THERAPEUTICS SECTION Bulletin

JANUARY 1996

THERAPEUTICS SECTION, MINISTRY OF HEALTH, WELLINGTON, NEW ZEALAND

Considered Advice

Recently the Ministry of Health was faced with a dilemma, which fell to the Therapeutics Section to resolve. The United Kingdom's Committee on Safety of Medicines published a letter to UK doctors advising them to alter the treatment of women taking low dose oral contraceptives containing desogestrel or gestodene. By their next menstrual cycle, these women were recommended to be on contraceptives containing the older progestogens. The advice was based on unpublished studies that we were unable to access.

Therapeutics Section's role is to balance the risks from the use of medicines with appropriate access to effective treatment. A large proportion of New Zealand women taking oral contraceptives are taking brands containing desogestrel or gestodene. What advice should we have given to New Zealand doctors?

To ensure we were doing the best we could in difficult circumstances, we urgently sought the advice of a group of experts and invited the manufacturers to participate in the meeting. The advice was that it was too soon to recommend changes to prescribing but that the information available to the Ministry should be made available to women taking these products as well as to doctors. We did this.

This issue is a good example of the usefulness of local expert advice in an acute situation. On a continuing basis the Ministry and the Minister of Health seek advice from several expert committees. In the area of medicine regulation the three most prominent are the Medicines Assessment Advisory Committee (MAAC), the Medicines Adverse Reactions Committee (MARC) and the Medicines Classification Committee (MCC).

All three play a key role in protecting public health. The work of MARC ensures that the risks of using medicines are minimised, while MAAC evaluates new medicines and new uses for medicines to see if they are safe and effective. The MCC considers how accessible these medicines should be for the public.

Often the valuable work of these committees goes unnoticed by the general public. It is timely, with the retirement of Professor Gavin Kellaway who has been chairing two of these committees in recent years, to reflect on how advisory committees add value to the work of the Section.

Professor Kellaway has been a member of MARC for 30 years and a member of MAAC for 25 years. He was, until he retired at the end of 1995, the chair of both committees. Gavin was the guest of honour recently at two farewell functions where the Ministry was joined by the Associate Minister, Hon Maurice Williamson, present committee members, and some past members. The tributes to his tireless efforts were well deserved and we all wish him well, as he pursues some of his many other, non-pharmacological interests.

Professor Gavin Kellaway looking with interest at the minutes of Medicines Assessment Advisory Committee meetings dating back to the early 1970's.

During Gavin's tenure there have been some notable achievements, going back as far as practolol, and the MARC advice to the then Department of Health about reports of life-threatening adverse reactions with this early beta-blocker. Because of that advice, New Zealand was the first country in the world to restrict the use of practolol (the UK took similar action a short time later) and New Zealand was spared the spate of severe adverse reactions seen elsewhere.

MARC also played a key role in assessing the evidence linking fenoterol and death from asthma. The Committee's advice to the Pharmacology and Therapeutics Advisory Committee via the Minister, resulted in the medicine being withdrawn from the Drug Tariff.

Similarly, MAAC identified concerns about possible hepatic and other side effects from the new non-steroidal anti-inflammatory agent benoxaprofen when assessing it for marketing consent. The medicine had already been approved in the UK and was subsequently withdrawn there, when the MAAC's concerns about rash and photosensitivity were borne out.

Another highlight of Gavin's term was the establishment of the Intensive Medicines Monitoring Programme (IMMP) in 1977. Amongst the first medicines monitored were several beta-blockers, now well-established as a relatively safe therapeutic class. IMMP continues to play a valuable post-marketing surveillance role thanks, in part, to the support it has received from Professor Kellaway.

The Ministry of Health has been well served by its technical committees from which we have come to expect sensible, practicable and well-founded recommendations. The leadership of the MAAC and the MARC now passes on to the next generation, in the form of Associate Professors Richard Robson of Christchurch and Tim Maling of Wellington. Both have served several years as committee members, and I know that both are very conscious of the example that they have been set.

Thank you Gavin for a job well done.

Bob Boyd, Manager

Professor Gavin Kellaway cutting his farewell cake.

Left to right: Hugh Baber, Assistant General Manager Health Regulation and Protection, Dr Ralph Richardson, former MAAC member and Dr Richard Girven from ESR.

Left to right: MAAC members, Professor Linda Holloway, Dr Bridget Robinson and Dr Rod Ellis-Pegler with Sheree Wellington, former secretary of MAAC.

New Therapeutics Staff

PETER ABERNETHY

Peter recently moved to the Therapeutic Information Resource in the Evaluation Team from the Ministry's Communications Section. Peter describes it as an interesting challenge to combine the use of his journalism experience with his BSc in physiology. He says his new position definitely beats dealing with the media, which has been a large part of his job for the past two years. Before Peter jumped the fence to work for the Ministry he was working as the national health reporter for Radio New Zealand, based in Wellington.

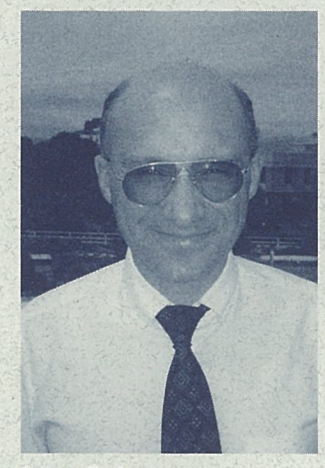
MIKE THOMPSON

Mike studied at the School of Pharmacy in London and subsequently spent 3 years in hospital/clinical pharmacy in the UK before joining Sandoz Pharma. There he spent time in medical information and technical services, before moving into clinical research, working mainly in the areas of immunology and dermatology. Immediately prior to joining the Therapeutics Section in May, Mike spent 4 years working as an international Clinical Project Manager at the headquarters of Sandoz in Basel, Switzerland.

BRIAN O'SULLIVAN

Brian received a degree in microbiology and biochemistry in Ireland and for the last few years has been working for the French Blood Transfusion Service (post-scandal) as an International Relations Officer. Additionally, he worked as a microbiologist in England and, when he first arrived to our shores, he was employed as a toxicologist with the Agricultural Compounds Unit of MAF. Brian is currently working on an Evaluation Team project to produce quality standards for blood products. At the conclusion of the project, he will join other Evaluation Team scientists assessing medicines. He says future plans include finding a decent pint of Guinness in this country.

Standing left to right: Mike Thompson, Peter Abernethy.
Seated: Brian O'Sullivan.



Arman Farjam

Rose Paki

ARMAN FARJAM

Arman has joined the Therapeutics Section as a medicine assessment Advisor in the Evaluation Team. He is a recent arrival in New Zealand from Dusseldorf, Germany where he worked for the pharmaceutical company Sankyo as head of their Human Pharmacology Department. Arman says his work there involved medicine development in all aspects of pre-clinical and clinical medical research, including some very detailed molecular biological work.

ROSE PAKI

Rose has joined the Therapeutics Section Compliance Team where she works as an assistant support officer. Rose's job largely involves dealing with company licences. Prior to this Rose was with the Department of Justice's Penal Section where she worked in the records section.

MERLE TURNER

Merle is an Assistant Advisor at the Auckland Regional Licensing Office, after having transferred over from the Licensing Section of the same office. She initially joined the Department of Health in 1973 after working as a primary school teacher and, since then, Merle has gained experience in a variety of roles in the public health area including providing support to the Auckland Medical Officer of Health.

CRISTINE DELLA BARCA

After graduating with a Diploma in Pharmacy from C.I.T., Cristine began her working life at Glaxo, firstly as an intern and then as a validation officer. She had a major involvement in the building and commissioning of the rotadisk facility at the company's Palmerston North site. More recently, Cristine worked as a medical representative for Eli Lilly as well as studying to complete a Diploma in Business and Administration. In September, Cristine joined the Therapeutics Section as a Medicine Control Advisor at the Wellington regional office.

KIM WILLCOX

Before commencing work as a Wellington-based Assistant Advisor in Medicine Control, Kim worked for the Occupational Registration Boards Secretariat of the Ministry of Health. This followed the completion of a Bachelor of Social Sciences in Psychology at the University of Waikato. Kim is enjoying her new position despite having to sort through triplicate copies of hundreds of controlled drug prescriptions to monitor the prescribing of controlled drugs.

Merle Turner

TONY GERRED

Tony joins the Medicine Control arm of the Compliance Team with a lengthy background in hospital pharmacy. After working in hospitals in England, Gibraltar and Germany, his New Zealand career began nearly twenty years ago as Chief Pharmacist of the West Coast Hospital Board. He later moved to Auckland as Pharmacist-in-Charge at Auckland Hospital and five years later became Chief Pharmacist of the Auckland Hospital Board, just in time to enjoy the 'interesting times' of transition through an Area Health Board to the creation of a Crown Health Enterprise. Tony is now based in the Hamilton Regional Licensing Office.

Left to right: Tony Gerred, Kim Willcox, Cristine Della Barca

LISA PEARSON

Lisa Pearson recently joined the Therapeutics Section as an Assistant Advisor, Medicine Control, based in Dunedin. Born and bred in Wellington, Lisa graduated from Otago University in 1991 with a Degree in Biochemistry and Microbiology. Before becoming a mother of one she worked as a laboratory technician for Fortex Group Silverstream and Healthcare Otago.

Lisa Pearson

Therapeutics Staff on the Move

Nicky Anderson	Returned from parental leave to the Auckland Regional Licensing Office
Carol Morris	To dispensing pharmacist at North Shore Hospital
Sheree Wellington	Gone travelling the world (we're all jealous!)
Ted Leigh	Enjoying retirement
Malene Hook	Working closer to home on Auckland's North Shore
Tania Paull	Gone 'temping' in Wellington
Connie Janes	Also 'temping' in Wellington
Kathy Daly	To dispensing pharmacist at Kenepuru Hospital
Arlene Lewer	Busy caring for new daughter Jessica
Rosemary Thompson	Now a community pharmacist in Lower Hutt

Auckland and Wellington Regional Offices Shift

The Auckland and Wellington Regional Licensing Office staff recently moved premises. Their new addresses, telephone and fax numbers are -

Auckland Regional Licensing Office

Level 2
31-35 Hargreaves St
PO Box 47 511
Ponsonby
Auckland

Telephone (09) 309 3035
Fax (09) 302 5061

Wellington Regional Licensing Office

1st Floor
Rossmore House
123 Molesworth St
PO Box 10 327
Wellington

See the staff list on page 7 for direct dial telephone numbers.
Fax (04) 499 6169

Therapeutics Section Staff List

	Special Responsibilities	Direct Dial Telephone
Bob Boyd	Manager	(04) 496-2088
Rosemary Cooney	Executive Assistant	(04) 496-2262

Business Support Team

Catherine Marnane	Senior Support Officer	(04) 496-2179
Rachael Trudgeon	Support Officer	(04) 496-2155

Special Projects Team

Susan Martindale	Team Leader	(04) 496-2092
Marilyn Anderson	Special Projects	(04) 496-2234

Evaluation Team

HEAD OFFICE, WELLINGTON

Mark Rowland	Team Leader	(04) 496-2091
Richard Griffith	Medicine Evaluation, MCC	(04) 496-2363
Khay Ooi	Traditional and Herbal Medicine	(04) 496-2339
Jeremy Brett	Secretary Generics Sub-committee, Biological Products	(04) 496-2097
Raymond Wilson	Medicine Evaluation, MAAC	(04) 496-2040
Alison Cossar	Medicine Evaluation	(04) 496-2460
Margaret Ewen	Therapeutic Information	(04) 496-2107
Stewart Jessamine	Medical Advisor	(04) 496-2274
Alexander Bolotovski	Medical Advisor	(04) 496-2078
Kathlyn Ronaldson	Secretary MARC	(04) 496-2365
Peter Abernethy	Analyst	(04) 496-2202
Brian O'Sullivan	Medicine Evaluation	(04) 496-2331
Mike Thompson	Secretary MAAC	(04) 496-2094
Arman Farjam	Medicine Evaluation	(04) 496-2098
Carol Smith	Secretary MCC	(04) 496-2096
David Stevens	New Medicine Applications	(04) 496-2093
Gary Twinn	Changed Medicine Notifications, Clinical Trials	(04) 496-2038

AUCKLAND REGIONAL LICENSING OFFICE

Myfanwy Fulford	Information Advisor	Phone (09) 309-3035 Fax (09) 302-5061

CHRISTCHURCH REGIONAL LICENSING OFFICE

Isobel Smith	Information Advisor	Phone (03) 366-7394 Fax (03) 366-1156

Compliance Team

	Special Responsibilities	Direct Dial Telephone
HEAD OFFICE, WELLINGTON		
Peter Pratt	Team Leader	(04) 496-2362
Trevor Nisbet	Medical Devices and Cosmetics	(04) 496-2364
Christine Deveson	GMP, Section 29 Meds, CD's	(04) 496-2378
Derek Fitzgerald	GMP and Medicine Recalls	(04) 496-2176
Lawrence Young	Medicine Control Co-ordinator	(04) 496-2136
Barbara Cavanagh	Support Officer	(04) 496-2191
Rose Paki	Support Officer	(04) 496-2090
AUCKLAND REGIONAL LICENSING OFFICE		
Glenys Riggir	Medicine Control Advisor	Phone (09) 309-3035
Gary Syme	Medicine Control Advisor	Fax (09) 302-5061
Nicola Anderson	Medicine Control Advisor	
Cecilia Niumagumagu	Assistant Advisor	
Merle Turner	Assistant Advisor	
HAMILTON REGIONAL LICENSING OFFICE		
Tony Gerred	Medicine Control Advisor	Phone (07) 834-0013
Michelle Bishop	Assistant Advisor	Fax (07) 834-0015
WELLINGTON REGIONAL LICENSING OFFICE		
Doug Longmire	Medicine Control Advisor	(04) 496-2439
Melissa Young	Medicine Control Advisor	(04) 496-2436
Cristine Della Barca	Medicine Control Advisor	(04) 496-2018
Anne Cherry	Assistant Advisor	(04) 496-2437
Kim Willcox	Assistant Advisor	(04) 496-2438
		Fax (04) 499-6169
CHRISTCHURCH REGIONAL LICENSING OFFICE		
Sheldon Ramer	Medicine Control Advisor	Phone (03) 366-7394
Nicky Harris	Assistant Advisor	Fax (03) 366-1156
DUNEDIN REGIONAL LICENSING OFFICE		
Denise Martin	Medicine Control Advisor	Phone (03) 479-2561
Lisa Pearson	Assistant Advisor	Fax (03) 477-6368

Head Office Therapeutics Section staff can be contacted by e-mail using the following Internet address:
first name.surname@mohwn.synet.net.nz

'Dear SCOTT' is Out

After the sponsor of a clinical trial has sent the requisite four copies* of the initial application to the Standing Committee on Clinical Trials (SCOTT), we ask that all subsequent correspondence about the trial is sent to the Therapeutics Section. SCOTT is contracted to the Ministry solely to make recommendations based on the application. Therefore any general queries and any correspondence arising from the Committee's evaluation is more appropriately handled by the Ministry.

The address for initial applications is:

Prof R Laverty Room 318 3rd Floor, Adams Building, Frederick Street, DUNEDIN

and thereafter the address is:

Manager, Therapeutics Section (attention Gary Twinn) Ministry of Health, 133 Molesworth St, WELLINGTON

We have had a number of queries about the definition of a 'new' medicine and how it relates to clinical trials. A company wishing to conduct a clinical trial using a medicine which already has consent to market in New Zealand does not require an exemption under Section 30 of the Medicines Act 1981. Therefore, even if the trial is assessing a new indication, no clinical trial application is needed. Where a clinical trial is to be carried out using a medicine that has not had consent to market, then the medicine is regarded as a new medicine and an application for exemption under Section 30 must be sought via an application to SCOTT.

Note - a medicine coated differently, or having a different strength or dose form than a medicine with consent to market, is a new medicine.

*A separate copy of the application and the fee should be sent directly to the Therapeutics Section.

Innovators Get Stronger Protection

The Therapeutics Section has recently published information on how the Medicines Amendment Act 1994 affects data about a medicine which has been provided in an application for marketing consent.

The amendment came into force in January 1995 and it protects registration data against unfair commercial use, either through disclosure or from being used to support a competing medicine application. This brings New Zealand into line with the trade agreement on intellectual property rights included in the GATT-Uruguay agreement, to which New Zealand is a party.

The document sets out the administrative process staff will follow when assessing innovative and generic applications to meet Government's obligations to provide stronger protection of intellectual property rights. Draft guidelines were circulated in January 1995 and comments from pharmaceutical companies have been considered and, where appropriate, incorporated into the final version which is now available on request.

The overall effect is that some sorts of information which have previously been released under the Official Information Act may now be withheld to protect the innovator companies from unfair commercial use of their information by their competitors.

This could result in a delay in the approval of generic products if data supplied in support of the applications relies on the existence of commercially sensitive information held by the Ministry about the innovative versions of the medicines. These data may now only be used to support a generic version where the manufacturer has the permission of the makers of the innovative medicine. Without this approval generic manufacturers cannot use their competitor's data for a set period of time (up to five years).

Ask for *"Administrative Guidelines for Protecting Confidential Supporting Information"* - see page 16 for details on how to order Therapeutics Section documents.

Comparing Adverse Reactions Across the Tasman

There can be considerable differences in the adverse reactions reported for the same medicine on different sides of the Tasman.

A recent conference on Adverse Drug Reactions held in Sydney in April presented an opportunity to compare notes about reports from both countries. In Australia the antibacterial flucloxacillin continues to be of concern. Australia now has more than 400 reports of hepatic reactions with flucloxacillin, possibly the highest rate of reporting of any country and far above New Zealand's reports which number less than 30 for a population one fifth the size of Australia's.

New Zealand's Intensive Medicine Monitoring Programme (IMMP) was of great interest to the Australians. In New Zealand a small number of medicines (seven at present) are intensively monitored. Doctors and pharmacists are asked to provide information about every patient prescribed these medicines and doctors are asked to report all adverse clinical events. From these known cohorts of patients, reliable estimates of the incidence of adverse reactions associated with particular medicines can be measured.

Particular achievements of New Zealand's IMMP were highlighted at the conference by Dr John McEwen of the Therapeutic Goods Administration. These included determining the incidence and risk factors for agranulocytosis with the antidepressant mianserin and very early confirmation that cough is an adverse reaction associated with ACE inhibitors.

Adverse Reactions Advisor Kathlyn Ronaldson, who attended the conference, says that the Australians view IMMP as particularly valuable because the data collected is able to give a good indication of the incidence of a particular adverse reaction, and its risk factors.

The conference also heard of the results achieved from the Australian spontaneous adverse reaction reporting programme. The conclusion was that post-marketing surveillance programmes are essential to detect adverse reactions not usually identified in pre-marketing clinical trials. These adverse reactions are particularly those that are rare, or occur after a latency period, or develop with prolonged use.

Hepatic reactions with flucloxacillin are a good example of reactions with a latency period. The first symptoms usually occur days or weeks following the completion of therapy, thus making identification of causal association difficult. The first case reports were not received in Australia until flucloxacillin had been on the market for more than a year.

No Grace Period

Section 23 of the Medicines Act 1981 allows the Minister of Health to grant provisional consent for a medicine to be marketed in this country, for situations where a clinical need is established but insufficient data is available for consideration of full consent. Provisional consent is granted for a maximum of two years and is not automatically renewable.

When an existing provisional consent expires and no new provisional or full consent has been obtained, the right to distribute the product lapses and it is treated as a new medicine. Supplies may then only be provided pursuant to Section 29 of the Act (which requires that companies report all supplies to the Ministry) and promotion or marketing activities are no longer allowed.

The Act does not allow for any period of grace, so applications for renewal of the provisional consent or transfer to a full consent should be submitted in sufficient time to allow for processing. The earlier the better, but allow four months for renewal. For transfer to a full consent please contact us as soon as possible, as this process can take as much time as that required to assess a new medicine application for a new chemical entity.

Applications for renewal can be fast-tracked and portions of the application fee can be waived depending on the level of demonstrated clinical need.

Introducing Bill

The legislation project team is optimistic that the Therapeutic Products Bill will be introduced in Parliament during 1996, after missing out in 1995.

Project Manager Susan Martindale says the Bill is regarded by both the Ministry and Government as a high priority and the delay in implementation is largely due to the slow-down in the legislative timetable in the lead up to MMP.

The project team is continuing to work on the development of the new Regulations and Rules which will need to be put in place after the Bill is enacted before the new legislation can become operational. This will involve further targeted consultation with affected parties, which is planned to start early in 1996.

An additional temporary project team member is being recruited to join Susan and Marilyn Anderson to help with this work.

CDs in the Workplace

The Medicines Assessment Advisory Committee (MAAC) is currently assessing a new medicine application provided electronically. The application was provided on CD-ROM which looks the same as a compact disk for a stereo except it contains data and software rather than music. In this case, the application came with its own hardware - fast personal computers with large screens (double the usual size), and their own software - all provided by the company to be returned after the evaluation is completed.

The first two parts of the application, including the administrative and summary data, expert reports, chemistry, manufacturing quality control and stability data were assessed within the Section by Evaluation Team Advisor Raymond Wilson.

Raymond rates this CANDA (computer assisted new drug application) highly, with some minor drawbacks. He says it took him about the same time to assess the first two parts of the application on CD (the CD contains the equivalent of 50 volumes of material) as it would have taken to assess it in hard copy.

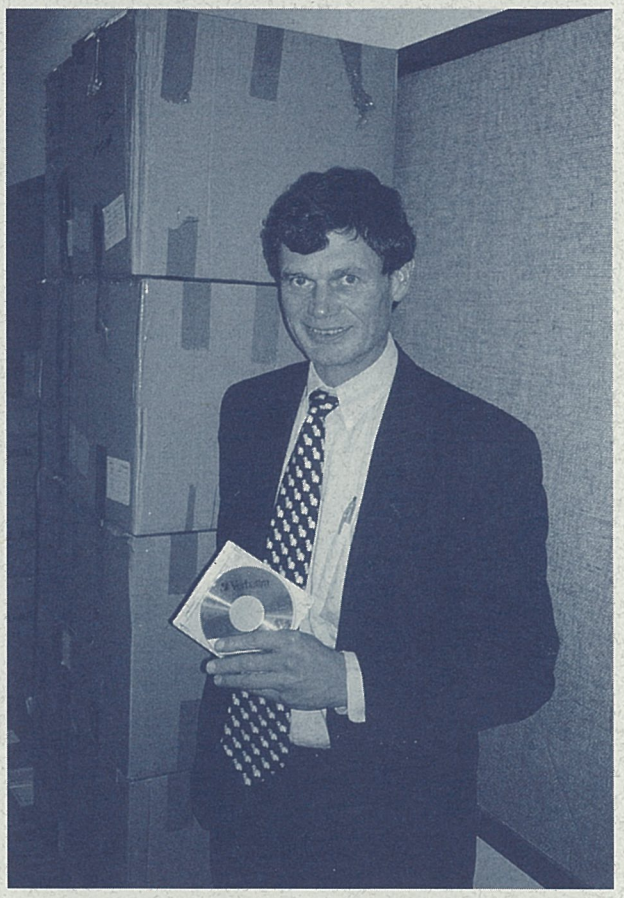
Compared to the one other previous CANDA he has assessed, Raymond says this was much more user-friendly, allowing both the application data and his report to be displayed on the screen at the same time. Material could be cut and pasted electronically from the application to the assessment report, enabling more detailed information to be easily incorporated.

Raymond says that this time around he needed a couple of hours training to get familiar with the operating system. However, with a little practice he believes his electronic assessments would definitely speed up.

One problem he found was a very vigilant electronic security system which regularly blanked out the screen with little warning and which required frequent re-keying of the password to reopen the system. Maybe he should have used this time to give his eyes a rest, because he also noticed that his eyes became very tired, which he attributes to long periods in front of the computer screen.

The toxicology and clinical trial data in the application are being assessed electronically by one other MAAC member, and a third is doing his assessment using the paper version.

CD vs paper – MAAC chair Associate Professor Richard Robson holding a CD containing the equivalent of 50 volumes of material.



GPs Caught in Net

Communicating via computer was an option trialed in November as a way of generating discussion amongst general practitioners about appropriate medicine use.

The Ministry of Health has been working with the Royal New Zealand College of General Practitioners to trial a distance education project using the GP computer network. This involved mailing out a video and resource book on the management of hyperlipidaemia based on the assessment of absolute risk (a rating of risk factors based on the latest available evidence). These were then used as a basis for electronic seminars, case studies and structured discussions.

A dozen rural GPs spread around the country from Kaikohe in the north to Te Anau in the south received the resource kit and then were connected electronically with each other, with the College and with the Ministry, via a computer network linked through telephone lines.

The network provided them with an on-line e-mail, electronic conference allowing the transfer of information between participants. The trial took place over three sessions and has still to be evaluated, but the initial response seems to be that the trial has been well worth the effort.

Animal, Vegetable or Mineral?

How do you determine what is a medicine and what is a medical device? Or, what is a dietary supplement and what is a herbal remedy?

These questions are important as the different categories are treated differently in legislation. Medicines are comprehensively controlled under the Medicines Act 1981 and require consent from the Minister of Health before they can be distributed. Foods are controlled under the Food Act 1981 and Dietary Supplement Regulations 1984. Medical device safety is monitored, but their access to the market is largely uncontrolled.

Deciding which category a particular product fits into can often be difficult. A recent example is a product which contains two powders which when mixed together produce oxygen for use in assisting people with breathing difficulty. Is it a device or a medicine?

To help in coming to a conclusion on these sorts of questions the Ministry of Health has its own internal Categorisation Committee. The Committee has representatives from the Food Section and from both the Compliance and Evaluation Teams within the Therapeutics Section.

The Committee recommends whether products are medicines, medical devices, related products, cosmetics, foods or dietary supplements. At issue usually is whether or not the product is intended to have a therapeutic purpose (that is, have an effect on a physiological function). If it does, then the product generally comes under the Medicines Act and so must fall into one of the first three categories. A database is maintained to help provide consistency of decision making.

As for the product which produces oxygen, the committee considered that because the oxygen was intended to be provided in circumstances where the gas would have a therapeutic effect the product should be treated as a medicine.

CMI Put to the Test

The consumer medicine information (CMI) project team and the CMI Working Party are now starting to put their theories into practice by doing their own consumer testing. This forms part of the development of a Code of Practice for providing information to consumers about Prescription and Restricted Medicines.

Three leaflets for Prescription Medicines, compiled in line with the Ministry's Draft Code of Practice for Consumer Medicine Information will be field tested in February 1996.

Patients dispensed three pre-selected medicines in the community pharmacies taking part in the survey, will be given the CMI for their medicine and asked to complete a questionnaire about the information they've been given. Forty pharmacies will be asked to distribute the questionnaires, half of which will act as controls for the survey.

CMI project leader Margaret Ewen says the survey will help ensure that the draft Code is on the right track and that the proposed requirements for CMI will provide the sort of information consumers want on their Prescription Medicines.

Focus groups of individuals from various ethnic groups, those who are high users of medicines and other special interest groups will be organised to ensure that the information needs of these consumers will be addressed.

Margaret says much of the direction for the survey and the focus groups came from the CMI Working Party which fine-tuned the draft Code at its third meeting which was held over two days in September.

The survey and the focus group discussions will be completed by May 1996 and the Working Party will meet a short time later to discuss the results and review the next stages of the project which will include an extensive round of consultation.

Margaret says in the meantime any pharmaceutical companies wishing to get a head-start in producing CMI are welcome to discuss with her the best way of doing this in line with the draft Code of Practice. Margaret's contact details are on page 6.

Note - CMI is a more precise term than CPI (consumer product information) and is now the preferred name for this project.

New Parts of GMP Code Published

Two new parts of the *New Zealand Code of Good Manufacturing Practice for the Manufacture and Distribution of Therapeutic Goods* have recently been published, along with an annex to an existing part of the Code.

The two new parts are:

Part 4: Wholesaling of Medicines and Medical Devices
Part 5: Uniform Recall Procedure for Medicines and Medical Devices

Parts 4 and 5 have been published together as one volume. Part 4 is for those who sell medicines and medical devices by wholesale, and includes guidelines on documentation, storage conditions, stock handling and other wholesaling activities. The Ministry's Medicine Control Advisors will be using this part of the Code to audit wholesalers. Part 5 gives guidance to those who are involved in initiating or controlling a medicine or medical device recall.

The other new publication is an annex to *Part 3: Compounding and Dispensing* which covers the compounding and dispensing activities carried out in hospital and community pharmacies. This part of the Code was published in 1993. The new publication, *Annex 1 (to Part 3): Compounding of Sterile Pharmaceutical Products,* is for use by those engaged in specialised sterile/aseptic work not covered by *Part 1: Manufacture of Pharmaceutical Products*.

All parts of the Codes of Good Manufacturing Practice are prepared in consultation with the industry and are regularly reviewed to ensure that they continue to meet the needs of the Ministry and the users.

The following GMP codes are currently available:

- *Part 1: Manufacture of Pharmaceutical Products*. Part 1 was published in 1993 and is intended primarily for use by the pharmaceutical manufacturing and medical gases industry.
- *Part 2: Manufacture of Blood and Blood Products*. Part 2 was also published in 1993 and will be revised in 1996. A working party, including members from the blood transfusion industry, will be established to consider the content of this part of the Code which will be expanded to include bone marrow collection, testing and processing.
- *Part 3: Compounding and Dispensing* plus *Annex 1 (to Part 3): Compounding of Sterile Pharmaceutical Products*
- *Part 4: Wholesaling of Medicines and Medical Devices*
- *Part 5: Uniform Recall Procedure for Medicines and Medical Devices*

See page 16 for ordering and cost information.

Improving Our Own Quality

Therapeutics Section GMP auditors expect companies to have fully documented quality systems for their manufacturing processes. We are now applying the same principle to ourselves.

The Compliance Team has a fully documented quality system for the processes involved in auditing and issuing of licences for medicines manufacture.

Advisor Derek Fitzgerald says that essentially the system has not changed and manufacturers are unlikely to notice any major differences. Nevertheless, internally the Section expects to be more efficient, have better records and be able to demonstrate that all actions were carried out correctly and that all decisions were fully considered.

The system covers Compliance Team processes such as:

- procedures for making licensing recommendations
- licence issue procedures
- policies on relevant issues
- auditor qualifications and training
- internal audit
- GMP audit conduct
- descriptive documents detailing operating procedures
- codes of ethics
- quality and policy statements.

The new quality system has been in place since April and will be very useful in negotiating mutual recognition agreements with other countries' regulatory authorities.

Last May, the Ministry's quality system was externally audited against the European Pharmaceutical Inspection Convention (PIC) standard and was found to measure up. Derek says the next step is to check that the Ministry's actions comply with the processes laid down in the quality system.

In with the In Crowd

New Zealand's entry into the Pharmaceutical Evaluation Reporting (PER) scheme may speed up the evaluation process for new medicine applications for new chemical entities.

Companies which already have approval to market an innovative product in one country can help to streamline the approval process in other countries if they consent to the sharing of evaluation reports between the regulatory agencies, where both countries are members of the PER scheme.

Evaluation Team Leader Mark Rowland says that now New Zealand can have access to evaluation reports from other PER scheme member countries, it will reduce the time spent on the evaluation process here. Normally a medicine application for a new chemical entity would be assessed in full by two Medicines Assessment Advisory Committee (MAAC) members, but where there is an appropriate evaluation report available through the PER scheme Mark says that the application would only need to be assessed by one MAAC member in full. Therefore the Committee could process applications more quickly and efficiently.

New Zealand was formally admitted as a PER scheme member at a meeting in Iceland in June 1995. Mark attended the meeting to hear that the other member countries felt that we had demonstrated the quality of our evaluation reports to put New Zealand on par with other PER scheme regulatory authorities.

Inspectors Meet

Manufacturing sterile products using special cabinets generated considerable interest at an international seminar recently.

Isolator technology involves the use of specially designed cabinets which allow manipulation of materials inside the sterile cabinet through gloved openings. Compliance Team Advisor Derek Fitzgerald says there is also considerable interest in isolator technology in New Zealand.

Derek says there are a number of potential uses locally, particularly within hospitals where they would be used to compound intravenous nutrient solutions, intravenous additives and reconstituted injectable drugs.

He says isolator technology is expensive, but cost effective when rated alongside traditional 'clean rooms', which are room-sized sterile environments that must meet strict standards.

At the seminar there was considerable discussion about the limits of isolator technology particularly in terms of guaranteeing sterility. He says there is some evidence that the existing alarms are not sensitive enough to detect contamination from background air arising from very small leaks into the cabinet.

Derek says the general consensus from the seminar is that the isolator technology is best used cautiously and as part of a 'clean room'-type system rather than as a replacement for it.

The seminar was co-ordinated by the European-based Pharmaceutical Inspection Convention (PIC) and Derek says the two and a half days presented a good opportunity for catching up with other auditors about different systems, expectations and standards used in other countries. Other topics up for discussion were:

- clean room environmental standards
- autoclaves, sterilisation and validation
- clean room personnel
- aseptic processes

The 1996 PIC technical seminar will be focusing on auditing computerised systems used in medicine manufacturing and will be held in Sydney so far a change the Europeans will be expected to travel to the southern hemisphere.

Thirty Something

Sunscreens claiming SPF protection of up to 30+ may soon comply with the joint Australian New Zealand Standard for sunscreens. At present the maximum SPF (sun protection factor) recognised by the Standard is 15+.

The limit is now likely to increase as the committee involved in reviewing the Standard has agreed that there is sufficient evidence to show a greater level of sun protection from sunscreens with SPF of 30+ compared to those with an SPF of 15+.

Following a round of public consultation, it is expected that the Standard AS/NZS 2604:1993 will be updated sometime in 1996.

While you are enjoying the summer sunshine remember that sunscreens should be used in association with other sunsmart behaviours -

- wear loose comfortable clothing that gives good coverage
- wear a hat that will shade your face, neck and ears
- wear sunglasses
- apply a sunscreen which is SPF 15 or greater and is also broad spectrum, 15 to 30 minutes before going in the sun and reapply every two hours
- keep an eye on the time. New Zealand sun is especially fierce between 11am and 4pm. This is when harmful UV rays are at their strongest
- invest in a sun-umbrella for instant portable shade
- make the most of the shade
- store sunscreens at temperatures below 25°C.

Schedule Rescheduled

Not before time, the First Schedule to the Medicines Regulations 1984 is to be reprinted in 1996. This will be a comprehensive, up-to-date listing of all Prescription, Restricted and Pharmacy-Only Medicines.

The most recent changes to the current regulations were published in the *New Zealand Gazette* on 7 September 1995. The Gazette notice will be superseded when the regulation amendment is published, and then subsequent amendments (made on the recommendation of the Medicines Classification Committee) will be notified in the Gazette again, until there is another catch-up reprint of the regulation schedule.

Therefore, when looking for the classification of a particular medicine, consult the Gazette notice first. If the medicine does not appear in the notice, then the First Schedule to the Regulations still holds. If you are still in doubt, we would be happy to advise the correct current classification status if you ask.

Fast Tracking

Applications for consent to market are dealt with in order of receipt, unless there is strong evidence that the public good would be served by fast tracking the assessment.

Eligibility for "fast tracking" a medicine assessment is based on two criteria, covering different aspects of "the public good". The first is where there is a need for the product because it fills a niche not being filled by existing therapies. The second is on the recommendation of PHARMAC, when there is evidence that there will be significant financial saving for the crown. Unfortunately, meeting the manufacturer's marketing timelines is not a convincing argument for granting fast tracking!

Labelling Exemptions

With the change to more flexible labelling requirements on medicines introduced at the beginning of 1995, there are now fewer circumstances where exemptions are necessary.

Changes to the 1984 Medicines Regulations which came into force on 1 January 1995, meant that more overseas labels were acceptable here, and reduced the amount of New Zealand specific requirements. This has resulted in fewer companies seeking labelling exemptions. However, a few requests for exemptions have been lodged that contain changes which were not merely a label change. For example a change of label because the medicine is to be manufactured at a different site, or the process has changed. In these instances, the medicine will not be granted a labelling exemption and a changed medicine notification will be eagerly awaited!

Naming of Parts

We need help in choosing a name for our planned new computerised information system. The Ministry has begun negotiating with Pharmasoft AB (a Swedish company) for a computer software system that will revamp its medicines evaluation, tracking and information systems and will enable the efficient administration of the new Therapeutic Products legislation.

The product is sold under the trade name REGULATOR (formerly known as SWEDIS) and the first parts of the modular system are expected to be up and running from about the middle of 1996. The new system will allow the Ministry to:

- produce up to date product information from the Section's files
- generate business reports
- record the Section's administrative processes and provide a tracking system for the processing of applications
- capture information about medicines and medical devices
- improve business efficiency and access to information
- issue product licences under the planned new Therapeutic Products legislation
- perform trends analysis of complaints about therapeutic products

It's planned the system will be accessible to the Section's clients (with protection for commercially sensitive data) and provide information about product evaluations and up-to-date news on the Section and its services. One of the major selling points of the new system is its flexibility, which allows access on a variety of levels and yet guarantees confidentiality where required. The system will also support work flow and document management within the Section.

We're looking for a suitable acronym for our database. Some of the options suggested to the project team include:

TARDIS - Therapeutic Analysis & Regulatory Drug Information System

and

START - System for Therapeutic Analysis Regulatory Tracking

But we think you can do better than this. Can you help?

Send you ideas to:

Peter Abernethy
Analyst
Therapeutics Section
Ministry of Health
133 Molesworth St Wellington
ph: 04-496-2202 fax: 04-496-2050

Prizes for the best entries are:

1st The complete Ministry of Health corporate outfit (an umbrella, pen and T-shirt) in corporate livery
2nd One free labelling exemption
3rd The name and address of Bob Boyd's hairdresser

Therapeutics Section Publications

The following publications can be ordered from:

David Stevens Therapeutics Section, Ministry of Health, PO Box 5013, Wellington, New Zealand

1. New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods

   (a) Part 1 – Manufacture of Pharmaceutical Products (1993). Cost $16 including GST.

   (b) Part 2 – Manufacture of Blood and Blood Products (1993). Cost $16 including GST.

   (c) Part 3 – Compounding and Dispensing and Annex 1: Compounding of Sterile Pharmaceutical Products (1995). No charge.

   (d) Part 4 and 5 – Wholesaling of Medicines and Medical Devices and Uniform Recall Procedure for Medicines and Medical Devices (1995). No charge.

2. Code of Good Manufacturing Practice for Cosmetics (1982).
3. Guidelines for Labelling Cosmetic Products (1990).
4. Guidelines as to Levels for Micro-organisms in Cosmetic Products.
5. Information on Silicone Gel Breast Implants (1994).
6. Safe Management of Medicines – A Guide for Managers of Old People's Homes (1994).
7. List of Sunscreens Offering Broad Spectrum and SPF 15+ Protection (Nov 94).
8. Medicines Distribution Guide (1993).
9. Notice to Applicants: EC Guide on New Medicine Applications IIA (1993). Cost - $20 including GST.
10. Guidelines for Classification of Products - as either Medicines, Related Products, Dietary Supplements, or Cosmetics (1990).
11. Fees for Service: Supplementary Information (1991).
12. Guidelines for Preparing Data Sheets (1989).
13. Guidelines for Compiling Applications for Contact Lens Solutions (1988).
14. Administrative Guidelines for Protecting Confidential Supporting Information (1994).
15. Interchangeable Multi-source Medicines (1996).

Interchangeable multi-source managers – which is the real one? ***Christmas 1995.***

In Our Next Issue

- **Trans Tasman sharing of evaluation reports**
- **Pharmacovigilance - a new science, or a new form of policing?**

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Editor: Margaret Ewen,
telephone (04) 496-2107, fax (04) 496-2340
Manager, Therapeutics Section: Dr GR Boyd

MINISTRY OF HEALTH
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