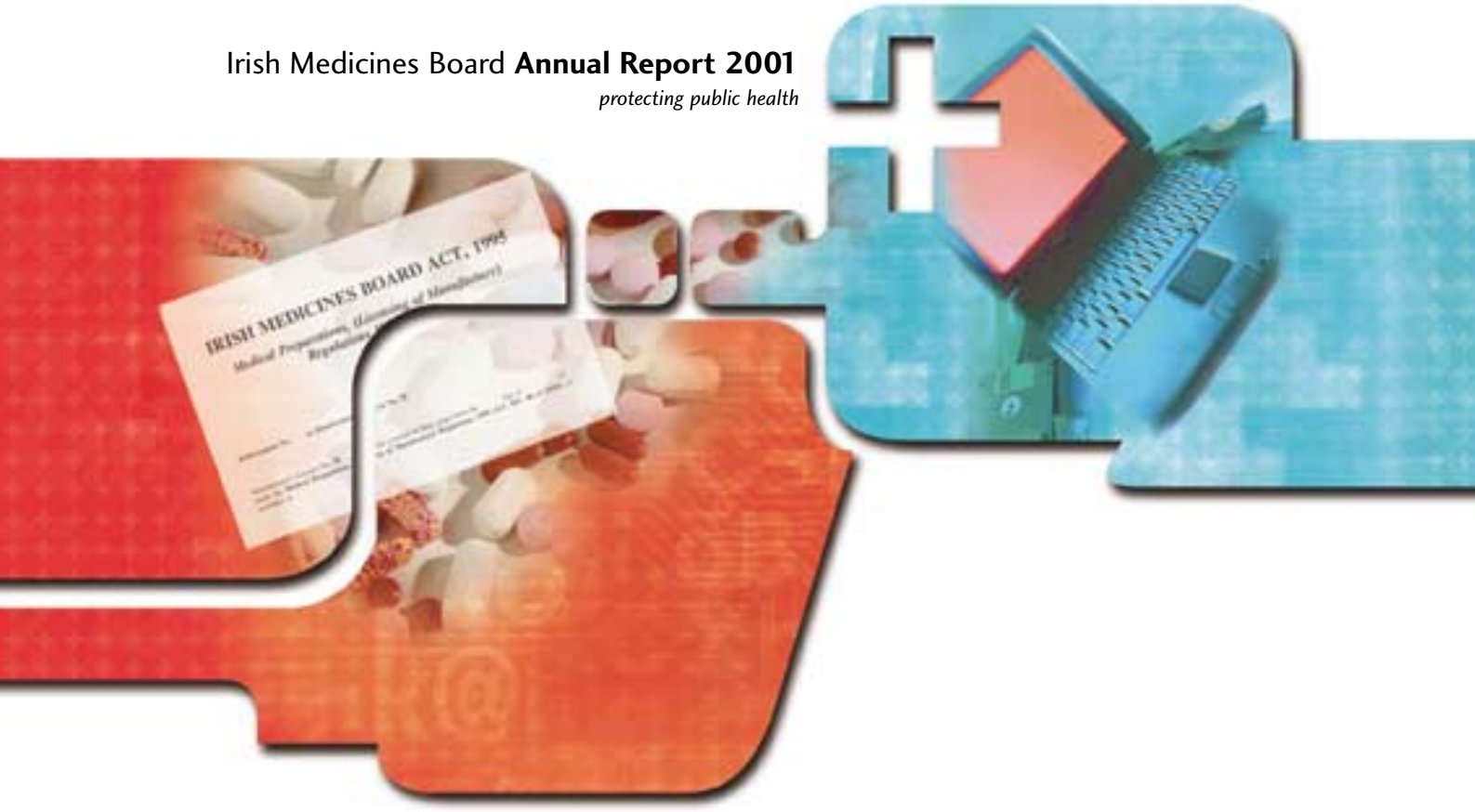
Irish Medicines Board **Annual Report 2001**

protecting public health



IRISH MEDICINES BOARD

Mission Statement

To protect and enhance the public and animal health through the regulation of human and veterinary medicinal products. The regulation of these products is founded on science and law (IMB Act and relevant EU and National legislation, primarily EEC 65/65 and EEC 81/851 as amended) to ensure their purity, potency, safety, efficacy and appropriate storage, transport and distribution.

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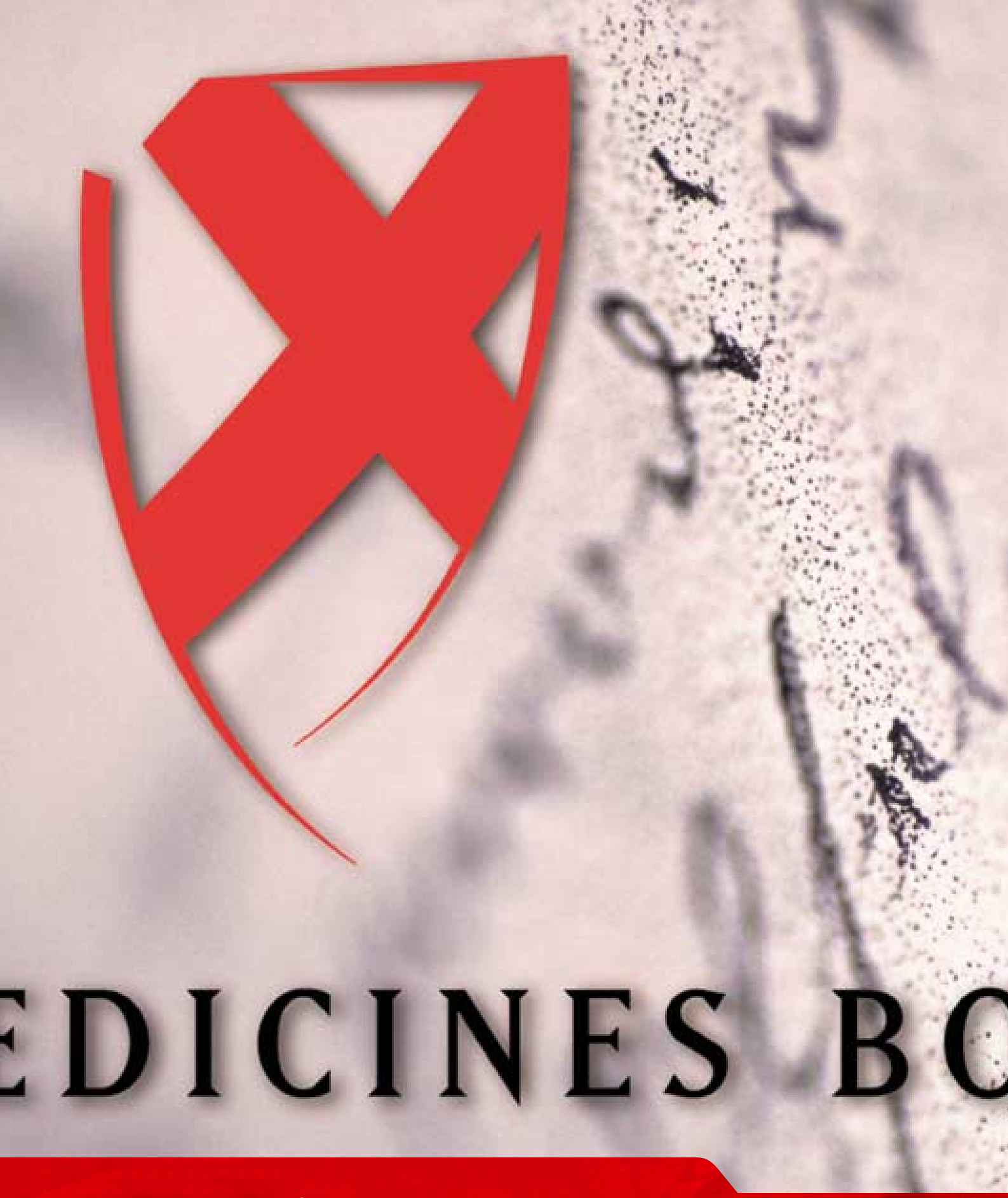


01 Corporate Information

Chairman's Report

I am pleased to present this the sixth annual report of the Irish Medicines Board (IMB). This report details the activities and Financial Statements of the IMB during 2001. It is satisfying to note that the core operations of the Board were again carried out without reliance on state subsidy.

The fundamental role of the IMB is to protect and enhance public and animal health, and we do this through the regulation of human and veterinary medical products. To do this effectively we must have a comprehensive strategy in place and must continually up-date and refine this strategy as we move forward and as the ever increasing demands of the external environment require. Our existing plan was completed and agreed in May 2000 to cover the period 2000 - 2003. Progress has been excellent reflecting very positively on management and staff, particularly so because significant adjustments were made to accommodate a searching review of our technological capability and our future needs against a background of less certain flows of income. More innovative technology and vigilant financial management will ensure that we can meet these demanding challenges ahead and remain self financing in our core business.

The increased emphasis on information sharing with various scientific bodies, the medical profession and pharmaceutical and herbal medicines organisations as well as our involvement in many expert national and international groups proved extremely beneficial, and is welcomed by all the professional staff of the IMB.

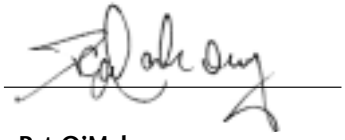
On the financial front, the year 2001 resulted in the IMB continuing to conduct its core activities at no cost to the State. The IMB achieved a reasonable surplus for the year - €379,194 before write-back of staff superannuation contributions (2000: €418,924). Fee income increased by 12% primarily due to a significant increase in income generated from the European licensing system. Costs increased by 18.7% with 5% of this increase attributable to increased legal costs. Inflation for the year was running at 4.9%, although the IMB noticed increases in excess of that in labour intensive services.

The balance of the increase is attributable to increased staff numbers and related staff costs. As with previous years, cash flow remained strong and the IMB is in a healthy position facing into 2002.

I would like to pay tribute to the Board members who so generously offer their valuable time and dedication to the IMB during the year. I also very much appreciate the work undertaken by our various expert sub committees whose members generously give the IMB unique access to best advice. Our staff members are to be congratulated for their enthusiastic and professional approach to their work.

We are most appreciative of the on-going constructive support received from the Minister for Health and Children and the Minister for Agriculture and Rural Development.

Continued professional co-operation between the IMB and these Departments has contributed and will continue to contribute to the provision of effective and efficient medicines. Our involvement in the EU bodies will also keep us to the forefront internationally in terms of professionalism and reputation.



Pat O'Mahony
Chairman

Board Members

Back row from left to right: Dr. Rory Lehane; Mr. Denis Cronin; Ms. Anne Nolan; Mr.PJ. O'Connor; Mr Aidan Murray.
Front row (L-R) Professor Kevin O'Malley; Ms. Aideen Murphy, Mr. Pat O'Mahony (chairman) and Ms. Breeda Dooley.

The IMB was appointed on 2nd March 2001 by the Minister for Health and Children, Mr. Micheal Martin TD in accordance with the powers conferred on him by subsection 2 of section 7 of the IMB Act, 1995 for the period ending 31st December 2005. The Board members are:

Mr. Pat O'Mahony (Chairman)

Mr. Denis Cronin

Ms. Breeda Dooley

Dr. Rory Lehane

Ms. Aideen Murphy

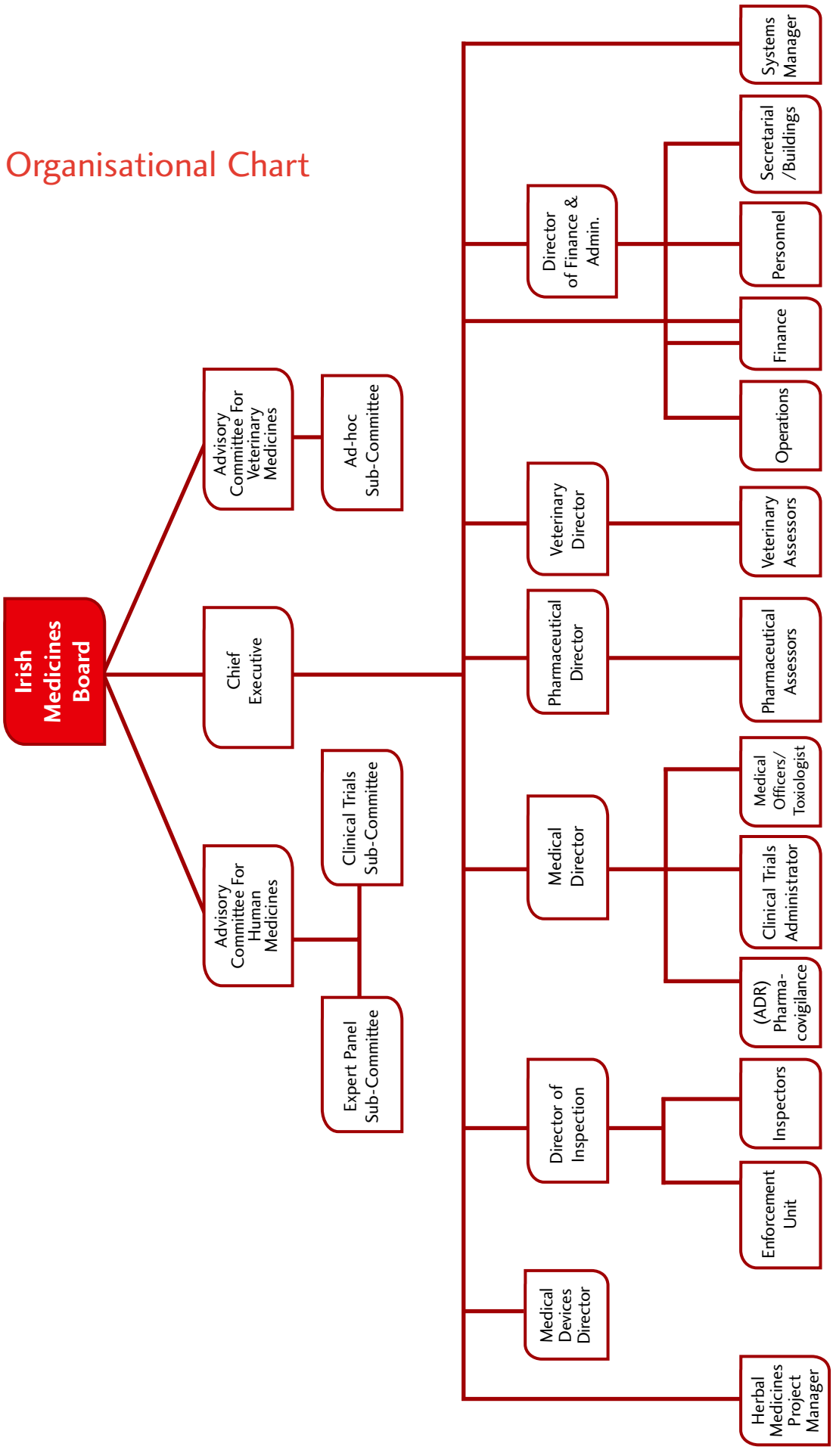
Mr. Aidan Murray

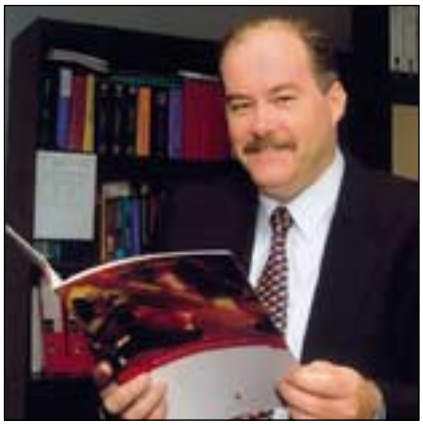
Ms. Anne Nolan

Mr PJ O'Connor

Prof. Kevin O'Malley

Organisational Chart





Chief Executive's Report

Overview of 2001

2001 was another very active year with a range of changes and challenges for the IMB. A new Board was appointed in March and nine full meetings were held during the year. The core work of licensing and post licensing activities continued as normal. The IMB made its contribution to the Lindsay Tribunal during the year and awaits the outcome with interest. In addition, the IMB became the competent authority for Medical Devices in 2001 and a new Department was created to deal with these matters. Finally, we completed our work on two major projects which are likely to be very significant for the future of the IMB: the Herbal Medicines Project and our IT Strategic Plan.

The European Medicines Regulatory System

The IMB participated actively in the European Medicines Regulatory System through its involvement in many committees and working parties in addition to its authorisation activities. The IMB also continued to represent Ireland at the European Pharmacopoeia.

Under the Centralised System, the IMB acted as Rapporteur/Co-Rapporteur for nine human medicinal products and four veterinary medicinal products, (including one maximum residue level application).

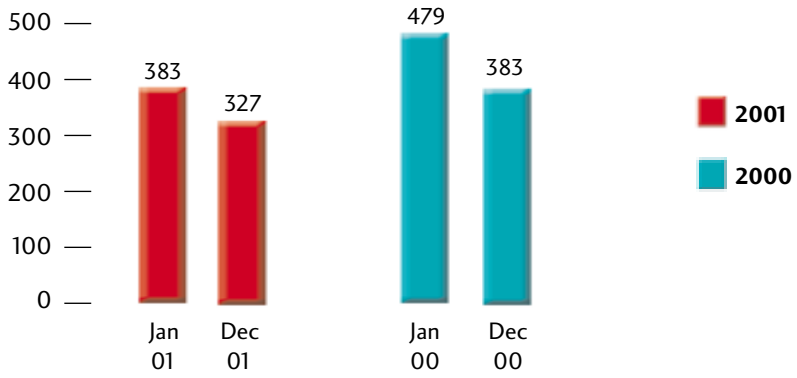
In the Decentralised System, the IMB received applications to act as Reference Member State for nineteen human medicines applications and fourteen applications for veterinary medicines. The IMB completed thirteen such applications in the human medicine area as well as ten in the veterinary medicine area.

In accordance with EC Directive 2001/83, a valid application under the Mutual Recognition procedure can only be refused by a Member State by raising a concern on the basis of significant risks to public health by day 55 of the procedure. The IMB continued to meet all timelines regarding any serious/potentially serious public health concerns in this procedure in 2001.

In the National System, the IMB received 174 national applications compared with 153 in 2000, and 108 in 1999, indicating that new national applications continue to increase following the introduction of the European licensing legislation in 1997.

The IMB continues to place a high priority on reducing the backlog of national applications with positive effect. The total number of applications still in progress decreased from 383 in January 2001 to 327 by the end of December 2001. This represents a reduction of 15% over the 12 month period.
In addition, the age profile of this work in progress has changed considerably with 53% of the products being received in the current year.

National Applications in Progress



Information technology continues to be an important topic on the EU agenda. The Common Technical Document and associated eCTD will bring new demands to the national system. The growth in electronic exchange of information across the EU in areas such as pharmacovigilance also brings challenges to the organisation.

The IMB's IT department was actively involved in a number of EU information technology initiatives in 2001, including EudraVigilance, eCTD and eDatabase technical implementation groups.

IMB IT Strategic Plan

In mid-2001 the Board approved the undertaking of a study to identify the potential benefits of increasing the use of information technology in its operations. Industry groups and their members were asked to provide feedback on IMB services, and the resulting information proved extremely useful in determining the business areas requiring the greatest attention. In October 2001, external consultants working with IMB personnel began the task of identifying specific business and IT initiatives that would assist in improving the efficiency and effectiveness of the Irish Medicines Board in the performance of its Human and Veterinary licensing activities. The purpose of the initiative was to benefit the IMB's operation and assist in meeting its objective of cost effective continuous improvement in the quality and level of service to its stakeholders. This project resulted in a recommended three-year change programme for the organisation which begins implementation in 2002.

The principal components of the proposed programme include the following:-

A. Business & Technology Infrastructure Projects
- Business Architecture & Organisational Structure Review
- Technical Infrastructure
- Document Quality Improvement

B. Technology Projects
- New Improved On-line Tracking & Application Services for the Web
- Workflow Technology
- Document Management Technology
- Management Information Systems

C. Business Transformation Projects

- Technology & Re-designed processes to support the National and European Licensing Activities for Human Medicines

Communications

Industry

During the year, the Board continued to enhance its communication with various groups with an interest in the medicinal products area. Four information days for industry stakeholders were held. These were dedicated respectively to Human Medicines which included a session devoted to the subject of Clinical Trials, Medical Devices (2) and Pharmaceutical Wholesalers. These meetings attracted over 500 attendees and positive feedback was received in all cases. The Board continued to play a major part in the Trinity College School of Pharmacy meeting for Qualified Persons in the Pharmaceutical Industry which was held in September 2001.

A number of other meetings with organisations and individuals with particular interests relevant to medicines were hosted by the IMB throughout 2001. These included meetings with the Animal & Plant Health Association (APHA), the Association of Pharmaceutical Manufacturers of Ireland (APMI), the Dental Technicians Association of Ireland, the Irish Association of Health Stores (IAHS), the Irish Health Trade Association (IHTA), the Irish Medical Devices Association (IMDA), the Irish Pharmaceutical Healthcare Association (IPHA) and the Irish Pharmaceutical and Chemical Manufacturers Federation (IPCMF).

The IMB website was updated to include a section devoted to the new area of Medical Devices. This section enables Applications for Registration to be made electronically for the first time among all the Agencies of the European system.

Publications

The IMB launched a number of valuable guidance documents as part of its communications efforts during 2001, which are available from our website *(http://www.imb.ie)*:-

- Guide To Information held by The Irish Medicines Board: This guide contains manuals prepared in accordance with sections 15 & 16 of The Freedom of Information Act 1997 (July 2001).
- Guide to Parallel Product Authorisations for Medicinal Products for Human Use and the associated forms for this procedure.
- Nine Medical Devices Regulatory guidance notes were published to provide guidance on how to comply with legislative requirements in this area.

Three editions of the IMB's newsletter were published and circulated to all PA and VPA holders, manufacturing and wholesale licence holders as well as other interested parties.

In the second of these, it was announced that future editions of the newsletter would only be published electronically on our web site and copies sent to interested parties by email. This will make the delivery of this important document more cost effective. Two editions of the Drug Safety Newsletter were also published and circulated to all registered medical and dental practitioners and pharmacists.

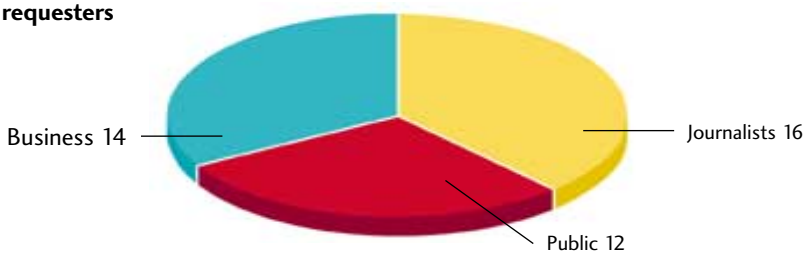
Guide To Information held by The Irish Medicines Board

IMB Drug Safety Newsletter

Freedom of Information

Forty two requests were received under the Freedom of Information (FOI) Act in 2001, eight (8) of which could be dealt with outside the FOI Act. This compares with 44 during 2000. Thus, the level of activity in this area appears to have stabilised.

Break-down of requesters



The IMB remains committed to transparency and openness within all legislative commitments and the requirements of commercial confidentiality. In 32 cases, the requests for information were granted, either wholly or in part. Two cases went to the internal review stage and one requester subsequently sought an appeal of the decision by the Information Commissioner. A decision on this appeal is pending. As of December 2001 there were two appeals pending a decision from the Information Commissioner.

International Liaison

The Board continued to support the Pan European Regulatory Forum (PERF) to assist preparations for the expansion of the European Union. This involved the participation of IMB staff as expert speakers to the various PERF groups.

During 2001 the Board was visited by regulatory colleagues from the UK (MCA and MDA), Norway, Romania and Malta, with the goal of sharing experiences and obtaining an understanding of the IMB's systems and their operations.

National Health Strategy

The IMB was pleased to be requested by the Minister for Health & Children to contribute its views on "strategic changes necessary to promote best health and well being" in the preparation of a new national Health Strategy. While recognising that there are many changes which can help to promote best health and well being, the IMB confined its comments to issues relating to those aspects of the Health Services with which it interacts i.e., Medicinal Products and Medical Devices. The IMB consulted with a number of organisations and with the public at large via its website prior to finalising its views. The IMB considered that there were four key issues which encompassed the main changes which it believed the new Strategy should cover, as follows:

- **Introduction of a statutory system for control of use of unauthorised medicinal products.**
- **Continued development of vigilance systems for medicines (Pharmacovigilance) and medical devices.**
- **Improving the availability of quality information regarding medicines/medical devices to all stakeholders taking particular account of Internet and IT developments.**
- **Recognising and responding positively to the pace and complexity of new technological developments in medicines/medical devices in the post human genome project era.**

In addition, the IMB participated actively in the Futures Working Group set up under the DHC Consultative Forum on the Health Strategy.

The Future

The IMB will need to deal with two important public inquiries in 2002: The Post Mortem Inquiry chaired by Ms Ann Dunne SC, which will investigate the use of post mortem human organs including their use as sources of medicinal products and the Vaccine Trials Inquiry of the Commission to Inquire into Child Abuse chaired by Ms Justice Mary Laffoy, which will include within its scope certain clinical trials of vaccines in residents of children's homes.

The IMB in 2002 is set to take on very important new challenges and activities in relation to the further development of the Herbal Medicines Regulatory System and the implementation of the Board's IT Strategic Plan. The former will be necessary for the ultimate implementation of the planned EU Directive in relation to this important area. The IMB emphasises that the Irish medicinal products regulatory authorities have indicated for many years the need for a suitable system for the regulation of herbal medicines. Indeed, this issue was identified in Annual Reports of the NDAB over a quarter of a century ago.

The IT Strategic Plan will be the single biggest project ever undertaken by the IMB and we hope that it can transform our information technology systems with consequential major benefits to the Board and its fee paying stakeholders. In the longer term, the IMB envisages an increasing proportion of its communication being carried out via electronic means. In addition, 2002 will see the transfer of more responsibilities from the DHC in the controlled drugs area.

The IMB is committed to supporting the regulatory systems in the countries joining the EU as part of the forthcoming enlargement and we hope to continue our support of PERF and other mechanisms in this regard in 2002. In addition, the IMB will make particular efforts to work with other EU Agencies in ensuring our staff receive harmonised training in new areas.

During 2001, the IMB requested its first fee increase since its inception. The IMB is required under the terms of the Irish Medicines Board Act 1995 to ensure that its fees cover the costs of its activities. The large increases in employment and building costs in the Dublin area since 1996, necessitates this fee increase.

I want to express my appreciation for the help and advice of the Board members and the members of our Advisory Committees and Sub-Committees throughout their term. I also wish to acknowledge the support of the staff of the Departments of Health and Children, and Agriculture, Food and Rural Development throughout the year.

Staff Matters

The IMB's staff continue to make important contributions to the various Committees involved in the regulation of medicinal products and medical devices (see Appendix II). In addition, staff members made a number of presentations relevant to the mission of the IMB. (See Appendices II and III.)

Dr. Mary Teeling resigned from her post as Medical Director in June 2001 after a one year leave of absence. Mary joined the National Drugs Advisory Board in 1987 as a Medical Assessor and become Medical Director in 1996. During her first few years at the Board, in addition to her work in assessment, Mary was also involved in pharmacovigilance, and her interest and commitment to this area of the Board's activities remained with her throughout her tenure. She was one of the Irish CPMP delegates from 1996 and was Vice-Chairperson from 1998 to 2000, when she also acted as the CPMP delegate to ICH. We wish Mary every success in her future career.

Dr. Joan Gilvarry was appointed as Medical Director in August.

Ms. Ann O'Connor was appointed as the Board's first Medical Devices Director in September. This appointment coincided with the Board taking over the role of national competent authority for medical devices from the DHC.

Dr JG Beechinor was appointed a member of Comhairle na Nimheanna (Poisons Council) in Feb 2001 for a three year period; Dr J Gilvarry was appointed to be a member of the National Immunisation Steering Committee; the Expert Committee on Contingency Planning for Biological Threats and the Board of the European Forum on Good Clinical Practice; Dr JM Morris was appointed a member of the National CJD Committee in Feb 2001 and Dr D Lyons was appointed as CPMP representative on the COMP.

I wish to welcome all new staff members to the Board and to express my personal appreciation to all the staff of the IMB for their continued support in achieving the Board's mission during 2001.

Frank Hallinan
Chief Executive

02 New Activities

protecting public health

New Activities

The IMB's work with the DHC in relation to the extension of the Board's activities by the transfer of responsibilities from the Department continued in 2001. In addition, work on the Herbal Medicines Project continued.

Medical Devices

The IMB became the competent authority for active implantable, general and *in-vitro* diagnostic medical devices in 2001. This followed the acceptance by the DHC of the report prepared by the IMB in the previous year, which outlined the implications of such a transfer. An active recruitment programme took place in the Autumn which resulted in the appointment of key technical staff who will carry out the functions of the Competent Authority required under legislation. Further details of the activity of the medical devices department can be found in Section 6 "Medical Devices".

Herbal Medicines

The Herbal Medicines Project, initiated in September 2000 in response to a request from the Minister for Health & Children, was successfully completed at the end of 2001. The final report has now been submitted to the Minister for Health and Children for his consideration. The work of the project and of the ad hoc Scientific Committee on Herbal Medicinal Products (SCHMP) during the course of 2001 is detailed in the following list.

a) Scientific Committee on Herbal Medicinal Products (SCHMP)

The Irish Medicines Board Scientific Committee on Herbal Medicinal Products (SCHMP) met a total of six times during the course of 2001. Drafts of proposed chapters of the final report were agreed at each meeting and then released for consultation.

b) On-going Consultation

A total of four separate consultation documents were circulated to interested organisations that had agreed to take part in the consultation process and had signed confidentiality agreements to protect the work in progress of the Herbal Medicines Project. Comments from interested organisations were considered by the SCHMP at its following meeting and responses to comments sent to each interested organisation after that meeting.

c) Herbal Medicines Project Final Report

Following the seventh meeting of the SCHMP held on 24th September 2001, the final report was agreed. The report was approved by the Expert Sub-Committee of the Advisory Committee on Human Medicines (ACHM) and subsequently by the ACHM in September. The Board endorsed the report in October.

The final report was released for public consultation through the Irish Medicines Board (IMB) website *(http://www.imb.ie)* for a period of eight weeks from 1st November to 27th December 2001. A total of 88 responses to the report were submitted to the IMB in that time. However, a total of 92 responses were submitted and considered by the time the report was finalised.

d) Establishment of a Traditional Medicinal Products Database

The traditional medicinal products information database is now also complete and includes a total of 2,246 products. 2,003 of these, are products for which information has been supplied by manufacturers and wholesalers to the IMB through the Herbal Medicines Project. The remainder are products currently on the IMB product authorisation database that could also fall within the scope of a proposed interim national scheme.

Updated and new information continues to be supplied by the industry for inclusion on the database.

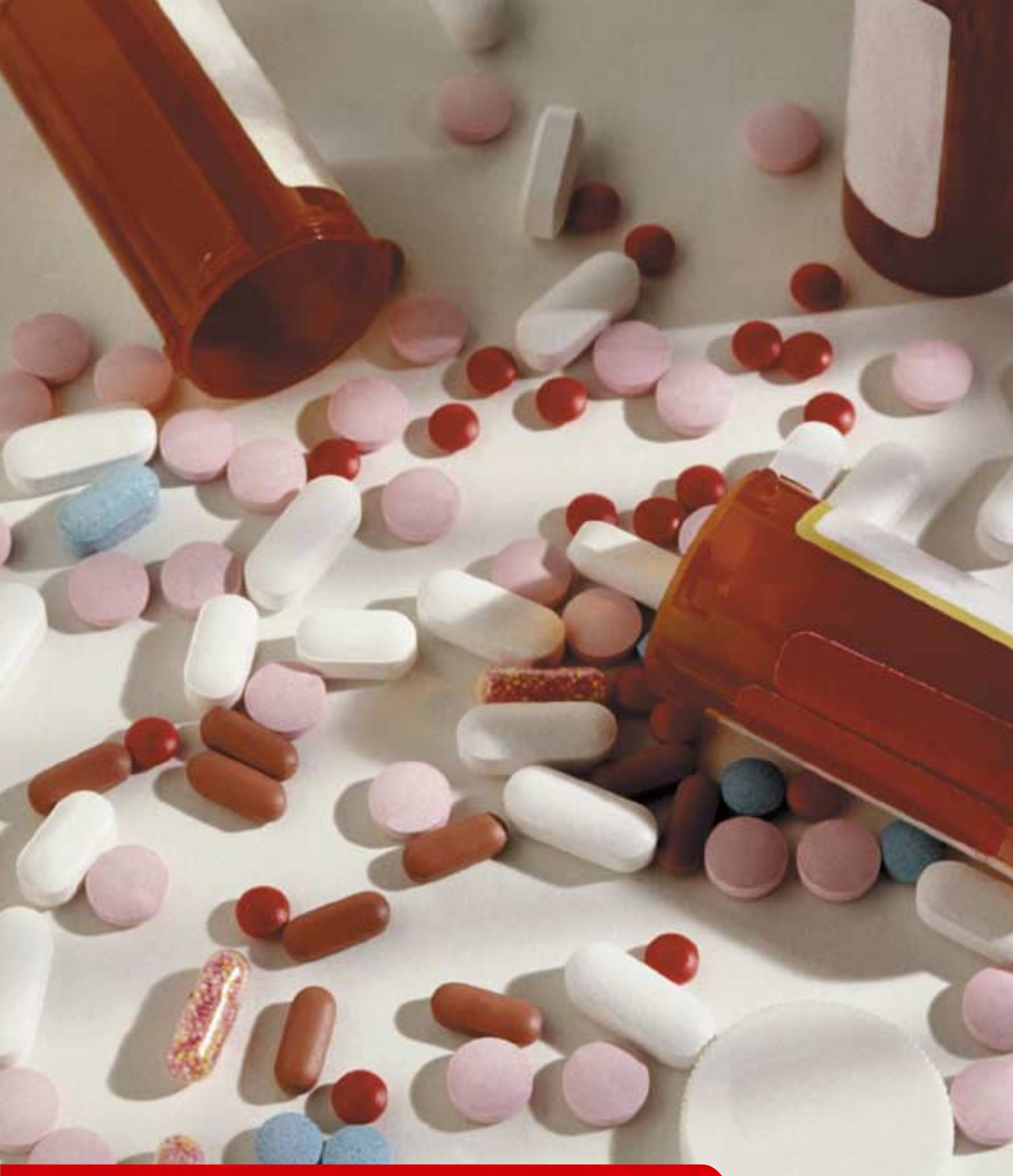
Controlled Drugs Project

In April 2001 the IMB, at the request of the Minister for Health and Children initiated a project to transfer the responsibility for licensing, regulation and inspection of controlled drugs under the Misuse of Drugs Act (1977) from the DHC to the IMB. This will involve the IMB undertaking the responsibility for ensuring national compliance in regard to the licensing and regulation requirements under this Act, and also providing statistical reports to the UN as part of our national obligation under the terms of the various UN Conventions on controlled drugs and precursor chemicals.

The IMB appointed a Controlled Drugs Project Manager who prepared a detailed proposal for the transfer of these functions from the DHC. This documented not only the responsibilities involved, but also the systems that will be necessary for the IMB to undertake this role. Meetings were held with the DHC to agree and finalise the proposal.

Although the legislation permitting the IMB to undertake this role has not yet been completed, progress has been made with regard to setting in place systems to enable the performance of the licensing, regulation and inspection functions for controlled drugs, which will ensure a smooth transfer of responsibility. This has primarily focused upon the need to introduce information technology to manage the processes involved in controlled drug licensing and regulation.

The IMB is in the process of assessing and introducing a database developed by the UN to manage aspects of controlled drug licensing and regulation. This database will provide a more efficient system for the generation of licences and the preparation of statistical reports for the UN. The Project Manager participated in an international meeting hosted by the UN in relation to this database, and is closely liaising with the UN during this stage of its introduction by IMB.



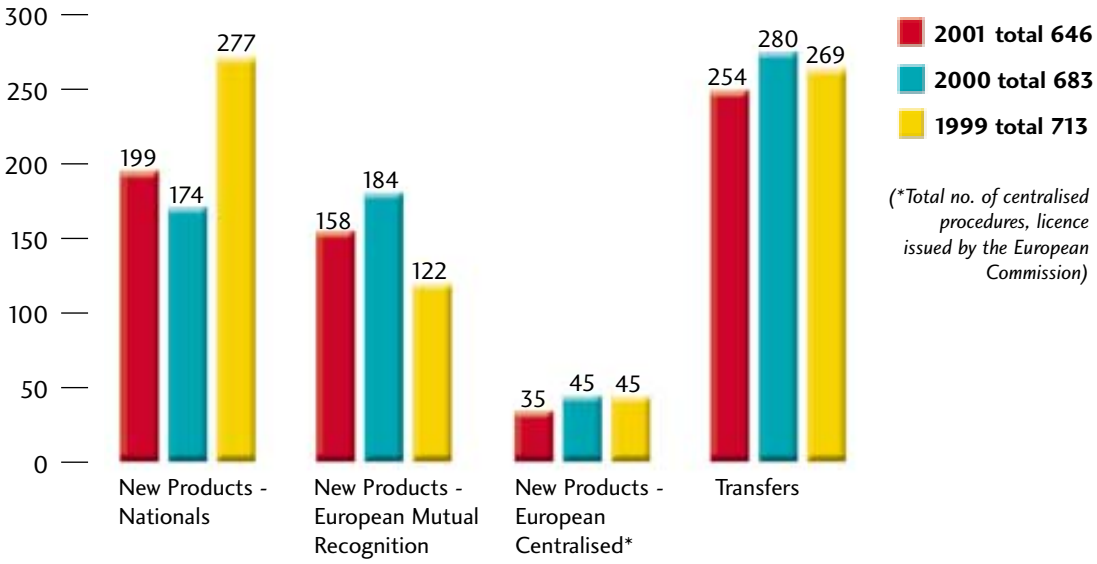
03 Human Medicines

protecting public health

Human Medicines

Licensing

During 2001, the IMB issued 646 product authorisations. The following table shows the distribution of these over the last number of years:



The median time for new product authorisations issued (excluding transfers) in 2001 was 45 weeks which was the same as 2000, but compares to 73 weeks in 1999. This represents the continued improvement in timelines by the Board.

During the year, 6,839 variations to product authorisations were issued for products authorised through the national or MR systems. The corresponding 2000 figure was 6,071 - this area has more than doubled in activity since 1998. Approximately 70% of all variations require pharmaceutical assessment.

Pre-Clinical (Pharmacology/Toxicology) Unit

The principal work of the unit during 2001 continued to be the examination and evaluation of the pharmacological and toxicological components of dossiers for new chemical entities submitted for marketing authorisation, where the IMB is acting as (Co-) Rapporteur or Reference Member State in a European procedure. The activity in this area has declined significantly from the high levels of 1998/99, allowing for increased input and improved quality of service to other units.

The unit works most closely with the Medical Department but there has been a steady increase in the number of referrals requiring toxicological evaluation in relation to pharmaceutical variations, clinical trials, enforcement, herbal medicines, pharmacovigilance and veterinary department. In addition, there were numerous requests for meetings and/or advice on pre-submission issues from pharmaceutical companies.

The most significant increase in workload during 2001 came from international collaborations. The Safety Working Party (SWP) held three meetings at the EMEA, in February, June and October 2001. The work of this group involves developing guidelines and scientific advice at the request of the CPMP or its Scientific Advice Review Group. The number of these projects and the level of involvement of the IMB delegate increased significantly in 2001.

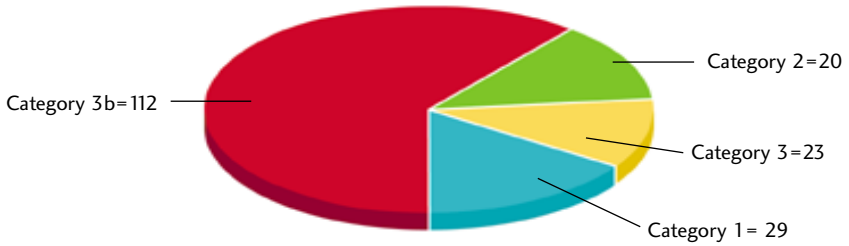
In addition, the IMB was involved in presentations at two training sessions run by or on behalf of the SWP.

Clinical Trials

The IMB's role in the Control of Clinical Trials Act is intended to protect the interests of participants. Clinical trials are forbidden unless the requisite permission has been obtained from the Board. The Board continued to meet the statutory time lines defined in the legislation and benefited greatly from the advice and expertise of the members of its Clinical Trials Committee.

There were 184 applications to conduct clinical trials during 2001 which was a substantial increase on the figure of 160 received during 2000.

These can be categorised as follows:



There were 259 amendment applications received.

Permissions to conduct 139 (a marginal increase compared to 2000) clinical trials were granted during 2001. There were 239 permissions to amend clinical trials (a drop of 6 compared to 2000). 115 clinical trial applications required pharmaceutical assessment. There were no clinical trials suspended by the IMB for safety reasons.

The European Clinical Trials Directive (2001/20/EC) was published in April 2001. Member States are required to legislate nationally in order to comply with the provisions of the Directive before May 2003 and apply the Directive provisions at the latest with effect from 1st May 2004. The Commission commenced a series of meetings in December 2001, aimed at developing guidelines to support the Directive.

In 2001, five GCP inspections were carried out prior to the resignation of the GCP inspector. A new inspector has now been recruited and the IMB will recommence inspections in this area in 2002.

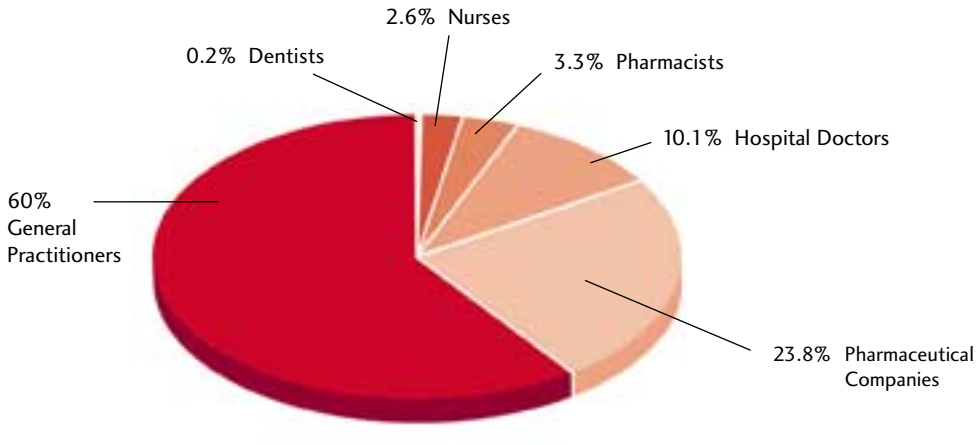
Pharmacovigilance

During 2001, the IMB received 2,282 adverse drug reaction (ADR) reports of national origin. This figure represents an increase of 62.2% over the volume of reports received in 2000, which in turn represented a significant increase in the reporting rate over the previous year. Thus, since 1999, we have seen an increase of over 100% in the total number of Irish ADR reports submitted. While this increase is welcomed as a sign of increasing awareness of pharmacovigilance on the part of health care professionals and an appropriate response to the initiatives taken by the IMB to stimulate reporting, it has significantly increased the workload of the unit.

During 2001, the IMB Board's continued to encourage ADR reporting using the downloadable version of the report form from the Board's website. Updated contact details were sought from healthcare professionals, who were encouraged to submit e-mail addresses to facilitate more rapid dissemination of information and to date, over 400 healthcare professionals have provided their e-mail details. During the year, use of the electronically available ADR report forms for healthcare professionals increased. This provided regular reminders about reporting in the Drug Safety Newsletter and in our regular publication in MIMS initiated during 2001.

A series of presentations on the value of pharmacovigilance and ADR reporting was also made to nurses and pharmacists, as part of their continuing education programmes.

The distribution of sources of reports in 2001 is detailed in the chart below. The reporting pattern in 2001 was consistent with that of previous years in terms of breakdown of sources.



All ADR reports were followed up with feedback information provided to reporters, as appropriate. Relevant ADR reports (i.e. all serious, suspected cases) notified directly to the IMB by healthcare professionals were forwarded to the appropriate Marketing Authorisation Holders (MAHs) and the EMEA within the agreed timeframes.

Information was provided in respect of all requests circulated via the rapid alert/infofax system by other Member States.

During 2001, a significant number of variations to product authorisations were initiated by the IMB following identification of specific safety issues identified through ADR reports, literature reviews etc., at either national or European level. These included the following:

Drug/Drug Class	Nature of Statement
Anti-epileptic agents, Cyclosporin, Digoxin, Non-nucleoside reverse transcriptase inhibitors, Oral Contraceptives, Protease inhibitors, Serotonin re-uptake inhibitors, Theophylline, Trazodone, Triptans, Warfarin	Introduction of statements on potential for interaction with *Hypericum perforatum* (St. John's wort)
Bupropion	Introduction of revised dose titration scheme, extension of contraindications and additional additional information on potential for interaction.
Combined Oral Contraceptives	(i) Revision of warnings on risk of Venous Thromboembolism (ii) Introduction of statements on potential for interaction with *Hypericum perforatum* (St. John's wort)
Epoetin alpha	Introduction of statements on development of pure red cell aplasia (PRCA)
Infliximab	Update of warning statements on tuberculosis, congestive heart failure, neurological effects and hypersensitivity reactions
Itraconazole	Updated warnings on cardiotoxic effects
Nucleoside reverse transcriptase inhibitors	Harmonisation of warnings on lactic acidosis. Introduction of statements on potential for interaction with *Hypericum perforatum* (St. John's wort)
Propofol Selective Serotonin re-uptake inhibitors	Additional warnings regarding use in sedation (i) Harmonisation of labelling on suicide warnings (ii) Introduction of statements on potential for interaction with *Hypericum perforatum* (St. John's wort)
Topiramate	Introduction of statements on ocular syndrome

A significant number of additional variations arising from issues reviewed at EU level will require implementation during 2002 (NSAIDs, dopaminergic agents, HRT products, levofloxacin).

The CPMP's Pharmacovigilance Working Party (PhVWP) met on eight occasions in 2001. During these meetings, the PhVWP considered 49 product-related issues at the request of the CPMP, compared with 48 in 2000. These included centrally authorised products, products subject to referral procedures and nationally authorised products for which no referral has been made. Forty seven product related issues were also discussed at the request of the competent authorities of the Member States. In addition, there was an increase in the number of other issues referred to the working party for review. The PhVWP continued its regular interaction with the FDA through video conferences held during working party meetings.

In line with pharmacovigilance legislation, the IMB incorporated MedDRA terminology into its adverse reaction monitoring system during 2001. In order to support electronic reporting to the EMEA work is also ongoing to support transmission of relevant reports in line with E2B requirements.

Products Withdrawn/Suspended For Safety Reasons

During 2001 the following medicinal products were withdrawn from the Irish and other markets for safety reasons:

Product Name	Reason for withdrawal
Cerivastatin	Voluntary withdrawal by the MAH from all worldwide markets following evaluation of reports of rhabdomyolysis and muscle disorders associated with its use.
Droperidol	Voluntary withdrawal by MAH following reassessment of benefit risk profile in relation to availability of the oral formulation.
Levacetylmethadol	Voluntary withdrawal by the MAH, following reassessment of the benefit risk profile of the product in the EU.

Drug Safety Newsletter

Topics reviewed in the two editions of the drug safety Newsletter in 2001 included:

- MMR vaccine
- Thioridazine
- Droperidol
- Bupropion
- Propofol
- Stavudine
- Didanosine
- Topical chloramphenicol
- Cerivastatin
- Gemfibrozil
- Itraconazole
- Clopidogrel
- Information on ADR reporting
- Clinical trials and product information

Quality Defects

A total of 30 reports of quality defects were received in 2001, as shown below in comparison with the outcome for 1999 and 2000:

	2001	2000	1999
Number of Minor Defects	21	16	9
Number of Major Defects	5	5	6
Number of Critical Defects	1	0	1
Number not justified/inconclusive	3	16	7
Total number quality defects received	**30**	**37**	**23**

Three reports were found to be unjustified, i.e., no defect was found with two products, and in one case, improper handling of the product at the point of administration rendered the product unusable, and the report was considered unjustified.

Of the 27 reports which were substantiated following investigation, one was considered to be a critical defect necessitating a batch recall. Additionally there were five major defects and twenty-one minor defects.

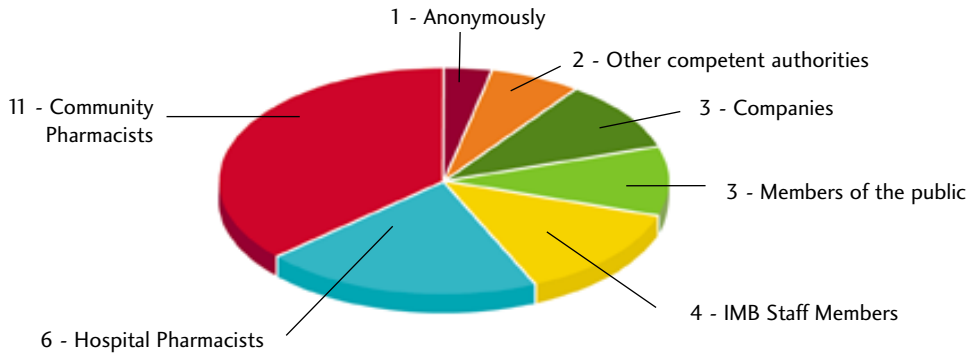
Details of the critical defects reported are as follows:

- For a syrup formulation prescribed for children, the cap was found to be defective, rendering the bottle non-closable after initial use of the product. Product packaged with the defective cap was recalled from the market.

Details of the major defects reported are as follows:

- For a parenteral product, it was observed that the rubber bung closure could be inadvertently removed from the vial when the outer aluminium seal was flipped off during use. A Caution In Use letter was issued to users.
- For an encapsulated product, capsules from three batches were found to be burst and leaking. Two batches were recalled from the marketplace, and a Caution in Use letter was issued to pharmacists for the third batch.
- For a parenteral product, glass particles were found in a number of sealed ampoules. The competent authority of the Member State concerned was notified, and that authority is overseeing and monitoring the corrective actions being put in place by the company concerned.
- For a parenteral product, a possible lack of robustness of the product packaging together with improper handling of the product resulted in a loss of solvent during reconstitution of the product. Revised handling instructions were approved for the labelling and packaging of this product, and a Caution in Use letter detailing proper handling procedures was issued to all users of the product. The packaging of this product is currently being evaluated for possible re-design requirements.
- For a tablet product, no Patient Information Leaflet was packaged with the product over a number of batches. This was corrected by the company concerned, and IMB is monitoring compliance of the product with the product registration details.

The reports came from:



Pre and Post Marketing Sampling

In 2001, analysis of medicinal products was carried out on behalf of the IMB by the Public Analyst's Laboratory, University College Hospital, Galway. A total of 54 medicinal products were submitted for analysis in 2001 (compared to 111 in 2000). The table below summarises the samples submitted during 2001:

Description	Number
Authorised Medicinal Products for Human Use & products manufactured in Ireland but not marketed here	11
Authorised Medicinal Products for Veterinary Use & products manufactured in Ireland but not marketed here	5
Unauthorised Medicinal Products for Human Use	38
Total	**54**

The enforcement samples submitted for testing during 2001 included conventional and traditional use medicines, as well as vitamin and mineral based products, and products marketed for weight loss purposes. One of these enforcement samples was confirmed as being a counterfeit product.

The analytical testing of authorised medicinal products included one product requiring microbiological testing. This was an eye drop formulation which was tested for preservative efficacy. This analysis was performed by an independent testing laboratory.

For the authorised medicinal products submitted for analysis in 2001, a total of three cases of non-compliance with specifications were reported. One product was found to be out of specification for preservative content, one was found to be out of specification for the concentration of active ingredient, and in two cases (including one of the above products) there were labelling deficiencies identified.

In addition, in eight instances, problems were encountered with the analytical methods provided by the marketing authorisation holder/manufacturer for the analysis of the products, and follow-up work was or is being carried out with the marketing authorisation holder/manufacturer as a result of the deficiencies identified. The IMB is concerned at the high percentage of methods requiring such follow up and emphasises to manufacturers their need to ensure that their analytical methods are adequately documented to facilitate their use by regulatory authorities control laboratories.

EU/International Activities

During the year IMB staff continued to devote significant effort to the international dimension of human medicines within the CPMP and its working parties, European Pharmacopoeia, European Commission and ICH, as outlined in Appendix II.

In addition the IMB continued to support the following meetings:

- Annual Meeting of the WHO Collaborating Centre
- Irish Society of Toxicology
- European Society of Toxicology

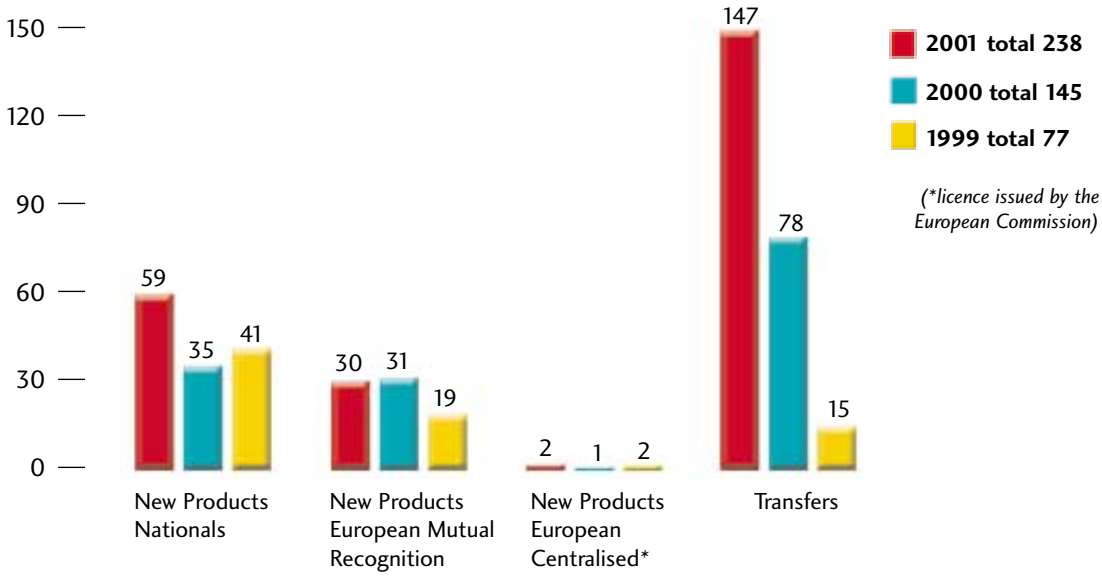
04 Veterinary Medicines

protecting public health

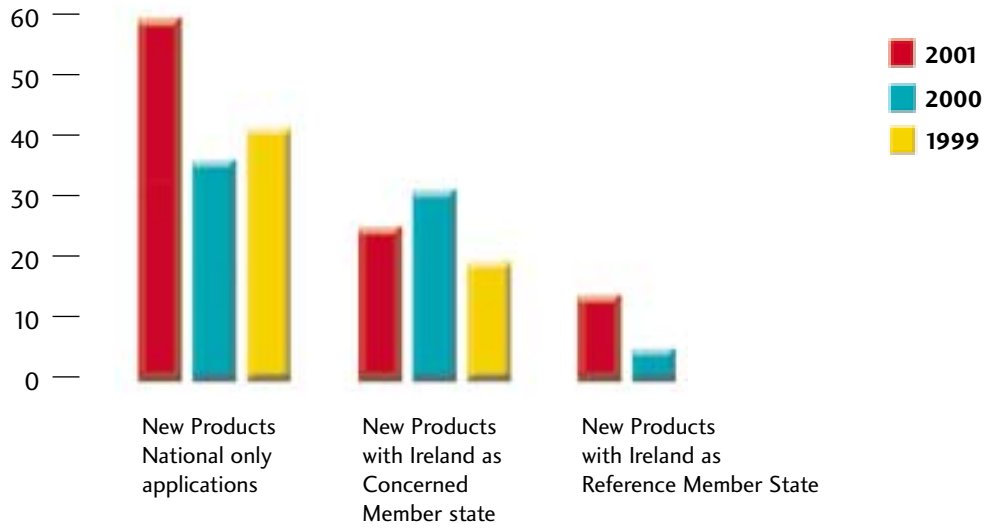
Veterinary Medicines

Licensing

During 2001, there was continued strong growth in authorisation activities across most licensing areas with 238 applications for new, or transferred licences issued compared to 145 in 2000 and 77 in 1999 as shown in the following graph:



In relation to new product authorisations issued, the following graph shows the progress achieved in the period 1999-2001:-

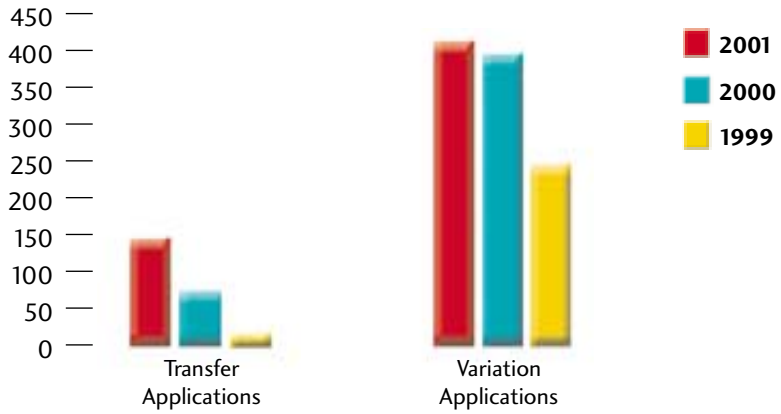


The number of national applications recorded as work in progress reduced from 73 to 31 throughout the year. In respect of mutual recognition applications, the IMB continued to perform well, as evidenced by a 2001 FEDESA survey and the number of companies requesting the IMB to act as Reference Member State during the current year. The implementation of the new IMB policy requiring applicants to furnish mock-up of product labels and packaging prior to authorisation or marketing has led to an increase in the time to authorisation of new products both in national and the Mutual Recognition procedures. This policy has been implemented to ensure that the labelling of authorised veterinary medicinal products complies with the outcome of the evaluation procedure and is necessary to ensure regulatory compliance.

IMB personnel have been active in the evaluation procedures in respect of applications to the European Medicines Evaluation Agency (EMEA) for a central authorisation. While the paucity of new applications for consideration by the EMEA continues to give cause for concern, the IMB personnel were appointed as rapporteur/co-rapporteur in respect of 4 applications for new products, MRL's or extensions of existing applications.

In relation to transfer and variation applications, excellent progress was also achieved coinciding with the near elimination of the backlog of renewal applications for veterinary pharmaceuticals. By year-end, some 602 renewal applications were issued and the work in progress had been reduced from 635 to 89. The progress in the issuance of the transfer and variation applications over the last 3 years is graphed below:-

Transfer & Variation applications issued



At December, the number of outstanding applications for transfer and variation applications were 28 and 141 respectively. In 2001, 421 variations to product authorisations were issued which represents a 6% increase on the corresponding 2000 figure. As in earlier years, approximately 80% of all variations required pharmaceutical assessment.

Clinical Trials

Under national legislation the DAFRD is obliged to consult with the IMB prior to authorising clinical trials in animals in regard to the technical aspects of applications. Clinical trial applications continued to show a decline from 14 in 1999 to 11 in 2000 and only 5 in 2001.

Some of this decline results from the outbreak of Food & Mouth Disease in Ireland, which restricted the movement of animals and veterinary personnel although some reflects the difficult development conditions for companies marketing animal health products.

Veterinary Vaccines

Progress on the evaluation of veterinary vaccines in compliance with the requirements of Council Directive 2001/82/EC is continuing. Two additional immunological assessors were recruited to assist in the overall workload of the unit and in the evaluation of the technical requirements in respect of the EU directive on use of materials of ruminant origin in veterinary vaccines. The evaluation of vaccines for compliance with the EU guideline on TSE was a particularly complex and important project conducted in 2001. Of 162 Annex I and II applications received in March 2001, compliance had been demonstrated for 61 products, assessments were completed for another 77 (EDQM assessments outstanding) and assessments were underway for the remaining 24. This performance has been achieved against a backdrop of training of new personnel and adoption of updated European wide approaches to the risk assessment of ruminant derived material. The IMB is very pleased that it was among the first EU regulatory authorities to achieve such progress.

In relation to other vaccine applications the key performance characteristics are given below:

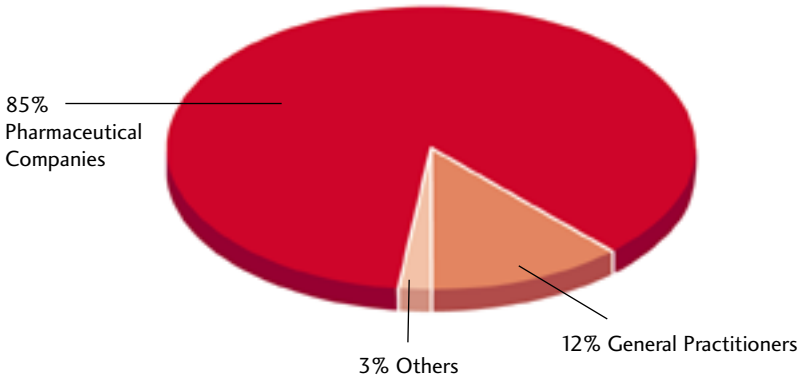
	2001	2000	1999
New national-only applications received	0	2	1
New national-only applications completed by IMB	1	0	0
New national-only applications issued by DAFRD	0	0	0
New MR applications received	6	12	12
New MR applications completed by IMB	5	15	4
New MR applications issued by DAFRD	5	9	3
Review applications received	20	71	60
Review applications completed by IMB	15	5	6
Review applications issued by DAFRD	7	5	3

While progress in the Mutual Recognition procedure has been good, there have been considerable delays in finalising the national-only new product applications. Some 37 vaccine variation applications were received during the year while 17 were issued by year-end. The time allocated for the submission of applications under the review programme has now expired and the IMB is making steady progress in the evaluation of the applications. It is estimated that it takes 12 to 18 months approximately to complete the evaluation on any particular product. Much work remains before the review of vaccines can be completed and it is expected that the additional resources given to the task will achieve closure by the end of 2003.

Veterinary Pharmacovigilance

The IMB received 51 reports of suspected adverse drug reaction (ADR) reports during 2001 compared with 50 in the previous year. Of the total number of suspected ADRs reported, 40 involved veterinary pharmaceutical products and 20 concerned vaccines. Two or more veterinary medicinal products were identified in seven reports.

ADR Reports by Source



Forty-four reports were received from the marketing authorisation holder, six directly from veterinary surgeons in practice and one from a regional veterinary laboratory. These suspected ADRs were reported in the following species: human (3 reports), cattle (25), horses (2), sheep (4), pigs (4), dogs (9), cats (3) and rabbit (1). Seven of the reports related to lack of efficacy. Of the remaining reports, the product(s) used was considered to have been probably or possibly associated with the observed reaction in 21 cases.

In relation to the serious ADRs that were associated with veterinary pharmaceutical products, 4 reports (detailing nine bovine deaths) were identified as probably/possibly related to the administration of anthelmintic boli. In all cases, the reactions reported were attributed to pharyngeal/oesophageal trauma. Although there remains a concern with the animal welfare implications of the use of anthelmintic boli, it is notable that numbers of boli sold annually and the reported incidence of ADRs are both declining. Also, it is noted that the incidence of deaths associated with the administration of such products was greatly influenced by a report originating from a single farm.

As a direct consequence of pharmacovigilance data submitted to the IMB, the labelling of two products has been amended to highlight the potential for the occurrence of certain ADRs.

The IMB considers that it is likely that there is a significant level of under reporting of suspected ADR's as evidenced by the low numbers of reactions reported directly to the IMB by veterinary surgeons and pharmacists. The IMB wishes to emphasise to stakeholders that spontaneous reporting of suspected adverse drug reactions is an inexpensive and effective method for ensuring continued safe and effective use of veterinary medicinal products following their introduction to the market place. The responsibilities of the MAH and the Competent Authority in relation to the handling of such data are well defined, but the gathering of relevant information is dependant on the contribution and cooperation of veterinary surgeons and other healthcare professionals.

The IMB gratefully appreciates and acknowledges the efforts of reporters in completing reporting forms and responding to requests for clarification. While an individual's experience may be limited to one or two cases it, when collated with data from other sources, may contribute considerably to the assessment of a potential safety hazard.

Persons licensed to sell or supply animal remedies are reminded of their legal obligation to notify the IMB of all suspected ADR's that come to their attention. In an attempt to promote veterinary pharmacovigilance, the IMB will:

1. Follow-up on all national reports received.
2. Publish annual reports on suspected adverse reactions.
3. Bring the pharmacoviligilance surveillance scheme to the attention of veterinary undergraduates.

Quality Defects

There was one report of a quality defect for a veterinary medicinal product received in 2001 in which the batch of product contained unlabelled vials. The IMB strongly encourages the reporting of quality defects by healthcare professionals and members of the public. Pre-paid green cards are available to pharmacies for reporting of quality defects.

Miscellaneous Veterinary Items

The initiative to facilitate the harmonisation of product labelling and Summary of Product Characteristics between Ireland and the U.K. begun in 2000 has been of limited success. To date, few companies have availed of this facility which had been devised in order to assist in the availability of an adequate range of veterinary medicinal product in Ireland. A meeting between the Veterinary Medicines Directorate and the IMB took place to review the progress achieved during the last quarter of 2001. However, in view of the fact that the use of the facility is dependent on the initiation by the animal health industry, there is little more that the IMB can do to facilitate the process.

In October 2001, the IMB suspended the authorisations for those benzathine penicillin containing antibiotics authorised for use in livestock. The basis for this action was to protect public health in a situation where it was not possible to determine a withdrawal period for residues in tissues of treated animals.

During the last quarter of 2001, the Veterinary Unit embarked on a major IT project which involves the electronic scanning of all administration and correspondence files for more than 1,100 applications. This work is well advanced and will ultimately lead to a better service in retrieving information for regulatory purposes.

The IMB continued to support the DAFRD in bringing prosecutions against users of illegal veterinary medicines.

EU/International Activities

During the year the IMB staff continued to devote significant effort to the international dimension of Veterinary Medicines within the CVMP and its working parties, as outlined in Appendix II.

05 Inspectorate

protecting public health

Inspectorate

Summary of Activity

The main statistical highlights of 2001 are shown in the attached charts compared to the equivalent figures for 1999 and 2000:

Inspections and Licensing

	2001	2000	1999
Inspections in Ireland	161	77	68
Foreign Inspections	7	5	3
Total	**168**	**82**	**71**

It can be seen that in all areas the Inspectorate Department activities have increased significantly over the period reflecting industry activity and increased IMB service levels. The inspections in Ireland included a project to inspect all wholesalers supplying non pharmacy retail outlets with over 100 outlets being inspected. IMB inspectors participated in a number of inspections related to centrally authorised and mutual recognition products in non - EEA countries.

Manufacturing/ Wholesale licence revocations

	2001	2000	1999
Licence Revocations	1 Vet Medicine	0	1 Human Medicines Wholesaler

New Manufacturing/ Wholesale licences issued

	2001	2000	1999
Human Medicine manufacturer	6	4	1
Veterinary Medicine manufacturer	2	1	1
Wholesaler	5	6	7
Total	**13**	**11**	**9**

Variations to existing Manufacturing/ Wholesale licences

	2001	2000	1999
Human Medicine manufacturer	136	69	50
Veterinary Medicine manufacturer	31	10	5
Wholesaler	23	10	3
Total	**190**	**89**	**58**

Numbers of Manufacturing/ Wholesale licences at year end

	2001	2000	1999
Human Medicine manufacturer	74	75	60
Veterinary Medicine manufacturer	24	22	17
Wholesaler	84	73	58
Total	**182**	**170**	**135**

Product Certification Activity

During 2001, the IMB issued 2,730 Product Certificates as shown below with the equivalent numbers for 1999 and 2000 for comparison:

	2001	2000	1999
Certification of Documents	525	372	532
Certificates of Free Sale	170	64	75
Certificates of Manufacture and Free Sale	10	28	30
Certificate of GMP	242	171	202
WHO Certificates	1,772	1228	748
Certificate of Export Sale	11	14	-
Total	**2,730**	**1,877**	**1,587**

2001 saw continued growth in the number of certificates issued. The increase in the number of WHO certificates reflects the IMB's policy of making the WHO Certificate of a Pharmaceutical Product the one of choice for an individual medicinal product.

Recalls

Medicinal Products for Human Use

The following table shows the total number and distribution of recalls of medicinal products for human use which took place in 2001 compared with 1999 and 2000:

	2001	2000	1999
Packaging issue	15	8	9
Stability issue	5	8	5
Non-compliance with authorisation	1	13	9
Product safety concerns	3	7	6
Non-compliance with specification	7	4	4
Other	7	6	6
Total Number	**38**	**46**	**39**

Despite the increased security measures applied during packaging operations packaging errors continue to be a significant cause of recalls. The IMB again emphasises the importance of proper line clearance and line set up to manufacturers.

Veterinary Medicinal Products

The following table shows the total number and distribution of recalls of veterinary medicinal products that took place in 2001 compared with 1999 and 2000:

	2001	2000	1999
Sterility issue	1	0	3
Stability issue	4	0	1
Non-compliance with Authorisation	11	2	1
Other	0	0	0
Total Number	**16**	**2**	**5**

Half of the recalls for 2001 related to the removal from the market of long acting penicillin injectables due to concerns over persistence of residues at the site of injection.

National

Some of the key GMP compliance issues which arose during inspections carried out in 2001 included:

- Role and training of contractors.
- Design of and acceptance criteria for process validation studies.
- In relation to deviations, the adequacy of corrective actions and the speed of their implementation.
- Assurance of GMP compliance of manufacturers of raw materials, particularly active pharmaceutical ingredients.
- Compliance of facilities used for the manufacture of sterile products with the environmental classifications set out in Annex 1 to the EU Guide to GMP.

A number of manufacturers of Active Pharmaceutical Ingredients were inspected during 2001 in relation to requests for Certificates of Good Manufacturing Practice. These inspections used the ICH Good Manufacturing Practice guide for Active Pharmaceutical Ingredients as the basis guidance for the IMB staff.

Regular liaison meetings were held jointly with industry representative bodies, the Animal and Plant Health Association (APHA), the Association of Pharmaceutical Manufacturers of Ireland (APMI) and the Irish Pharmaceutical and Chemical Manufacturers Federation (IPCMF). A wide range of GMP related issues of mutual interest were discussed. It is intended that these meetings will continue into the future.

A pilot study of the adherence of manufacturers and marketing authorisation holders to pharmacovigilance reporting requirements was initiated during the latter part of 2001.

Two inspections of the Cork Centre and one inspection of the National Blood Centre (Dublin) of the Irish Blood Transfusion Service were carried out during 2001. Inspections were also carried out at the donor clinic (D'Olier Street), two mobile donor clinics and at two storage sites for raw materials for mobile clinics.

EU / International Activities

Progress on the implementation of Mutual Recognition Agreements (MRAs) on GMP inspection continued to be variable during 2001. The following was the status of the MRAs at the end of 2001 in all the countries for which discussions were in progress:

Canada

The implementation of this MRA continued to be delayed during 2001.

Japan

Significant progress was made on the implementation of this MRA and signing was completed during 2001. An 18 month preparatory phase was due to commence on the 1st January 2002.

New Zealand

The MRA relating to medicinal products for human use has been in force since the beginning of 1999. For veterinary medicinal products the transitional period was due to conclude at the end of 2001, but was, in fact, extended.

Switzerland

Implementation of this MRA was postponed on a number of occasions during 2001.

USA

A preliminary review by the EU of the inspection system of the U.S., Food and Drug Administration was carried out during 2001. An IMB Inspector was a member of the EU group which carried out on site review.

The three year transitional period expired at the end of 2001. By that time the inspectorate of only one Member State had been evaluated by the U.S. Discussions on a formal extension of the transition period were in progress at year end. The IMB looks forward to the progress in this area.

Members of the Inspectorate continued to participate actively in the Ad Hoc Working Party of GMP Inspection Services at the EMEA and the Pharmaceutical Inspection Co-Operation Scheme (PIC/S). A number of guidelines and internal recommendations for the use of inspectors were adopted / revised by the PIC/S including:

- PIC/S GMP guide for Blood Establishments (PE 005-1) (new)
- Guidance on Parametric Release (PI 005-1) (new)
- Recommendation on the Validation of Aseptic Process (PI 007-2) (revised)

A number of revised or, new annexes to the EU Guide to GMP were implemented during 2001:

- Annex 1 "Manufacture of Sterile Medicinal Products" (paragraph 42 revised)
- Annex 6 "Manufacture of Medicinal Gases" (revised)
- Annex 15 "Qualification and Validation (new)

The following new annexes were due for implementation on the 1st January 2002:

- Annex 16 "Certification by a Qualified Person and Batch Release"
- Annex 17 "Parametric Release".

In addition, the following were ongoing at year end:

- Annex 1 - proposed revision of environmental requirements
- Annex 13 "Manufacture of Investigational Medicinal Products".

The proposed revision of Annex 13 to take account of requirements of Clinical Trials Directive, 2001/20/EC, was released for six months consultation in November 2001.

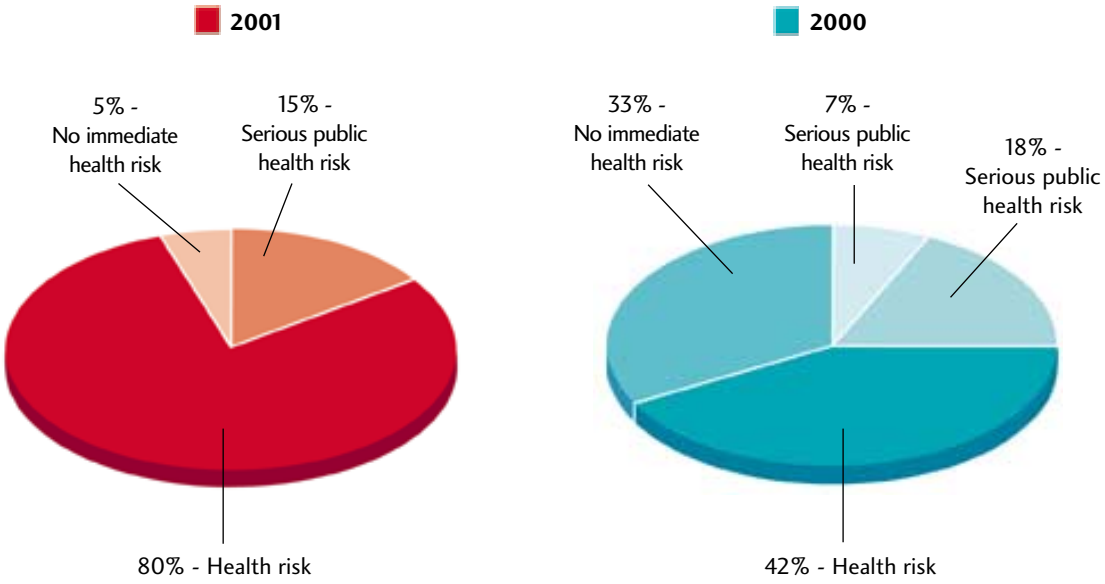
A common position on a Directive on Blood Transfusion was reached by the Council of Health Ministers towards the end of 2001. Further drafting of the Directive text was due to take place during 2002.
A Joint Audit Programme for EU GMP Inspectorates was developed during 2001 and actual audits were scheduled to commence during 2002. These will also be used for the purpose of a PIC/S formal re-assessment.

As part of the preparations for full accession to the EU, Protocols to the European agreement on Conformity assessment and Acceptance of industrial products (PECA) were developed by the EU, individually, with the Czech Republic and Hungary. These PECAs cover a number of areas including GMP inspection and include a formal assessment by the EU. For Hungary, the PECA relating to GMP inspection for human and veterinary medicinal products became operational on the 1st December 2001. The PECA relating to GMP inspection for human medicinal products from the Czech Republic was due to become operational on the 1st January 2002. The implementation of these PECAs means that batches of relevant medicinal products imported from these two countries do not require to be re-tested in the EU. Release by a Qualified Person remains a requirement.

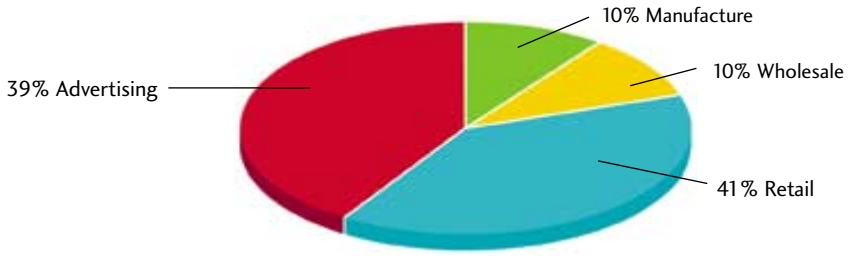
Enforcement

The IMB recruited four additional enforcement officers in 2001. The increase in enforcement capability and public awareness of the role of the enforcement function in the IMB in safeguarding public health will lead to an increased detection and reporting of breaches of medicinal product legislation. The total number of cases investigated in 2001 was 244 compared with 155 in the period March to December 2000. The closure of enforcement cases increased from 5.8 per month to 13.1 per month, reflecting the increased resources in this area and enabled a timelier conclusion of investigations.

The breakdown of cases in 2000 and 2001 in the context of our categorisation on the basis of risk to public health is shown below:



The following chart shows the distribution of cases by Sector in 2001:



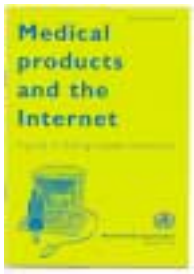
The enforcement unit targeted the advertisement sector for compliance action in 2001. The area of advertising of medicinal products accounted for 39% of all cases in 2001 compared with 3% in 2000. Offences included the advertising of Prescription only Medicines and unauthorised medicinal products. The effective liaison between the media, other publishers and business supplying these products has resulted in increased awareness and understanding of the Medical Preparations (Advertising) Regulations 1993-1996. This increased co-operation led ultimately to fewer such breaches in the second half of 2001.

Illegal wholesale dealing of medicinal products accounted for 10% of breaches, an increase from 8% in 2000. The majority (64%) of offences in this category related to unlicensed wholesaling. The true reflection of this problem is in the number of retail outlets selling unauthorised medicinal products and/or product confined to sale from pharmacy outlets including Prescription only Medicines.

The retail sector of the market accounted for 41% of cases. Ten percent of retail cases related to pharmacies and 90% of cases related to non-pharmacy outlets including grocery retail outlets, petrol stations, healthfood shops and ethnic product retail outlets. The types of medicinal products being retailed were mostly found to be Prescription only Medicines in cream and tablet forms.

Illegal trade in mail order supply of medicinal products continues to be a significant issue requiring enforcement action. In 2001, 18% of all cases involved mail order supply versus 27% in 2000. The reduction reflects the improved liaison with other Member States, US Regulatory authorities and others. The increased international supply of medicines via Internet purchase is of particular public health concern. "Internet Prescriptions" increase the avoidance of accountability by suppliers and diminish the essential traceability of unauthorised medicinal products being used in Ireland, particularly Prescription only Medicines. The increasing use of the Internet in Irish homes will require continued focus on this area in the interest of protecting public health. One Internet site supplying Prescription only Medicines to the International market and operating from Ireland was closed down as a result of Enforcement Action. Two other Internet sites supplying within Ireland were also closed. Eight Internet sites ceased to advertise the supply of medicinal products in Ireland. The IMB advises Irish consumers and companies operating in this area that mail order supply, including Internet supply, of medicinal products is illegal in Ireland.

The IMB also agrees with the WHO view in its publication "Medical Products and the Internet: A Guide to finding reliable information" that there are many reasons why medicinal products bought via the Internet could represent a danger to the user. The IMB therefore advises very strongly that consumers be cautious about buying medical products on the Internet. The IMB will be cooperating with colleagues in other law enforcement and regulatory agencies at home and abroad in monitoring this area in future years.



Slimming products continued to be a matter for concern, rising from 10% of cases in 2000 to 13% in 2001. These products were investigated because of their medicinal claims, presentation and/or their ingredients. One such unauthorised product was recalled from the market as it contained a Prescription only Medicine. Many such products that amended their claims continued to be available as they then fall outside the medicinal product legislation.

Inadequate traceability of medicinal products is a common feature of all cases investigated. The associated problems of not being able to guarantee the quality, safety and efficacy of such unauthorised products reaching the market may have an adverse affect on public health and safety. Enforcement unit action detected and investigated two counterfeit products on the market in 2001 and many products without authorisations in this jurisdiction. Both counterfeit products were being sold in non-pharmacy retail outlets in small quantities but available to anyone entering such outlets. Neither product is believed to have returned to the market following enforcement action.

On-going communication with the IMB's stakeholders has led to a greater understanding and in most cases acceptance of the benefits of ensuring that compliance with medicinal product legislation is more actively enforced than heretofore. Ultimately, this will result in greater consumer protection in relation to medicinal products. The public, and many in the industry and in the business community, have responded well to the Enforcement Unit in the provision of and clarification of information in relation to the medicinal products legislation. This has made a major contribution to the prevention of breaches of the Regulations. Prevention activities represent about 50% of the Enforcement Unit activities. The Enforcement Unit is proactive in its investigations to bring about compliance with the law and to remove potentially dangerous and unauthorised medicinal products from the market place at the earliest possible time. The Enforcement Unit, operating to the highest principles and standards of law enforcement, has applied a policy of openness and transparency. It has sought compliance rather than prosecution in most cases where no serious public health risk was at issue, to encourage the elimination of breaches of the legislation. The IMB's first prosecution occurred in June 2001 and resulted in the conviction for the supply of a Prescription only Medicine without a prescription, by mail order, and without a Product Authorisation. The Court fined the defendant £3,000. As indicated above, the advertisement sector was targeted for compliance action in 2001 and in each successive year new targets will be chosen in order to eliminate illegal activities in the targeted sectors.

06 Medical Devices

protecting public health

Medical Devices

Summary of Activity

In 2001, the Irish Medicines Board (IMB) took over the role of Competent Authority (CA) for medical devices in Ireland, commencing with designation of the IMB as the CA for *in-vitro* diagnostic (IVDs) medical devices by way of S.I. No. 304 of 2001 in late June. More significantly, the CA role for general medical devices (GMD) and active implantable medical devices (AIMD) was legally transferred from the DHC by way of S.I. No. 444 of 2001 in September 2001. The transfers are in line with current government policy and followed the acceptance of a report prepared by the IMB outlining the implications of such a transfer.

In its new role as the CA for medical devices, the IMB is responsible for ensuring safe and effective use of medical devices on the Irish market. This is done by way of both pre-market and post-market surveillance. Given that medical devices are governed by the new approach Directives, a greater responsibility is placed on the manufacturer for self-regulation, which is supported thereafter by post-market surveillance. This is a key difference between the regulation of medicines and medical devices.

During the year, significant progress was made in ensuring a smooth transfer of Competent Authority functions which included the development of a quality system for the medical devices department, preparation, consultation and issuance of guidance notes for stakeholders, supporting databases and a designated medical devices website with a high data content. A successful recruitment programme in accordance with the detailed plan submitted to the DHC took place in September/October, which resulted in the appointment of the Medical Devices Director and key technical staff. Two information days, one targeted at the IVD industry and the second targeted at the general medical device and active implantable medical device industry were held, in September and November respectively, to inform stakeholders of the new systems which were put in place to support the functioning of the new Medical Devices Department of the IMB. Both days proved very successful and were used to launch the medical devices website and the first on-line electronic registration form for medical devices in Europe.

Panels of experts were developed both for IVDs, AIMDs and GMDs which will be used to provide expertise to the Medical Devices Department as the need arises. Currently there are 15 nominated experts for IVDs and 44 for AIMDs and GMDs. It is envisaged that an Advisory Committee will be set up when the legal basis is resolved. Terms of reference have been developed to support the formation of such a committee.

The general policy of developing and enhancing liaison with key stakeholders including medical device manufacturers, European Commission, key Member States, the Irish Notified Body, NSAI and the DHC was progressed. Active participation also occurred in international activities.

Vigilance

Vigilance reports were received from manufacturers, users and European Competent Authorities for medical devices. During the year, a voluntary user reporting system was developed which was welcomed by healthcare professionals and hospital services. In the period under review, a total of 80 vigilance reports were received from the above sources that resulted in the issuance of one Competent Authority report to Member States of the EU and EEA. On average two user reports were received from Irish hospitals per month.

Vigilance Report	September - December
Number of User Reports	7
Number of Reports from other Member States	46
Number of Reports from Manufacturers	27
Total	**80**

A number of key vigilance activities arose as a result of the 80 reports received, including most notably 14 recalls of medical device products from the Irish market. One vigilance report relating to a paediatric heart valve was categorised as serious. A Competent Authority report was circulated in respect of this product to all member states of the EEA.

Other Vigilance Activities	September - December
Number of Recalls	14
Number of Irish Competent Authority Reports generated in Ireland	1
Number of Serious incidents	1
Number of Investigations open at Year end	43

Certificates of Free Sale

The issuance of certificates of free sale also transferred from the DHC as part of the responsibility for medical devices. A new system was developed which allowed for the electronic receipt of applications. During the period September to December a total of 45 certificates of free sale were issued. Turn around time was two working days if all documentation was correct.

Registration

For low risk medical devices and IVDs, manufacturers are obliged to register with the IMB as the National Competent Authority in the state where those devices are manufactured. Registration can be done electronically by way of the new electronic form, which is the first of its kind in Europe. In the Sept to Dec period, a total of 61 manufacturers registered, many of these successfully using the electronic registration form. A total of 782 IVDs devices and 32 GMDs were registered. All manufacturers previously on the register at the DHC were requested to re-register with the IMB to ensure the accuracy of the IMB database. A working group was also set up to develop guidelines for dental technicians. The Dental Technicians Association of Ireland is represented by two members and the group also includes an academic and two representatives of the Medical Devices Department. The following tables represent summaries of the registrations made in 2001.

Number of devices, grouped by device product family placed on the register in 2001: General Medical Devices

Device Product Family	Number of Devices
Reusable Instruments	2
Active Implantable Devices	0
Non-Active Implantable Devices	0
Dental Devices	16
Ophthalmic and Optical Devices	7
Diagnostic and Therapeutic Radiation Devices	0
Anaesthetic & Respiratory Devices	0
Electro-Mechanical Medical Devices	0
Technical Aids for Disabled People	0
Hospital Hardware	4
Single Use Devices	3
Total	**32**

In-vitro Diagnostic Medical Devices

Device Product Family	Number of Devices
In-vitro Diagnostic Medical Devices	782

Number of Organisations registered in 2001

Device Group	Manufacturer's	Authorised Representative's	Importer
GMD	19	5	0
IVD	21	16	0

Classification of Devices registered in 2001

Device Group	GMD	IVD
Class I Devices	15	-
Custom-Made Devices	14	-
System & Procedure Pack	3	-
Other (GMD)	0	-
List A	-	41
List B	-	43
Self Test	-	2
Other (IVD)	-	696
Total	**32**	**782**

Notified Body Issues

Responsibility for designation of the Irish Notified Body now rests with the IMB. This has resulted in monthly meetings with the National Standards Authority of Ireland (NSAI). An application was received from the NSAI for designation as a Notified Body under Directive 98/79/EEC during quarter 4. An initial review was carried out in the last quarter and it is hoped to progress this application in 2002.

EU/International Activities

Attendance occurred at a number of key international meetings namely expert meeting for IVDs and GMDs where the IMB represented Ireland as a Member State for the purposes of the CA obligations under the Medical Devices Directives. Furthermore, we actively participated in a number of working groups namely, Notified Bodies Operations Group (NBOG), which has been set up to improve the standard of Notified Bodies and designating authorities in the EU. We were also represented at the Vigilance Working Group, TSE and Eudamed Working Groups.

07 Financial Statements

protecting public health

Corporate Information

Bankers:
Allied Irish Bank
Lower Baggot Street
Dublin 2

Solicitors:
Eugene F. Collins
Temple Chambers
3, Burlington Road
Dublin 4

Head Office:
Block A
Earlsfort Centre
Earlsfort Terrace
Dublin 2

Auditor:
Comptroller and Auditor General
Dublin Castle
Dublin 2

Corporate Governance

The Irish Medicines Board (IMB) was established under the terms of the Irish Medicines Board Act, 1995, and is governed by a Board which was appointed by the Minister for Health & Children. The Board of the IMB (the Board) consists of a Chairman and eight unremunerated non executive members.

The IMB is committed to the highest standards of Corporate Governance and is in the process of implementing the Department of Finance "Code of Practice for the Governance of State Bodies". This Code of Practice which was issued to the Irish Medicines Board in January 2002 incorporates many of the principles under which the IMB operates, taking account of the size and legal nature of the organisation. Initiatives that the IMB have taken include the finalisation in 2002 of an extensive Code of Conduct for all staff, committee and Board members. The IMB is also in the process of establishing an audit sub-committee of the Board and reviewing the internal audit needs of the organisation. The IMB already applies the highest standards of disclosure and transparency in respect of interests held by staff, committee and Board members.

Remuneration Policy - Board Members and Executive Directors

Remuneration and travel expenses paid to Board members are disclosed in note 14 to the Financial Statements. The Chairman receives remuneration in accordance with instructions received from the Minister for Health and Children in accordance with the Irish Medicines Board Act, 1995. Other Board members receive travel expenses in accordance with circulars issued by the DHC. The Chief Executive Officer is remunerated in accordance with guidelines issued from Government and other Executive Directors are paid in accordance with DHC pay scales. The Chief Executive's salary is disclosed net of Superannuation contributions in note 15 to the Financial Statements.

Internal Control

The Board is responsible for the IMB's systems of internal control. Such systems can only provide reasonable and not absolute assurance against material misstatement or loss.

"Internal Control : Guidance for Directors on the Combined Code" (the Turnbull "Guidance") was published in September 1999. Although the guidance is primarily directed towards private and listed companies subject to the Companies Acts (1963 to 1996), the IMB is currently reviewing the applicability of the guidance to its operations.

In addition, the Board confirms that there is an ongoing process for identifying, evaluating and managing the significant risks faced by the IMB. This process is regularly reviewed by the Board via the report of the Chief Executive Officer.

Management are responsible for the identification and evaluation of significant risks applicable to their areas of business together with the design and operation of suitable internal controls. These risks are assessed on a continual basis and may be associated with a variety of internal or external sources including control breakdowns, disruption in information systems, natural catastrophe and regulatory requirements. Management report fortnightly on operational issues and risks and how they are managed to the Executive Committee. The Executive Committee's role in this regard is to review on behalf of the Board the key risks inherent in the affairs of the IMB and the system of actions necessary to manage such risks and to present their findings on significant matters via the Chief Executive Officer to the Board.

The Chief Executive reports to the Board on behalf of the executive management on significant changes in the work of the IMB and on the external environment which affects significant risks.

The Director of Finance and Administration provides the Board with monthly financial information which includes key performance indicators. Where areas for improvement in the system are identified the Board considers the recommendations made by the Executive Committee.

An appropriate control framework is in place with clearly defined matters which are reserved for Board approval only or, as delegated by the Board, for appropriate Executive approval. The Board has delegated the day-to-day management of the IMB and established appropriate limits for expenditure authorisation to the Executive. The Chief Executive is responsible for implementation of internal controls, including internal financial control.

Going Concern

The Board has a reasonable expectation, at the time of approving the Financial Statements, that the IMB has adequate resources to continue its operations for the foreseeable future. For this reason, it continues to adopt the going concern basis in preparing the Financial Statements.

Statement of Board Members' Responsibilities

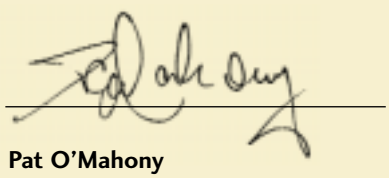
The Board is required by the Irish Medicines Board Act, 1995 to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the Irish Medicines Board.

In preparing those statements the Board is required to:

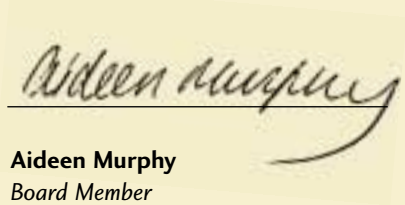
- select suitable accounting policies and apply them consistently
- make judgements and estimates that are reasonable and prudent
- disclose and explain any material departures from applicable accounting standards, and
- prepare the financial statements on a going concern basis unless it is inappropriate to presume that the Irish Medicines Board will continue in existence.

The Board is responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the Irish Medicines Board and which enable it to ensure that the financial statements comply with the Act. It is also responsible for safeguarding the assets of the Irish Medicines Board and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

On behalf of the Board



Pat O'Mahony
Chairman



Aideen Murphy
Board Member

Report of the Comptroller and Auditor General
For Presentation to the Houses of the Oireachtas

I have audited the financial statements on pages 47 to 56 under Section 18 of the Irish Medicines Board Act, 1995.

Respective Responsibilities of the Board and of the Comptroller and Auditor General

The accounting responsibilities of the Board Members are set out in the Statement of Board Members' Responsibilities on page 45. It is my responsibility, based on my audit, to form an independent opinion on the financial statements presented to me by the Board and to report on them.

Basis of Opinion

In the exercise of my function as Comptroller and Auditor General I conducted my audit of the financial statements in accordance with auditing standards issued by the Auditing Practices Board and by reference to the special considerations which attach to State bodies in relation to their management and operation.

An audit includes examination, on a test basis, of evidence relevant to the amounts and disclosures in the financial statements. It also includes an assessment of the significant estimates and judgements made in the preparation of the financial statements and of whether the accounting policies are appropriate to the Board's circumstances, consistently applied and adequately disclosed.

I planned and performed my audit so as to obtain all the information and explanations that I considered necessary to provide me with sufficient evidence to give reasonable assurance that the financial statements are free from material misstatement whether caused by fraud or other irregularity or error. I also evaluated the overall adequacy of the presentation of information in the financial statements.

Pension Costs

Without qualifying my opinion I draw attention to the Accounting Policies note on Superannuation which explains why the Board has not complied with the disclosure requirements of Financial Reporting Standard 17.

Opinion

In my opinion, proper books of account have been kept by the Board and the financial statements, which are in agreement with them, give a true and fair view of the state of affairs of the Irish Medicines Board at 31 December 2001 and of its income and expenditure and cash flow for the year then ended.

Gerard Smyth
For and on behalf of the
Comptroller and Auditor General
10 July 2002

Accounting Policies

Historical Cost Convention

The Financial Statements are prepared in accordance with generally accepted accounting principles under the historical cost convention and comply with the financial reporting standards of the Accounting Standards Board.

Income Recognition

Income is recognised in the financial statements on the following basis:

- In the case of applications for Product Authorisations (new applications, variations to existing authorisations, or transfers) and Clinical Trial applications, income is recognised in the financial statements when a valid application form is received.
- In the case of Wholesale and Manufacturing Licences and maintenance of Product Authorisations, fees are payable annually and a full year's income is accrued in each financial year.

Expenditure Recognition

Expenditure is recognised in the financial statements on an accruals basis as it is incurred.

Reporting Currency and Currency Translation

The Financial Statements are prepared in euros and have been converted into Irish pounds for comparative purposes using the fixed rate of exchange of € 1 = IR£ 0.787564, as set on 1 January 1999. This rate has also been applied to the comparative figures for 2000.

Transactions in currencies other than Euro are recorded at the rates ruling at the date of the transactions or at a contracted date. Monetary assets and liabilities are translated into Euro at the balance sheet date or at a contracted date. Exchange differences are dealt with in the income and expenditure account.

Tangible Assets

Tangible Assets are stated at cost less accumulated depreciation. Depreciation is calculated in order to write off the cost of tangible assets over their estimated useful lives by equal annual instalments.

The estimated useful lives of tangible assets by reference to which depreciation has been calculated are as follows:

Leasehold Property:	28 years
Fixtures and Fittings:	5 years
Computer Equipment:	3 years

Taxation

The Irish Medicines Board is exempt from liability to Corporation Tax under Section 32 of the Finance Act, 1994.

Debtors

Known bad debts are written off and specific provision is made for any amount the collection of which is considered doubtful. A further general provision is also maintained.

Superannuation

The superannuation scheme operated by the Irish Medicines Board is in accordance with the Local Government (Superannuation Revision) (Consolidation) Scheme, 1986. It is an unfunded statutory scheme and benefits are met from current income as they arise.

The charge to salaries and wages is stated gross of superannuation deductions of €206,881: IR£162,932 (2000 - €72,616 : IR£57,190). The surplus for the year on page 8 is then shown both before and after superannuation transactions for the year. The income and expenditure reserve on the balance sheet is split between retained reserves and superannuation reserves in the note on page 49.

The above accounting treatment, which is consistent with all State Bodies under the Local Government Body Superannuation scheme, is not in accordance with the requirements of Financial Reporting Standard 17. For accounting periods ending on or after 22 June 2003 the Standard will require financial statements to reflect at fair value the assets and liabilities arising from an employer's superannaution obligations and any related funding and to recognise the costs of providing superannuation benefits in the accounting periods in which they are earned by employees. As a transitional measure the Standard requires that the present value scheme liabilities be disclosed in the notes of the 2001 financial statements. In 2001 the Board was not in a position to comply with the requirements of FRS 17 as it did not obtain an actuarial valuation of the scheme's liabilities.

Library

No value has been placed on the books, audio-visual resources and electronic databases in the library. Expenditure on these items is written off in the year in which it is incurred.

Leases

All leases are treated as operating leases and the rentals thereunder are charged to the Income and Expenditure account on a straight line basis over the lease period.

Statement of Income and Expenditure

For the year ended 31 December 2001

	Note	2001 €	2000 €	2001 IR£	2000 IR£
Fee Income	2	7,817,728	6,924,327	6,156,961	5,453,351
Sundry Income		850,255	475,413	669,630	374,418
		8,667,983	**7,399,740**	**6,826,591**	**5,827,769**
Salaries and Wages	3	5,363,812	4,624,741	4,224,345	3,642,280
Other Operating Costs	4	2,634,968	2,090,891	2,075,206	1,646,711
Depreciation	1	290,009	265,184	228,401	208,849
		8,288,789	**6,980,816**	**6,527,952**	**5,497,840**
Surplus for the year before write back of Superannuation contributions		379,194	418,924	298,639	329,929
Staff Superannuation Contributions		206,881	72,616	162,932	57,190
Surplus for the year		586,075	491,540	461,571	387,119
Balance brought forward		3,685,905	3,194,365	2,902,886	2,515,767
Balance carried forward		**4,271,980**	**3,685,905**	**3,364,457**	**2,902,886**

All income and the surplus for the year arises from continuing activities. The IMB had no recognised gains or losses other than those dealt with in the Income and Expenditure Account.

Pat O'Mahony
Chairman

Aideen Murphy
Board Member

The accounting policies on pages 47 to 48 and the notes on pages 52 to 56 form part of the financial statements.

Balance Sheet As at 31 December 2001

	Note	2001 €	2000 €	2001 IR£	2000 IR£
Tangible Assets	1	500,902	368,651	394,492	290,336
Current Assets					
Debtors and Prepayments	5	1,924,167	1,246,783	1,515,405	981,921
Stock of Stationery		5,172	5,984	4,073	4,713
Cash at Bank and in Hand	11	2,012,885	1,595,964	1,585,276	1,256,924
Short Term Deposits		2,124,073	2,416,520	1,672,843	1,903,164
		6,066,297	5,265,251	**4,777,597**	4,146,722
Creditors - Amounts falling due within one year					
Creditors and Accruals	6	2,295,219	1,947,997	1,807,632	1,534,172
Net Current Assets		3,771,078	3,317,254	2,969,965	2,612,550
Total Net Assets		**4,271,980**	3,685,905	**3,364,457**	2,902,886
Financed by					
Income and Expenditure Reserve	10	4,271,980	3,685,905	3,364,457	2,902,886
		4,271,980	3,685,905	**3,364,457**	2,902,886

Pat O'Mahony
Chairman

Aideen Murphy
Board Member

The accounting policies on pages 47 to 48 and the notes on pages 52 to 56 form part of the financial statements.

Cash Flow Statement For the year ended 31 December 2001

	Note	2001 €	2000 €	2001 IR£	2000 IR£
Reconciliation of surplus to net cash inflow from operating activities					
Surplus for year		586,075	491,540	461,571	387,119
Depreciation charge		290,009	265,184	228,401	208,849
Increase in Debtors		(677,384)	(920,608)	(533,483)	(725,038)
Decrease in Stocks		812	(1,124)	640	(885)
Increase in Creditors - amounts falling due within one year		347,222	702,106	273,460	552,953
Deposit interest		(109,914)	(94,381)	(86,564)	(74,331)
Bank interest and charges		4,554	4,758	3,587	3,747
Gain on Disposal of Fixed Assets		(533)	(279)	(420)	(220)
Net Cash Inflow from Operating Activities		**440,841**	447,196	**347,192**	352,194
Cash Flow Statement					
Net Cash Inflow from Operating Activities		440,841	447,196	347,192	352,194
Return on Investments and Servicing of Finance	7	105,360	89,624	82,978	70,585
Capital Expenditure	7	(421,728)	(282,016)	(332,138)	(222,106)
Management of Liquid Resources	7	292,447	(71,383)	230,321	(56,219)
Increase in Cash		**416,920**	183,421	**328,353**	144,454
Reconciliation of net cash flow to movement in net funds					
Increase In Cash		416,920	183,421	328,353	144,454
Decrease In Short Term Deposits		(292,447)	71,383	(230,321)	56,219
Change In Net Funds		124,473	254,804	98,032	200,673
Net Funds at start of year		4,012,485	3,757,681	3,160,087	2,959,414
Net funds at end of year	8	**4,136,958**	4,012,485	**3,258,119**	3,160,087

The accounting policies on pages 47 to 48 and the notes on pages 52 to 56 form part of the financial statements.

Notes to the Financial Statements For the year ended 31 December 2001

1 Tangible Assets

	Fixtures & Fittings €	Computer Equipment €	Leasehold Property €	Total €	Total IR£
Cost					
Balance as at 1 January 2001	534,440	1,229,368	75,373	1,839,181	1,448,473
Additions for the year	110,019	312,242	-	422,261	332,558
Disposals for the year	(2,766)	(9,142)	-	(11,908)	(9,378)
As at 31 December 2001	**641,693**	**1,532,468**	**75,373**	**2,249,534**	**1,771,653**
Depreciation					
Balance as at 1 January 2001	400,449	1,056,623	13,459	1,470,531	1,158,137
Charge for the year	83,245	204,072	2,692	290,009	228,401
Disposals for the year	(2,766)	(9,142)	-	(11,908)	(9,378)
As at 31 December 2001	**480,928**	**1,251,553**	**16,151**	**1,748,632**	**1,377,160**
Net Book value at 31 December 2001	**160,765**	**280,915**	**59,222**	**500,902**	**394,493**
Net Book value at 1 January 2001	**133,991**	**172,745**	**61,914**	**368,650**	**290,336**

2 Fee Income

	2001 €	2000 €	2001 IR£	2000 IR£
Clinical Trials	128,539	134,021	101,233	105,550
Human Medicine - National Fees	3,580,038	3,693,303	2,819,509	2,908,713
Human Medicine - European Fees	2,623,195	1,624,377	2,065,934	1,279,301
Veterinary Medicine - National Fees	662,532	799,262	521,786	629,470
Veterinary Medicine - European Fees	264,782	136,295	208,533	107,341
Inspectorate Department	552,682	532,837	435,272	419,643
Medical Devices	5,960	-	4,694	0
Reduction In Bad Debts Provision	-	4,232	0	3,333
	7,817,728	**6,924,327**	**6,156,961**	**5,453,351**
Fee Income can also be analysed as follows :				
Income recognised on a cash receipts basis	5,722,928	4,836,865	4,507,172	3,809,341
Income recognised on an accruals basis	2,094,800	2,087,462	1,649,789	1,644,010
	7,817,728	**6,924,327**	**6,156,961**	**5,453,351**

3 Salaries and Wages

	2001 €	2000 €	2001 IR£	2000 IR£
Salaries and Wages	4,912,785	4,241,289	3,869,132	3,340,287
Social Welfare Costs	451,027	383,452	355,213	301,993
	5,363,812	**4,624,741**	**4,224,345**	**3,642,280**

The average number of staff employed during the year was 140 (2000 - 133).

Staff employed at 31 December 2001 can be analysed across the following departments : -

	2001	2000
Medical Technical	10	11
Pharmaceutical Technical	15	19
Veterinary Technical	6	3
Inspectorate Technical	7	7
Medical Devices Technical	2	2
Enforcement Technical	5	1
Herbal Medicines Technical	1	1
Controlled Drugs Technical	1	-
Administrative and Operational Staff	91	87
Pensioners	4	4
	142	135

4 Operating Costs

	2001 €	2000 €	2001 IR£	2000 IR£
Accommodation Costs	878,991	932,839	692,262	734,671
Travel, Representation and Training	408,186	348,317	321,473	274,322
Legal Costs	434,322	58,666	342,056	46,203
Stationery, Publications and Postage	240,849	221,460	189,684	174,414
Other Operating Costs	672,620	529,609	529,731	417,101
	2,634,968	2,090,891	**2,075,206**	1,646,711

5 Debtors *(all due within one year)*

Trade Debtors	559,989	325,209	441,027	256,123
Prepayments	116,338	230,323	91,624	181,394
Other Debtors	1,247,840	691,251	982,754	544,404
	1,924,167	1,246,783	**1,515,405**	981,921

Included in Other Debtors is an amount of EUR1,108,867 (IR£873,304) in respect of legal costs incurred by the IMB in their participation in the Tribunal of Enquiry of Infection with HIV and Hepatitis (of persons with Haemophilia and related matters.) While the award of costs by the Chairperson of any Tribunal is a discretionary matter, solicitors to the IMB have expressed the view that it has been the unequivocal practice and custom of all similar tribunals to award costs to any party that is legally represented before it and who has co-operated in its dealings with the Tribunal. The IMB has co-operated fully with the Tribunal and are confident that it will recover all costs on the same basis as occurred in case of the Tribunal of Enquiry into the Infection of Anti-D with Hepatitis C.

6 Creditors *(amounts falling due within one year)*

	2001 €	2000 €	2001 IR£	2000 IR£
Trade Creditors	267,133	437,807	210,384	344,801
Accruals	2,028,086	1,363,526	1,597,248	1,073,864
PAYE/PRSI	-	146,664	0	115,507
	2,295,219	1,947,997	**1,807,632**	1,534,172

7 Gross Cash Flows

Returns on Investment and Servicing of Finance:				
Deposit Interest	109,914	94,382	86,565	74,331
Bank Interest and Charges	(4,554)	(4,758)	(3,587)	(3,747)
	105,360	89,624	**82,978**	70,584
Capital Expenditure				
Payments to acquire Tangible Fixed Assets	(422,261)	(282,296)	(332,558)	(222,327)
Receipts from sales of Tangible Fixed Assets	533	280	420	221
	(421,728)	(282,016)	**(332,138)**	(222,106)
Management of Liquid Resources				
Payments to acquire Short Term Deposits	292,447	(71,383)	230,321	(56,219)
	292,447	(71,383)	**230,321**	(56,219)

8 Analysis of Changes in Net Funds

Cash at Bank and in Hand	2,012,885	1,595,964	1,585,276	1,256,924
Short Term Deposits	2,124,073	2,416,520	1,672,843	1,903,164
	4,136,958	4,012,484	**3,258,119**	3,160,088

9 Administration Expenses

Surplus for the year was calculated having charged : -				
Auditor's Remuneration	**8,500**	5,028	**6,694**	3,960

10 Income and Expenditure Reserves

The Income and Expenditure Reserve disclosed in the Balance Sheet on page 50 comprises the following :

Retained Reserves	3,523,922	3,144,727	2,775,313	2,476,674
Staff Superannuation Contributions	748,058	541,178	589,144	426,212
	4,271,980	3,685,905	**3,364,457**	2,902,886

11 Cash and Bank Balances	2001 €	2000 €	2001 IR£	2000 IR£
Current Account Balances	280,587	204,866	220,980	161,345
Deposit Account Balances	1,731,656	1,389,755	1,363,790	1,094,521
Cash on Hand	642	1,343	506	1,058
	2,012,885	**1**,595,964	**1,585,276**	1,256,924

12 Lease Commitments

Operating Leases

Amounts payable during the next twelve months in respect of leases which expire				
- within one year	859	654	677	515
- between two and five years	1,150	1,139	906	897
- after five years	606,300	606,300	477,500	477,500

The operating lease amounts include an annual commitment of EUR606,300 : IR£477,500 (2000 - EUR 606,300 : IR£477,500) in respect of the Board's premises at Earlsfort Terrace, Dublin 2.

13 Capital Commitments

No capital commitments had been entered into by the IMB at either 31st December 2000 or 2001.

14 Board Remuneration

Chairman's Salary	21,197	19,746	16,694	15,551
Board Member's Travel Expenses	4,665	2,473	3,674	1,948
	25,862	**22,219**	**20,368**	**17,499**

15 Staff Remuneration

Chief Executive's Salary	91,768	92,709	72,273	73,014
(Stated net of Superannuation Contributions)	**91,768**	**92,709**	**72,273**	**73,014**

16 Related Party Transactions

There have been no transactions with related parties which require disclosure under Financial Reporting Standard 8.

17 Contingent Liabilities

Anti-D Immunoglobulin

In early February 1994 the Irish Medicines Board was advised that Hepatitis C could have been transmitted through Anti-D Immunoglobulin produced from Irish blood plasma and manufactured by the Blood Transfusion Service Board. The Board has received letters before action and has been sued, with the Blood Transfusion Service Board, the Minister for Health and Children, Ireland and the Attorney General, in legal proceedings by a number of persons arising out of alleged infection by the Anti-D product. Further letters and proceedings are anticipated. The Board does not admit liability in these cases and thus will be defending them in full. In the settlements concluded to date, the IMB has not incurred any liability arising from the Anti-D Immunoglobulin cases and on that basis does not anticipate that any such liability will arise in the future. The DHC established a Tribunal of Enquiry to review the circumstances surrounding the infection of Anti-D with Hepatitis C. The Tribunal's findings were published in March 1997 and are available to the public from the Government Publications Office. The DHC also established a Tribunal for the purpose of providing ex-gratia compensation to persons infected with Hepatitis C through the use of the Anti-D Immunoglobulin product. Where an award made by the tribunal has not been accepted the claimant can pursue legal action.

18 Prompt Payment Of Accounts Act 1997

The report on the IMB's compliance with the requirements of the Prompt Payment of Accounts Act 1997 is contained in a separate section of the Annual Report.

19 Exchange Rates

The exchange rates used in preparing these Financial Statements were as follows : -

2001 EUR 1 = £0.787564 = STG£0.60 = BFR 40.3399

2000 EUR 1 = £0.787564 = STG£0.6125 = BFR 40.3399

20 Conversion To The Euro

All accounting systems in the IMB were converted over to the Euro on 1 November 2001. Detailed testing was carried out on test databases prior to the conversion and the changeover took place successfully. The costs associated with the changeover were not significant.

21 Approval of Financial Statements

The Financial Statements were approved by the Board on 29th May 2002.

08 Appendices

protecting public health

Appendix I
Executive Committee Members and Committees

Executive Committee

Dr. Frank Hallinan	Chief Executive
Dr. J. G. Beechinor	Veterinary Director
Dr Joan Gilvarry	Medical Director
Mr. John Lynch	Director of Inspection
Ms Suzanne McDonald	Systems Manager
Dr. J. Michael Morris	Pharmaceutical Director
Ms Ann O'Connor	Medical Devices Director
Ms. Rita Purcell	Director of Finance and Administration

Advisory Committee for Human Medicines

Professor Kevin O'Malley (Chairman)
Ms Eugenie Canavan
Dr Kevin Connolly
Professor Owen Corrigan
Dr Paule Cotter
Professor Ted Dinan
Professor Desmond Fitzgerald
Dr Mary Horgan
Dr Rory Lehane
Dr Kate McGarry
Mr Tom McGuinn
Dr Patrick Sullivan

Advisory Committee for Veterinary Medicines

Mr. Patrick J O'Connor, Chairman
Dr. Thomas Barragry
Mr. Patrick Brangan
Mr. Rory Breathnach
Ms. Eugenie Canavan
Dr. Anne Cullinane
Mr. Timothy Kyne
Mr. Desmond Leadon
Mr. John McArdle
Mr. Tom McGuinn
Mr. Paul Mulville

Clinical Trials Sub-Committee of Advisory Committee for Human Medicines

Dr. Patrick Sullivan (Chairman)
Dr. Liam T. Bannan
Professor David Bouchier-Hayes
Dr. Paul Browne
Professor Ted Dinan
Professor Desmond Fitzgerald
Dr. L. Grogan
Dr. Tom Peirce

Expert Sub-Committee of the Advisory Committee for Human Medicines

Professor Des Fitzgerald
Dr Brendan Buckley
Dr. Colin Buckley
Dr Mary Cafferkey
Dr. Owen Carey
Professor Martin Clynes
Professor Louis M. T. Collum
Dr. Peter Conlon
Dr. Kevin D. Connolly
Prof. Ted Dinan
Dr. George Duffy
Dr. Stephen Flint
Dr. Owen Hensey
Dr. Mary Horgan
Professor Hilary Humphreys
Dr. Gerry D. Hurley
Dr. Kevin Kelleher
Dr. Mary Keogan
Dr John McCaffrey
Dr. Patricia McCormack
Mr. T. McGuinn
Dr. David McInerney
Dr. Malachi McKenna
Professor Kingston Mills
Dr. Fiona Mulcahy
Dr. Frank Murray
Dr John O'Connor
Dr. Rosemary O'Connor
Dr. Veronica O'Donoghue
Dr. Janice Redmond
Dr. Mark Rodgers
Dr. Martina Scallan
Professor Brian Sheppard
Dr. John Stack
Dr. Brion Sweeney
Dr. Douglas Veale

Scientific Committee on Herbal Medicinal Products

Dr. D. Corrigan (Chairperson)
Dr. D. Clare
Ms. N. Darrell
Prof. E. Ernst
Mrs. I Hook
Ms. G. Lavelle
Ms. H. McCormack
Dr. K. Chan-Mullen
Dr. H. Sheridan

The Irish Medicines Board wishes to acknowledge the work of the experts without whose continuous support the Irish Medicines Board would have difficulty in carrying out its statutory functions. We wish particularly to express our appreciation to the following experts, who have left the committees during 2001 and to wish them every success in the future:

Dr Rosemary Boothman
Mr Albert Costelloe
Mr Declan Hickey
Professor Irene Hillary
Professor Michael Lambert
Professor Brian Leonard
Ms Claire McSweeney
Dr Grace Mulcahy
Dr. Iona Pratt
Dr Owen Smith

Appendix II
Meetings attended by staff members on behalf of the IMB

CPMP
COMP
CVMP
Mutual Recognition Facilitation Group (MRFG) & 'Breakout' Meetings
CPMP Safety Working Party
CPMP Efficacy Working Party
CPMP/CVMP Quality Working Party
CPMP Biotechnology Working Party
CPMP Pharmacovigilance Working Party
CPMP Working Party of Good Clinical Practice
CPMP Scientific Advice Review Group
CPMP ad hoc Working Party on Excipients
CPMP ad hoc Working Party on Blood Products
CPMP ad hoc Working Party on Anti-Cancer Agents
CPMP ad hoc Working Party of GCP Inspectors
CPMP ad hoc Working Party on Update on the Note for Guidance on the SPC
CPMP ad hoc Working Party on use of Thiomersal in Medicinal Products
CVMP Efficacy Working Party
CVMP Immunologicals Working Party
CVMP Pharmacovigilance Working Party
CVMP ad hoc Group on Availability of Veterinary Medicines
Emacolex
EMEA ad hoc Meeting of GMP Inspection Services
EMEA Management Board
EMEA Management Board Working Group on Fees
EMEA QRD Group
EMEA Working Party on Herbal Medicinal Products
ICH M2 Support Group
EU Commission Experts Meeting for Medical Devices
EU Commission Experts Meeting for In vitro Diagnostic (IVD) Medical Devices
EU Commission Pharmaceutical Committee Meeting
EU Commission EUDRANet Technical Implementation Group
EU Commission EUDRAVigilance Technical Implementation Group
EU Commission eSubmissions Technical Implementation Group
EU Commission Notice to Applicants Working Party
EU Council Meeting on Clinical Trials Directive
EU Council Meeting on Blood Transfusion Directive
European Pharmacopoeia Commission
Working Group Meeting on Vigilance for Medical Devices
Meetings of Heads of Regulatory Agencies of Human Medicinal Products
Meetings of Heads of Regulatory Agencies of Veterinary Medicinal Products
Annual Meeting of the European Society of Pharmacovigilance
Annual Meeting of the WHO Collaborating Centre
National CJD Advisory Committee
National Immunisation Committee (Ireland)
National Immunisation Steering Committee
Pan European Regulatory Forum PIC/S Committee of Officials
Veterinary Mutual Recognition Facilitation Group

Appendix III
Meetings attended by staff members as invited speakers

- Ms Niamh Arthur spoke on 'Structure and functions of IMB' to Post-graduate employees in pharmacovigilance at the University of Hertfordshire; on 'The IMB & Pharmacovigilance: Reporting ADRs, who, what, when, why & how' to the Eastern Regional Health Authority. Post-graduate Training Course for Nurses; on ' The IMB Pharmacovigilance'. 'Definition & Classification of ADRs', 'Recognition & Prevention of ADRs', Reporting ADRs, who, what, when, why & how' to the Irish Centre for Continuing Pharmacy Education, Post-graduate Training Programme for Pharmacists.
- Mr Brendan Casey spoke at the Concept Heidelberg/European Compliance Academy Modern API Facilities Conference in Cork on "GMP requirements for API Production - An Inspector's View".
- Dr D Dempsey presented lectures on 'Regulatory Status of Herbal Medicinal Products' to the Irish Centre for Continuing Pharmaceutical Education, Dublin, on 'Regulation of Herbal Medicines' to the Irish Herb Society, Dublin and on 'Regulation of Traditional Medicines - Changing Times' to the Irish Centre for Continuing Pharmaceutical Education, Cork.
- Dr. Joan Gilvarry gave lectures on 'Informed Consent and the EU Directive' at the European CT Conference in Brussels; on 'How Ireland will implement the CT Directive' at the European Conference on Clinical Trials in Berlin; on 'Clinical Trials Regulation in Ireland, Challenges in Clinical Trials' in Cork; on 'Consent and the EU Directive' at a Clinical Trials Conference in London and on 'Directive and Implications to Ireland' at the EU Clinical Trials Meeting in London.
- Dr F Hallinan gave Lectures on "Current EMEA Developments Affecting Pharmaceutical Manufacturing " at the Parenteral Drug Association (PDA) Meeting in Sicily in April 2001 and on "National Agency Perspective on the Outcome of Review 2001" at the British Institute of Regulatory Affairs Conference in York in Sept 2001.
- Dr V Irwin spoke on "Use of transgenic animals and plants in the manufacture of medicinal products: quality and safety aspects" and chaired the transgenic animals/plants session at Drug Information Association meeting in Barcelona Spring 2001.
- Dr David Lyons spoke on Good Clinical Practice in Clinical Trials at the Institute Formation Industrie Pharmaceutique in Paris, on Bioequivalence and Bioavailability the CPMP perspective at the Turkish Ministry of Health symposium on harmonisation, Istanbul, and on Scientific Advice for Orphan Medicinal Products at the IIR Seminar in London.
- Mr John Lynch spoke on "Irish Inspections - Observations" at the IPCMF / ISPE / FAS GMP Conference in Cork.
- Dr M Morris gave Lectures on "Process Validation Requirements" at the Annual ESRA/EMEA Meeting: Update on Quality in Amsterdam, 13/2/01; on "Validation during drug development" at a Pharmaceutical Consultancy Services Seminar on "Good Development Practice" in Strasbourg; on proval changes" at the ISPE/IPCMF Conference on "International Developments in GMPs, Regulations and Compliance-implications for Ireland" in Cork; on CTD at the CEFIC/APIC Conference in Vienna; on "Quality:- overall summary" at the EMEA Training meeting on CTD for Quality/Biotech assessors in London.
- Dr. T. Mitchell gave a presentation on EU regulatory procedures for biotechnology products at the University of Warwick Biotechnology Course; on "Pharmacogenetics: Applications & Implications, Present and Future" at the Society of Pharmaceutical Medicine meeting on Royal Society of Pharmaceutical Medicine in London; on "Regulatory Procedures/ Orphan Drugs" at the Regulatory Affairs Professionals Society Meeting in Madrid and on Regulatory Viewpoints on Pharmacogenetics in Clinical Trials at the Drug Information Association 3rd Annual Workshop on Pharmacogenetics in Lisbon.
- Mr Stan O'Neill made a presentation at a Honeyman Sterilisation Ltd. Course on Sterilisation: Principles and Practice on the topic of "Sterilisation" in Dublin.
- Dr. P. Salmon spoke at the Annual Introduction to European Regulatory Affairs at the European Society Regulatory Association Meeting in Brussels.
- Ms Linda Wolfe spoke on "Experience with Validation of Clinical Trial Materials - An Inspector's Viewpoint" at the PDA Conference on Process Validation for Manufacturing of Biologics and Biotechnology Products in Berlin.

Appendix IV
Publications

Beechinor, JG, Buckley, T & Bloomfield, FJ. Prevalence and public health significance of blemishes in cuts of Irish beef. The Vet Record 149, 43-44.

Beechinor, JG, & Bloomfield, FJ.(2001): Variability in residue concentrations of tilmicosin in cattle muscle. The Vet Record 149, 182-183.

Beechinor, JG, Buckley,T & Bloomfield,FJ. (2001): Prevalence of injection site blemishes in primal cuts of Irish pork. Irish Vet J. 54, 121-122.

Killalea SM, Krum H. (2001): Systematic review of the efficacy and safety of Perhexiline in the treatment of ischaemic heart disease. Am J Cardiovasc Drugs 1(3):193-204.

O'Hare P, Bilous R, ***Mitchell T*** et al. (2001): Low-dose ramipril reduces microalbuminuria in type 1 diabetic patients without hypertension: results of a randomised controlled trial International Diabetes Monitor / Nephrology, 13,3 Section 176, p 42, , no. 3.

Irwin, V. (2001) Prospects for producing biopharmaceuticals using transgenic higher animals or plants, Irish Pharmacy Journal, 79:4 143-145.

Appendix V
Prompt Payment of Accounts Act 1997

The Prompt Payment of Accounts Act came into operation on 2nd January 1998. The Irish Medicines Board (the IMB) comes under the remit of the Act. The payment practices of the IMB are reported on below for the year ended 31st December 2001 in accordance with Section 12 of the Act.

(a) It is the policy of the IMB to ensure that all accounts are paid promptly. Cheques are issued as required to ensure timely payments. In the event of a dispute between the IMB and a supplier, there is a procedure in place whereby all contact between the IMB and the supplier, concerning the dispute, is recorded.

(b) The system of internal control incorporates such controls and procedures as are considered necessary to ensure compliance with the Act. These controls are designed to provide reasonable, and not absolute, assurance against material non-compliance with the Act.

(c) There were no late payments during the year ended 31st December 2001 and accordingly no interest was paid in the year.

(d) The IMB has adopted procedures in accordance with guidelines issued by the Department of Enterprise, Trade and Employment in relation to the disclosure of relevant information.

Statement By Responsible Officer

The Irish Medicines Board (IMB) confirms that it is complying with the Prompt Payment of Accounts Act, 1997 as described in the statement and practices outlined above.

Rita Purcell
Director of Finance and Administration.

Glossary

ADR: Adverse Drug Reaction

AIMD: Active Implantable Medical Device

APHA: Animal and Plant Health Association

API: Active Pharmaceutical Ingredient

APMI: Association of Pharmaceutical Manufacturers of Ireland

CA: Competent Authority

COMP: Committee for Orphan Medicinal Products

CPMP: Committee for Proprietary Medicinal Products

CJD: Creutzfeldt Jakob Disease

CTD: Common Technical Document

CVMP: Committee for Veterinary Medicinal Products

DAFRD: Department of Agriculture, Food and Rural Development

DHC: Department of Health and Children

EC: European Community

ECTD: Electronic Common Technical Document

EDQM: European Directorate for Quality of Medicines

EEA: European Economic Area

EMEA: European Agency for the Evaluation of Medicinal Products

EU: European Union

FDA: Food and Drug Administration

FEDESA: European Federation of Animal Health

FOI: Freedom of Information

GCP: Good Clinical Practice

GMD: General Medical Device

GMP: Good Manufacturing Practice

HIV: Human Immunodeficiency Virus

HRT: Hormone Replacement Therapy

IAHS: Irish Association of Health Stores

ICH: International Conference on Harmonisation

IHTA: Irish Health Trade Association

IMB: Irish Medicines Board

IMDA: Irish Medical Devices Association

IPCMF: Irish Pharmaceutical and Chemical Manufacturers Federation

IPHA: Irish Pharmaceutical Healthcare Association

IVD: In-Vitro Diagnostic

MA: Marketing Authorisation

MAH: Marketing Authorisation Holder

MCA: Medicines Control Agency

MDA: Medical Devices Agency

MR: Mutual Recognition

MRA: Mutual Recognition Agreement

MRL: Maximum Residue Limit

NBOG: Notified Bodies Operations Group

NDAB: National Drugs Advisory Board

NSAI: National Standards Authority of Ireland

NSAID: Non Steroidal Anti Inflammatory Drug

PA: Product Authorisation

PERF: Pan European Regulatory Forum

Ph.Eur.: European Pharmacopoeia

PhVWP: Pharmacovigilance Working Party

PIC/S: Pharmaceutical Inspection Co-Operation Scheme

SCHMP: Scientific Committee on Herbal Medicinal Products

SWP: Safety Working Party

TSE: Transmissible Spongiform Encephalopathy

UN: United Nations

VPA: Veterinary Product Authorisation

WHO: World Health Organisation

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