancy tests.

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[1] Contains 20 mg/ml of progesterone (INN)* and 2 mg/ml of estradiol benzoate (INN)

[2] Contains 50 mg/ml of progesterone (INN) and 3 mg/ml of estradiol benzoate (INN)

[3] Contains 10 mg of norethisterone (INN) acetate and 0.02 mg of ethinylestradiol (INN) per tablet

[4] Contains 50 mg of ethisterone (INN) and 0.05 mg of ethinylestradiol (INN) per tablet

[5] Contains 10 mg of dimethisterone (INN) and 0.05 mg of ethinylestradiol (INN) per tablet

[6] A copy of the statement can be obtained from the World Health Organization on request

[7] Laurence, M. et al., Hormonal Pregnancy Tests and Neural Tube Malformations, Nature, Vol. 233, October 15 1971, pp 495-496

[8] Gal, I., Risks and Benefits of the Use of Hormonal Pregnancy Test Tablets, Nature, Vol 240, November 24 1972, pp 241-242

[9] Sever, L. E., Hormonal Pregnancy Tests and Spina Bifida, Nature, Vol. 242, April 6 1973, pp 410-411

* INN stands for International Nonproprietary Name proposed by WHO.

The Minister of Health also stated that apart from the pregnancy-testing products mentioned, there were a number of other hormonal preparations available in Australia for medical uses such as the treatment of breast cancer, which could also be used for pregnancy testing. The Department would require that product literature for those preparations contain a specific warning that they not be used for pregnancy testing, and the manufacturers and importers are being advised accordingly.

Although a number of contraceptive pills contain similar types of substances, they are used in much lower doses and are administered to prevent pregnancy. Thus, women on the pill had no cause for worry if they complied with recommended instructions. However, the practice of taking multiple doses of the pill on a few occasions in the event of doses being missed should be avoided. Similarly increased doses of the contraceptive pill should not be taken as a pregnancy test.

accumulations and depressed very low density lipoprotein. These studies, together with various sophisticated biochemical analyses with studies of enzymatic involvement, which have recently been attempted, give hope that at least some of the obscurities may be removed in the not too distant future and perhaps pave the way for a more rational and less empiric line of therapy.

INFECTIOUS MONONUCLEOSIS

INFECTIOUS MONONUCLEOSIS is a disease which, because of its various clinical manifestations in adolescence and young adults, may imitate a number of other infections. Conversely, there is always a temptation to label a febrile disease with otherwise undiagnostic features with the title of infectious mononucleosis.

The Paul-Bunnell test for heterophil antibody remains an important test in the diagnosis of infectious mononucleosis. Unfortunately, in childhood infections it often fails to become positive and this is also occasionally the case in classical disease in young adults. With the relatively recent discovery of the EB (Epstein-Barr) virus, a further marker has become available to study the epidemiology of this disease. A number of excellent prospective studies have shed light on childhood infections with the EB virus. In the Cleveland family study, it was found that EB virus infections in childhood were rarely associated with obvious symptoms and signs which would suggest a clinical diagnosis of infectious mononucleosis.[1] Most cases of non-bacterial tonsillitis or pharyngitis were found to be due to other viruses, often adenoviruses. In the Alaskan Islands survey, 100% of primary infections were found to occur in children under the age of three years, but no distinctive clinical illness was observed.[2] It is possible, therefore, that some of the children with clinical infectious mononucleosis described by Hubble and his co-authors in this issue (page 863) were suffering from infections with viruses other than the EB virus.

Hubble *et alii*, in their retrospective study in Perth, have confirmed many of the well-known features of this illness. Two peaks of infection, one in the under ten years age group and another between the ages of 15 and 24 years have been well documented, the first perhaps representing early childhood infections acquired from the patient's mother. The earlier peak amongst adolescent females is also well described and perhaps attributable to earlier sexual maturity.

Estimates of the crude annual incidence of heterophil antibody-positive infectious mononucleosis in general populations have ranged widely, and are clearly dependent upon the type of patients studied and the method of reporting.[3]

It is of interest that the Western Australia group have been unable to confirm the seasonal incidence of the disease reported by other workers. Such differences, if present, might have been revealed by the study of a more precisely defined population over a longer period of time; on the other hand, they may reflect the generally milder climate of the Australian temperate zone, compared with that of the countries in which the classical studies of infectious mononucleosis have been carried out. A study by C. R. Boughton of a hospital series of "glandular fever" cases in Sydney also found no significant seasonal variation in the admission rate.[4] Studies of the epidemiology of infectious mononucleosis which are performed retrospectively and without adequate virological[3] confirmation must necessarily be limited in value. Undoubtedly, many of the patients described did have infectious mononucleosis, but it is probable that some others were suffering from infections with agents such as cytomegalovirus and toxoplasmosis. More conclusive results will only be obtained from prospective studies using the EB virus as a marker for this disease.

[1] Henle, G., and Henle, W., *J. Infect. Dis.*, 1970, 121: 303.
[2] Tischendorf, P., Shramek, G. J., Balagtas, R. C., *et alii*, *J. Infect. Dis.*, 1970, 122: 401.
[3] Heath, C. W., Brodsky, A. L., and Potolsky, A. I., *Amer. J. Epidemiol.*, 1972, 93: 46-52.
[4] Boughton, C. R., MED. J. AUST., 1970, 2: 529.

BIRTH DEFECTS AND ORAL CONTRACEPTIVES

SINCE the first suspicions that some birth defects may be associated with exposure to sex hormone therapy,[1] oral contraceptives,[2,3] or hormonal pregnancy tests[4] during embryogenesis, more data have accumulated.[5] It appears that some infants, whose mothers have been administered progestogen/oestrogen hormones during the earliest part of pregnancy, may have an increased incidence of vertebral, anal, cardiac, tracheal, oesophageal, renal or limb anomalies (acronym: VACTERL).[6]

In a recent controlled study from New York, reported in *The New England Journal of Medicine*,[7] it was found that 15 (14%) of 108 mothers of malformed children were exposed to hormonal pregnancy tests, or supportive hormone therapy, or had "breakthrough" pregnancies while on oral contraceptives, while only four (4%) of 108 control mothers of normal children were thus exposed. In the survey, the malformed children all had limb-reduction defects, which are defined as loss of an arm or leg or part thereof. There was a slight increase in the rate of twins among the affected infants, but only one of any pair was malformed. Of these mothers who became pregnant while taking oral contraceptives one was using a sequential type, and others used combination-type preparations. It was significant that affected children with histories of exposure to orally administered hormones were all male. This seems to imply that oral hormones have some type of sex-specific effect on the developing fetus. Of less certain significance is the finding that the rate of limb-reduction defects has increased by 33% since 1963, while the rate of malformations of all types has decreased about 6%. It is conjectured that this change has been apparent only since the introduction of oral

[1] Levy, E. P., Cohen, A., and Fraser, F. C., *Lancet*, 1973, 1: 611.
[2] Nora, J. J., and Nora, A. H., *Lancet*, 1973, 1: 941.
[3] Kaufman, R. L., *Lancet*, 1973, 1: 1396.
[4] Oakley, G. P., Flynt, J. W., Falek, A., *Lancet*, 1973, 2: 256.
[5] Balci, S., Say, B., Pirner, T., and Hicsönmez, A., *Lancet*, 1973, 2: 1098.
[6] Nora, J. J., and Nora, A. H., *New Engl. J. Med.*, 1974, 291: 731 (October 3).
[7] Janerich, D. T., Piper, J. M., and Glebatis, D. M., *New Engl. J. Med.*, 1974, 291: 697 (October 3).

contraceptives, but this view awaits confirmation, and is expressed cautiously.

One conclusion of the study is that endogenous hormonal insufficiency may be present in those mothers who exhibit a breakthrough pregnancy while taking an oral contraceptive, or need supportive hormone therapy during pregnancy, and who then subsequently have a malformed child.

It is obvious that the great majority of pregnancies in which these drugs are used do not give rise to malformed infants. If progestogen/oestrogen hormones do produce malformations, it is at a low frequency rate, and probably operating in a predisposed mother. However, recommendations have been voiced that it would be wise to discontinue hormonal pregnancy tests, and to demonstrate that there is no pregnancy present before initiating oral contraceptive administration.[6,7]

RELAXATION OF REQUIREMENTS ON SMALLPOX VACCINATION

AUSTRALIANS long had a strict policy on smallpox vaccination requirements for arriving travellers. This has caused irritation from time to time on the part of people from overseas who are accustomed to the casual policy in some countries, and it has, within the bounds of prudence and commonsense, been modified a little in recent years. Nevertheless, a strict policy has been only too easy to justify and may well have saved us from serious outbreaks of the disease.

With the success of the World Health Organization's campaign to control smallpox, the ultimate goal of eradicating the disease now seems not too much to hope for. This had led to a more relaxed attitude overseas, even in places like the United Kingdom and the United States. However, as we pointed out[1] when commenting on these changes some years ago, Australia, because of its geographical nearness to areas where smallpox is still epidemic, is scarcely in a position to take a lead in relaxing its guard against the disease.

Now, however, there is to be some further relaxation for travellers arriving in Australia, but still within the bounds of prudence and commonsense. An announcement made by the Commonwealth Minister for Health, Dr D. N. Everingham, on November 12, 1974, states that as from that date travellers who cannot be vaccinated because of a medical condition will no longer be compelled to enter quarantine on arrival, provided they have not come from, or stopped over at, countries infected with smallpox. Previously, all travellers without valid vaccination certificates were obliged to spend 14 days in quarantine unless they had spent the 14 days prior to arrival in the United States or Canada, or in those Pacific islands on the direct air route to Australia.

Dr Everingham said that the relaxation had been decided on after careful weighing up of the potential risks to the Australian community. However, certain essential safeguards were still necessary and would be rigorously enforced. Travellers seeking exemption must have a medical certificate, issued within the 12 months before embarkation and signed by a registered medical practitioner, stating that vaccination against smallpox was inadvisable because of a medical condition. The condition must be specified. The exemption did not extend to travellers from countries where smallpox was still endemic, or where the disease had been recorded in the previous 12 months.

At the present time, according to the Minister's statement, only four countries have endemic smallpox—Ethiopia, Pakistan, India and Bangladesh. To determine which countries are included, the Health Department will use as its guide the *Weekly Epidemiological Record*, in which the World Health Organization lists countries infected within the previous year. It is emphasized that travellers who simply land in these countries *en route*, as transit passengers, will be exempted, but not people who stop over.

The medical conditions which will qualify travellers for exemption are (i) pregnancy; (ii) history or presence of eczema or other skin diseases considered by the traveller's doctor to be a contraindication to smallpox vaccination; (iii) states of immunological deficiency which are (*a*) subsequent to treatment which depresses immunity (for example, deep X-ray therapy, administration of corticosteroids, alkylating and cytotoxic drugs) or (*b*) hypogammaglobulinaemic conditions; (iv) nephrosis; (v) organ transplants; (vi) general malignant disease. In addition, travellers accompanied by a doctor or nurse, for whom hospital care is likely for 14 or more days after arrival, will be exempted. There is no change in the rule regarding infants under 12 months of age; they will continue to be automatically exempt.

All travellers admitted in this way without vaccination will be given a form advising them to seek immediate medical attention if they become ill during the first six weeks after arrival. It is emphasized that the relaxation applies only to travellers with the medical conditions specified. Any other travellers arriving without valid vaccination certificates, or entering from smallpox-infected countries, will still have to go into quarantine.

In a concluding comment, Dr Everingham said that the World Health Organization was confident that smallpox would be totally eradicated from the world within a few years. However, in the meantime, Australia was determined to maintain its smallpox-free record and—with the exception of the present relaxation—would continue to take strict precautions with incoming travellers.

[1] MED. J. AUST., 1971, 2: 456 (August 28).

142/70/1441

18 February 1975

The Manager,
Roussell (N.Z.) Ltd,
P.O. Box 37111,
AUCKLAND

Dear Sir,

AMENERONE FORTE

The Department is aware of recent evidence associating the use of hormonal pregnancy tests in early pregnancy with birth defects.

Despite the rarity of this association concern is felt at the continued availability of your product on the New Zealand market.

Your comments on recent references in the literature to this association and your proposals for the continued marketing of this product will be examined with interest by the Department.

Yours faithfully,

D.A.A.

(D.A. Andrews)
for Director,
Division of Clinical Services

B/u for Dr. Andrews 17/3/75

~~Dr. Parsons~~ 18.2.
Miss ~~Foote~~ [illegible]
~~Dr. [illegible]~~
~~Dr. [illegible]~~
~~Dr. [illegible]~~
~~Dr. Phillips~~

(Similar letter sent to Schering about Primodos [illegible])

F