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

27 APR 2017

[redacted]

Ref: H201701217

Dear [redacted]

Response to your request for official information

Thank you for your request of 6 April 2017 under the Official Information Act 1982 (the Act) for

"archival records for Amenorone Forte".

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.

Request	Response
Archival records for Amenorone Forte	Attached is: A copy of the archived records for Amenorone Forte

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

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

Reply 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.

Section 9(2)(a)

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

142/70/1441

13 June 1975

Section 9(2)(a)
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. A.

(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

[redacted]
Roussel (N.Z.) Limited,
P.O. Box 37111,
AUCKLAND.

Dear [redacted]

Further to our letter of 26 May, concerning the withdrawal 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

F

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. ~~Dr [illegible]~~
2. ~~[illegible]~~
3. ~~[illegible]~~
4. Dr Griffith
5. F M

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.

Section 9(2)(a)

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

I :/H

142/70/1441

1 May 1975

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

Dear [redacted]

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

F

2) BU 18/5/75
gaw.

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."

"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.

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 Amenorone 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 usage 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.

Section 9(2)(a)

Dr Phillips JPV

142/70/1441

Amenerone Forte.

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

This conveyed that Roussell 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.

Roussell then asked if marketing of Amenerone Forte could be continued for secondary amenorrhoea. I [illegible] that the company would be [illegible] [illegible] writing and [illegible] would take no further action until a letter is received.

What is your opinion concerning continued use for this purpose.

Ian

JPV This product must receive the same treatment as Primodos oral & following the [illegible] DAAC recommendation we should seek removal from the market

JPV

F 11

142/70/144/

(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.

The Committee agreed that packet inserts should be in non-technical language.

A Therapeutic Note on oral contraceptives is being planned.

(b) Minipress

When this drug was given consent for marketing the firm agreed to limit distribution to hospitals and not advertise the drug's availability, and it was pleasing to note that the firm had complied with these requests. The firm has applied to have this drug put on the Drug Tariff.

Members felt that for applications of this type clinical experience should be obtained in Australasia, and that data on placental transfer should be provided.

The Committee agreed that Minipress could now be made available for wider distribution.

(c) Clinical Trials

Dr Paul advised that Hospitals Division has sent a follow-up circular regarding Ethical Committees.

(d) Medicines Bill

The Second Draft of the Bill is nearing completion. When it is finalised, permission will be sought from the Minister of Health to circularise it to all interested parties, including members of this Committee.

(e) Rybarex and Rybarvin Inhalant

The firm has decided to withdraw these products from the market.

4. DEFERRED DRUGS

Fenoxoron

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of this drug subject to the provision of satisfactory quality control data.

It was thought that drugs should be monitored for 2 - 3 years after consent to distribution has been granted and that initial distribution could be limited to doctors who were willing to report on efficacy, any adverse reactions and side effects. If such a scheme was put into action it would eliminate some of the present delays in giving consent to marketing.

A scheme of this type would be very complex and would require a great deal of planning. There could be difficulties in ensuring continuing co-operation of the recording doctors.

142/70/1441

IAW
CJB

13 March 1975

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

Dear Sir,

ANSHLACHE 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 Data 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 DO =1 B/u to M. 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 I). Eight patients were given

TABLE I
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	1 (5%)	2 (9%)	9 (17%)	20 (18%)
Total	10	9	116	77
	22		222	

Duogynon or Duogynon Simplex; in the remaining cases the preparations used were unknown; other preparations available for pregnancy testing or attempting to produce withdrawal bleeding in non-pregnant patients are Amenorone forte (Roussel), Menstrogen (Organon) and Norcdyl 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. DOGGAN.

[1] Fraser, 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, 1972, 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

142/70/1441

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.

---

[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: 203.
[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: 48-52.
[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 Hiesbmez, A., *Lancet*, 1973, 2: 1038.
[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.[1]

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.

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

142/70/1441

12 March 1970

[illegible] Ltd.,
P.O. 1403,
AUCKLAND.

Dear Sirs,

Thank you for the information in your letter of 9 March, that you have changed the housemarkings for two of your products.

Yours faithfully,

[illegible]
for Director
Division of Public Health

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

[illegible] 17/3/75

~~[illegible]~~ 18.2.
Miss [illegible]

([illegible])

Dr. [illegible]
[illegible]
[illegible]
[illegible]

142
70/1941

ROUSSEL

Roussel (N.Z.) Limited
Bristol House
12 Albert Street
Auckland 1

PJO:PS

9th March, 1970

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

Dear Sir,

I would like to advise you that we have changed the housemarkings for two of our products. The new tablet markings are as follows:

Amenorone Forte	Face I	R(breakline)L
	Face II	A
Decaserpyl 10mg	Face I	R(breakline)L
	Face II	D(breakline)10

Yours faithfully,
Roussel (N.Z.)Limited,

Section 9(2)(a)

Area Manager.

RECEIVED
10 MAR 1970
HEALTH DEPT.
HEAD OFFICE

P.T.
11/3

Thanks

Phone: 370-636
C.P.O. Box 4018
Cables: Rousselab - Auckland

ROUSSEL

Roussel (N.Z.) Limited
Bristol House
12 Albert Street
Auckland 1

MIB/SAB

20th February, 1969

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

Dear Sir,

Thank you for your letter of 17th February, reference 142/70/1411 on the subject of Anenorene Forte.

We regret to advise that there has been a delay in the preparation of specimen labels, however, we hope to have the specimens for you within 1 weeks.

Yours faithfully,
ROUSSEL (N.Z.) LIMITED

Section 9(2)(a)

F.C. Pruett

Phone: 370-636
C.P.O. Box 4018
Cables: Rousselab - Auckland

IDO:SC

142/70/1441

17 February 1969

Area Manager,
Roussel (N.Z.) Ltd,
C.P.O. Box 4018,
AUCKLAND.

Dear Sir,

I refer to previous correspondence on the subject of Amenorone Forte. Would you please advise the present situation.

Yours faithfully,

(I.D. Ogden)
for Director,
Division of Public Health

ROUSSEL

Roussel (N.Z.) Limited
Bristol House
12 Albert Street
Auckland 1

KHB:MHS

3rd December, 1968

Director,
Division of Public Health,
Department of Health,
P.O. Box 5013,
WELLINGTON.

Dear Sir,

We have your letter of the 29th November reference 142/70/1441 regarding the labelling of Mucomorone Forte.

We have just returned proofs of the labels in question to our United Kingdom principals and hope to have suitable specimens for submission to your department before the end of December.

Yours faithfully,
Roussel (N.Z.) Limited,

Section 9(2)(a)

Area Manager.

Phone: 370-636
C.P.O. Box 4018
Cables: Rousselab - Auckland

IDO:SJS

142/70/1441

25 November 1968

The Area Manager,
Roussel (N.Z.) Ltd,
C.P.O. Box 4018,
AUCKLAND.

Dear Sir,

Would you please advise if there has been any word from your United Kingdom principals on the re-labelling of Amenorone Forte.

Yours faithfully,

(I. D. Ogden)
for Director,
Division of Public Health

ROUSSEL

Roussel (N.Z.) Limited
Bristol House
12 Albert Street
Auckland 1

KHb:MkS

24th September, 1968

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

Dear Sir,

Thank you for your letter of the 20th September reference 142/70/1411 relating to our letter of the 23rd August on the subject of Amenorone Forte.

We have forwarded your recommendations to our principals in the United Kingdom who have been requested to supply us with amended labels at an early date. We will forward them to you as soon as they are received by us.

Yours faithfully,
Roussel (N.Z.) Limited,

Section 9(2)(a)

Area Manager.

RECEIVED
26 SEP 1968
HEALTH DEPT.
HEAD OFFICE

40-636

Phone: 370-636
C.P.O. Box 4018
Cables: Rousselab - Auckland

IDO:BCH

142/7 /1441

20 September 1968

Roussel (N.Z.) Ltd,
P.O. Box 12170,
Penrose,
AUCKLAND, 6.

Dear Sirs,

On 23 August you were advised that the labels proposed for your product Amenorone Forte were deficient in several respects. Would you please advise what steps have been taken to meet those deficiencies.

Yours faithfully,

(I. D. Ogden)
for Director,
Division of Public Health

IDO:VL

147-70-1441

147-70-1444

Roussel (NZ) Ltd,
P.O. Box 12170,
Penrose, AUCKLAND 6.

11 July 68

AMENORONIL FORTE	Tablet	50 mg	Methisterone	
		0.5 mg	Ethinyloestradiol	3 tab.

Nil

To comply with Regulation 37 of the Poisons Regulations 1964 the words 'Restricted Drug' on the bottle must appear in a line separate to other words. On the carton the height of this statement must be increased to not less than ½ inch in height. To comply with Regulations 14,16 and 25 of the Food and Drug Regulations 1946, the statement of dose on the bottle must be amended to non serif capital letters of not less than 1/16th of an inch in height and on the carton to 1/12th of an inch in height.

(1) [illegible] 30/8.

(2) Clinical Services

(3) Bkup 22/9/68

By: ~~22-10-68~~ ~~22-11-68~~ ~~20-12-68~~ ~~15-2-69~~ 15-3-69 B.A.R.

DRUG ACTION SHEET

Food and Drugs Act 1947

___ New Drug Notification (S.11B)

X Application for consent s 11B(2)-s 11C(2)

X Changed Drug Notification (S.11C)

___ Deposit of further particulars (s 11D)

___ Notification of investigational drug and application approval investigator (s 11E)

Any previous notification application: Date:

Nature:

Date of deposit of this communication 11.7.66

Notification/Application by: Manufacturer:

True Name Roussel (NZ) Ltd., True Name: Roussel Labs. Ltd.,

Full Address: P.O. Box 12-170 Full Address: London,

Penrose, Akld. 6. England

TRADE NAME Amenorrone Forte

Non-Proprietary Name

Formula: Each Tablet Contains

Ethisterone B.P. 50mg.

Ethinylestradiol B.P. 0.05mg.

Form of Drugs: Tablet

Therapeutic class:

Proprietors proposed method of distribution to public

Present Statutory Restriction R.D. (

Recommended Restriction (by/Date

GENERAL ACTION (If any further comments - please continue overleaf.)

(1) Mr Ogden (a) Notification complete
(b) ~~Notification not complete (see reverse of form),~~
(c) Request for early distribution (Cross out if not applicable)

(2)

(3) Mr Reed 1/8

(4) Mr Ashforth 9/8

(5) Dr Murphy Acknowledge

(6) Mr Ogden (Reply to firm)

(7)

(8)

Recommended Disposal	Initials	Date
Accept as notification		
Reject " "		
Grant Consent		
Decline Consent		

The following information marked "2" is required to complete this notification.

(a) (i) Address of depositor of notification.
(ii) True name and address of the manufacturer.

(b) The name under which the drug will be distributed.

(c) A full statement of the ingredients, named by descriptive or non-proprietary names, including details of the quantities in which they are contained in the drugs.

(d) A description of the form or forms of the drug.

(e) The proposed or recommended dosage and frequency of dose, and the manner in which the drug will be recommended to be administered, applied, or otherwise used.

(f) The purposes for which the drug will be recommended to be used, and the claims to be made in respect of its usefulness.

(g) Reports of any tests made to establish the safety of the drug for the purposes for which and in the manner in which it is intended to be used.

(h) Reports of any tests made to control the strength, quality, purity, or safety of the drug.

(i) The intended method of distribution of the drug in New Zealand.

(j) A specimen of every label proposed to be used on packages containing the drug.

(k) If the drug is to be manufactured, prepared, or packed in New Zealand, the name and address of the place or places where the manufacture, preparation, or packing is intended to be carried out.

FURTHER COMMENTS

DEPARTMENT OF HEALTH, HEAD OFFICE

DRUG LABEL COMMENT SHEET

TRADE NAME AND FORM AMENORONE FORTE

PACK 3 tab bottle

Deficiencies are indicated by the symbol "x" in the right hand column. Partial deficiencies and particular defects may be emphasised by underlining of appropriate words.

Ref.	Reg. No.	Requirement	Deficient
POISONS REGULATIONS			
A	37	Poisons classification on upper part of main panel of label (i.e. in the same panel as the name of the drug) in non-serif capital letters not less than $\frac{1}{4}$"/$\frac{1}{8}$" in height, or 1/20 height of the container whichever is the less	
		Poisons classification to appear ~~as specified above~~ in separate line to other wording — RESTRICTED DRUG	x x
		PRESCRIPTION POISON or POISON P.P.	
		POISON S1	
		Where alternative POISON S2 not used	
B	43	Second schedule poison alternative statements not appearing or not conspicuously printed	
		"Caution: it is dangerous to exceed the stated dose"	
		"Caution: to be taken strictly as directed"	
		"Caution: to be used strictly as directed"	
C	23	Does poisons classification appear on all advertising material?	Yes / No
D	42	Directions for use on drug for external application	
E	50	Antihistemine warnings, "Do not use during pregnancy without medical direction" and "Do not drive a motor vehicle within 6-8 hours after taking this drug".	
		Further antihistamine warning where drug for nasal or external use "Prolonged or repeated use should not be carried out without medical advice"	
FOOD AND DRUG REGULATIONS			
A	14,16	Name of the drug in non serif capital letters not less than $\frac{1}{2}$"/1/16" in height	
		Recommended dose in same panel as name in non-serif capital letters not less than $\frac{1}{2}$"/1/16" in height	x x
		True name and address of manufacturer in non-serif capital letters not less than $\frac{1}{12}$"/1/16" in height	
B	181	Declaration of alcohol	
		In precise form set down in reg. 181	
C	184	Compliance with specific requirements for biological preparation	

Ref.	Reg. No.	Requirement	Deficient
D	179,187	Quantitative and qualitative declaration of ingredients expressed in terms of G.M.C. approved name, B.P. or B.P.C. name or true scientific description	
E	25	All statements in uniform colour or uniform background	
3. MEDICAL ADVERTISEMENTS REGS.			
A	18	Directions for use	
B	15 (F & D) (reg.183) (and 182)	Statement "DANGER" - this preparation should not be used except under medical direction" on labels and advertisements for glandular preparations or extracts or synthetic substances of similar physiological effect	
4. RECOMMENDATIONS NOT SPECIFICALLY COVERED BY LAW			
A	Nil	Warning on preparations containing aspirin "Caution, this preparation should not be administered to children under 2 years of age without medical advice"	
B	Nil	Dosage recommendation for fluid medicines in metric system preferred	
5. FURTHER COMMENT			

Checked	
Inits.	Date

DEPARTMENT OF HEALTH, HEAD OFFICE

DRUG LABEL COMMENT SHEET

TRADE NAME AND FORM AMENORONE FORTE

PACK 3 Tab outer carton

Deficiencies are indicated by the symbol "x" in the right hand column. Partial deficiencies and particular defects may be emphasised by underlining of appropriate words.

Ref.	Reg. No.	Requirement	Deficient
POISONS REGULATIONS			
A	37	Poisons classification on upper part of main panel of label (i.e. in the same panel as the name of the drug) in non-serif capital letters not less than ¼"/⅛" in height, or 1/20 height of the container whichever is the less	X
		Poisons classification to appear as specified above — RESTRICTED DRUG	X
		Poisons classification to appear as specified above — PRESCRIPTION POISON or POISON P.P.	
		Poisons classification to appear as specified above — POISON S1	
		Poisons classification to appear as specified above — Where alternative POISON S2 not used	
B	43	Second schedule poison alternative statements not appearing or not conspicuously printed	
		"Caution: it is dangerous to exceed the stated dose"	
		"Caution: to be taken strictly as directed"	
		"Caution: to be used strictly as directed"	
C	23	Does poisons classification appear on all advertising material?	Yes / No
D	42	Directions for use on drug for external application	
E	50	Antihistamine warnings, "Do not use during pregnancy without medical direction" and "Do not drive a motor vehicle within 6-8 hours after taking this drug".	
		Further antihistamine warning where drug for nasal or external use "Prolonged or repeated use should not be carried out without medical advice"	
FOOD AND DRUG REGULATIONS			
A	14,16	Name of the drug in non serif capital letters not less than ½"/1/16" in height	
		Recommended dose in same panel as name in non-serif capital letters not less than ½"/1/16" in height	X
		True name and address of manufacturer in non-serif capital letters not less than ½"/1/16" in height	
B	181	Declaration of alcohol	
		In precise form set down in reg.181	
C	184	Compliance with specific requirements for biological preparation	

Ref.	Reg. No.	Requirement	Deficient
D	179,187	Quantitative and qualitative declaration of ingredients expressed in terms of G.M.C. approved name, B.P. or B.P.C. name or true scientific description	
E	25	All statements in uniform colour or uniform background	
3. MEDICAL ADVERTISEMENTS REGS.			
A	18	Directions for use	
B	15 (F & D) (reg.183) (and 182)	Statement "DANGER" - this preparation should not be used except under medical direction" on labels and advertisements for glandular preparations or extracts or synthetic substances of similar physiological effect	
4. RECOMMENDATIONS NOT SPECIFICALLY COVERED BY LAW			
A	Nil	Warning on preparations containing aspirin "Caution, this preparation should not be administered to children under 2 years of age without medical advice"	
B	Nil	Dosage recommendation for fluid medicines in metric system preferred	
5. FURTHER COMMENT			

Checked	
Inits.	Date

Roussel (N.Z.) Limited

73A GREAT SOUTH ROAD, PENROSE, AUCKLAND 6
P.O. Box 12-170, Penrose
Telephone 597-733 — Telegrams: Rousselab, Auckland

ROUSSEL

KHB:MMS

9th July, 1968

H 7

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

Dear Sir,

We submit the following details pertaining to our product Amenorone Forte under Section 11C; 1 (b) of the Food & Drug Amendment Act 1968:-

Imports Name : Roussel (N.Z.) Limited, Auckland

Manufacturers Name : Roussel Laboratories Ltd., London, England.

Product Name : Amenorone Forte

Pack & Form : Packs of 3 tablets

Labelling : New as per specimens

Your early consent to market would assist us.

Thanking you in anticipation.

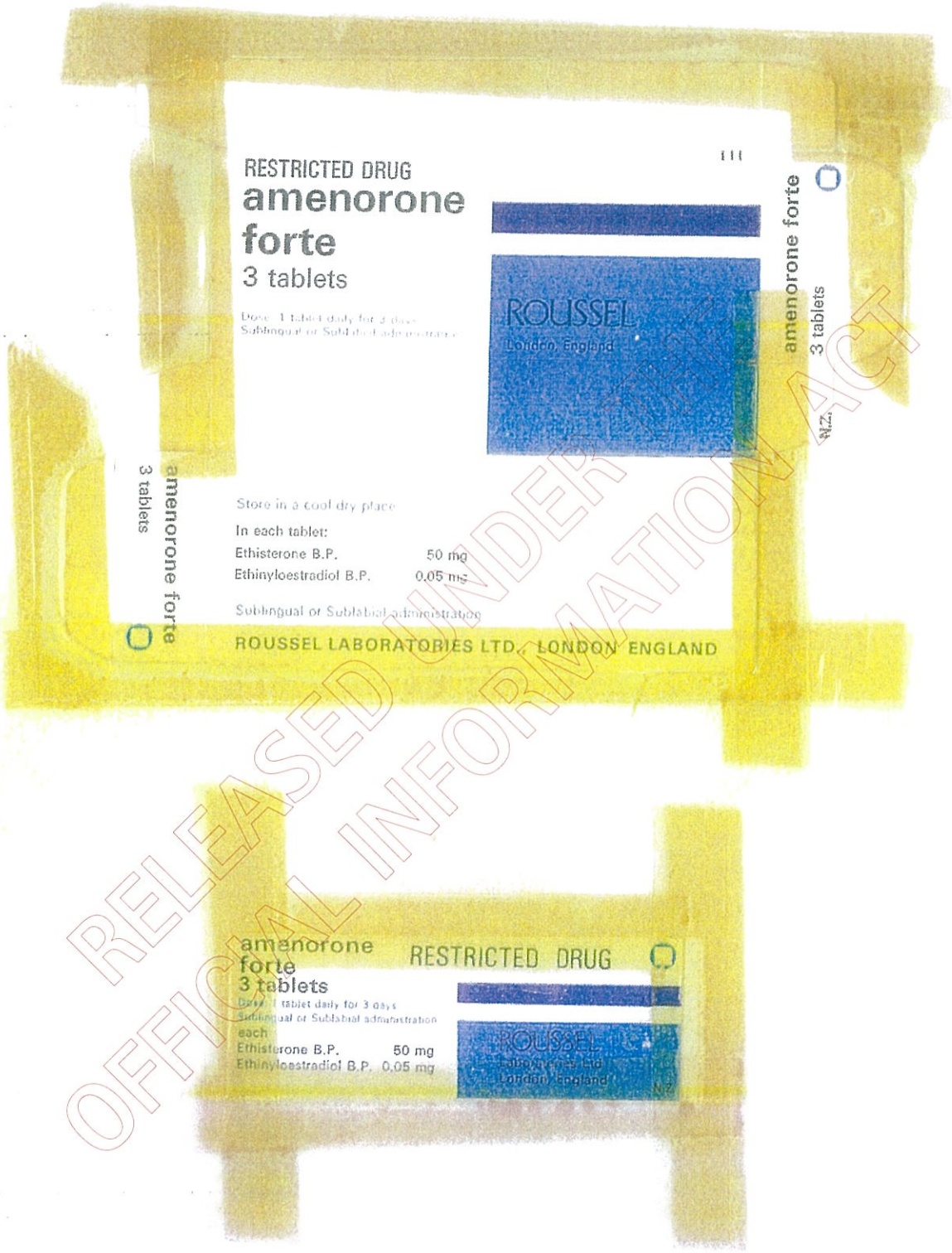
Yours faithfully,
Roussel (N.Z.) Limited,

Section 9(2)(a)

Area Manager.

RECEIVED
11 JUL 1968
HEALTH DEPT.
HEAD OFFICE

11/7/68



File

APPLICATION FOR REGISTRATION OF A STOCK REMEDY

NAME OF PREPARATION:

PURPOSE OF USE:

COMPOSITION:

NAME AND ADDRESS OF APPLICANT:

DATE OF APPLICATION:

Department of Health,
P.O. Box 3013,
WELLINGTON.

Roussel (NZ) Ltd.,
P.O. Box 12-170,
Penrose,
Auckland 1.

Dear Sir,

Your letter of 9.7.68 forwarding information about the drug Amenorone Forte has been received. You will be advised as soon as possible whether in the opinion of this Department the notice complies with the requirements of the Food and Drugs Amendment Act 1968.

Yours faithfully,

J Grace.

for Director-General of Health