

# *Annual Report 1986*



**ndab**

NATIONAL DRUGS ADVISORY BOARD

An Bord Comhairleach Naisiunta Druganna

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**ndab**

**NATIONAL DRUGS ADVISORY BOARD**  
AN BÓRD COMHAIRLEACH NAISIÚNTA DRUGANNA  
63-64 ADELAIDE RD., DUBLIN 2.  
TEL: 764971/7 TELEX: 90542.

BM/mm

19th October 1987

Mr. P.W. Flanagan,  
Secretary,  
Department of Health,  
Custom House,  
Dublin 1.

Dear Sir,

As you are, no doubt, aware, the Chairman of the Board will formally present the Board's Annual Report for 1986 to Dr. Rory O' Hanlon, T.D., Minister for Health on Thursday 22nd October 1987 at 6.00pm at the Board's offices.

I am directed by the Board to request the pleasure of your company at this presentation and I will be grateful for your confirmation that you will attend.

I enclose a copy of the 1986 Annual Report, in advance of the formal presentation, for your information.

Yours faithfully,

Brendan Murphy,  
Secretary.

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**NATIONAL DRUGS ADVISORY BOARD**  
**An Bórd Comhairleach Náisiúnta Druganna**

# **Annual Report 1986**

**Charles Lucas House,  
63-64 Adelaide Road, Dublin 2.**

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## NATIONAL DRUGS ADVISORY BOARD

The National Drugs Advisory Board was established by the Minister for Health in 1966 by the National Drugs Advisory Board (Establishment) Order 1966 (S.I. No. 163 of 1966) under the Health (Corporate Bodies) Act 1961. The functions of the Board are set out in Article 4 of this Order as amended by the National Drugs Advisory Board (Establishment) Order 1966 (Amendment) Order 1974 (S.I. No. 178 of 1974) and the National Drugs Advisory Board (Establishment) Order 1966 (Amendment) Order 1985 (S.I. No. 220 of 1985) and are as follows:-

- (a) to organise and administer a service for obtaining and assessing information as regards the safety of new and reformulated drugs and in particular, their toxicity and other adverse effects,
- (b) to organise and administer a service for obtaining and assessing reports on the adverse effects of drugs in use in the State,
- (c) to advise the Minister and others concerned as to the precautions or restrictions, if any, subject to which drugs may be marketed or continued in use in the State,
- (d) if requested by the Minister, to consider and report to him on the arrangements to be made for the quality control of drugs, for the registration and inspection of the premises of drug manufacturers, importers and wholesalers, and for the sampling and testing of drugs,
- (e) if requested by the Minister, to advise on the licensing of the manufacture, importation,

distribution and sale of drugs, on the standards of manufacturing practice (including quality control) of manufacturers of drugs and on the certification for export purposes or for any other purposes of drugs,

- (f) if requested by the Minister and subject to such conditions as he may approve, to arrange for the collection and dissemination of information in respect of drugs, their pharmacological classification and therapeutic efficacy and in respect of economies in prescribing,
- (g) if requested by the Minister, to make recommendations regarding standards for the composition, purity and strength of drugs and for the methods of testing drugs,
- (h) to consider and report to the Minister on such general or particular matters in regard to drugs as he may refer to the Board for advice,
- (i) to exercise such powers as a competent authority or otherwise for the purposes of the implementation of the Directive No. 81/851/EEC (a) of the Council of the European Communities as may be assigned to the Board by the Minister in pursuance of the European Communities Act, 1972 (No. 27 of 1972).

### NOTE

- (a) Official Journal of the European Communities No. 2317 6/11/1981 (Pages 1-15)

## BOARD

K. O'MALLEY	<i>M.D., Ph.D., F.R.C.P.I.; F.R.C.P.(Ed.), Professor of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin — Chairman.</i>
T. B. BARRAGRY	<i>Ph.D.(NUI), M.V.M.(NUI), M.V.B., M.R.C.V.S., Senior Lecturer in Veterinary Pharmacology and Therapeutics, Faculty of Veterinary Medicine, University College, Dublin.</i>
M. CURTIN	<i>M.D., F.R.C.P.I., D.C.H., D.P.H., B.Sc., Consultant Paediatrician, Regional Hospital, Limerick.</i>
G. R. FITZGERALD	<i>M.B., B.Ch., F.R.C.P., Consultant Physician, Ardkkeen Regional Hospital, Waterford.</i>
T. A. McGUINN	<i>B.Sc.(Pharm.), F.P.S.I., Chief Pharmacist, Department of Health, Dublin.</i>
K. McGARRY	<i>M.B., B.Ch., F.R.C.P.I., D.C.H., Consultant Physician, Our Lady's Hospital, Navan.</i>
P. F. NOWLAN	<i>M.V.B., M.Sc.(Tox.), M.R.C.V.S., Lecturer in Laboratory Animal Science and Manager, Wellcome Research Animal Laboratories, University of Dublin.</i>
M. O'DWYER	<i>M.B., D.C.H., Family Practitioner, Blackrock, Co. Dublin.</i>
T. V. O'DWYER	<i>M.B., F.F.C.M.I., D.C.H., L.M., D.Obst., (R.C.O.G.), Senior Medical Officer, Department of Health, Dublin.</i>
D. P. O'MAHONY	<i>M.D., Lecturer, Department of Pharmacology, University College, Cork.</i>
G. G. SHAW	<i>B.Pharm., M.A., Ph.D., M.P.S., F.T.C.D., Professor of Pharmacology and Director, School of Pharmacy, University of Dublin.</i>
J. STRONGE	<i>M.B., B.Ch., M.A.O., F.R.C.O.G., Master, National Maternity Hospital, Holles Street, Dublin.</i>
R. F. TIMONEY	<i>Ph.D., M.Sc., F.P.S.I., F.R.S.C., Professor of Pharmaceutical Chemistry, School of Pharmacy, University of Dublin.</i>
M. G. T. WEBB	<i>M.B., M.Phil., F.R.C.P.I., F.R.C.Psych., Professor of Psychiatry, University of Dublin.</i>
D. WHITE	<i>M.R.C.V.S., Senior Supervisory Research Officer, Veterinary Research Laboratory, Abbotstown, Castleknock, Co. Dublin.</i>

## COMMITTEE ON EVALUATION AND TOXICITY

\*PROFESSOR R. TIMONEY *Chairman*

M. L. CONALTY *M.D., F.R.C.Path., D.P.H., Dublin.*

T. D. FEELEY *M.Sc., Ph.D., M.Chem.A., F.R.I.C., Public Analyst's Laboratory, Regional Hospital, Galway.*

I. B. HILLARY *M.D., F.R.C.Path., D.P.H., D.C.H., Associate Professor Medical Microbiology (Virology), University College, Dublin.*

B. LEONARD *M.Sc., Ph.D., Professor of Pharmacology, University College, Galway.*

\*MR. T. A. McGUINN

\*DR. D. P. O'MAHONY

## COMMITTEE ON DRUG USAGE AND ADVERSE REACTIONS

\*Dr. M. CURTIN

*Chairman*

J. FEELY *M.B., B.Sc., M.A., M.D., F.R.C.P.I., Professor of Pharmacology and Therapeutics, University of Dublin.*

\*DR. G. R. FITZGERALD

\*DR. K. McGARRY

\*Dr. M. O'DWYER

\*DR. T. V. O'DWYER

\*PROFESSOR K. O'MALLEY

\*DR. J. STRONGE

\*PROFESSOR M. G. T. WEBB

*\*Denotes member of the Board*

## VETERINARY COMMITTEE

*MR. P. F. NOWLAN	<i>Chairman</i>
*DR. T. B. BARRAGRY	
J. BARRETT	<i>M.R.C.V.S., Hillcrest, Dunboyne, Co. Meath.</i>
J. D. COLLINS	<i>M.V.M., M.S.(Calif.), M.R.C.V.S., Ph.D., Associate Professor Farm Animal Clinical Studies, Faculty of Veterinary Medicine, University College, Dublin.</i>
W. DONNELLY	<i>B.V.M., M.Sc., D.V.M., M.R.C.V.S., Superintending Senior Research Officer, Veterinary Research Laboratory, Abbotstown, Castleknock, Co. Dublin.</i>
N. DOWNEY	<i>Ph.D., Sc.D., M.R.C.V.S., An Foras Talúntais, Grange, Dunsay, Co. Meath.</i>
M. A. GARGAN	<i>B.Ag.Sc., Agricultural Inspector, Department of Agriculture, Kildare Street, Dublin 2.</i>
D. P. LEADON	<i>M.A., M.V.B., M.Sc., M.R.C.V.S., Irish Equine Centre, Johnstown, Co. Kildare.</i>
*PROFESSOR G. G. SHAW	
*MR. D. WHITE	

*\*Denotes member of the Board.*

## OFFICERS OF THE BOARD

### **Medical Director**

ALLENE I. SCOTT *M.D., F.R.C.P., F.R.C.P.(I)*

### **Deputy Medical Director**

MARIE T. BURNS *M.B., D.A., F.F.A., R.C.S.I.*

### **Medical Assessor**

MARY McCARTHY *M.B., Ch.B., M.Sc.*

### **Secretary**

BRENDAN MURPHY

### **Assistant Secretary**

MICHAEL CASEY

### **Pharmacists**

BEATRICE HUGHES	<i>B.Sc.(Pharm.), M.Sc., M.P.S.I.</i>
CHRISTL KLOOS	<i>B.Sc.(Pharm.), M.Sc., M.P.S.I.</i>
VINCENT MORLEY	<i>B.Sc.(Pharm.), M.P.S.I., Dip.Chem.Eng.</i>
MARY RAFTER	<i>B.Sc.(Pharm.), M.P.S.I.</i>

### **Inspector**

JAMES F. O'DOWD	<i>M.P.S.I.</i>
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### **Adverse Reactions Recording Secretary**

OLIVE M. LOWE	<i>S.R.N.</i>
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## **INTRODUCTION**

**by the Chairman**

Nineteen eighty six has been a busy and exciting year for the Board and the staff. Two events set in train in 1985 were to provide major challenges for the Board. First it had been mooted that it would be timely to have the function, structure and staffing of the Board examined by an outside agency because of the advent of the Board's involvement in the veterinary medicines licensing scheme and also as an aid to assessing the Board's requirement in relation to computerisation and word-processing.

Craig Gardner reported their findings and recommendations to the Minister for Health and these were made available to the Board in March. As the report addressed a wide range of issues pertinent to many aspects of the Board's work it served as a useful review and a number of the recommendations seemed reasonable. Areas addressed included the role of the Board as the competent authority, appellate system, enforcement of regulations, role of Committees, role of various officers of the Board, administrative structure, manpower and computerisation. The most important aspect on which the Board was not able to agree was on estimates of manpower requirements. The Department of Health who commissioned the report and the Board had a number of meetings. The final outcome in relation to staffing was a compromise and one that the Board felt could permit the backlog of work as well as our new commitment on the veterinary medicines side to be met.

However, a major proviso is that the Craig Gardner estimates for secretarial staffing assumed a saving of 25% pursuant to the introduction of word-processing. In the absence of progress on computerisation and word-processing the Board and staff perceive our operation to be seriously understaffed clerically. These difficulties were being discussed with the Department of Health at year's end. The Board's major concern is with the backlog of work and it seems that now there will be no long-term solution until computerisation and word-processing are installed.

Plans for computerisation and word-processing have been extant for nearly a decade and yet we are not in a position to implement them. Having brought the matter to an advanced stage of planning we find that the financial cuts make progress impracticable. This is particularly unfortunate as the type of operation run by the Board is suited to computerisation and word-processing. It is lamentable that in this day and age the Board does not have available to it facilities for word-processing. It seems to be a false economy given the proven value of this type of technology.

Secondly and in parallel with the above the Veterinary Committee had its first meeting under the Chairmanship of Mr. P. Nowlan in August. A number of new staff appointments mainly in relation to the veterinary medicines scheme were being processed in 1986 and this work should be completed in early 1987.

The implementation of the Veterinary Medicines Scheme, action on various recommendations by the consultancy group as well as the existing backlog on human medicines puts a very considerable strain on the staff of the Board. Notwithstanding this situation, the staff approached the challenge in a positive and helpful way. In this regard we acknowledge the constructive input of the main trade union involved on behalf of the staff, the Local Government and Public Services Union.

The Clinical Trials Bill, 1986 was presented in the Seanad early in the year. The Board accepted the initial draft as a basis for critical comment and a document was forwarded to the Minister detailing the perceived shortfalls.

Following discussions with officers of the Department of Health (and representations by other parties), subsequent versions of the Bill have shown vast improvement. From the Board's point of view it is vital that its role in the implementation of the Clinical Trials Bill is clearly defined.

I am concerned about our responsibilities for monitoring adverse drug reactions. This section of the Board needs to be expanded if we are to fulfill our statutory obligations in this vital area.

Two members of the Board retired from service in 1986. Dr. Philip Brennan has been a member of the Board since 1980. He has served diligently and with good humour and wisdom. Dr. Brendan Duffy resigned from the Board in October. Again Dr. Duffy served the Board in a most expert fashion over the past nine years. Dr. Kathleen McGarry was appointed to the Board in September and it is a pleasure to welcome her to the Board.

In September, the 1985 Annual Report was presented to the Minister for Health, Mr. Barry Desmond. The Board is of the view that it is important to have a formal meeting with the Minister on an annual basis so as to appraise him not only of the work of the Board but of the aspirations of the Board and staff for the future.

It is a pleasure to acknowledge the hard work and efforts of the staff of the Board over the year in question. As mentioned above this has been a particularly difficult year and yet their approach has never been less than professional and helpful. The Board is continually in contact with the officers of the Department of Health and it is a pleasure to acknowledge their helpfulness and courtesy which assists the smooth running of the affairs of the Board. As always our dealings with the pharmaceutical industry have been on a high professional level.

The coming year will be no less challenging than 1986. It is the Board's intention that the veterinary medicines licensing scheme be fully under way at the beginning of the year with a whole range of activities including manufacturers' licensing, product authorisations and the review programme functioning smoothly. While this is a major new task the many other aspects of the Board's work will continue and develop during the year. I am confident that the Board and staff of the Board are well up to this challenge.

**KEVIN O'MALLEY**

*Chairman*

# **1. LICENSING ACTIVITIES**

## **(a) ACTIVITIES IN RELATION TO ASSESSMENT OF APPLICATIONS**

### **Product Authorisations**

During 1986, 711 applications for product authorisations to market medical preparations were received by the National Drugs Advisory Board.

The Board examined and assessed these applications together with applications outstanding at the end of 1985. It recommended acceptance of 388 applications (91 in respect of review products). Of the remainder, 103 applications were withdrawn; 277 were held awaiting the provision of additional information and 2,097 were under consideration at the 31st December 1985. Applications received over the last 5 years are shown in Table 1.

Table 2 shows the number of applications received since the inception of the product authorisation scheme on 1st October 1974 and the position pertaining at the 31st December 1986.

## **(b) COMMENTS ON APPLICATIONS**

### **CLINICAL INFORMATION**

The Board would like to remind applicants that the purpose of premarketing assessment is to establish the conditions of use which ensure optimal benefit and least risk for the patient. To this end it would be valuable for the applicant to consult regularly with his medical advisers to avail of their expertise in directing the clinical investigations in relevant areas. Three main aspects are apparent: duration of study, at risk groups and drug interactions.

#### **1. Duration of Studies**

A trend has been noted in recent years for applicants for authorisations to present submissions prematurely, in particular without sufficient long term evidence of safety.

Products such as anxiolytics, non-steroidal anti-inflammatory drugs, those for the management of peptic ulcer disease, and anti-depressants, for example, are likely to be used for prolonged periods in clinical practice even if such prolonged use is not formally approved.

In the past, unexpected adverse effects have developed after long term use which are quite distinct from those seen after short term administration. It is important, therefore, for applicants to consider carefully the likely pattern of use of such products and to provide as much evidence as possible to establish the safety and efficacy of such long term use when making their initial submission.

#### **2. Clinical Risk Situations**

The Board has been concerned that a considerable number of applications has been made for novel ingredient products in which insufficient study has been directed to possible problems associated with the use of the product in the elderly, or in those with significant renal or hepatic dysfunction, or relevant enzymatic abnormalities. Almost 15% of the applications received for products containing novel active ingredients neglected to supply the requisite information which would permit either an assessment of safety in use for such special groups or the delineation of the required conditions for appropriate use in the groups at risk.

#### **3. Interactions**

Almost 20% of applications relating to products containing novel active ingredients failed to provide an adequate evaluation of the drug's interaction potential. Very often manufacturers relied on a list of other active ingredients taken concurrently with the medicine under consideration. Even where a significant risk was theoretically likely, no steps had been taken to evaluate the risk systematically.

**TABLE 1**  
**EUROPEAN COMMUNITIES (Proprietary Medicinal Products) REGULATIONS 1975**  
**and**  
**MEDICAL PREPARATIONS (Licensing, Advertisement & Sale) REGULATIONS 1984**  
**APPLICATIONS FOR PRODUCT AUTHORISATION TO MARKET**  
**received by**

**NATIONAL DRUGS ADVISORY BOARD**

<b>Applications in hand at 1st January:-</b>	<b>1982</b>	<b>1983</b>	<b>1984</b>	<b>1985</b>	<b>1986</b>
Under consideration	1436( 600)	1914( 928)	1566( 740)	1549( 579)	1816( 494)
Held awaiting additional information	275( 55)	140( 46)	405( 128)	436( 67)	338( 41)
No. of applications received	<u>966( 468)</u> <u>2577(1123)</u>	<u>895( 238)</u> <u>2949(1212)</u>	<u>759( — )</u> <u>2730( 868)</u>	<u>641( — )</u> <u>2726( 646)</u>	<u>711( — )</u> <u>2865( 535)</u>
<b>Recommendations issued to Dept. of Health</b>					
Withdrawn	468( 134)	720( 244)	565( 199)	464( 108)	388( 91)
Suspended	55( 15)	258( 100)	80( 23)	108( 3)	103( 29)
	— —	— —	— —	— —	— —
<b>Applications in hand at 31st December</b>					
Under consideration	1914( 928)	1566( 740)	1649( 579)	1816( 494)	2097( 392)
Held awaiting additional information	140( 46)	405( 128)	436( 67)	338( 41)	277( 23)
	<u>2577(1123)</u>	<u>2949(1212)</u>	<u>2730( 868)</u>	<u>2726( 646)</u>	<u>2865( 535)</u>
Existing Product Authorisations suspended	—	—	—	—	1
Authorisation Amendments notified and approved	225	277	523	544	— (See Note (b))
Existing Authorisations withdrawn/cancelled	146	118	79	88	104
Existing Authorisations renewed and issued to Dept. of Health	455	180	147	301	171

**NOTE:**

- (a) The figures in brackets denote applications for product authorisations under the review of established drugs.  
(b) The procedure for dealing with applications and amendments was revised during 1985 — See page 13.

TABLE 2  
**EUROPEAN COMMUNITIES (Proprietary Medicinal Products) REGULATIONS 1975**  
**and**  
**MEDICAL PREPARATIONS (Licensing, Advertisement and Sale) REGULATIONS 1984**  
**APPLICATIONS FOR PRODUCT AUTHORISATION TO MARKET**  
**received by**  
**NATIONAL DRUGS ADVISORY BOARD**

1974-1986

No. of applications received	9983	(3510)
Recommendations to Department of Health	6515	(2745)
Withdrawn	1092	( 350)
Suspended	2	( — )
Applications in hand at 31st December 1986		
Under Consideration	2097	( 392)
Held awaiting additional information	277	( 23)
	9983	(3510)
Existing Product Authorisations withdrawn	698	

**NOTE**

The figures in brackets denote applications under the review of established drugs.

**BIOAVAILABILITY**

The Board has reviewed the circumstances under which it will require evidence of in vivo bio-availability and has made the following recommendations:-

1. All dosage forms in which the active ingredient depends on a novel or unconventional mechanism for delivery to the patient. This would include percutaneous and buccal delivery systems; oral medications claiming sustained or controlled rate of release; implants; etc.
2. All anti-infectives presented other than in solution.
3. Dose forms containing an active ingredient which is highly potent, short-acting, or with a low therapeutic ratio.
4. Dose forms, the formulations of which differ significantly from the standard conventional one.

Evidence of bioavailability in-vitro will, as a rule, be required in most circumstances including those listed above.

Depending upon the nature of the product and the active ingredient, multiple dosing until a steady-state has been achieved, may be required, in addition to single dose studies.

**PHARMACEUTICAL INFORMATION**

**Sample Submission for Product Authorisation Consideration**

Details of the requirements for product samples to be submitted in connection with product authorisation assessment are set out in Part I, section 19, of the Board's Guidelines.

On occasion, the Board receives large amounts of samples or large dispensing packs. These are generally far in excess of requirements. The Board suggests that smaller samples should be provided. Should the sample size prove inadequate additional samples can be requested.

**Specialised and/or Automated Analytical Control Methods**

The increasing sophistication of analytical equipment available has led to the replacement of many standard analytical methods by more highly specialised methods, which in turn may lend themselves to automation.

While recognizing the advantages of such methods for routine quality-control, the Board considers it necessary, unless otherwise justified, that where product analysis utilizes instrumentation that is expensive, advanced and/or automated to a degree that is not generally available in a standard control laboratory, an alternative method utilizing standard equipment should also

be provided. Such alternative methods should ideally be based on a similar principle to that of the routine method employed and, in all cases, should be supported by validation results.

### **Sulphites in parenteral preparations**

Sulphites are widely used as preservatives in the pharmaceutical and food industries, and are reported to produce a broad spectrum of severe adverse reactions including anaphylaxis, in sensitive subjects. Although the exact incidence of sensitivity is unknown, it has been estimated that 5-11% of asthmatics may be sensitive, but 30% of reported cases have occurred in subjects without a history of asthma. Bisulphite has been found to be mutagenic in bacterial and mammalian cell cultures. Sulphites also react spontaneously with many intracellular compounds including the pyrimidine constituents of DNA.

The Board has in particular noted with concern the inclusion of sulphites as anti-oxidants in some amino acid solutions intended for parenteral nutrition. Parenteral infusion by-passes the entero-hepatic detoxification mechanism, and tissues generally are thus exposed to higher free sulphite levels. Since amino acid solutions are routinely used for long periods in the care of pre-term infants and other metabolically compromised patients, the Board does not intend to approve new or renewal applications for amino-acid solutions containing sulphites.

### **Time Scale for Processing Applications for Product Authorisations**

A review was undertaken of the time taken for the processing of the 388 applications for products for which recommendations were issued to the Department of Health by the Board during 1986. The results of this review are as follows:

#### **Time taken from receipt of applications to issue of recommendations to the Department of Health**

	<b>No. of Applications</b>	<b>%</b>
Under 6 months	46	11.9
6 months to 12 months	96	24.7
12 months to 24 months	106	27.3
Over 24 months	140	36.1
	<u>388</u>	<u>100.0</u>
Minimum time	2 months	
Maximum time	83 months	
Average time	24 months	

The Board would like to draw attention to a few matters which might facilitate processing of applications:-

1. In the case of products containing novel ingredients products, although initial assessment may be commenced quite soon after receipt by the staff, a presentation to the Committees has often to be delayed because of the absence of information important to the full evaluation of data. This is particularly significant in presentation of clinical data. (See page 9 [on Duration of Studies]).
2. There is often an inordinate delay in the supply of additional information required to support an application. The interval is further extended by the time which elapses between receipt of these data and their assessment. In part this is due to staff shortage, but the fault is compounded by the slowness of applicants responses. It is doubly unfortunate, since many of the queries could have been avoided. In the interest of expediting the procedure applicants should ensure that all evidence in support of applications is supplied as requested in the guidelines, and is accurate.

### **(c) RENEWAL OF PRODUCT AUTHORISATIONS**

In 1986, 518 product authorisations issued or renewed in 1981 fell due for renewal. 82 of these product authorisations were not renewed for various reasons and the remaining 436 applications for renewal were being prepared for issue at the year's end.

The numbers of product authorisations, showing the year of renewal, for which the product authorisation had not been issued by the 31st December 1986 is shown in Table 4.

The Board regrets the delay being experienced by companies in receiving the renewal document. The preparation and issue of renewal product authorisations was approximately 26 months in arrears at the end of the year. It is hoped that staffing changes, in the short term, and the application of computer technology in the longer term, will improve matters.

TABLE 4

#### **RENEWAL OF PRODUCT AUTHORISATIONS**

<b>Year of Renewal</b>	<b>No. Awaiting Issue</b>
1981	1
1982	107
1983	248
1984	207
1985	382
1986	436
<b>TOTAL</b>	<u>1381</u>

#### (d) AMENDMENTS OR VARIATIONS TO PRODUCT AUTHORISATIONS

The Board received 1596 applications for amendments in the terms of product authorisations during 1986. These applications, together with 472 awaiting assessment at the 31st December 1985 were considered and assessed during 1986 and the details are shown in Table 5.

The new procedure and form introduced in 1985 to facilitate implementation of amendments and variations continued to operate. Some difficulties were experienced by holders of product authorisations in receiving approval to the amendments due to the delay in the renewal of existing product authorisations.

It would facilitate processing of the applications for amendment, if the applications were sent to the Variations Section and not to individual officers of the Board.

There are a number of matters to which the attention of applicants is directed:

1. If an application for an authorisation is still under consideration and a formal product authorisation has not been issued, proposed alterations or additions to that application should not be presented as amendments to product authorisations but should simply be forwarded with a covering letter.
2. If an existing product authorisation is due for renewal and amendments to the original supportive data are proposed by the applicant, these should be incorporated into the renewal application, and attention drawn to the changes as required.

TABLE 5

#### APPLICATIONS FOR AMENDMENTS AND VARIATIONS TO PRODUCT AUTHORISATIONS

received by the  
**NATIONAL DRUGS ADVISORY BOARD**  
for the year ended 31st December 1986

	No.	%
Amendments awaiting assessment at 31st December 1985	472	
Amendments received:-		
(a) requiring medical assessment	353	22.1
(b) requiring pharmaceutical assessment	1243	77.9
	<u>2068</u>	<u>100.0</u>
<b>Amendments Approved</b>		
By endorsement of the product authorisation	641	31.0
By letter	805	38.9
Awaiting renewal	129	6.3
Amendments withdrawn	68	3.3
Amendments not approved	17	0.8
Amendments awaiting assessment at 31st December 1986	408	19.7
	<u>2068</u>	<u>100.0</u>

## **(e) WITHDRAWAL OF EXISTING PRODUCT AUTHORISATIONS**

The Board was notified of the withdrawal of 89 product authorisations during 1986. In most cases this was a commercial decision by the companies concerned.

## **(f) EUROPEAN COMMUNITY**

### **Committee for Proprietary Medicinal Products (CPMP)**

Preparatory to the implementation of further Directives 87/19/EEC and 87/21/EEC much of the time of the Committee and its working parties during 1986 was directed toward the development of new guidelines to be employed by applicants using the multi-state procedure. This involved a number of amendments and additions to existing guidelines made on the basis of additional experience in the area of drug control.

In this regard the Board would like to draw to the attention of applicants the availability in 1987 of the Board's guidelines, amended, with particular attention to the format, to take into account the guidelines from the CPMP shortly to be finalised.

### **Expert Reports**

One of the innovations of the new CPMP procedure is the introduction of a requirement for expert reports for each of the three main sections of the dossiers namely, pharmaceutical, pharmacological-toxicological (i.e. preclinical animal studies) and clinical sections.

The Board required expert reports to accompany applications for 'new ingredient' products from 1st January 1986 and for new formulation and reformulations of established active ingredients from 1st April 1986.

As a result of this year's experience a number of comments on the expert reports are made in the hope that future reports may avoid some of the inadequacies.

1. Many of the reports consisted simply of a summary of the data included in the evidence supporting the application
2. On occasion there were significant discrepancies between the statements in the summaries and the results in the body of the application.
3. Relatively few experts presented a critical appraisal of the data and its significance, or a conclusion of the value of the product on the basis of their experience.

Of 50 such reports received most contained acceptable summaries of the pharmaceutical sections (32) but fewer provided satisfactory summaries of the preclinical (29) and clinical sections (17). In fewer than 10 applications did the expert reports include a reasoned discussion, commentary and assessment of the data provided in support of the applications.

Applicants are reminded that the main purpose of the expert report is the critical evaluation of the investigations conducted on the product, and of the information derived from the investigations to permit a reasoned evaluation of the quality, safety and efficacy of the product not only by the expert but by the assessor.

## **(g) MANUFACTURING LICENCES**

In 1986, 5 applications for manufacturing licences under the Medical Preparations (Licensing of Manufacture) Regulations 1974 and 1975 were received by the Board. In addition, 4 applications were under examination at the 31st December 1985. Recommendations were made to the Minister for Health in respect of 5 of these applications and the remaining 4 applications were under examination at the 31st December 1986. Twenty applications for amendments to existing licences were also received over the year. At the end of the year there were 54 licensed manufacturers of medical preparations in this country. Table 6 shows the applications received for the last 5 years.

TABLE 6

**MEDICAL PREPARATIONS (Licencing of Manufacture) REGULATIONS 1974 and 1975****APPLICATIONS FOR MANUFACTURING LICENCES RECEIVED**

by the

**NATIONAL DRUGS ADVISORY BOARD**

	1982	1983	1984	1985	1986
Applications in hand at 1st January:-					
Under examination	5	3	5	6	4
No. of applications received during the year	<u>3</u>	<u>6</u>	<u>4</u>	<u>5</u>	<u>5</u>
	<u>8</u>	<u>9</u>	<u>9</u>	<u>11</u>	<u>9</u>
Recommendations issued to the Department of Health	5	4	2	7	5
Applications withdrawn	—	—	1	—	—
Applications in hand at 31st December:-	<u>3</u>	<u>5</u>	<u>6</u>	<u>4</u>	<u>4</u>
	<u>8</u>	<u>9</u>	<u>9</u>	<u>11</u>	<u>9</u>
Amendments to existing Licences	7	15	14	5	20
Existing Licences withdrawn	2	—	1	7	1
Existing Licences renewed	2	4	30	6	9

**(h) WHOLESALE LICENCES**

Three applications for wholesale licences under the Medical Preparations (Wholesale Licences) Regulations 1974 were received by the Board in 1986. In addition, 4 applications were under examination at the end of 1985. These applica-

tions were assessed by the Board and recommendations issued to the Department of Health in respect of 2 applications. Five existing licences were renewed during the year and at the end of the year, there were 84 wholesalers licensed under these regulations. Table 7 shows the number of applications received during the past 5 years.

TABLE 7

**MEDICAL PREPARATIONS (Wholesale Licences) REGULATIONS 1974****APPLICATIONS FOR WHOLESALE LICENCES RECEIVED**

by the

**NATIONAL DRUGS ADVISORY BOARD**

	1982	1983	1984	1985	1986
Application in hand at 1st January:-					
Under examination	2	4	3	6	4
No. of applications received	<u>7</u>	<u>4</u>	<u>7</u>	<u>3</u>	<u>3</u>
	<u>9</u>	<u>8</u>	<u>10</u>	<u>9</u>	<u>7</u>
Recommendations issued to the Department of Health:	4	3	4	5	2
Applications withdrawn	1	2	—	—	—
Applications on hand at 31st December:-					
Under examination	<u>4</u>	<u>3</u>	<u>6</u>	<u>4</u>	<u>5</u>
	<u>9</u>	<u>8</u>	<u>10</u>	<u>9</u>	<u>7</u>
Amendments to existing Licences	1	6	1	1	1
Existing Licences withdrawn	4	2	1	5	1

## (i) INSPECTIONS

A total of 49 inspections were undertaken by the Board's Inspector during the year. These inspections can be classified as follows:-

(i)	Inspections under the Medical Preparations (Licensing of Manufacture) Regulations 1974 and 1975	
	New applications	6
	Existing licence-holders	24
(ii)	Inspections under the Medical Preparations (Wholesale Licences) Regulations 1974	
	New applications	2
	Existing licence-holders	6
(iii)	Inspections in respect of certificates for export	5
(iv)	Inspections under the Convention for the Mutual Recognition of Inspections in respect of the Manufacture of Pharmaceutical Products.	6
		<u>49</u>

## (j) COMMENTS ON INSPECTIONS

### Inspections of Manufacturers

Many companies had instituted further upgrading of facilities to give better standards of Good Manufacturing Practice. The re-location of one company to a new facility was noted with satisfaction. It was clear that the benefits of the move more than justified the expenditure involved. In another company, planned re-development has reached an advanced stage in respect of their sterile facility and it is expected that it will be fully operational in mid-1987. The facility will have the latest technology to enhance its performance. A third company has redeveloped its plant and is rapidly increasing its out-put. It is a further source of satisfaction that the companies are indigenous manufacturers. It is also worthy of comment that another indigenous company has developed a sophisticated facility to handle total parenteral nutrition products and is providing this service to the major hospitals in the country. Two large international companies have commissioned major developments of Irish facilities during the year and both are expected to be in production by mid-1987. These developments have necessitated many interim inspections to ensure compliance with requirements, which will in turn enable these units to be licensed soon after completion.

### Inspection of Wholesalers

Due to pressure of work, limited inspections were undertaken. Security continues to be a serious problem. (It would appear that criminal elements have directed their attention to medicines/drugs as a possible source of gain.) However, most premises are now well protected by both mechanical devices and security patrols. Record systems have been much improved with the expanded use of computerisation. The Board would remind wholesalers of the need to notify the Department of Health and the Board of any intended changes in premises or activities covered by their licence in order to obtain approval.

### Other inspections

During the year, the Board's Inspector inspected five pharmaceutical manufacturing plants in order to advise the Minister for Health on certification for export purposes. One was a manufacturer of a drug substance; three were manufacturers of medical devices and one was a licensed manufacturer of medicinal products and required appropriate certification for export of a product not marketed in Ireland. The remaining facility inspected was a laboratory which provides a number of testing services for pharmaceutical manufacturers in Ireland.

Under the terms of the Convention for the Mutual Recognition of Inspections in respect of the Manufacture of Pharmaceutical Products, five inspections were undertaken on behalf of the Department of Health and Social Security in the United Kingdom, and one inspection on behalf of the National Board of Health of Denmark.

## (k) LICENSING FEES FOR HUMAN MEDICINES

During the year, the Minister for Health revised the fees payable in respect of applications for product authorisations for the marketing of medical preparations in Ireland with effect from the 1st March 1986. The new fee structure is as follows:

(a)	New products	£415
(b)	Review products	£210
(c)	Renewals	£210
(d)	Additional dosage strength	£85

The fee charged for "review products" is in respect of the review of generic products under the Medical Preparations (Licensing, Advertisement and Sale) Regulations 1984.

The Medical Preparations (Amendment of Fees) Regulations 1986 increased the fee for a manufacturing licence from £600 to £650 per annum and the fee for a wholesale licence from £260 to £300 per annum plus £100 for each additional wholesale outlet with effect from the 1st March 1986.

## **(I) CONVENTION FOR THE MUTUAL RECOGNITION OF INSPECTIONS IN RESPECT OF THE MANUFACTURE OF PHARMACEUTICAL PRODUCTS**

The Pharmaceutical Inspection Convention (PIC) has been set up in order to contribute towards the removal of obstacles in the international trade of pharmaceutical products, having due regard to public health aspects. It is a means of ensuring, through official inspections, that strict quality assurance and control of the manufacture of pharmaceutical products is carried out in accordance with appropriate standards of good manufacturing practice (GMP).

By the end of December 1986, the Convention was in operation in fourteen countries, namely, Austria, Denmark, Finland, the Federal Republic of Germany, Hungary, Iceland, Ireland, Liechtenstein, Norway, Portugal, Romania, Sweden, Switzerland and the United Kingdom.

In order to ensure the efficient functioning of the Convention as well as its uniform application in all Contracting States, a permanent committee was established in accordance with Article 8 of the Convention. This committee is composed of officials from the competent authorities of the Contracting States. In 1986 the Committee was chaired by Mr. T. Witschi (Switzerland), the deputy Chairman being Mr. L. C. Kinnander (Sweden).

During 1986 the Committee held two meetings, one in June in Sigtuna, Sweden and one in November in Geneva. The main items discussed were the mutual training of inspectors, the extension of the Convention to other countries, and the broadening of the basic rules of good manufacturing practice (GMP) established under the Pharmaceutical Inspection Convention, by the elaboration of further guidelines on the manufacture of ingredients. The format of inspection reports exchanged under the terms of the Convention and practical aspects of the operation of the Convention were also discussed.

One of the important tasks of the Committee is that of promoting the training of pharmaceutical inspectors of the member countries. This has been carried out so far by means of seminars dealing with various aspects of the manufacture and quality control of pharmaceutical products in relation to the Basic Standards of Good Manufacturing Practice established under the Convention.

The seminars contribute to ensuring uniformity of understanding and interpretation of the Basic Standards on the part of inspectors.

In June 1986 a seminar was organized in Sigtuna, on behalf of the Committee of Officials, by the Swedish pharmaceutical authority. It dealt with the subject of premises for the manufacture of pharmaceutical products. Inspectors and health officials from Convention countries, and from Australia, Canada, Belgium, Italy and Spain attended the seminar.

The Committee of Officials reviewed the means so far provided for the mutual training of inspectors of the PIC Contracting States and discussed possibilities for improvement in the future. A working group has examined the subject and made recommendations to the Committee. One of the possibilities proposed by the working group was the organization of joint visits to pharmaceutical manufacturers by inspectors of different countries. Most members recognized that such visits could facilitate the assurance of common interpretation of the Convention and of a common appreciation of the manufacturing standards applied as compared with PIC rules of GMP.

In view of the increasing number of applications for accession to the Convention, the Committee decided to lay down guidelines setting out in detail a step-by-step accession procedure. Those guidelines were adopted in June 1986 and have proved very useful since their implementation. In the course of 1986 Belgium applied for accession and the Committee of Officials should reach a decision in this respect at its first meeting in 1987. Other European countries which have indicated their intention to join the Convention and have taken the first necessary steps for that purpose are Spain, Italy, Czechoslovakia and France. The Australian, Canadian and US health authorities continued to follow the activities taking place in the framework of the Convention and sent representatives to the PIC Seminars.

Table 8 shows requests received under the Convention for information reports on the general standards of manufacturing practice and Table 9 shows information reports requested by the Board from signatory countries of the Convention.

TABLE 8

**REQUESTS RECEIVED FOR INSPECTION REPORTS UNDER  
THE PHARMACEUTICAL INSPECTION CONVENTION**

	Denmark	United Kingdom
Requests awaiting inspection at 31st December 1985	—	4
Requests received during 1986	<u>1</u> <u>1</u>	<u>8</u> <u>12</u>
Inspections undertaken and Reports completed	1	5
Requests awaiting reports at 31st December 1986	<u>—</u> <u>1</u>	<u>7</u> <u>12</u>

TABLE 9

**REQUESTS MADE BY THE BOARD FOR INSPECTION REPORTS  
UNDER THE PHARMACEUTICAL INSPECTION CONVENTION**

	Austria	Federal Republic of Germany	Finland	Iceland	Switzerland	United Kingdom
Requests awaiting reports at 31st December 1986	—	—	2	—	1	1
Requests made during 1986	<u>1</u> <u>1</u>	<u>1</u> <u>1</u>	<u>1</u> <u>3</u>	<u>1</u> <u>1</u>	<u>1</u> <u>2</u>	<u>2</u> <u>3</u>
Reports received	—	1	2	1	1	2
Requests awaiting reports at 31st December 1986	<u>1</u> <u>1</u>	<u>—</u> <u>1</u>	<u>1</u> <u>3</u>	<u>—</u> <u>1</u>	<u>1</u> <u>2</u>	<u>1</u> <u>3</u>

## 2. POST-MARKETING SURVEILLANCE

### (a) SIDE EFFECTS REPORTED TO THE BOARD DURING 1986

During 1986 the National Drugs Advisory Board received 1,188 reports of adverse reactions from which 2,454 side effects were recorded. These results represent an increase of approximately 20% in reporting.

Thirty-four per cent of side effects were related to drugs affecting the central nervous system (almost half of these concerned analgesics). Just over a quarter of the effects were associated with anti-infectives. These proportions are not too dissimilar from the prescribing patterns, in that anti-infectives account for just under 30% of all prescriptions and drugs affecting the central nervous system for just over 30%.

Seventeen deaths were reported in association with drugs. However of these, four (1 cot death and 3 cardiovascular) were unlikely to be drug-related. Another death with malignant neuroleptic syndrome was likely the consequence of additive toxicity. One death occurred during a radio-graphic procedure. Although use of nomifensine was discontinued in January 1986 two deaths were reported consequent to adverse reactions recorded late in 1985.

Twenty nine drug interactions were reported in 1986. Ten of these were examples of additive effects e.g. hypotension with concurrent use of diuretics, beta-blockers, and vasodilators, or combinations of sympathomimetics. Eight resulted in increased toxicity through addition, and seven interactions related to interference with the effect of one of the drugs. Four were unexpected.

General practitioners were responsible for 39% of the reports, while 19% came from hospitals. Intensive hospital monitoring added a further 7%. Pharmacists supplied 19% of reports and companies almost 16%.

### (b) COMMENTS ON SIDE EFFECTS REPORTED TO THE BOARD DURING 1986

#### Specific matters

1. Four reports of cases of malignant neuroleptic syndrome (MNS) were received, associated with the use of phenothiazine and butyrophenone neuroleptics. Death resulted in one instance in which several phenothiazines were used concurrently. While adequate control of major psychoses is often very difficult, psychiatrists and physicians in general should keep in mind the

increased risk of MNS with higher dosages of these drugs and should be particularly conscious of this when depot intramuscular preparations are being used.

2. Practitioners are increasingly aware of the possibility of drug dependence in patients on prolonged benzodiazepine therapy. While with the longer acting members of the group, the effects of discontinuing therapy are more insidious in onset, the symptoms following withdrawal of short acting benzodiazepines appear early and acutely.

It is generally found that patients who have been on prolonged therapy or have received high dosage will almost all experience agitation, restlessness and anxiety on discontinuing therapy. These may last from a few hours to several weeks and may be very unpleasant.

To minimise such effects, the use of benzodiazepines in therapy should be more restricted, of short duration, (a maximum of 4 to 6 weeks at a time) and with the lowest doses possible.

3. **Lofepramine**

Lofepramine, an antidepressant, the activity of which relies to a significant extent on its conversion to desipramine, has been reported with an increasing number of anticholinergic side effects. When using this drug it is important to appreciate its similarity to the other tricyclic antidepressants.

4. **Mianserin**

For some time it was thought that mianserin was relatively free of the epileptogenic features of the tricyclic antidepressants. Recent reports, however, suggest they may increase cerebral irritability and produce epileptic convulsions.

5. **Non-Steroidal Anti-Inflammatory Drugs (NSAID)**

In 1983 the National Drugs Advisory Board warned of the risk of deterioration in renal function in patients on NSAID in whom such function was already compromised, especially in the elderly. The Board has received reports of significant renal dysfunction associated with most of the drugs in this category, occurring particularly in the older age group with prolonged treatment. It is probable that the prostaglandin synthetase inhibition characteristic of these drugs is the cause.

It is suggested that patients in the older age group and those with known renal dysfunction should have regular monitoring of renal function during prolonged use of NSAID.

In addition a number of cases of renal papillary necrosis have occurred in association with aspirin, indomethacin, ibuprofen and naproxen. The mechanism of this reaction is not fully known.

6. **Aminophylline/Theophylline**

Of those products for oral use containing the above, all but a very few are of the sustained release type. A number of the reported side effects have been associated with the concurrent use of short-acting and long-acting dose forms, while others have occurred as a result of the inappropriate timing of dosage of the sustained release forms. It is important that these be used in a regimen which takes account of the pattern and duration of their pharmacological action. Experience has clearly shown that the differences in release characteristics of the various sustained-release formulations do not permit interchange of the different products. The patient requires a separate and distinct regimen if there is a need to change from one product to another.

7. **Nifedipine**

This substance, a calcium channel blocker used for the management of hypertension, has been associated with a number of unexpected side effects, some of which are probably due to hypersensitivity; others possibly arise following prolonged use. Reactions include pancytopenia, hepatitis and peripheral neuropathy; more recently, gingival mucosal hyperplasia has been reported.

8. **Oestrogen and Progestogens**

The Board noted that the so called 'low dose' oestrogen: progestogen combinations and a progestogen alone have been associated with a number of reports of thromboembolic disease. Practitioners should continue to keep any patients on such agents under close and regular surveillance even if the dosages of the oestrogen and progestogen are low even if progestogen alone is used.

9. **Erythromycin**

A few reports have been received of changes in auditory acuity and vestibular function associated with use of erythromycin. While this macrolide has been relatively free of such problems, the possibility of ototoxicity should be kept in mind especially if high dose regimens are used.

## 10. Contrast Media in Radiography

The many potentially serious side-effects reported in association with these agents highlight the need for the immediate availability of trained personnel and adequate resuscitation facilities whenever systemic parenteral contrast media are being administered.

## NOTICES SERVED TO DOCTORS, DENTISTS AND PHARMACISTS

### 1. Aminophylline/Theophylline

Most of the oral preparations currently available containing the above active substances are of the 'sustained release' type, i.e. delivering the drug by slow release in the intestinal tract over hours after administration.

Such a delivery system allows a reduced frequency of dosage, once or at most twice daily, and generally avoids the peaks in plasma levels associated with adverse reactions.

However, each sustained release formulation has its own individual characteristics and as a consequence, the different formulations are not interchangeable. Should the doctor wish to transfer his patient from one product to another he should change first to conventional dose forms and then titrate dosage with the alternative sustained release formulations.

### 2. Benzodiazepines

The benzodiazepine tranquillisers used as anxiolytics and as hypnotics have been available for over 25 years. They have now replaced barbiturates and have proved of great therapeutic value, with relative freedom from side effects.

These properties, have led to extensive and prolonged use. Unfortunately in the last 10 years it has become obvious that most of the benzodiazepines are capable of inducing dependence if use is extended over months. This is of particular importance in the case of the benzodiazepines used as anxiolytics.

While the Board has noted a general decrease in the number of patients receiving the tranquillisers in the past 10 years, it has also found that there are still many patients maintained on benzodiazepines for periods of several years without interruption.

It is a characteristic of the benzodiazepines that their anxiolytic and hypnotic effects continue with prolonged use and do not usually require "topping up" by an increase in dosage. As a consequence it is all too easy to renew prescriptions continually. Nonetheless, to avoid dependence production it would be wise to keep the duration of use short — 4 to 6 weeks at the most — and using the lowest therapeutically effective dose.

Discontinuation of therapy will not then lead to

the appearance of unpleasant symptoms of withdrawal such as agitation, restlessness and anxiety.

## (c) SPECIAL POST MARKETING SURVEILLANCE 1986

### 1. Alprazolam

The National Drugs Advisory Board has received only a few reports of side-effects associated with this substance during 1986 (an incidence of 0.5%), consisting mainly of rashes.

### 2. Amiodarone

This drug, use of which is restricted, has been associated with reports of side-effects during 1986, the most significant of which related to persistent abnormalities in liver function. The total incidence of side effects was 4.2%.

### 3. Captopril

This drug, available in general practice as an antihypertensive, had a reported incidence of side effects of 0.25% during 1986. An additional point of interest noted was the apparent greater sensitivity in the elderly to adverse effects.

### 4. Enalapril

Since the recent introduction of this medication on to the market, side effects were reported as occurring in association with this drug with an incidence of 2%. Special attention was drawn to the occurrence of renal dysfunction.

### 5. Nabumetone

An incidence of 3% has been recorded for side effects reported in association with this drug during 1986. Of importance to note are reports of peptic ulceration, gastrointestinal bleeding, and thrombocytopenia — i.e. the pattern generally associated with non-steroidal anti-inflammatory drugs.

### 6. Ranitidine

An incidence of 0.17% has been recorded for side effects reported in association with this drug. One case of hepatitis was reported but a full relationship has not yet been established.

## (d) CONGENITAL ABNORMALITIES

During 1985 there was a significant increase in the number of congenital abnormalities observed in the four Dublin maternity units under observation. The total incidence almost reached the peak recorded in 1980. The increase appeared to be due to a rise in numbers of cases of Down's Syndrome,

congenital heart disease and limb deformities. No relationship can as yet be established between these results and drug ingestion or viral infections during 1984. (See Table 10)

## **(e) DRUGS SPECIALLY CONSIDERED**

### **Canthaxanthin**

The Board has informed any companies known to have marketed medical preparations containing canthaxanthin in Ireland, (i.e. many 'suntan' products) that these will not be recommended for authorisation in view of the risk of ocular toxicity with prolonged use.

### **Eye Drops**

**(5% guanethidine + 1% adrenaline)**

**(5% guanethidine + 0.5% adrenaline)**

In November 1986, the two higher strengths (named above) of these eye drops were voluntarily withdrawn from the market after reports of cicatrizing changes of the conjunctiva and cornea in some patients who had been on continuous therapy for a number of years.

It is known that guanethidine and/or adrenaline topical preparations have the potential to cause hyperaemia and inflammatory changes in the conjunctiva, and reversible cicatrizing changes have previously been reported as a sequel of such prolonged inflammation.

The changes are slow in onset (over 1-2 years), and regular six monthly examination of the conjunctiva should allow treatment to be discontinued in those patients who have started to develop cicatrization before irreversible change occurs. Nevertheless, since it is not always possible to guarantee a six monthly slit-lamp examination in patients on continuous therapy, the two higher strengths were voluntarily withdrawn and stocks recalled.

The incidence of adverse effects is considerably reduced with the lower strength preparations (3 + 0.5, and 1 + 0.2). It is important however, to conduct slit-lamp examinations of the cornea and conjunctiva at six monthly intervals in patients on such continuous therapy, so that it may be withdrawn at the first sign of conjunctival damage.

### **Mianserin ("Tolvon") and blood dyscrasias**

To date, 279 cases of white blood cell disorders, usually granulocytopenia or agranulocytosis, have been reported in approximately 11 million patients treated world wide — none has so far been reported in Ireland. The reactions have usually occurred after 4-6 weeks treatment, were generally reversible on cessation, and whilst observed in all age groups, appeared to be more common in the elderly.

It is important that patients be kept under regular review, especially in the early stages of treatment. A full blood count is recommended every four weeks in the first three months of therapy, with continued clinical monitoring thereafter, especially for signs of infection such as fever, sore throat, and stomatitis. Should any of these symptoms develop in a patient on mianserin, treatment should cease and a full blood count be carried out.

### **Sustained-Release Preparations**

An increasing number of established active ingredients is being formulated as sustained or controlled release preparations in addition to standard dose forms. Theophylline-containing products, analgesics, some non-steroidal anti-inflammatory drugs, nitrate coronary vasodilators, some  $\beta$ -adrenoceptor blockers are examples.

The Board is concerned that prescribers should not assume that all sustained release formulations of the same active ingredient are bioequivalent when presented by different manufacturers. A number of reports have come to the attention of the Board in which loss of therapeutic control or even adverse effects have resulted when patients stabilised on one sustained release preparation have been transferred to another.

Doctors should therefore maintain their patients on the particular preparation which has given satisfactory control. If it is deemed necessary to change, it may be preferable to transfer to conventional dose forms before restabilising on an alternative sustained release formulation. In any event the patient should be kept under regular surveillance until optimal control has been re-established.

### **Labelling statements in relation to "inactive" ingredients**

Certain ingredients in formulations of medical preparations, regarded as 'inactive' in terms of therapeutic effects may be of significance for patients with particular disorders. Obvious examples include sucrose for patients with diabetes mellitus, alcohol, parabens in patients with aspirin or local anaesthetic hypersensitivity, gluten in persons with enteropathy.

The Board recommends that the presence of such agents in a formulation should be stated on the label for the benefit of the prescriber, dispenser and consumer. It is possible that there will be an increasing number of such ingredients, but at present the need for such statements is being negotiated individually.

TABLE 10

## TOTAL NUMBER OF CONGENITAL ABNORMALITIES FOR COOMBE, NATIONAL MATERNITY, ROTUNDA AND ST. JAMES HOSPITALS

Number		1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985
270-272	Congenital Disorders of Metabolism	0	2	3	3	3	6	0	9	5	5	9
740	Anencephalus	66	52	63	65	67	42	30	29	19	28	18
741.0	Spina Bifida with Hydrocephalus	22	13	17	21	22	23	8	15	6	12	18
741.9	Spina Bifida without Hydrocephalus	38	11	18	20	11	15	18	23	8	9	6
742	Hydrocephalus	12	19	31	19	14	15	9	3	8	8	6
743	Congenital Abnormalities of the Nervous System other than those above	19	15	21	16	23	11	15	9	7	6	13
743.3	Spinal Cord Congenital Abnormalities (i.e. Myelias)	7	17	21	18	15	14	9	3	4	1	27
744	Congenital Eye Abnormalities	0	0	0	6	6	15	8	4	2	5	22
745	Congenital Abnormalities of Ear, Face, Neck (NOT including Cleft Palate)	17	2	10	64	44	26	7	13	13	17	17
746	Congenital Abnormalities of Heart	54	43	43	69	69	123	41	29	37	30	94
747	Congenital Abnormalities of Circulatory System	7	3	3	8	0	37	1	17	8	7	12
748	Congenital Abnormalities of Respiratory System	11	18	17	4	17	17	11	8	6	7	20
749	Cleft Palate and Hare Lip	14	18	9	32	27	29	29	10	21	8	22
750	Congenital Abnormalities of the Alimentary Tract above the Pylorus. (NOT including Cleft Palate)	18	8	5	14	19	23	17	12	15	12	21
751	Congenital Abnormalities of the Alimentary Tract below the Pylorus including Anus, Liver and Umbilical Hernias	18	16	13	20	22	85	30	25	21	14	31
752	Congenital Abnormalities of Genital Tract — Male and Female	12	3	11	21	36	84	62	24	41	43	70
753	Congenital Abnormalities of Urinary Tract including Bladder, Ureter and Urethra	19	16	10	43	48	112	16	26	33	17	60
754	Talipes (Club Foot etc.)	34	14	22	38	58	77	88	42	73	86	134
755	Congenital Abnormalities Limbs NOT Talipes	64	23	21	115	44	134	72	113	12	91	143
756	Congenital Abnormalities Musculo-Skeletal System including Skull if no Brain Damage — NOT including Limbs but including Diaphragmatic Hernias	18	20	15	45	55	45	43	19	64	33	47
757	Congenital Abnormalities of the Skin, Hair and Nails	45	4	0	26	57	41	32	189	34	33	35
758	Congenital Abnormalities of the Endocrine System and Spleen	8	7	2	6	5	2	2	0	4	5	10
759	Gross or Multiple Congenital Abnormalities (i.e. Monsters etc.)	5	10	19	26	9	10	6	3	4	1	1
759.3	Mongolism or Down's Syndrome	24	18	18	41	33	43	32	15	24	13	46
759.5	Sex Chromosome Abnormalities	10	12	6	13	7	29	13	38	4	6	6
Total No. of Congenital Abnormalities .....		542	364	398	753	711	1058	598	678	478	495	888
Total No. of Live Births .....		21555	22154	22554	23653	24262	25081	24583	23586	22455	21680	21483
Total No. of Deliveries .....		24055	22885	23416	24479	24426	25312	24660	25202	23891	22490	22878
% Incidence of Congenital Abnormalities .....		2.0%	1.42%	1.71%	3.18%	2.91%	4.17%	2.42%	2.69%	2.0%	2.20%	3.88%

## Drugs Information Books

During 1986, the Board issued the following publications to medical and dental practitioners and to pharmacists:-

- (a) Drugs Information Book No. 32 —  
MEDICATIONS IN THE ELDERLY
- (b) Report of Side-Effects Associated with the  
Use of Drugs — 1985

## (f) SAMPLING AND ANALYSIS OF MEDICAL PREPARATIONS

A total of 150 samples were submitted to the Public Analyst's Laboratory, Regional Hospital, Galway, for analytical testing under the agreement between the Western Health Board and the National Drugs Advisory Board, on which a total of 3,093 tests were carried out. The results are presented in Table 11.

TABLE 11  
SAMPLING AND ANALYSIS OF MEDICAL PREPARATIONS 1986

	Drug Substances	P.A. Applications	Inspector's Samples	Preparations taken from Market	Suspected Defective Products	Adverse Reactions Reported	Total
Samples awaiting results on the 31st Dec. 1985	—	—	—	29	—	—	29
Samples submitted	18	51	8	63	6	4	150
	<u>18</u>	<u>51</u>	<u>8</u>	<u>92</u>	<u>6</u>	<u>4</u>	<u>179</u>
Satisfactory Results	17	47	7	76	2	3	152
Unsatisfactory Results	—	1	1	—	1	—	3
Samples awaiting results on the 31st Dec. 1986	1	3	—	16	3	1	24
	<u>18</u>	<u>51</u>	<u>8</u>	<u>92</u>	<u>6</u>	<u>4</u>	<u>179</u>

The 18 samples in respect of drug substances were submitted for testing to ensure conformity with specifications.

The 50 samples in respect of applications for product authorisation to market medicinal products were submitted for assay to verify the analytical methods submitted by the applicant.

In relation to the 3 samples where unsatisfactory results were reported, the matter was taken up with the companies concerned. In the case of the inspector's sample, this result necessitated further work on the company's assay method and this work was continuing at the end of the year. In the case of the sample submitted by a retail pharmacist when reporting a quality defect, this defect was rectified by the introduction of a quality control check on an excipient.

In the remaining case, the company's method of assay was unsatisfactory and the matter was being pursued with the company at the end of the year. The product authorisation held by the company was suspended pending a resolution of the problem.

## (g) RECALLS

During 1986, the Board was notified of 7 recalls of medical preparations from the market in Ireland.

Six of these recalls were notified to the Board by the companies concerned who kept the Board informed of the action taken at all stages and the outcome of the withdrawal. The remaining recall was notified to the Board by a hospital and all stocks of the suspected batch were immediately withdrawn and destroyed.

## (h) QUALITY DEFECTS

Fifty-three quality defects were reported in various products during 1986. None of these required batch recall. Most were defects in the physical characteristics of the products which were corrected by changes in manufacturing procedures. Classification of the quality defects reported are shown in Table 12.

TABLE 12  
QUALITY DEFECT REPORTS 1986

Class of Preparation	Total No. of Reports	No. of Defects Proved	Container	Labelling	Physical Characteristics	Chemical Properties	Contamination Particles	Micro-biological
Large Volume Parenterals	0							
Small Volume Parenterals	7	2	1		1			
Solid Unit Dose Forms	30	29	1	2	26			
Liquids, Oral Suspensions	5	4			1		2	1
Topical Preparations	2	1			1			
Paste	1							
Powder	1	1		1				
Inhalers	5	4			4			
Eye Drops	2	1			1			
<b>TOTALS</b>	<u>53</u>	<u>42</u>	<u>2</u>	<u>3</u>	<u>34</u>	<u>0</u>	<u>2</u>	<u>1</u>

Eleven reports related to side effects with no defect in quality.

### 3. CLINICAL TRIALS

#### Clinical Trials

The Board considered 218 applications for clinical trial approval in 1986. The majority concerned preparations in advanced stage of development or already on the market. Of these about half related to bioavailability or pharmacokinetic studies in special groups.

Of the total applications received 198 were approved, with some modification in 15 of the protocols provided. Approval was in all cases subject to the conditions outlined in the Board's Annual Report 1985.

#### Legislation on Conduct of Clinical Trials

The opportunity was afforded to the Board amongst other interested bodies to make comments in depth on the progressive drafting of the Clinical Trial Bill in its progress through the various legislative stages. Many provisions already applied by the Board in its contact with clinical trialists will be reflected in the legislation. It is hoped that in the near future the roles, responsibilities and protection for intending investigators and participants will be clearly and satisfactorily defined.

### 4. VETERINARY MEDICINES

The European Communities (Veterinary Medicinal Products) Regulations 1986 will come into effect on 1st January 1987.

The purpose of these Regulations is to give statutory effect in this country to the requirements of the two EEC Directives (81/851/EEC and 81/852/EEC) relating to veterinary medicinal products.

The principal effects of these Regulations are:-

- (a) to require that a person shall not place a new veterinary medicinal product on the market on or after 1st January 1987 save in accordance with the provisions of EEC Council Directive 81/851/EEC and with a product authorisation granted or renewed by the National Drugs Advisory Board which has been designated the competent authority for the purpose of these Regulations;
- (b) to require that a person shall not manufacture a veterinary medicinal product or import such a product from a country other than a Member State of the EEC save in accordance with EEC Council Directive 81/851/EEC and with a manufacturer's licence granted or renewed by the National Drugs Advisory Board; and
- (c) to require the progressive application of the Directives to veterinary medicinal products which were on the market prior to 1st January 1987.

During 1986 the Board appointed a Veterinary Committee under the Chairmanship of Mr. P. F. Nowlan. The main responsibilities of this Committee are the evaluation of the safety, quality and efficacy of veterinary medicinal products with

particular reference to the target species involved and man. (The names of the members of this Committee on 31st December 1986 are shown on the facing sheets of this report).

To facilitate compliance with the European Communities (Veterinary Medicinal Products) Regulations 1986 the Committee has drawn up a number of guidelines for use by applicants for veterinary medicinal product authorisations or for veterinary medicinal product manufacturing licences. The former are in formats similar to those outlined in the Directives 81/851/EEC and 81/852/EEC.

Copies of the following guidelines are being circulated to the industry and additional copies may be obtained from the Board's offices.

1. Guidelines for Applications for Product Authorisations in respect of Veterinary Medicinal Products containing Novel Active Ingredients.
2. Guidelines for Applications for Product Authorisations in respect of Veterinary Medicinal products containing Established Active Ingredients.
3. Explanatory Leaflet for Manufacturers.

Attention is drawn to the requirements that all manufacture of veterinary medicinal products within the State is subject to licensing as of 1st January 1987, and that any veterinary medicinal product must be authorised prior to its introduction onto the market.

The review of veterinary medicinal products is due to commence and applications for authorisation for products in the first category should be forwarded as soon as possible to the Board. The order of review is tabulated below together with the dates by which products of the class specified require authorisation:

## Fees for Veterinary Licences

In October 1986, the Board was informed by the Department of Health that the fees for veterinary licences would be at the same level as those for human medicines. The proposed fee structure for veterinary licences which has been established by the Minister for Health with the consent of the Minister for Finance is as follows:

Fees commencing  
on 1st January 1987

### Type of Licence

Manufacturing licence	£880
	*£440

### Product Authorisations

(a) New products	£560
(b) Review products	£284
(c) Additional dosage strengths	£115

\*Where the applicant holds a licence to manufacture human medicines and intends to manufacture veterinary medicines on the same premises the fee payable for the veterinary manufacturing licence is £440 — which will represent half the human medicine fee from 1st March 1987.

## 5. OTHER MATTERS

### The Federation of Irish Chemical Industries

During 1986, exchange of views of matters of mutual interest continued between the Board and the Federation of Irish Chemical Industries.

On the 3rd June 1986, a meeting was held between officers of the Board and representatives of the Federation's Proprietary Medicines Division Standing Committee to discuss the steps to be taken in relation to the marketing of aspirin-containing preparations in the light of a preliminary report on Reye's Syndrome. It was agreed that the following precautionary measures

Class of Veterinary Medicinal Product	Specified Date
Products of the following classes on the market before 1st January 1987.	
(a) Oestrogenic, androgenic and gestagenic hormones; anabolic agents; penicillins	(a) 1st October 1987
(b) Cephalosporins and other anti-infectives	(b) 1st October 1988
(c) Corticosteroids and other hormones; autocoids; anthelmintics; antifungals; antiparasitics; metabolic and haematinic drugs	(c) 1st October 1989
(d) Substances affecting the central nervous system, including anaesthetics, tranquillisers, stimulants, and analgesics; anti-inflammatory agents; diuretics and substances acting on the cardiovascular system	(d) 1st October 1990
(e) Substances acting locally i.e. on skin, eye, ear, nasopharynx, gastrointestinal tract, etc. Diagnostic agents	(e) 1st October 1991
(f) Miscellaneous not included above	(f) 1st October 1991

Applicants are reminded that the necessary applications must be made 12 months prior to the dates specified above.

should be taken:-

1. All paediatric dose forms of aspirin will be confined to pharmacies, to be supplied on prescription only.
2. All aspirin-containing preparations will carry an additional warning on the pack — "This product should not be given to children, particularly those under twelve years of age, without medical advice".

A meeting took place on the 22nd July 1986 between members of the Board and its officers and representatives of the Federation to discuss the Federation's views on the Clinical Trial Bill 1986. The following topics were covered in the discussion:- definition of a clinical trial; range of studies included within that definition; role of the National Drugs Advisory Board and/or other scientific bodies; ethics committees; participants and informed consent; insurance matters; information and reports relevant to a clinical trial; transitional provisions.

The Federation's views were sought on the draft "Guidelines for the Manufacture of Active Starting Materials" prepared by the Committee of Officials of the Pharmaceutical Inspection Convention. Correspondence ensued with the Federation on the "Report of the Working Party Convened by the Faculty of Paediatrics of the R.C.P.I. on the Packaging of Drugs in relation to Child Safety"; on its opposition to the level of fees proposed for the veterinary medicines licensing schemes and on the question of the availability of aspirin and paracetamol-containing preparations.

### **Irish Pharmaceutical Union**

During 1986, correspondence took place with the Union on its poster for display in pharmacies warning of the dangers of giving analgesics to children and on products confined to pharmacies. In November the views of the Union were sought by the Board on the availability to the consumer of products containing either aspirin or paracetamol as a single active ingredient. It is expected that discussions will take place with the Union on this matter in 1987.

### **Medical Devices**

No progress was made on the question of the introduction of an Irish register of manufacturers of sterile medical devices and surgical products during 1986. A number of queries was received from overseas companies seeking information on the legislation governing such products in Ireland.

The Board is still awaiting a response from the Department of Health in relation to its request, referred to in the 1985 Annual Report, for discussions with a view to establishing a more formal arrangement for the inspection of such manufacturers by its Inspector.

### **Pharmaceutical Society of Ireland**

In November 1986, the views of the Society were sought by the Board to assist it in its consideration of the availability to the consumer of products containing either aspirin or paracetamol as the single active ingredient. It is expected that discussions on this subject will continue into 1987.

### **W.H.O. Fellowships**

During the week commencing 10th March 1986, the Board provided a training programme for two World Health Organisation fellows from Pakistan.

Visits to a number of pharmaceutical manufacturing and wholesaling companies were included in this programme. The Board is appreciative of the co-operation and hospitality extended to the visiting pharmacists by these companies during their visits.

## **6. GENERAL**

### **Board**

The names of the members of the Board and its Committees on 31st December 1986 are shown on the facing sheets of this report.

The Board was informed on the 5th March 1986 that Dr. Maura O'Dwyer had been reappointed, by the Minister for Health, to membership of the Board for the period ending 11th July 1989. On the 29th August 1986, the Board was informed that Professor K. O'Malley had been reappointed Chairman of the Board by the Minister for Health for the period ending the 11th July 1989. Professor M. G. T. Webb was also re-appointed to the Board for the same period and Dr. Kathleen McGarry, Our Lady's Hospital, Navan was appointed to replace Dr. P. Brennan.

The Board passed, at its September meeting, a vote of thanks to Dr. Brennan for his considerable contribution to its deliberations during his period of membership, where his knowledge, opinion and common sense were of great value to the Board in reaching its decisions.

At the same meeting, the Board established its third Committee — the Veterinary Committee. Details of its composition and responsibilities are described elsewhere in this Report.

A formal presentation of the Board's Annual Report for 1985 was made to the Minister for Health, Mr. Barry Desmond, T.D., after the September meeting of the Board. This presentation was attended by the members and staff of the Board, representatives of the national daily newspapers and of the medical and pharmaceutical press. The presentation was followed by an informal reception.

In November 1986, Dr. B. S. Duffy tendered his resignation as a member of the Board to the Minister for Health. The Board regretted the loss of his expertise in its deliberations and, as in the case of Dr. Brennan, passed a vote of appreciation for his contribution to the Board's work during his period of membership.

The Board, the Committee on Evaluation and Toxicity and the Committee on Drug Usage and Adverse Reactions each held 10 meetings during the year and five meetings of the Veterinary Committee were also held. In addition, a special meeting of the Board took place on the 4th April 1986 to discuss the Report to the Department of Health on the Review of the National Drugs Advisory Board undertaken by Craig Gardner, Management Consultants.

### **Management Consultancy Assignments — Craig Gardner**

In December 1985, the Department of Health appointed Craig Gardner, Management Consultants to undertake a management consultancy assignment to assist the Minister for Health and the Board in determining its immediate and future needs.

The terms of reference for the review were as follows:

1. to examine and report on the adequacy of the existing constitution and management structure of the Board in the light of its present envisaged functions and responsibilities;
2. to make recommendations on the staffing levels (numbers and types) required for the efficient discharge of the Board's functions;
3. to examine and report on the procedures and systems required to discharge the Board's functions and to identify any ideas where cost-effective computerised systems might be installed.

A Project Control Group was established to undertake the following functions:—

- (a) to agree, and modify where appropriate, the direction of the study and the assignment Work Programme;
- (b) to consider the first drafts of the plans emerging from the various tasks, understand the basis, nature and implications of recommendations, and obtain approval thereof;
- (c) to provide guidance to the consultants on any matters arising during the course of the work.

Several meetings of the group took place in the early part of the year

Interviews and meetings took place during January and February with the appropriate officers of the Department of Health; some members of the Board; the entire staff of the Board; the appropriate officers of the Department of Agriculture, the Federation of Irish Chemical Industries and the appropriate officers of the Department of Health and Social Security and the Central Veterinary Laboratory in the United Kingdom.

The final report was presented to the Department of Health in March 1986 and the consultants recommendations were set out under the following headings:

### **1. The Organisational Plan**

- (i) the Board to become the competent authority for both the human and veterinary schemes and, in due course, for clinical trials and medical devices;
- (ii) the Board to assume a wider policy and management role and that the Committees finalise detailed assessment and inspection work;
- (iii) the internal management systems to be changed to accommodate the executive role;
- (iv) an extra Committee to be established to deal with veterinary products;
- (v) the post as Medical Director to become a post as Chief Executive with changes in role and responsibilities;
- (vi) four heads of function viz. pharmacy, medical, veterinary and administration to report to the Chief Executive;
- (vii) all support services to be centralised under the Board Secretary;
- (viii) the composition of the Board to be altered to take account of its enhanced role;
- (ix) changes to take place in relation to appeals, and enforcement;
- (x) less work to be submitted to Committee and Board levels.

### **2. The Systems Plan**

- (i) two computer systems to be installed, one to provide word processing and one to provide systems for application tracking, adverse reactions recording and fee accounting;

- (ii) detailed changes to take place in systems and procedures which will produce clerical savings in the following areas: assessment work; work related to inspections; adverse reactions recording work; other general clerical activity.

### 3. The Staffing Plan

- (i) the required increase in capacity to deal with existing and new work to be provided through a combination of: additional posts; computerisation; changes in work practices,
- (ii) the following seven additional posts to be created: one Senior Pharmacist; one Senior Veterinary Assessor; one Medical Assessor; one Pharmacist Inspector; one Veterinary Assessor; one Assistant Secretary and one Clerk/Typist,
- (iii) staffing levels to be reviewed if the assumptions on which they are based should alter;
- (iv) changes in work practices to be introduced to increase productivity.

### 4. Other Issues

- (i) consideration to be given to the need to replace key people over the next period of years when recruiting to fill the additional posts recommended;
- (ii) opportunities for greater bilateral cooperation with other regulatory bodies to be explored;
- (iii) sampling work to be increased;
- (iv) the fee system to be fundamentally reviewed;
- (v) a planned approach to be adopted to implementation of the recommendations in the report.

The Board considered this Report at a special meeting on the 4th April 1986 and its comments thereon were submitted to the Department of Health on the 15th April 1986. A meeting between representatives of the Board and the Department of Health took place on 30th April 1986 to discuss the Report and the Board's comments. The Department was in general agreement with the recommendations of Craig Gardner in relation to the organisation, systems and staffing appropriate to the Board's developing role. The Board, on the

other hand, had serious reservations in relation to the conclusions and recommendations of the Report particularly with regard to the limited staffing proposals made in the report as being adequate to meet the Board's expanded role. In this regard, the Board emphasises the need to review the staffing levels if the assumptions on which they are based should alter.

Co-operation with the consultants, on the Review of the Board, by the unionised staff of the Board was received on the 10th January 1986 following consideration by the Local Government and Public Services Union of the terms of reference, background and objectives for the Review on the basis of a number of conditions being agreed. In particular, the recommendations on staffing levels (numbers and types) were to be the subject of direct discussions with the Union. The Union, following consideration of the Report, submitted its comments thereon to the Board on the 7th August 1986 and a meeting, between representatives of the Board and the Union took place on the 13th August 1987 to discuss these comments. In general, the views of the Board and the Local Government and Public Services Union coincided to a large extent.

On the 26th August 1986, Craig Gardner submitted a plan, at the request of the Board, for the design, development and implementation of word-processing and computer systems recommended in their Report. The Board authorised Craig Gardner to proceed to the first stage of the systems development plans (i.e. the completion of the specifications for the word-processing and systems requirements) following a meeting of its Steering Committee on Computerisation which was established to oversee this consultancy assignment. Following interviews with the appropriate officers of the Board, Craig Gardner submitted its report "Application Systems Requirements Specifications" to the Board on the 1st December 1986. This report was considered by the Steering Committee on 5th December 1986 and by the Board at its meeting on the 16th December 1986. The Board agreed that Craig Gardner should proceed to the next stage of its investigations on the basis of the recommendations made in its report.

### Staff

The number, sex, title/grade of the staff of the Board are shown in Table 12.

Over recent years, references were made in Annual Reports to the staff difficulties experienced by the Board. Following the submission of the Board's comments on the "Review of the National Drugs Advisory Board" undertaken on behalf of the Department of Health by Craig

Gardner, Management Consultants, discussions were held with the appropriate officers of the Department of Health on the level of staffing necessary to undertake the additional work which would devolve on the Board in implementing the requirements of the E.E.C. Veterinary Directives and in clearing the backlog of work arising from the human medicines licensing scheme.

Accordingly, the approval of the Minister for Health was conveyed to the Board on the 25th September 1986 for the creation of the following permanent and temporary posts:—

# 1. Professional Staff

- (a) *Permanent Posts*  
 1 — Senior Veterinary Officer  
 1 — Veterinary Officer  
 1 — Senior Pharmacist  
 1 — Inspector  
 1 — Medical Assessor
- (b) *Temporary Posts*  
 2 — Pharmacists

TABLE 13  
 NUMBER OF STAFF EMPLOYED BY THE BOARD 1979-1986

TITLE/GRADE		Staff of the Board at 31st October											
		1979		1980		1981		1982		1983		1984	
		M	F	M	F	M	F	M	F	M	F	M	F
<b>Medical</b>													
Medical Director	(a)	—	1	—	1	—	1	—	1	—	1	—	1
Deputy Medical Director		—	1	—	1	—	1	—	1	—	1	—	1
Medical Assessor		—	1	—	1	—	1	—	1	—	1	—	1
Adverse Reactions Recording Secretary		—	1	—	1	—	1	—	1	—	1	—	1
<b>Pharmaceutical</b>													
Pharmacists		1(b)	3	1(b)	3	1(b)	3	1(b)	3	1	3	1	3
Inspector		1	—	1	—	1	—	1	—	1	—	1	—
<b>Administrative &amp; Clerical</b>													
Secretary		1	—	1	—	1	—	1	—	1	—	1	—
Assistant Secretary		1	—	1	—	1	—	1	—	1	—	1	—
Clerical Supervisor Grade IV		—	—	—	—	—	—	—	1	—	—	1	—
Clerk/Typist Grade III		—	2	—	2	—	3	—	3	—	3	—	3
Clerk/Typist Grade II		—	8	—	7	—	7	—	8	—	8	—	8(c)
Paperkeeper/Messenger		1	—	1	—	1	—	1	—	1	—	1	—
		5	17	5	15	5	17	5	19	5	19	5	19
TOTAL		22		20		22		24		24		24	

(a) M — Male; F — Female

(b) One part-time pharmacist

(c) Two temporary Clerk/Typists — Grade II to replace permanent officers on career breaks.

## 2. Administrative/Clerical

- (a) *Permanent Posts*
  - 1 — Clerical (Health Board — Grade IV)
  - 1 — Clerical (Health Board — Grade III)
- (b) *Temporary Posts*
  - 8 — Clerk/Typists (Health Board — Grade II)

Negotiations with the Local Government and Public Services Union on the proposed level of staffing took place during October and despite the Union's reservations regarding the proposal to create "temporary" positions agreement was achieved with the Union to co-operate with the Board's new functions in the field of veterinary medicines as soon as the additional staff was recruited and a number of issues in relation to the grading of existing staff were resolved.

These posts were advertised in the national daily newspapers and the appropriate professional journals in October 1986 and interviews were held during November and December. It is expected that appointments to these posts will be made early in 1987.

Because of the pressure of work, attendance at training courses by the Board's professional, administrative and clerical staff was severely curtailed. Mrs. Beatrice Hughes completed her course of lectures in biotechnology at the National Institute for Higher Education in Glasnevin in February 1986. The National Institute of Biological Standards and Control in London kindly provided a special programme of training for Mrs. Mary Rafter on blood products, viral products and bacterial products for one week in July 1986. The Board is indebted to the Institute for its assistance in arranging this programme.

The Board approved career breaks for two of its Clerk/Typists — Grade II.

No new measures designed to promote further the achievement of equal opportunity between men and women were adopted during the year. In the light of the present staff structure (as set out in Table 13), it is felt that the existing measures meet acceptable standards.

**7. STATEMENT OF ACCOUNTS  
OF  
NATIONAL DRUGS ADVISORY BOARD  
FOR THE YEAR ENDED  
31st DECEMBER 1986**

**AUDITORS' REPORT  
TO THE MEMBERS OF NATIONAL DRUGS ADVISORY BOARD**

We have audited the annexed accounts in accordance with approved Auditing Standards. In our opinion, proper books have been kept by the Board and the accounts as set out are in accordance therewith. We received all the information and explanations which we considered necessary for our audit and in our opinion, the accounts give a true and fair view of the state of affairs of the Board as at 31 December 1986 and of its operation for the year ended on that date.

*Touche Ross & Company  
Chartered Accountants.*

**NATIONAL DRUGS ADVISORY BOARD**

**63/64 ADELAIDE ROAD, DUBLIN 2**

**INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED**

**31st DECEMBER 1986**

	<b>1986 IR£</b>	<b>1985 IR£</b>
Income Receivable (Note 1)	654,728	522,471
Less: Expenditure (Schedule A)	<u>671,721</u>	<u>624,555</u>
Excess of (Expenditure over Income)	(16,993)	(102,084)
Taxation	<u>(9)</u>	<u>(988)</u>
	(17,002)	(103,072)
Balance brought forward: 1 January 1986	<u>21,427</u>	<u>124,499</u>
Balance carried forward: 31 December 1986	<u><u>4,425</u></u>	<u><u>21,427</u></u>

# NATIONAL DRUGS ADVISORY BOARD

63/64 ADELAIDE ROAD, DUBLIN 2

## SCHEDULE A

### SCHEDULE OF EXPENDITURE FOR THE YEAR ENDED

31 DECEMBER 1986

	1986 IR£	1985 IR£
<i>Establishment:</i>		
Rent and Rates	129,579	127,876
Insurances	6,251	14,084
Repairs and Maintenance	19,831	14,804
Light and Heat	9,004	7,459
Cleaning	11,157	11,055
Depreciation (Note 3)	11,433	8,835
	<u>187,255</u>	<u>184,113</u>
<i>Administration:</i>		
Wages and Salaries (Note 2)	325,766	310,459
Travel Expenses	22,066	23,616
Printing, Postage & Stationery	57,935	54,179
Publications & Subscriptions	5,798	7,475
Leasing Charges	2,090	2,394
Sampling and Analysis	26,049	24,083
Advertising	13,704	—
Computer Analysis	—	100
Assessment Fees	—	6,071
Consultancy Charges	19,420	—
Auditors Fees	1,600	1,500
Legal Fees	625	1,377
Telephone and Telex	8,264	7,307
Sundry Expenses	1,001	1,733
	<u>484,318</u>	<u>440,294</u>
<i>Financial:</i>		
Bank Interest and Charges	<u>148</u>	<u>148</u>
	<u>148</u>	<u>148</u>
<b>Total Expenditure</b>	<b><u>671,721</u></b>	<b><u>624,555</u></b>

**NATIONAL DRUGS ADVISORY BOARD**  
**63/64 ADELAIDE ROAD, DUBLIN 2**  
**BALANCE SHEET AS AT 31 DECEMBER 1986**

	1986		1985	
	IR£	IR£	IR£	IR£
<i>Fixed Assets (Note 4)</i>		16,567		15,010
<i>Current Assets</i>				
Debtors and Payments in Advance	8,526		805	
Stock of Stationery and Oil	5,998		6,790	
Cash on Hand and at Bank	<u>1,815</u>		<u>5,856</u>	
	<u>16,339</u>		<u>13,631</u>	
<i>Less: Current Liabilities</i>				
Accrued Expenses	25,389		7,214	
Bank Overdraft	<u>3,092</u>		<u>—</u>	
	<u>28,481</u>		<u>7,214</u>	
<i>Net Current (Liabilities)/Assets</i>		<u>(12,142)</u>		<u>6,417</u>
<i>Total Net Assets</i>		<u><u>4,425</u></u>		<u><u>21,427</u></u>
<i>Financed By:-</i>				
Income and Expenditure Account		<u><u>4,425</u></u>		<u><u>21,427</u></u>

# NATIONAL DRUGS ADVISORY BOARD

63/64 ADELAIDE ROAD, DUBLIN 12

## NOTES ON AND FORMING PART OF THE FOREGOING ACCOUNTS

FOR THE YEAR ENDED 31 DECEMBER 1986

	1986	1985
	IR£	IR£
<b>1. Income Receivable</b>		
Department of Health Grant	654,700	520,000
Deposit Interest	<u>28</u>	<u>2,471</u>
	<u>654,728</u>	<u>522,471</u>
<b>2. Salaries</b>		
Salaries have been shown net of Superannuation and Widows and Orphans Fund contributions. Deductions are made under the Local Government (Superannuation) Act 1956 and Local Authority and Widows and Orphans Pension Scheme. Since the Board is not obliged to maintain a separate fund, no liability has been included in the Accounts in respect of the deductions, nor has any provision been made in respect of future payments which may arise and which will have to be carried by the Board out of future revenue.		
<b>3. Depreciation</b>		
Depreciation has been charged to write off the cost of Furniture and Fittings on a rate of 20% p.a. Straight Line.		
<b>4. Fixed Assets</b>	<b>Furniture &amp; Fittings</b>	
Cost	<b>1986</b>	<b>1985</b>
Balance 1 January 1986	44,174	39,060
Additions during year	<u>12,990</u>	<u>5,114</u>
Balance 31 December 1986	<u>57,164</u>	<u>44,174</u>
<b>Accumulated Depreciation</b>		
Balance 1 January 1986	29,164	20,329
Charge for Year	<u>11,433</u>	<u>8,835</u>
Balance 31 December 1986	<u>40,597</u>	<u>29,164</u>
<b>Net Book Value</b>		
31 December 1986	<u><u>16,567</u></u>	<u><u>15,010</u></u>