MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

133 Molesworth Street
PO Box 5013
Wellington 6140, New Zealand
T +64 4 496 2000
W www.medsafe.govt.nz

27 SEP 2017

[redacted]

Ref: H201703568

Dear [redacted]

Response to your request for official information

Thank you for your request of 4 September 2017 under the Official Information Act 1982 (the Act) for:

"the main points I wish to raise with you are:

1. *The MHRA inquiry into Primodos started on the 25th March, 2015, with a call for evidence. The inaugural meeting was held on the 14th October, 2015.*
   - On the 19th March, 2017, The Sun and The Guardian newspapers in the United Kingdom ran stories about Primodos and other Hormone Pregnancy Tests, calling it a scandal.
   - On the 20th March, 2017 Medsafe published a request for people in New Zealand affected by Primodos to come forward, fully two years after the call for evidence from Medsafe's sister organisation.
   -The Inquiry closed on the 24th April, 2017. I was assured by Rowan Pollock of Medsafe on the 4th May, 2017, that I would receive a copy of the information gathered in New Zealand which was to be sent to the MHRA.
2. *Medsafe's response to my OIA request for communication between the MHRA and Medsafe regarding Primodos was, "the "document(s) alleged to contain the information requested does not exist".*
   Does this mean there has been no communication between the MHRA and Medsafe regarding HPTs, nor a request from the MHRA for information?
3. *Medsafe reported in the media, 20th March, 2017 that the Department of Health "removed stocks from pharmacies". The evidence provided to me by Medsafe's OIA request refers only to the manufacturers removing the drugs. Clearly the Department of Health relied on the manufacturers to remove stocks and did no follow up to ensure none remained. Medsafe's claim in the media that the Department removed stocks is disingenuous.*
4. *Roussell's letter dated 19 June,1975, refers to a Clinical Services Letter No.150 sent by the Department of Health, stating "… this action plus the information which appeared in your Clinical Services letter No. 150, will ensure that all retail pharmacies have cleared the Amenorone Forte stocks…".*
   In a RNZ Checkpoint media clip John Campbell read a statement from yourself. In the statement you say "…a Clinical Services Letter was released in May 1975, withdrawing systemic hormonal pregnancy testing."

Why then was the response to my request for this information declined on the basis that no documents existed?

5. *Question 9 asked for evidence of Notices for publication in the NZ Gazette regarding the introduction and revocation of HPTs including but not limited to Primodos.*
   My search of the NZ Gazette archive revealed 3 entries for Primodos from 1966 to 1971 but no notification of revocation by the Department of Health. Your response to me was,"the "document(s) alleged to contain the information requested does not exist".
6. *The NZ experience in 1962 of the effects of Thalidomide gave clear indications that harm caused to unborn babies had significant long term health and social effects. It is hard to believe that the Department of Health whose role it was to ensure the safety of medicines made no effort to inquire into the health of mothers prescribed HPTs and their babies, thirteen years on from Thalidomide. Health authorities are responsible for the health and wellbeing of the population. It is inconceivable that no meetings were held to discuss the Department of Health's responsibilities to those affected by HPTs. The response to my request for information as to what actions the Department of Health took was, "...the "document(s) alleged to contain the information requested does not exist".*

   In summary, it appears that Medsafe has made little or no effort to seek or provide the information I originally requested. The lack of information regarding communication between Medsafe and the MHRA is a yawning gap.

I therefore seek responses to the following:

7. *"When was Medsafe first aware of the MHRA Inquiry into Primodos and other HPTs?*
8. *How was Medsafe made aware of the MHRA Inquiry given that Medsafe's response to my original question 2, was that no such documents existed. Please provide this and other documentation outlined in my original OIA request.*
9. *Why did Medsafe wait for over 2 years from the time the MHRA called for information, to action the call for information from those who may have taken the drugs in New Zealand?*
10. *Provide a copy of Medsafe's report to the MHRA about Primodos and other HPTs use in NZ or advise the status of the report.*
11. *Provide a copy of the Clinical Services Letter No. 150 and any other documents that show the actions taken by the Department of Health before and after withdrawal of HPTs as outlined in my original OIA questions 6 and 7.*
12. *Provide minutes of the Department of Health committee(s) responsible for the health and well being of women who were prescribed HPTs and their children, from March 1975 to December 1975, including those of the Medicines Advisory Committee."*

[Supplementary questions from attachment to OIA response]

13. *Why has Medsafe reported that the Department of Health removed stocks from pharmacies when clearly that was not undertaken by the department.*
14. *Why has Medsafe alleged that the ".. .document(s) alleged to contain the information requested does not exist* [with regards to Clinical Services Letter No. 150]*?*

15. *Following the Thalidomide recall in 1961, local health officers found stock in pharmacies and hospitals some six months later. Why were no similar efforts made to ensure HPT drugs were removed in 1975?*

[Additional information provided via email on 7 September 2017]

16. *I enclose a link to video of Theresa May answering questions about toxic Hormone Pregnancy Tests given to women in the 1960's and 70's.*
In the video May says that the MHRA are due to release their report into Hormone Pregnancy Tests and the actions of the Health Department (of the time), in October this year.
British MPs are calling for an inquiry.
I would like to know what the Ministry of Health's intentions are with regard to the effects of HPTs on women and babies in New Zealand.

Before I address your specific concerns I think it would be helpful to explain some of the evolution of medicines regulation in New Zealand.

During the 1970s, medicines were regulated by the therapeutics and utilisation section of the former Department of Health. The legislation under which medicines were regulated at that time was the Food and Drug Act 1969. This Act has since been replaced by the Medicines Act 1981. The Ministry of Health became responsible for the regulation of medicines when it came into being on 1 July 1993. Medsafe, the New Zealand Medicines and Medical Devices Safety Authority was set up as a business unit of the Ministry of Health in 1997 as the agency responsible for the regulation of therapeutic products in New Zealand. Medsafe now administers the Medicines Act 1981 and Medicines Regulations 1984.

The legislation in place at the time Primodos was approved and subsequently withdrawn was the Food and Drug Act 1969. Under this Act, the amount and type of data required from a sponsor wishing to distribute a new medicine in New Zealand was considerably less than is required today.

In my response I have grouped related questions together. These are referenced to the number assigned to your requests above.

Under section 9(2)(a) and section 9(2)(g)(i) of the Official Information Act 1982, I have decided to withhold some information to protect the privacy of natural persons and to maintain the effective conduct of public affairs through the free and frank expression of opinions. In some instances we have been unable to locate any documentation referred to in your request. Therefore your requests have been refused under section 18(e) of the Official Information Act 1982. Specific grounds are noted in the responses below and in each document where information has been redacted.

1, 2, 7, 8 and 10. Communication between the United Kingdom and Medsafe regarding Hormone Pregnancy Tests

In the response to your initial OIA request (H201701896), your question was interpreted to refer to the 2017 inquiry being undertaken by the Medicines and Healthcare products Regulatory Agency (MHRA). Medsafe has not received a request for information from the MHRA in relation to this recent enquiry. However, I can confirm that Medsafe did receive

a request for information from the MHRA in 2015. I apologise for any confusion this may have caused.

Correspondence relating to the 2015 request is attached to this response. One case report that had been submitted to the Centre for Adverse Reactions Monitoring (CARM) concerning the medicines ethinyloestradiol and norethisterone in combination was provided to the MHRA in 2015. This report is also attached. In this report, the suspected medicines were reported to be ethinyloestradiol and norethisterone, but the brand name was not stated. Although the reported dose for each medicine is not consistent with the formulation of either Primodos or Amenorone Forte, it is possible that the dose was not reported or recorded correctly. However, to ensure that the MHRA had access to all possible cases, Medsafe decided to provide this information.

In 2015, CARM had not received any case reports in which Primodos was reported as the brand name of the suspected medicine which resulted in congenital anomalies in a baby.

3, 13 and 15. Removal of stocks from pharmacies

We are unable to locate any documentation on the Department of Health processes for drug recalls in the 1960s and 1970s. The recall code has developed over the years and in 2017 the recall process is significantly different to what would have been in place in 1975, when the hormonal pregnancy tests were withdrawn. For example, recalls can now be transmitted via email to healthcare professionals.

I note your concerns regarding the responsibilities of the Department of Health in the hormonal pregnancy tests recall as detailed in the media release on the Ministry of Health and Medsafe websites. We are currently reviewing the wording of the Ministry of Health's media release and will update the statement if necessary.

4, 11 and 14. Clinical Services Letter No. 150

Clinical Services Letters are publically available on the Ministry of Health website in the Ministry of Health Library (www.health.govt.nz/about-ministry/ministry-health-library). Search the Online Library Catalogue for 'Clinical Services Letter'. A copy of the Clinical Services Letter No. 150 is attached. Please accept my apologies for not providing a copy of the Clinical Services Letter in your first request or pointing you to the website link.

Clinical Services Letter No. 79 is also attached for your information as this mentions hormone pregnancy tests.

5. Notices for publication in the NZ Gazette

This request was previously refused under section 18(e) of the Act as the document(s) alleged to contain the information requested does not exist. This phrase was used because the Ministry of Health does not hold these documents.

Gazette Notices are held by Archives New Zealand. Please contact Archives New Zealand directly if you wish to obtain copies of these documents.

6 and 11. Correspondence showing what actions the Department of Health took to contact women or their GPs.

We are unable to locate any documentation on the Department of Health processes at this time; however, I have attached relevant minutes from the Ministerial Expert Advisory Committees for your information (please see response to question 12 below). All the information from the product files of both Primodos and Amenorone Forte were provided in your previous request (OIA H201701896).

9. Why did Medsafe wait for over 2 years from the time the MHRA called for information, to action the call for information from those who may have taken the drugs in New Zealand?

In 2015, Medsafe provided information to the MHRA (see above). At this time there was only one possible New Zealand case. No concerns were raised with us by the public at this point so it was presumed that there had not been an issue in New Zealand. We also noted that the New Zealand recall was initiated because of overseas cases not local cases.

Information about hormonal pregnancy tests was published on the Medsafe and Ministry of Health websites in 2017 after public interest increased in New Zealand.

12. Provide minutes of the Department of Health committee(s), from March 1975 to December 1975, including those of the Medicines Advisory Committee

The following documents are attached:

- Minutes of the Drug Assessment Advisory Committee meeting held on Wednesday 19 March 1975.
- Minutes of the Drug Assessment Advisory Committee meeting held on Wednesday 16 July 1975.
- Minutes of the Drug Assessment Advisory Committee meeting held on Wednesday 30 November 1977.
- Minutes of the Committee of Adverse Drug Reactions held on Wednesday 9 April 1975.

I have provided minutes outside of the time frames you requested for completeness. Please also note that the entire meeting minutes, not only the relevant sections, are attached to provide an indication of the extent of documentation at this time.

16. Ministry of Health's intentions with regard to the effects of HPTs on women and babies in New Zealand

Medsafe is awaiting the outcome of the current UK inquiry as Medsafe understands new information has been identified in the United Kingdom. New Zealand does not have access to this new information so will be reviewing this once it is available to assess its context in relation to the use of these products in New Zealand.

To summarise, the information released relating to your request is itemised below, with copies of documents attached as outlined in the table below.

Table 1 Documents provided in response to OIA H201703568	
Email correspondence	
1	Email 21/07/2015
2	Email 19/08/2015
3	Email 02/09/2015
4	Email 02/09/2015 plus CARM case report
5	Email 08/09/2015
Clinical Services Letters	
6	Clinical Services Letter No. 150
7	Clinical Services Letter No. 79
Meeting minutes	
8	Minutes of the Meeting of the Committee on Adverse Drug Reactions held on 9 April 1975 (page 7)
9	Minutes of the Meeting of the Drug Assessment Advisory Committee held on 19 March 1975 (page 8)
10	Minutes of the Meeting of the Drug Assessment Advisory Committee held on 16 July 1975 (page 3)
11	Minutes of the Meeting of the Drug Assessment Advisory Committee held on 30 November 1977 (page 9)

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

Sent by: Chris James/MOH

21/07/2015 09:02 a.m.

To: Rowan Pollock/MOH@MOH,
cc:
bcc:

Subject: Fw: Hormone Pregnancy Tests and Congenital Abnormalities

Hi Rowan

Can you please take a look at this one and see if we can provide info to [redacted]

Thanks

Chris

Chris James | Acting Group Manager | Medsafe | Ministry of Health | [redacted]

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A MEDSAFE UNIT OF THE MINISTRY OF HEALTH

[redacted]

----- Forwarded by Chris James/MOH on 21/07/2015 09:02 a.m. -----

From: [redacted]
To: [redacted]
Cc: [redacted]
Date: 20/07/2015 10:23 p.m.
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Janelle and Michael and Chris,

Here at the MHRA I am working on several interesting projects relating to medicines for women and I wonder if I may ask you for some input from NZ on a specific issue?

The project relates to **Hormone Pregnancy Tests (HPTs)** which were marketed in the UK between the 1950s and 1970s to diagnose pregnancy, before the introduction of more effective tests. The MHRA is to undertake an Expert Review to determine if there is any association between HPTs and **congenital abnormalities**, which have been reported in some of the children of mothers who used HPTs. One of my tasks is to identify case reports of congenital abnormalities associated with HPTs from relevant national and international datasets.

I attach a summary table of the products which were available in the UK (none is currently licensed) and the active ingredients in each. We have found out that HPT products were available in several other countries, including Australia where a product called Duogynon was licensed.

I wonder if you may be able to answer the following questions please:

1) Were HPT products ever approved for use in NZ and if so, what were these products and their active ingredients?
2) Have the NZ expert advisory committees (e.g. the MARC) discussed HPTs at any

time?

3) Are there any reports relating to HPTs in the CARM dataset and if so, are you able to share a summary of these reports with the MHRA?

We would very much appreciate any relevant information you can provide on this issue,

Best wishes,
9(2)(a)

Section 9(2)(a) BM DM FRCOG
Senior Medical Assessor
Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)

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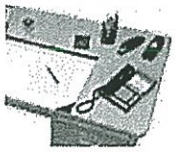
MHRA is a centre of the Medicines and Healthcare Products Regulatory Agency

COMPOSITION OF HORMONE PREGNANCY TESTS_UK PRODUCTS.doc



Sent by: Chris James/MOH

19/08/2015 09:10 a.m.

To: Janelle Ashton [redacted]
cc: Michael Tatley [redacted], Susan Kenyon/MOH@MOH,
bcc:

Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Thanks Janelle.

Yes I think it would be helpful for us to respond to [redacted] so if you could prepare whatever you need to I will send on to the MHRA with Medsafe's information.

Chris

Chris James | Acting Group Manager | Medsafe | Ministry of Health | [redacted]

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

Janelle Ashton Dear Chris In response to this req... 18/08/2015 06:35:12 p.m.

From: Janelle Ashton [redacted]
To: [redacted]
Cc: Michael Tatley [redacted]
Date: 18/08/2015 06:35 p.m.
Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Chris
In response to this request, I identified that Amenorone Forte was approved in NZ 31/12/1969 to 01/06/1975.
This is the only product I found that had been approved in NZ but if there are others, please let me know.

I searched the CARM database for reports combining Ethinyloestradiol and Ethisterone (the active agents in Amenorone) reporting congenital abnormalities but there were none.
I then searched for reports combining Ethinyloestradiol and Norethisterone and found one identifying multiple congenital malformations which was reported to CARM in July 1976 (a year after Notification Date of Amenorone).
The patient is described as a 32 F and Gestation Period of first exposure is reported as "?5/52" .
There are no dates of administration but there has been an indication '2 days' added in red probably by a staff member at the time although there is nothing else to indicate a duration of treatment.

If you want to provide these details, I will get them prepared into a case report.

I have been working through the MARC reports from our 50 years as we re-file in our post-fire system. There were regular 'Maternity' cases provided to the MARC from another committee but I have not checked any of them at this point.

Hope this helps.
Regards
Janelle

Janelle Ashton | Manager Information Systems | New Zealand Pharmacovigilance Centre [https://nzphvc.otago.ac.nz]
NZPhvC, PO Box 913, Dunedin 9054, New Zealand | DDI: Section 9(2)(a) | Fax: Section 9(2)(a)
Section 9(2)(a)

From: Section 9(2)(a)
Sent: Monday, 20 July 2015 10:23 p.m.
To: Janelle Ashton; Michael Tatley; Section 9(2)(a)
Cc: Section 9(2)(a)
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Janelle and Michael and Chris,

Here at the MHRA I am working on several interesting projects relating to medicines for women and I wonder if I may ask you for some input from NZ on a specific issue?

The project relates to **Hormone Pregnancy Tests (HPTs)** which were marketed in the UK between the 1950s and 1970s to diagnose pregnancy, before the introduction of more effective tests. The MHRA is to undertake an Expert Review to determine if there is any association between HPTs and **congenital abnormalities**, which have been reported in some of the children of mothers who used HPTs. One of my tasks is to identify case reports of congenital abnormalities associated with HPTs from relevant national and international datasets.

I attach a summary table of the products which were available in the UK (none is currently licensed) and the active ingredients in each. We have found out that HPT products were available in several other countries, including Australia where a product called Duogynon was licensed.

I wonder if you may be able to answer the following questions please:

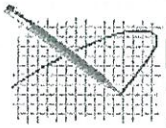
1) Were HPT products ever approved for use in NZ and if so, what were these products and their active ingredients?
2) Have the NZ expert advisory committees (e.g. the MARC) discussed HPTs at any time?
3) Are there any reports relating to HPTs in the CARM dataset and if so, are you able to share a summary of these reports with the MHRA?

We would very much appreciate any relevant information you can provide on this issue,

Best wishes,
9(2)(a)

Section 9(2)(a) BM DM FRCOG
Senior Medical Assessor
Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)



Sent by: Secttion 9(2)(a)

02/09/2015 01:42 a.m.

To: Section 9(2)(a)
cc:
bcc:

Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Chris,
I am just following up on the emails below regarding HPTs, as we do not yet appear to have received any information from NZ since your email in late July.

The first meeting of the UK Expert Working Group on HPTs is being held in mid-October and so it would be most helpful to receive any information and/or data by Monday 14th September latest.

Many thanks for your co-operation,

9(2)(a)

Section 9(2)(a) BM DM FRCOG
Senior Medical Assessor
Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)

Stay connected : mhra.gov.uk/stayconnected

MHRA is a centre of the Medicines and Healthcare Products Regulatory Agency

From: Section 9(2)(a)
Sent: 21 July 2015 06:19
To:
Cc: Section 9(2)(a)
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

Dear 9(2)(a)

Thank you for your email. I will get one of the team to have a look into what information we have and can easily access. Will get back to you shortly.

Thanks

Chris

Chris James | Acting Group Manager | Medsafe | Ministry of Health | Section 9(2)(a)

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A BUSINESS UNIT OF THE MINISTRY OF HEALTH

----- Forwarded by Chris James/MOH on 21/07/2015 09:02 a.m. -----

From: [redacted]
To: [redacted] Section 9(2)(a) [redacted]<
Cc: [redacted] Section 9(2)(a)
Date: 20/07/2015 10:23 p.m.
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Janelle and Michael and Chris,

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We would very much appreciate any relevant information you can provide on this issue,

Best wishes,
9(2)(a)

Section 9(2)(a) BM DM FRCOG
Senior Medical Assessor

Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)

Sent by: Section 9(2)(a)
02/09/2015 04:25 p.m.

To: Section 9(2)(a)
cc: Michael Tatley; Section 9(2)(a)
bcc:

Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Hi Chris
9(2)(a) follow-up email of today has actioned my completion of this 'Case Report' for you.
I have extracted the detail from the very limited information on the one CARM report that looks a possible match and have compiled the attached Word document.

I have added a section "Other Comment" to show the results of trying to match the limited CARM report details.
I have looked at the medicines options in the MHRA listing compared to the Medsafe Product listing and to the details in the CARM database as the CARM case report says ethinyloestradiol 0.5mg and norethisterone 5mg. I cannot find a product with the same formulation and believe it is probably a transcription error.

Michael has reviewed the Case Report and I have left the document in Word format so that you can make alterations if you wish.

Let me know if you need anything further.
Janelle

Janelle Ashton | Manager Information Systems | New Zealand Pharmacovigilance Centre [https://nzphvc.otago.ac.nz]
NZPhvC, PO Box 913, Dunedin 9054, New Zealand | DDI: Section 9(2)(a)
Section 9(2)(a)

From: Section 9(2)(a)
Sent: Wednesday, 19 August 2015 9:10 a.m.
To: Janelle Ashton
Cc: Michael Tatley; Section 9(2)(a)
Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Thanks Janelle.

Yes I think it would be helpful for us to respond to 9(2)(a) so if you could prepare whatever you need to I will send on to the MHRA with Medsafe's information.

Chris

Chris James | Acting Group Manager | Medsafe | Ministry of Health | Section 9(2)(a)

From: Janelle Ashton
To: Section 9(2)(a)

Cc: Michael Tatley
Date: 18/08/2015 06:35 p.m.
Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Chris
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Janelle Ashton | Manager Information Systems | New Zealand Pharmacovigilance Centre [https://nzphvc.otago.ac.nz]

NZPhvC, PO Box 913, Dunedin 9054, New Zealand | DDI: Section 9(2)(a)
Section 9(2)(a)

From: Section 9(2)(a) [mailto: Section 9(2)(a)
Sent: Monday, 20 July 2015 10:23 p.m.
To: Janelle Ashton; Michael Tatley; Section 9(2)(a)
Cc: Section 9(2)(a)
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

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Best wishes,

9(2)(a)

Section 9(2)(a) BM DM FRCOG
Senior Medical Assessor
Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)

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MHRA is a centre of the Medicines and Healthcare Products Regulatory Agency

MHRA_CARM ID 005803.doc

CARM REPORT
June 1976

Report No. 005803

Report Received: 25/06/1976
Source: Hospital Doctor

Patient: Pregnant Female 32yrs
Height: [redacted]
Weight

Suspect Medicine(s): Ethinyloestradiol /Norethisterone

Medicine details have been recorded as Ethinyloestradil 0.5mg and Norethisterone 5mg taken orally for 2 days.
No product name has been identified ***

Onset Date: Gestation recorded as " ? 5/52 "

Event description:

Multiple congenital abnormalities
cleft lip and palate
Hypoplastic ext auditory meatus and appendages
Thoracic hemivertibrae
Absent L Radius with hypoplastic thumb
? VSD
Genitourinary tract anomalies

Outcome: No indication

Follow-up information: Request for "Clarification of gestation period of exposure to the drugs"

Other Medical Conditions: None

Other Comments: [redacted]

Fw: Hormone Pregnancy Tests and Congenital Abnormalities
Chris James to Jo Prankerd 22/09/2017 12:02 p.m.

Chris James | Group Manager | Medsafe | Ministry of Health | Section 9(2)(a)

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

[redacted]

----- Forwarded by Chris James/MOH on 22/09/2017 12:02 p.m. -----

From: Chris James/MOH
To: Section 9(2)(a)
Date: 08/09/2015 04:21 p.m.
Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Dear 9(2)(a)
I understand that Amenorone Forte was approved in NZ (from 1969 up until 1975). The active ingredients were norethisterone acetate (50mg) and ethinylestradiol (0.05mg). I can find no record of Duogynon in our system.
Attached is information from one report from CARM from 1976.

I hope this information is useful.

Chris

PDF
MHRA_CARM ID 005803.pdf

Chris James | Acting Group Manager | Medsafe | Ministry of Health | Section 9(2)(a)

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

[redacted]

Section 9(2)(a) Dear Chris, I am just following up o... 02/09/2015 01:42:30 a.m.

From: Section 9(2)(a)
To: Section 9(2)(a)
Cc: Section 9(2)(a)
Section 9(2)(a)
Section 9(2)(a)
Date: 02/09/2015 01:42 a.m.
Subject: RE: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Chris,
I am just following up on the emails below regarding HPTs, as we do not yet appear to have received any information from NZ since your email in late July.

The first meeting of the UK Expert Working Group on HPTs is being held in mid-October and so it would be most helpful to receive any information and/or data by Monday 14th September latest.

Many thanks for your co-operation,

9(2)(a)

Section 9(2)(a) BM DM FRCOGduog

Senior Medical Assessor
Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)

Stay connected : mhra.gov.uk/stayconnected

MHRA is a centre of the Medicines and Healthcare Products Regulatory Agency

From: Section 9(2)(a)
Sent: 21 July 2015 06:19
To:
Cc: Section 9(2)(a)
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

Dear 9(2)(a)

Thank you for your email. I will get one of the team to have a look into what information we have and can easily access. Will get back to you shortly.

Thanks

Chris

Chris James | Acting Group Manager | Medsafe | Ministry of Health | Section 9(2)(a)

----- Forwarded by Chris James/MOH on 21/07/2015 09:02 a.m. -----

From: Section 9(2)(a)
To: Section 9(2)(a)
Cc: Section 9(2)(a)
Date: 20/07/2015 10:23 p.m.
Subject: Hormone Pregnancy Tests and Congenital Abnormalities

Dear Janelle and Michael and Chris,

Here at the MHRA I am working on several interesting projects relating to medicines for women and I wonder if I may ask you for some input from NZ on a specific issue?

The project relates to **Hormone Pregnancy Tests (HPTs)** which were marketed in the UK between the 1950s and 1970s to diagnose pregnancy, before the introduction of more effective tests. The MHRA is to undertake an Expert Review to determine if there is any association between HPTs and **congenital abnormalities**, which have been reported in some of the children of mothers who used HPTs. One of my tasks is to identify case reports of congenital abnormalities associated with HPTs from relevant national and international datasets.

I attach a summary table of the products which were available in the UK (none is currently licensed) and the active ingredients in each. We have found out that HPT products were available in several other countries, including Australia where a product called Duogynon was licensed.

I wonder if you may be able to answer the following questions please:

1) Were HPT products ever approved for use in NZ and if so, what were these products and their active ingredients?
2) Have the NZ expert advisory committees (e.g. the MARC) discussed HPTs at any time?

3) Are there any reports relating to HPTs in the CARM dataset and if so, are you able to share a summary of these reports with the MHRA?

We would very much appreciate any relevant information you can provide on this issue,

Best wishes,

9(2)(a)

Section 9(2)(a) BM DM FRCOG
Senior Medical Assessor
Benefit Risk Management Group

MHRA
151 Buckingham Palace Road, London, SW1W 9SZ, UK
Tel: Section 9(2)(a)
E-mail: Section 9(2)(a)

DEPARTMENT OF HEALTH,
P.O. BOX 5013,
WELLINGTON.

16 May 1975

CLINICAL SERVICES LETTER NO. 150

TO MEDICAL AND DENTAL PRACTITIONERS

(Copy to Proprietors of Retail Pharmacies)

Dear Sir/Madam,

HORMONAL PREGNANCY TESTS

Recent evidence has associated the use of hormonal pregnancy tests in early pregnancy with congenital abnormalities. In view of the questionable safety of these formulations and the availability of reliable alternative methods for pregnancy testing, the department is recommending that systemic hormonal pregnancy testing preparations be withdrawn from the market. Both the Drug Assessment Advisory Committee and the Committee on Adverse Drug Reactions have supported the department's proposal.

THE DRUG TARIFF

The Drug Tariff lists in a single Schedule those preparations which are available as pharmaceutical benefits, and any restrictions on their availability. Any special conditions are indicated alongside the name of each drug and, where necessary, these conditions are explained in Part I of the Schedule (*"Definitions"*).

Amendments to the Tariff are issued three times a year, on 1 April, 1 August, and 1 December and are cumulative. The Tariff, therefore, is contained in only two documents, the principal Drug Tariff and the most recent amendment.

As amendments are made in the availability of drugs, the drug concerned must first be deleted from the Tariff and is included in the list of deletions in the Drug Tariff Amendment; its amended form is then included in the list of additions. These two lists also specify any items which are deleted entirely or are added to the Tariff for the first time.

Items which appear in an amendment for the first time, or which appear with an alteration in availability, are denoted by an asterisk.

The Drug Tariff also covers other matters relating to pharmaceutical benefits, such as the period of supply and practitioners' supply orders.

Major changes made in a revision of the Drug Tariff or in an amendment are explained in an accompanying Clinical Services Letter.

PRACTITIONERS' SUPPLY ORDERS

There is provision under the Drug Tariff for supplies of most pharmaceutical benefits to be obtained on a practitioners' supply order form. Supplies of these forms, including the special form to be used for narcotics, may be obtained from the local medical officer of health.

These supply orders should not be used as a source of drugs for dispensing to patients other than in an emergency. They are intended to cover immediate treatment before supplies can be obtained in the ordinary way. They may also be used to obtain materials for personal administration to a patient, such as injections.

Items for use in the consulting room, such as diagnostic materials, disinfectants, or solutions for the storage of instruments, are not acceptable as a charge under the Drug Tariff. In accordance with the Tariff, supply orders are subject to scrutiny by the department.

Yours faithfully,

A. W. S. Thompson. D. A. Andrews.

(A. W. S. Thompson)
Director,

(D. A. Andrews)
Deputy Director,

Division of Clinical Services.

Dr A. W. S. THOMPSON

Clinical Services Letter No. 1 was published on 30 September 1957, the first in the series of Prescribers' Notes which have continued ever since. All have appeared over the signature of Dr A. W. S. Thompson. But the present issue will be the last signed by him, since he retires on 27 May. It is fitting, therefore, that a brief tribute to him should appear in a publication he considered of great importance and to which he devoted much time and thought over the years.

Dr "Bill" Thompson came to New Zealand in November 1946 as the Medical Officer of Health for the Auckland District. He was soon to make a considerable impact on the medical scene in that city and beyond through his flair for public health combined with his administrative skills. It was with some reluctance that he moved to Wellington following his appointment as Director of the Division of Clinical Services on 1 September 1955.

His achievements in that position during the intervening years have been too numerous to list. Most notable has been his work in the field of primary medical care where his success has been evident from the excellent working relationship his Division has with the medical profession. Several important advisory committees have functioned to good purpose under his chairmanship and guidance.

Another outstanding success, which gave him particular satisfaction, was the introduction in 1959 of the visiting practitioner scheme.

Dr Thompson will be remembered by many of us with affection. We shall miss his Irish wit, his sense of humour, his encyclopaedic memory, his erudition, his wisdom and, most of all, his humility.

He plans to spend his retirement in England and we wish him well.

(H. J. H. Hiddlestone)
Director-General of Health.

BY AUTHORITY:
A. R. SHEARER, GOVERNMENT PRINTER, WELLINGTON, NEW ZEALAND—1975
61628B—75 G

DEPARTMENT OF HEALTH,
P.O. BOX 5013,
WELLINGTON.

22 April 1968.

CLINICAL SERVICES LETTER NO. 79

TO MEDICAL PRACTITIONERS

Dear Doctor,

MATERNITY BENEFIT CLAIM FORM (MAT. B.5)

To overcome the difficulty experienced by doctors in obtaining satisfactory patients' certificates, the new print of form Mat. B.5 allows for the completion of the patient's certificate prior to the post-natal examination. The claim will be accepted if it is signed and dated by the patient towards the end of the lying-in period. The co-operation of doctors is requested to ensure that claims are properly completed by patients.

SUPPLEMENTARY BENEFITS (PHARMACEUTICAL)

If a patient requiring a drug which is not in the Drug Tariff cannot reasonably be expected to pay for it, application may be made by the practitioner to the Director of this Division for approval of a special supply. This provision normally applies to drugs for the treatment of chronic conditions and authority is not given retrospectively. Anti-obesity preparations and special foods cannot be authorised in this way.

Care should be taken to supply the following information:

(a) The name of the drug and dosage.

(b) Brief clinical details, and

(c) A statement to the effect that the patient would find it a hardship to pay for the drug.

Please use this service with discretion so that it may continue as at present without curtailment or petty restrictions.

Drugs authorised as Supplementary Benefits are normally issued only through hospital board dispensaries.

P.T.O.

PREGNANCY TESTS

The Drug Tariff specifically excludes payment for pregnancy tests. This would include combinations of progestogens and oestrogens used for this purpose.

Incidentally, these combinations are not, in fact, considered to be satisfactory. The new hormonal tests are cheap and reliable.

Yours faithfully,

A. W. S. Thompson.

(A. W. S. Thompson)
Director,

T. L. Hayes

(T. L. Hayes)
Assistant Director,

Division of Clinical Services.

Vacancies in General Practice

Alexandra, Central Otago, urgently requires another doctor. No purchase or goodwill required. Houses to lease or purchase available, finance beyond normal lending limits can be arranged. This rapidly growing town, centre of a prosperous fruit and sheep farming area, has a splendid climate (average rainfall 12 inches), excellent high school, swimming pool, new 18-hole golf course, fishing, ice skating within 3 miles. Public hospital and maternity annexe 6 miles. Two present doctors are seriously overworked. Inquiries: Mrs V. M. Boyd, Box 86, Alexandra.

Methven, a pleasant country town with a district population of 2,500, offers a vacancy for a sole practitioner. Maternity hospital (six beds) averages 50 patients a year. District high school. Chemist. House and surgery available to rent or purchase. Excellent prospects. Inquiries: County Clerk, Ashburton County Council, P.O. Box 43, Ashburton.

R. E. OWEN, GOVERNMENT PRINTER, WELLINGTON, NEW ZEALAND—1968
4,400/4/68—46519 G

MINUTES OF THE MEETING OF THE COMMITTEE ON ADVERSE DRUG REACTIONS HELD IN THE COMMITTEE ROOM, 1ST FLOOR, MACARTHY TRUST BUILDING, LAMBTON QUAY, WELLINGTON, AT 10.30 A.M. ON WEDNESDAY, 9 APRIL 1975

PRESENT

Dr M. Watt (Chairman)
Dr D.A. Andrews
Dr W.N. Clay
Dr G.S.M. Kellaway
Professor A.D. Macalister
Professor E.G. McQueen
Dr A.H. Paul
Dr J.S. Phillips
Dr R. Saunders
Miss S. Porter (Secretary)
Mrs E.C. McKenzie (Minute Secretary)

1. APOLOGIES

Dr C.M. Luke

2. INTRODUCTION

The Chairman introduced Dr Phillips who had recently been appointed Principal Medical Officer with the Division of Clinical Services.

3. MINUTES

The minutes of the meeting held on 13 November 1974 were confirmed.

4. MATTERS ARISING FROM THE MINUTES

(a) Hospital Monitoring

(i) Auckland

Nothing new to report. Dr Kellaway advised that a bulletin on adverse reactions, for internal circulation within Auckland Hospital, was being produced every 2 months; the latest one dealt with digoxin.

(ii) Wellington

The reporting programme was proceeding satisfactorily. Approximately 200 patients had been involved in the 6 months that the programme had been in operation. A report would be issued to staff shortly.

(iii) Christchurch

Progress had not been made in establishing a continuing reporting programme. A pharmacologist had not yet been appointed.

(iv) Dunedin

Professor McQueen advised that they were still attempting to sustain spontaneous reporting. There was not an intensive monitoring programme at present.

(b) Computer Terminal for New Zealand Centre

Professor McQueen advised that they are now awaiting delivery of the hardware.

A mathematics graduand had been employed over the long vacation to convert the N.Z. Computer filing system into a form comparable with that used by the U.K. Committee on Safety of Medicines. This would result in a substantial amount of additional data being stored for reference.

The data stored would be accessible at certain times during the day. Queries from practitioners could be answered within a few hours.

(c) Reactions to Penicillin (Therapeutic Notes)

The draft had not yet been received by the Department of Health. It was agreed that this item be omitted from the agenda in the future.

(d) Practolol

The Department was congratulated on the admirable way in which this situation had been handled. The firm had cooperated fully throughout.

New Zealand was the first country to restrict the availability of Practolol. The United Kingdom had followed but with stricter controls.

From sales figures submitted by the Company, it was noted that sales had dropped markedly in February 1975.

The Chairman said that this matter showed the value of spontaneous reporting of adverse drug reactions. There had been sufficient local information to enable a decision to be made.

The Standing Committee on Therapeutic Trials was experiencing problems with an application for a trial of a chemically similar drug. This was being looked at more cartiously as a consequence of practolol reactions. No decision had as yet been reached by members of the Committee.

In many cases, initial clinical trials did not involve sufficient numbers to enable adverse reactions to show up and it was not until the drugs had been released for more extensive use that they became apparent.

Professor Simpson had provided a list of various adverse drug reactions to practolol experienced at the Dunedin Hypertension Clinic. Professor McQueen asked if these should be included in the general file. It was felt that their inclusion could produce biased results.

It was agreed that a Bulletin on Beta-Blockers in general be issued.

(e) Minomycin and Giddiness

The papers prepared by Dr Macintosh on tetracyclines was to be issued as a Bulletin. It was agreed that the last sentence of this report be omitted and that the names of various investigators be listed at the end with the bibliography.

It was agreed that it would be helpful if any adverse drug reactions reported in the weekly report of HEW were drawn to the attention of the Committee.

(f) Rauwolfia and Breast Cancer

Professor McQueen said that Professor F.O. Simpson had collected data in the Dunedin Hypertensive Clinic which suggested that there may be a relationship between rauwolfia and neoplasms.

Although reports to date were not conclusive, it was agreed that the Committee's attitude on the subject should not be changed.

(g) Index to Bulletins

Copies of previous Bulletins were available on request.

5. COMMITTEE REPORTS

(a) New Zealand

Professor McQueen asked whether a 3 year review should be done this year or the review deferred for a year and a ten year review be published in 1976.

It was felt that a 10 year survey may not be relevant and it was agreed that the 3 year survey should be done with a special 10 year review in the form of an article to be included in the Annual Report.

(i) Intensive Monitoring by General Practitioners Preliminary survey in Otago and Southland.

The number of adverse drug reactions reported over the three month period by the doctors participating varied between 1 and 70. There was a great difference in the interpretation of what constituted an adverse drug reaction and this would obviously have to be made entirely clear before any further survey was initiated.

(ii) Visit to Australia Regarding Intensive Drug Surveillance Projects

Professor McQueen reported on a conference in Melbourne under the auspices of the Commonwealth Department of Health. This dealt with intensive monitoring, both in hospitals and in general practice.

Professor McQueen felt that something further should be done in this country to set up a programme of intensive reporting by general practitioners. The Pilot Study had highlighted the difficulties in setting up such a scheme. General practitioners could not be expected to carry out intensive monitoring for longer than 3 months at a time.

Dr Clay commented on the way in which a scheme set up in Auckland several years ago concerning the reporting of non-infectious diseases had operated.

Dr Saunders mentioned that many general practitioners were now using computers for their accounts and that it might be possible to extend this service to incorporate the recording of adverse drug reactions.

Dr Kellaway thought it was necessary to set up a small sub-committee to set out the aims, objectives, and method of implementation if a further intensive monitoring programme was to be set up.

It was agreed that a sub-committee comprising Professor McQueen, Dr Macintosh, Dr Jenner (representing the Department of Health) and Dr R. West, be set up to consider the question and to report back to the Committee.

It was considered that the Pilot Study had been valuable in that it highlighted the problems to be contended with.

It was noted that the Hamilton, Australia, survey was still not in operation after 2½ years of planning.

(b) Australian Drug Evaluation Committee

(i) 1. Minutes of the 45th and 46th A.D.R.A.C. Meeting Reports

For information.

2. Chlorhexidine Ototoxicity

For information.

(ii) Minutes of the 58th Meeting of the A.D.E.C.

1. Minocycline and Foetal Malformations.

Dr Macintosh would be modifying his paper in view of this report and the contra-indications would include pregnancy.

(iii) Minutes of the 59th Meeting

1. Metiamide

For information.

(iv) Minutes of the 60th Meeting

For information.

(c) British Committee on Safety of Medicines

(i) U.K. Committee reports on Practolol

For information.

(ii) Prazosin and Loss of Consciousness

For information.

(d) Danish National Health Service

For information.

(e) German Federal Republic on Drug Commission

For information.

(f) Swedish A.R. Committee

For information.

(g) WHO

(i) Adverse Reactions to Contrast Media

Professor McQueen said that he had received reports of adverse reactions as well as requests from radiologists for information and advice on management.

(ii) Rauwolfia Alkaloids and Breast Cancer

For information.

(iii) Finnish Data Drug Information No. 142, 28/1/75 Re Digoxin

For information.

(iv) Adverse Reactions Reporting (Sweden). Information Sheet Number 18, 17/2/75 : Reporting Obligatory

The reporting of all adverse drug reaction is now compulsory in Sweden. It did not appear, however, that penalties were imposed for non-compliance.

(v) Hormonal Testing Preparations - Drug Information Number 144, 11/2/75 : Withdrawal in Australia

Two hormonal pregnancy testing preparations are marketed in New Zealand. At its last meeting the Drug Assessment Advisory Committee recommended that these products be withdrawn from the market.

Moved Kellaway/Macalister

THAT this Committee support the Department in obtaining the withdrawal of hormonal pregnancy tests from the market.

Carried

(vi) Resignation of Dr Venulet, Senior Project Officer, WHO

Professor McQueen advised that Dr Venulet's resignation was due to the expiry of his exit permit from Poland.

6. FURTHER BUSINESS

(i) 1. A.D.R. Numbers Game

(i) 2. Special Article : The New England Journal of Medicine, 291 1974 pp 824 - 828 : Hershel Jick

Dr Kellaway advised that 3 deaths caused by adverse drug reactions had been reported in Auckland. He was not confident that this was the total number as it was difficult to trace the numbers from patients' medical records.

Dr Kellaway agreed to write to Dr Jick and ask for any statistics that are available.

(ii) Minocycline : (Morbidity and Mortality, 24, 1975)

For information

(iii) Smallpox Vaccination

Reports had been received of severe adverse reactions to smallpox vaccinations. The vaccine currently available appeared to be stronger. It was thought that some doctors might be using the wrong technique when vaccinating.

It was agreed that this be mentioned in a Clinical Services Letter or a Letter to Doctors.

(N.B. This was included in a Circular Letter to Medical Practitioners dated 1 April 1975.)

(iv) Minipress (Prazosin)

Dr Andrews advised that early in 1974 consent to limited marketing was granted and in November 1974 the Drug Assessment Advisory Committee approved Minipress for wider distribution.

The last meeting of Pharmacology and Therapeutics Advisory Committee recommended availability under the Drug Tariff from retail pharmacy without restriction.

The amendment to the Drug Tariff was at printer's proof stage when Dr Hallwright, one of the trialists of this drug, advised that many of his patients had adverse reactions to the drug and he thought that it

should not be widely available. None of the adverse drug reactions which occurred in the multi-centre trials had been reported to this Committee or to the company.

The Department then decided to restrict the availability of prazosin to "Hospital Board Specialist" only.

Professor McQueen thought that some action should be taken to ensure that investigators be made aware that adverse drug reaction should be reported immediately and not when results of trials are collated.

Many investigators are not aware of this requirement and it was agreed that the Standing Committee on Therapeutic Trials should advise the Department of their requirements in this regard and it would be incorporated in the reprint of the Department's Drug Distribution Booklet.

It was agreed that Professor McQueen request investigators of this drug to advise all adverse drug reactions and a reference to these be made in the next Annual Report.

(v) B-Agonists and Antagonists in Asthmatic Subjects

This would be covered by the Bulletin to be issued on Beta-Blockers.

7. GENERAL

(i) Obstetric Regulations

Dr Paul advised that these regulations had been under consideration for a long time. The Regulations would require the notification of all foetal abnormalities on a standard form which would enable follow up action to be taken.

The form was discussed and although it was considered desirable that more information could be incorporated, especially with relation to "at risk" drugs, it was agreed that this would probably cause further delay. This precluded inclusion in the present form. The information could be obtained on follow up.

(ii) Tricyclic Antidepressants and Adrenalin

Professor Macalister referred to the wide usage of tricyclic antidepressants in the treatment of enuresis. He was concerned that many dentists and dental nurses might not be aware of the possible interaction of these drugs with adrenaline and noradrenaline.

(iii) Bulletins

It was requested that Bulletins be addressed to "Medical and Dental Practitioners" instead of "Medical Practitioners and Dentists" and this was agreed.

8. DATE OF NEXT MEETING

The next meeting was set for 10.30 a.m. on Wednesday 17 September 1975, (morning tea will be served at 10.15 a.m.)

The meeting closed at 1.45 p.m.

Signed: _____ (Chairman)

Date: _____

MINUTES OF THE 14th MEETING OF THE DRUG ASSESSMENT ADVISORY COMMITTEE HELD ON WEDNESDAY, 19 MARCH 1975, IN THE BOARD ROOM 7TH FLOOR, MACARTHY TRUST BUILDING, LAMBTON QUAY, WELLINGTON AT 9.00 A.M.

PRESENT: Dr D.A. Andrews (Chairman)
Professor P.B. Herdson
Dr M. Kingsford
Dr P.W. Moller
Dr G.F. Shanks
Mrs E.C. McKenzie (Secretary)

IN ATTENDANCE:

Mr N.J. Bennoson
Dr K.H. Goh
Dr J.S. Phillips
Miss S. Porter
Mr I. Witty

APOLOGIES:

Professor T.V. O'Donnell
Dr G. Kellaway

1. INTRODUCTION:

The Chairman opened the meeting and introduced Dr Phillips, the new Principal Medical Officer and Dr Goh, the new Pharmacologist appointed to the Department.

2. DATE OF NEXT MEETING:

The next meeting will be held on Wednesday, 16 July 1975.

3. MINUTES:

The minutes of the 13th meeting, having been circulated, were taken as read and confirmed.

4. MATTERS ARISING FROM THE MINUTES:

(a) Eraldin (Practolol)

The Chairman outlined the events which had occurred since the last meeting.

An increasing number of adverse reactions had been reported, including some considered irreversible. The Pharmacology and Therapeutics Advisory Committee decided at its December 1974 meeting to restrict practolol to Hospital Board Specialist availability. At a later date Professor McQueen sought the opinion of all members of the Committee on Adverse Drug Reactions and they unanimously recommended that further restriction was necessary. After discussions with the Department, the manufacturer initiated a recall to retail level and the

Department decided to delete practolol from the Drug Tariff as from 1 April 1975. The drug will, however, still be available from hospital pharmacies to the small number of patients who require it, and application for free supplies may be granted under Section 99.

The Department is concerned about the possibility of general practitioners initiating treatment and the Committee agreed that this should be discouraged.

New Zealand is the first country to take definite action to restrict availability. The firm, I.C.U. (N.Z.) Limited, has been extremely co-operative throughout the whole proceedings.

(b) Minipress (Prazosin)

This Committee has reviewed Minipress on three occasions and at the last meeting recommended that general distribution be permitted.

The Company had previously restricted advertising and availability as requested. The last meeting of the Pharmacology and Therapeutics Advisory Committee recommended availability from retail pharmacy without restriction.

The amendment to the Drug Tariff was at printer's proof stage when Dr Hallwright, one of the trialists of this drug, advised that many of his patients had adverse reactions to the drug and he thought it should not be widely available. None of the adverse drug reactions which occurred in the multi-centre trials had been reported to the Committee on Adverse Drug Reactions or to the company.

The Department decided to restrict the availability of prazosin to Hospital Board Specialists only.

There was no decision required by this Committee on the matter, however, it will need to be reconsidered by the Pharmacology and Therapeutics Advisory Committee.

Professor Herdson reaffirmed that the original decision to handle this drug within the Department was incorrect and he was critical of the conduct of the multi-centre trial and of the firm.

(c) Hiper

The Chairman advised of a meeting with principals of the company and they did not disagree with the statement that the data provided was "too good" and they have agreed to conduct bioavailability testing in New Zealand.

There was discussion on the attitude that should be taken when faked data is suspected and it was felt that in such cases the credibility of the company must always be in doubt.

(d) Seguilar

The firm has asked the Committee for a definition of "ethnic groups relevant to New Zealand".

Discussion followed and it was agreed that trials carried out in Commonwealth countries and the U.S.A. were preferable as members were concerned at their lack of knowledge of the trialists in non-English speaking countries. The Committee considered that the original criticism was an unreasonable one in this case, although there is some evidence of clonal differences between some races.

It was agreed that some cases were studied for only a short length of time and in respect of oral contraceptives longer term cohort studies produce more meaningful results.

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.

The firm is to be asked if they have noted any differences in drug responses in various ethnic groups.

(e) Medicines Bill

The Departmental Draft of the Medicines Bill will be distributed in the near future and a short summary will be provided for members. Time will be made available at the next meeting for discussion of the draft Bill.

(f) Drug Monitoring

Dr Kellaway's paper was tabled and it was agreed to defer discussion to the next meeting. The Department will also prepare a paper for distribution prior to the next meeting.

5. DECLINED DRUGS:

(a) Ipradol

The Committee decided to confirm their original decision to decline this drug due to the lack of clinical supporting data, lack of comparison with appropriate drugs, inadequate numbers of clinical trials in countries other than Austria and Germany and inadequate quality control data.

The Committee will consider the further data submitted and any new papers which may be submitted at the July meeting.

There was discussion on the Committee's responsibility in respect of the need for certain drugs when there are many similar drugs on the market already.

Members felt that they were concerned with the safety and efficacy of drugs and should not be concerned with economic factors. Any other attitude would be politically unacceptable.

Some firms are submitting applications prematurely. The Committee is particularly careful in assessing drugs that have not been accepted elsewhere, but does not want any such submissions to be delayed before they are referred to them.

It was agreed that the Department discuss the problem of submissions not supported by sufficient data with the Pharmaceutical Manufacturers' Association.

(b) Nebcin

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of this drug subject to the firm agreeing to refrain from advertising, that it be restricted to hospital specialists only, that ongoing data especially on nephrotoxicity and ototoxicity be provided, that adverse reactions be reported by users and that satisfactory quality control data be provided.

The firm is to be asked to comment on the possibility of Nebcin destroying bacteroides with resultant dangers of superinfections in the bowel.

The Committee expressed concern at the over-use of antibiotics in general practice and discussed the action of clindamycin and lincomycin in destroying bacteroides.

6. NEW DRUGS:

(a) Lopresor and Betaloc

The Committee decided to defer this drug pending receipt of further data on long term clinical studies, particularly with regard to immunological abnormalities, reporting of adverse drug reactions and satisfactory quality control data.

The firm is to be complimented on the good presentation of the submission and advised that pre-clinical animal and toxicoloty data were satisfactory.

(b) Sotacor

The Committee decided to defer this drug pending receipt of further data on long term clinical studies, particularly with regard to immunological side effects, reporting of adverse drug reactions and satisfactory quality control data.

The firm is to be complimented on the good presentation of the submission and advised that pre-clinical animal and toxicology data were satisfactory.

The firm is to be asked for further information on the incidence of adeno-carcinoma in the pituitary gland of Beagles.

(c) Panquil

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.

(d) Pharmaton

The Committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of this drug due to the lack of evidence of safety and efficacy, inadequate quality control data and the failure to conform with the requirements of the Committee for combination drugs.

(e) Androcur

The Committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of this drug due to the lack of local clinical data, pre-clinical and toxicology data and unsatisfactory bioavailability and quality control data.

The firm is to be advised that this submission was poorly presented and if reports with journal references are submitted, bibliographies should be provided.

(f) Apernyl

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.

(g) Pro-Diaban

The Committee decided to defer this drug due to insufficient evidence of long term efficacy, lack of comparison with other similar drugs, unsatisfactory quality control data and lack of comment on the possibility of myocardial infarction.

The firm is to be advised that this submission was poorly presented, the indexing was inadequate, data were repetitive and meaningless, e.g. reports of one doctor with only one patient, and that better correlation of data is required.

The pre-clinical animal and toxicology data were satisfactory.

(h) Epilim

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 bioavailability and quality control data, provided that distribution is limited to specialist use only with ongoing reporting required for assessment at the November 1975 meeting.

The advertising need not be restricted and the firm is to be advised of the Committee's concern at the lack of long term studies and requested to provide further data on hepatic and renal toxicity.

(i) Nicolex

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 animal toxicology and teratology data.

(j) Xadine

The Committee decided to defer this drug until further information (as already requested), satisfactory bioavailability and quality control data are provided.

(k) Rivotril

The Committee decided to defer this drug until data on long term clinical trials carried out in more countries, long term hepato-toxicity data, testing for chronic toxicity, more information on blood level studies, paediatric side effects, satisfactory bioavailability and quality control data are provided.

Professor Herdson undertook to enquire about the incidence of cysts in pituitary glands of Beagles.

(1) Cornkil

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of this new drug.

Members were advised that in the case of all new, changed and Drug Tariff applications WHO and New Zealand Adverse Drug Reaction Reports are now checked routinely for information.

7. CHANGED DRUGS

(a) Cystex

Members stated that they were against self diagnosis and self treatment of potentially serious conditions and that this should be discouraged.

The Committee decided to defer this drug pending receipt of comparative studies and satisfactory quality control data.

The Department is to review all over-the counter products promoted for the treatment of urinary symptoms.

The Chairman advised that the draft Medicines Bill does not include provision for a Poisons Committee and that it may be appropriate eventually for this Committee to deal with the scheduling of drugs.

8. GENERAL

(a) "Stand-in" Members

It was agreed that "stand-in" members be nominated if a member cannot attend, however such a person should be mutually acceptable and have had sufficient time to become familiar with the data to be considered.

(b) Minutes

The Chairman advised that minutes of the meetings of the Australian Drug Evaluation Committee are received routinely by the Department and asked if members thought that the format of our minutes should be along the lines of the Australian minutes.

Members stated that the current minutes were sufficient. Members asked that when deferred or declined drugs are resubmitted the reason for deferral or declining be included in the summary.

(c) Cabinet Sub-committee on Efficiency in the State Services - Report on Pharmaceutical Services

This report, carried out by a private company, has been completed, but not published yet.

The report looked at cost, overall administration and efficiency, and although favourable, it was very superficial, glossing over any problem areas which are controversial, or where improvements or savings could be made, and therefore the report was disappointing.

A copy of the report, when published, will be sent to all committee members.

(d) Ferrum H.

The firm has been asked to comment on the lack of response in three patients, and to provide proof of efficacy and statistics of usage. All three cases have occurred in Dunedin, however, it may be occurring in other centres but not being recognised or reported.

It was agreed that informal enquiries be made: Professor Herdson in Auckland, Dr Moller in Christchurch, and the Department in Wellington and Waikato.

(e) Progyluton

The Committee agreed that the warnings regarding discontinuation during pregnancy and the connection between oestrogenic substances and thrombosis were not sufficient.

The warning to discontinue use during pregnancy should also be incorporated with the statement on page 1 "Progyluton is not a contraceptive".

The warning regarding thrombosis should be amended to highlight this contra-indication.

(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.

(g) Dental and Dermatology Departmental Consultant Advisors

It is hoped that these will be appointed shortly and members will be advised of the appointees.

(h) Camalox

The acid "rebound" effect of calcium carbonate has been well established for many years and the Committee agreed that the Department should handle this application.

(i) Phase I Clinical Trials

The Chairman advised that Phase I Clinical Trials may be carried out in the near future by Dr B.N. Singh of Auckland.

These would be the first Phase I Clinical Trials to be carried out in New Zealand and are unusual outside the U.S.A.

(j) The question of future proposals to reconsider the availability of existing drugs on the market as new drugs of a similar nature become available, was queried. It was considered that this was a present function, in many cases, of the Pharmacology and Therapeutics Advisory Committee.

The meeting closed at 4.45 p.m.

Confirmed D. C. Anderson (Chairman)

Date 16 July 1975

File Ref: 140/25/1

MINUTES OF THE FIFTEENTH MEETING OF THE DRUG ASSESSMENT ADVISORY COMMITTEE HELD ON WEDNESDAY 16 JULY 1975 IN THE BOARD ROOM, 7TH FLOOR, MACARTHY TRUST BUILDING, WELLINGTON AT 10.00 A.M.

PRESENT: Dr D.A. Andrews (Chairman)
Prof. P.B. Herdson
Dr G.S.M. Kellaway
Dr M. Kingsford
Dr D. Macintosh
Dr P.W. Moller
Prof. T.V. O'Donnell
Dr G.F. Shanks
Mrs E.C. McKenzie (Secretary)

IN ATTENDANCE:

Mr M.J. Bennoson
Dr K.H. Goh
Mr R.C. Griffith
Dr J.S. Phillips
Miss S. Porter
Dr A.G. Scott
Mr I.A. Witty

1. INTRODUCTION

The Chairman opened the meeting and introduced Professor O'Donnell who had been nominated by the Department of Health to replace Professor J.D.K. North on the Committee, Dr Macintosh who had been nominated by the Medical Association of New Zealand to take Professor F.N. Tastier's place on the Committee, Dr Scott the new Deputy Director of the Division of Clinical Services and Mr Griffith a new pharmacist appointed to the Department.

The Chairman advised that the daily fee for members has been increased from $32.00 to $45.00. A submission by the Department for the fee per drug to be increased from $2.00 is to be considered by Treasury shortly.

2. DATE OF NEXT MEETING

The next meeting will be held on Wednesday 26 November 1975. The first meeting for 1976 will be held on 17 March.

Members were asked if they felt it was necessary to increase the number of meetings per year from 3 to 4. It was agreed that the number of meetings remain at 3 for the time being.

3. MINU

The minutes of the 14th meeting, having been circulated, were taken as read, and confirmed.

4. MATTERS ARISING FROM THE MINUTES

(a) Ferrum H.

The Chairman advised that the possible solution for the lack of response to this drug was that the needles used were too short and some of the iron was being injected into fatty tissue. The firm has advised that they have increased the size of the needles from 1 inch to 2 inches.

Ferrum H is used infrequently because of the doubts of its effectiveness. Its total use is low.

(b) Drug Monitoring

(c) Medicines Bill

It was agreed that these two items be considered at the end of the meeting if time permitted.

(d) Survey of Over-the-Counter Products Promoted for the Treatment of Urinary Symptoms

The Department feels that the labelling of urinary antiseptics is misleading in some cases and this is to be followed up. Another solution to the problem is the scheduling of urinary tract infections in the Schedule to the Food and Drug Act 1969.

The question of whether a review of all over-the-counter products is to be carried out was raised. The Chairman advised that this was not possible at present. Reviews are carried out by the Department as problems arise with each group. The U.S.A. and U.K. are reviewing all over-the-counter products and if information received from them is applicable to New Zealand over-the-counter products, these will be followed up.

The Committee agreed that the Department had a responsibility to check the safety of over-the-counter preparations in conjunction with misleading labelling.

(e) Nicalex

Since the last meeting this drug has been scheduled a Prescription Poison by the Poisons Committee. This drug was originally referred to the Committee at the request of one of the members, in particular for assessment of its efficacy. Consent to distribution was recommended subject to the provision of satisfactory animal toxicology and teratology data.

The firm has advised that these data are not available due to the length of time the drug has been available on the market overseas.

The Committee agreed that the animal toxicology and teratology data were not required and decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Nicalex.

(f) Minipress (Prazosin)

This drug was considered at the last Pharmacology and Therapeutics Advisory Committee and the action taken by the Department to restrict availability to Hospital Board Specialists only was approved by them.

(g) Hormonal Pregnancy Tests and Births Defects

The two hormonal pregnancy tests available in New Zealand were withdrawn from the market as from 1 June 1975.

(h) Cabinet Subcommittee on Efficiency in the State Services - Report on Pharmaceutical Services

The Chairman advised that three-monthly reports on progress on the recommendations must be made to the State Services Commission. Computer pricing of prescriptions is high on the list of departmental priorities. A feasibility study of world-wide tendering for drugs has been recommended but not received with enthusiasm, and submissions are being made by interested parties, e.g., the Pharmaceutical Manufacturers Association. The sampling method of payments to pharmacists is being investigated by the DSIR Applied Mathematics Section.

The question of animal toxicology testing of new drugs was raised by Dr Shanks. There is however, no organisation in New Zealand equipped to carry this out at the present time and it was agreed that such testing should either be done fully or not at all. At the present time it is impracticable but nevertheless ultimately desirable.

(i) Dental and Dermatology Departmental Consultant Advisers

Dr R. Parks has been appointed Dermatology Adviser and Mr D.B. Adams has been appointed Dental Adviser.

(j) Cysts in Pituitary Glands in Beagles

Professor Herdson tabled a paper showing that the normal incidence of cysts in pituitary glands of beagles is high.

5. DEFERRED DRUGS

(a) Mynah

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

6. DECLINED DRUGS

(a) Triazure

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Triazure subject to the labelling being amended to emphasis the drug's teratology, that pregnancy and the possibility of pregnancy should be definite contraindications, that the drug should not be used in children at all, that availability should be restricted to appropriate specialists, i.e., rheumatologists and dermatologists, that advserse drug reactions be reported by users and that satisfactory quality control data be provided.

The Committee also recommended that this drug not be made available under section 99 except to appropriate specialists.

(b) Berotec

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Berotec.

(c) Ipradol

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Ipradol.

(d) Cefatrexyl

The firm has advised that it considers long-term studies dangerous as serum sickness occurs after 10-12 days of treatment.

The Committee decided to defer this drug pending receipt of more information on the U.S.A. acceptance, more information on serum sickness, e.g., the firm's definition of serum sickness and its incidence; further data on nephrotoxicity in humans and the provision of satisfactory quality control data.

7. NEW DRUGS

(a) Loxapac

The Committee decided if the indications for Loxapac are to include anxiety and neurosis, to defer this drug pending receipt of long-term studies for these indications and the provision of satisfactory quality control data.

However, if the indications are to be limited, the Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Loxapac subject to the removal of all references to all indications except "the treatment of schizophrenia and psychotic states associated with organic brain syndromes or mental retardation", and the provision of satisfactory quality control data.

(b) Dantrium

The Committee decided to defer this drug pending receipt of further information on long-term cardiac effects, satisfactory data on quality control and bio-availability, further information on the difference between spasticity in upper and lower limbs, further data on side-effects, e.g. arrythmias, anti-nuclear factor, and hepatotoxicity.

(c) Parlodel

The Committee decided to defer this drug pending receipt of further clinical data especially on the inhibition of lactation, further data on the incidence of venous thrombosis, and the provision of satisfactory quality control data.

An informal suggestion is to be made to the firm to carry out clinical trials in New Zealand. Its use with L.Dopa as an anti-Parkinson drug was noted with interest.

(d) Depramine

The Committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of the new therapeutic drug Depramine due to the lack of comparative bio-availability studies and bio-equivalence data and unsatisfactory quality control data.

(e) Clinoril

The Committee decided to defer this drug pending receipt of comparative studies with another anti-inflammatory, e.g., indomethacin, particularly in regard to the incidence of side-effects in long-term studies, and the provision of satisfactory quality control data.

The firm is to be advised that the pre-clinical data were satisfactory.

(f) Pexid

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Pexid subject to the provision of satisfactory quality control data, that advertising be limited and include a warning on possible hepatic toxicity in long-term use, that availability be restricted to appropriate specialists, that its use be monitored closely and reports be submitted to the Committee. In particular the Committee would like more data concerning the pharmacokinetics of the drug and also concerning the origin of raised enzyme values.

The firm is to be advised that the submission was well presented and that the pre-clinical data were satisfactory.

The Committee agreed that if they recommended a drug for specialist use only then it is appropriate that the Department decline applications from general practitioners under section 99.

(g) VM26-Sandoz

The Committee decided to defer this drug pending receipt of further information on the histological stages at which it has been administered in Hodgkin's disease, more clinical and histological data on the treatment of other indications, justification for use of the solvent and the provision of satisfactory quality control data.

(h) Duranest

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

(i) Madopar

The Committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of the new therapeutic drug Madopar due to the lack of comparative studies with Sinemet, unsatisfactory quality control data, lack of long-term toxicity studies, and the lack of data on calcium and bone metabolism.

(j) Amikin

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Amikin subject to the firm agreeing to refrain from advertising, that availability be restricted to hospital specialists only, that on-going data especially on nephrotoxicity and ototoxicity be provided, that adverse reactions be reported by users and that satisfactory quality control data be provided.

(k) Sectral

The Committee decided to defer this drug pending receipt of further data on anti-nuclear factor, long-term clinical studies particularly with regard to immunological side-effects and adequate documentation of safety, further toxicity data and the provision of satisfactory quality control data.

There was discussion on the future general policy on B- blockers taking practolol into account. It was agreed that general guidelines be suggested by members for consideration at the next meeting.

(l) Prostin F2α

The Committee decided to recommend that the Minister of Health consent to the distribution in New Zealand of the new therapeutic drug Prostin F2α subject to the firm agreeing to restrict advertising, that availability be restricted to appropriate specialists and the provision of satisfactory quality control data.

8. GENERAL

(a) Aldactone

The information sent to members was supplied voluntarily by the firm. Professor McQueen does not consider that any action is required at this stage however it will be considered by the Committee on Adverse Drug Reactions at their next meeting.

(b) Drug Testing - Antibiotics

The Committee expressed concern at the lack of progress towards the establishment of laboratory facilities for sterility testing, the bio-assay of antibiotics and biological testing.

The Chairman advised that it was 2 years since the first meeting was held between the DSIR, N.H.I. and the Department on this matter. The delay has been unfortunate but a bacteriologist has now been appointed at N.H.I. to initiate such testing. Although the bio-assay of antibiotics and also the testing of vaccines will eventually be included in the programme, the sterility testing of large volume I.V. solutions must have the highest priority.

(c) Rauwolfia

The information provided was considered and no comment was made.

(d) Crescormin

The Swedish firm of Kabi has approached the Department to investigate the possibility of obtaining human pituitary glands in New Zealand for processing and thus ensuring continuity of supply to New Zealand. The Department has been led to believe that processing might eventually take place in Auckland Hospital.

Human pituitary glands are currently sent to U.S.A. for processing and this is done very cheaply. Professor Herdson advised that there is no shortage of human pituitary glands from post-mortems in New Zealand and he asked to be advised if the other proposals eventuate. Professor Herdson expressed his opposition to any payment for the collection of human pituitary glands.

(e) Systemic Absorbtion of Clobetasol (Dermovate)

This drug is absorbed in greater quantities than other similar steroid creams. The firm will issue a warning that no more than 50 gm/week be used in adults and less for children. The Committee agreed with the Department that this drug should be restricted to specialist use only.

(f) Aldecin Inhaler

A changed drug notification has been received for the intranasal use of Aldecin Inhaler in cases of allergic and perennial rhinitis. For this purpose a special intranasal adaptor will be supplied in the already existing Aldecin Inhaler pack.

The Committee agreed with the utilisation of the same container for both indications if different adaptors are provided.

(g) Parenteral Nutrition

A paper setting out the Australian Drug Evaluation Committee's action was tabled.

The Committee asked the Department to obtain further information for consideration at the next meeting.

(h) Drug Cost - Drug Tariff

The Chairman advised that the period of supply in the Drug Tariff will be reduced from 7 days to 5 days in an attempt to reduce costs. This will come into effect on 1 August 1975.

An extensive survey both before and after 1 August will be carried out to assess its effect and to discover if doctors will find a loophole in the reduction of the period of supply.

The meeting closed at 5.08 p.m.

Chairman: Val Scott

Date: 26. 11. 75.

MINUTES OF THE 22ND MEETING OF THE DRUG ASSESSMENT ADVISORY COMMITTEE HELD ON WEDNESDAY 30 NOVEMBER 1977 IN THE BOARD ROOM, 7TH FLOOR, MACARTHY TRUST BUILDING, LAMBTON QUAY, WELLINGTON COMMENCING AT 9.00 AM.

PRESENT:

Dr A.G. Scott (Chairman)
Professor P.B. Herdson
Professor L.B. Jellett
Professor G.S.M. Kellaway
Dr M. Kingsford
Dr D. Macintosh
Professor T.V. O'Donnell
Dr G. Shanks
Miss L.G. Woolstencroft (Secretary)

IN ATTENDANCE:

Mrs M.S. Combly
Dr K.H. Goh
Mr R.C. Griffith
Dr J.S. Phillips
Miss L. Stanaway
Mr R.M. Trow
Mr R. Withington

There were no apologies.

The chairman opened the meeting and welcomed all members, especially Professor Herdson who had recently returned from overseas.

1. DATES OF NEXT YEAR'S MEETINGS:

It was proposed and accepted that the committee meets next year on the following dates:

22 February
14 June
11 October.

2. MINUTES OF THE LAST MEETING:

The minutes of the 21st meeting having been circulated, were taken as read and were confirmed subject to a few minor typographical corrections being made.

3. MATTERS ARISING FROM THE MINUTES:

(1) Intensified Adverse Drug Reaction Reporting Scheme

The chairman reported that at the recent Committee on Adverse Drug Reactions' meeting it had been pointed out that the Drug Assessment Advisory Committee would be interested to know about reactions and events being reported by doctors. A six monthly review was suggested.

Several members had already received by post a copy of a review on the adverse events reported in the first six months of the scheme. This information had been circulated to all doctors in private practice along with a sheet of "Intensified Monitoring" stickers for use on patient records.

There was considerable discussion on the form in which the review of these reports was presented. It was suggested that the presentation of the number of events reported with individual products could lead to unwarranted comparison of the safety of these products. It would also be possible to relate the number of reports to the figures of sales in an unsound manner. It was further pointed out that most of the reports had been unsubstantiated, although it was realised that over zealous checking of reports could have the effect of cutting down reporting rates.

It was agreed that some form of feed-back was necessary to encourage practitioners to continue to report adverse events. It was felt however that this could be achieved without presenting the individual figures in relation to each product. Alternatively if the figures were to be presented, and it was accepted that the Committee on Adverse Drug Reactions and the World Health Organisation do present individual figures, then they should be qualified by comment on their reliability and a warning of the dangers of wrong interpretation. It was requested that the committee's view-point be presented to the Medical Assessor of the Committee on Adverse Drug Reactions.

The members of the committee were pleased to hear that general adverse drug reaction reporting had increased by approximately 50% since the intensified adverse drug reaction reporting scheme had come into effect.

It was reported that Auckland Hospital had done a two months survey on the numbers of patients having stopped the use of a medicine on the scheme without giving any reasons. Out of 44 patients no longer receiving the medicines, there were two possible and two definite cases where adverse drug reactions had occurred and not been reported. It had been decided to do a two month

survey every six months and forward the information obtained to Professor McQueen. This would provide some idea of the level and accuracy of the figures received if the Auckland Hospital figures were comparable with other hospitals.

The department advised that an intensified adverse drug reaction reporting scheme card with a covering letter had been sent to all retail pharmacists as, with the marketing of Cimetidine and Labetalol, retail pharmacies were now involved in the scheme.

The department also advised that following the request made by the committee at its last meeting a further circular was sent to hospital pharmacists-in-charge to clarify the nurses' position and responsibility regarding the scheme.

It was understood that Professor G. McQueen had written to the Pharmaceutical Manufacturers' Association requesting the association to provide the finance for half the salary of an assistant to work on the scheme. The committee supported this request. At present the P.M.A. are printing the pharmacist reporting cards three times a year and will update the cards as required. It was reported that the association had been most helpful in supporting the scheme and promoting it amongst its members.

(2) Tartrazine Hypersensitivity

The committee was informed that no reply has yet been received from the National Jewish Hospital and Research Center, Denver.

(3) Depo Provera

It was reported that the company had advised the department that the American Food and Drug Administration had requested the withdrawal of the new drug application for Depo Provera. If this was not done by the company they had been warned that the application would be rejected.

The committee reaffirmed its opinion that this product is of value in New Zealand.

(4) Urotrast

The department had had no reply from the manufacturer regarding the regulatory history of Urotrast in Australia.

Other queries have also not been answered.

(5) Medicines Bill

The committee was advised that the Medicines Bill had been deferred to the next Parliamentary Session.

(6) Mr S. Smith

It was reported that a letter had been sent to Mr Smith following the previous meeting. The chairman read the letter received in reply. The committee agreed that no further action should be taken.

4. DEFERRED MEDICINES:

(1) Benoral

The committee felt that the further information provided was insufficient and inadequate to satisfy their queries regarding long term studies, therefore they decided to defer consideration of this medicine until satisfactory data were supplied.

It was noted that the Australian Drug Evaluation Committee had requested further information on clinical efficacy or blood levels with regard to different dosage regimens based on twice daily or four times daily treatment. It was agreed that the company should be asked to supply these data to the Drug Assessment Advisory Committee as they become available.

(2) Topisolone

The committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of the new medicine Topisolone owing to the dangers of its use being disproportionate to its benefits. There were also outstanding quality control queries.

(3) Vivalan

The committee reaffirmed its decision to defer this medicine for more data on long term usage. The quality control queries raised earlier had been resolved.

Members strongly rejected the suggestion by the firm that the application to distribute Vivalan be considered on the basis that it be included in the intensified adverse drug reaction reporting scheme. The scheme was not intended to supplant the requirement for long term clinical trials. Information on these are still necessary and should be supplied with the application. It was felt that there should have been sufficient usage in the United Kingdom to supply these data.

5. NEW MEDICINES

(1) Noristerat

The committee decided to defer consideration of this medicine for further information on the frequency of dosage required for efficacy, long term safety data relating to a continuous use period of two years and quality control data.

While the packet insert refers to the duration of effect as being 12 weeks, there is the suggestion elsewhere that the medicine is effective for only up to eight weeks.

The committee also requested that updated references be supplied by the company since a number of references in the application were very dated and unreliable. It was noted in studies in Peru that 50% of the women had discontinued the medicine for "medical reasons" but no indication was given of what these reasons were.

(2) Dolobid

The committee decided to defer consideration of this new medicine for further information on long term usage, more information on gastro intestinal side effects including blood loss in the gastro intestinal tract, bioavailability and quality assurance.

It was pointed out that a considerable number of the patients were on concomitant medication and that there was a great reduction in numbers after 12 weeks' treatment.

(3) Cinopal

The committee decided to defer consideration of this medicine for further information on long term usage particularly in view of the gastro intestinal side effects reported in animals. There was a shortage of data on hepatic and renal toxicity testing. Further comment was required on the fine opacities found in the eyes of dogs. Further information is also needed on some quality control aspects.

(4) Vaspid

The committee decided to defer consideration of this medicine for further information on long term usage and to support claims that there are no systemic effects or local atrophy of the skin. The company should also be asked if there are any published articles on the clinical trials as it was felt that investigators would wish to publish their findings on this interesting medicine.

(5) Depixol

The committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of the new medicine Depixol. Further data on the pharmacokinetics in man, metabolism and quality control of the medicine are required. Also necessary is further information on long term usage and side effects. Concern was expressed about the incidence of extra pyramidal effects and depression resulting from therapy.

The committee were of the opinion that this was a poor application and they found it difficult to assess how many long term patients had been involved.

(6) Zaroxolyn

The committee decided to defer consideration of this medicine for further information on bioavailability. It is an insoluble substance with potential bioavailability problems. Some quality control matters remain to be resolved. No further clinical studies are required.

(7) Phasecon

The committee decided to recommend that the Minister of Health decline consent to distribute in New Zealand the new medicine Phasecon.

Further data on efficacy in long term usage, relative efficacy with other products and on quality control are required. The affiliations of the investigators should be provided with the efficacy data. Questions were also raised on the high rate of intermenstrual bleeding and its cause, the lack of assurance on possible fluid retention, and the ability to conceive after cessation of therapy.

It was requested that the company be reminded that data written in English were required. If Phasecon is resubmitted the articles presented in German should be translated.

(8) Florone

The committee decided to recommend that the Minister of Health decline consent to the distribution in New Zealand of the new medicine Florone.

Further data would be required on safety in long term usage, comparative efficacy, side effects including the danger of absorption and quality control.

The members considered the application to be very badly compiled and presented. It was impossible to follow the cross references and the summaries were inadequate. It was requested that the company be told of the committee's opinion of the presentation and the difficulty experienced in evaluating this medicine.

(9) Seatone

The committee decided to recommend that the Minister of Health decline consent to distribute in New Zealand the new medicine Seatone.

Insufficient information was provided on all aspects. The information that was provided was considered contradictory and unimpressive. It was noted that some patients were reported as actually deteriorating whilst under therapy.

(10) Information Submitted on Medicines Deferred

Members commented on the difficulty experienced in dealing with medicines deferred from previous meetings. It was thought that recommendations would be easier to reach and more consistent if companies resubmitted all the information when the medicine came before the committee again. In order to facilitate this, members agreed to return all the information, provided by the company, to the department. This would be returned to the company for storing until the medicine next came before the committee.

If members wish to retain, personally, any information this can be requested on their behalf, from the company.

6. CHANGED MEDICINES

(1) Parlodel

(a) Pre-menstrual Tension and Menstrual Disorders

The committee recommended that the Minister of Health decline consent to distribute the medicine Parlodel for the new indications of pre-menstrual tension and menstrual disorders. It was felt that these disorders were not serious enough to warrant the high risk of side effects especially if conception occurred during or following treatment.

(b) Parkinsonism

Although it was felt that the efficacy of Parlodel on its own was not established for this indication and the side effects were troublesome, the committee decided that for patients failing on other available medicines, the use of bromocriptine

was justified in spite of the risk of associated side effects.

The committee therefore recommended that the Minister of Health consent to the distribution in New Zealand of Parlodel for the new indication Parkinsonism subject to its restriction to use by neurologists only.

The company's advice on the bioavailability of the 10 mg capsule should be sought.

(c) The committee approved the precautions recommended by the company as a result of the findings of malignant uterine tumours in rats.

It was proposed that a Clinical Services Letter be written on the subject laying stress on the proposal that Parlodel be used only when other medicines have failed and when the possible benefits to patient outweighed the associated risks. Attention should be drawn to the gynaecological precautions recommended.

7. GENERAL BUSINESS

(1) Oestrogen Therapy - Contra Indications and Warnings

At the November 1976 meeting of this committee it was recommended that certain warnings be required in the literature on oestrogen containing products. Following that meeting a circular was distributed to all companies marketing oestrogens in New Zealand. The replies of two companies who objected to some of the conditions in the circular were brought to the attention of the committee.

Members believed it to be their duty to caution practitioners and/or the public on possible risks associated with such preparations and that it was up to the company to prove that the risks were not associated with their product.

The committee therefore reaffirmed their original decision regarding warnings required on products containing oestrogens. It was suggested that some firms may wish to preface the warning with the words "Statistical evidence suggests that".

(2) Tegretol

Information regarding a two rat toxicity study with Tegretol (carbamazepine) was presented to the committee.

The committee received and noted the data but no action was considered necessary at this time.

(3) Dr Moller's visit to the Food and Drug Administration

Dr Moller's report was received with interest and members looked forward to hearing further from Dr Moller upon his return.

(4) Epilim

The committee decided to defer consideration of derestricting Epilim until June 1979. This product will be considered by the Pharmacology and Therapeutics Advisory Committee in the interim with regards to its availability as a pharmaceutical benefit.

(5) Clofibrate

A paper from I.C.I. (N.Z.) Limited regarding carcinogenicity reports on Clofibrate arising from work by another company was discussed. No action was deemed to be necessary at this time.

(6) Committee on Safety of Medicines

(a) Oral Contraceptives

A letter recently received from the Committee on Safety Medicines in the United Kingdom was presented to members. The committee agreed that the information on oral contraceptives should include a warning on the increased risk of vascular problems in smokers especially in the later age groups.

(b) Hormonal Pregnancy Tests

A letter recently received from the Committee on Safety of Medicines on the association of hormonal pregnancy tests with congenital abnormalities was tabled.

This subject had been discussed at the March 1975 meeting and as a result the two hormonal pregnancy tests available in New Zealand were withdrawn from the market as from 1 June 1975. No further action is therefore necessary.

(7) Cefoxitin

A letter received from Dr P.J. Little regarding the availability of Cefoxitin in New Zealand was placed before the committee for their information.

Cefoxitin is expected to come before the committee at the February 1978 meeting.

(8) Salbutamol

A special report received from Allen & Hanburys Limited on the occurrence of leiomyomata following long term administration of salbutamol sulphate to rats had been distributed to members for their information. No action was considered necessary at this stage.

The chairman closed the meeting at 4.00 p.m. having thanked the members for their attendance and wished them the compliments of the season.

Certified: I.M. Scott
Chairman

Date: 22 Febry 1978.