IRISH MEDICINES BOARD

news LETTER

MEDICINAL PRODUCTS

JANUARY – APRIL 2004 Issue No. 17

IRISH MEDICINES BOARD, EARLSFORT CENTRE, EARLSFORT TERRACE, DUBLIN 2 TEL: 01 676 4971 FAX: 01 676 7836 EMAIL: FOI@IMB.IE

GENERAL

Michael Morris is the new president of the Council of Europe Pharmacopoeia

During the March meeting in Strasbourg, the European Pharmacopoeia Commission elected Michael Morris (Ireland) as its new president for a term of three years, following Henning Kristensen (Denmark). Dr Morris will take up his duty on 16 June 2004 after the celebration of the 40th anniversary of the European Pharmacopoeia.

EU PRESIDENCY MEETINGS

Ireland's presidency of EU meetings in the areas of medicines and medical devices began on 12 January, when the IMB hosted the 13th meeting of Competent Authorities for Medical Devices in Dublin, with the Department of Health and Children. The meeting was opened by the Minister for State at the Department of Health and Children, Mr Brian Lenihan, and a dinner was hosted by the Minister for Health and Children, Mr Michál Martin, who stressed the importance of the medical device industry in Ireland. Later in the month on 21 – 22 January, the CEO of the IMB, Mr Pat O'Mahony, chaired meetings of Heads of Agencies and Heads of Veterinary Regulatory Authorities. The informal meetings of the Committee for Proprietary Medicinal Products, the Committee for Orphan Medicinal Products and the Mutual Recognition Facilitation Group were held in Dublin on 29 – 30 April. Further meetings are planned for later in the six months' period of the presidency.

Ms A. O'Connor, Medical Devices Director, IMB; Mr M. Martin, Minister for Health and Children; Mr W. Higgins, Chairman of the Advisory Committee for Medical Devices; Mr C. Brekelams, Head of the Unit with responsibility for Medical Devices at the DG Enterprise of the EU Commission

Mr P. O'Mahony, Chief Executive of the Irish Medicines Board; Mr M. Martin, Minister for Health and Children; Mr P O'Mahony, Chairman of the Irish Medicines Board

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VETERINARY INFORMATION DAY

The 2004 Veterinary Information Day will take place in the Great Southern Hotel, Dublin Airport, on 1 July, 2004 between 10.00 am and 4.00 pm. A major part of the day's programme will be an update on the proposed changes to the Animal Remedies legislation in Ireland, as well as an update on the impact of the changes brought about by the EU review of the veterinary medicines directive (2001/82/EC). The IMB veterinary team as well as invited colleagues from the Department of Agriculture and Food will be available during the course of the day to address questions from delegates. Enquiries and bookings to Emily Hassett on 676 4971 ext 3320 or by email **emily.hassett@imb.ie**.

IMB INSPECTORATE INFORMATION DAY

The Inspectorate Department plans to hold an Information Day for manufacturers and other interested parties on 15 October 2004, at the CityWest Hotel, Saggart, Co. Dublin. This will be a full day event, and Inspectorate staff will present on a number of Good Manufacturing Practice- and Inspectorate-related topics of current interest.

Details relating to this Information Day will be made available in early July 2004 on the IMB website at www.imb.ie. This will provide a general outline of the topics which will be covered at the Information Day, and booking and registration details will be made available on the website at that time also.

NEW STAFF APPOINTMENTS

since our last Newsletter include

Zoe Nelson,	*Inspector*
Helene Plein,	*Toxicologist*
Jan Guerin,	*In-vitro Diagnostic Specialist*
Joanne Gallagher,	*Veterinary Immunologist*
Maeve Lally,	*Pharmaceutical Assessor*
Thomas Harty,	*Scientific Officer*
Bryan Cavanagh,	*Veterinary Technical Officer*

HUMAN MEDICINES

NEW LEGISLATION AND GUIDELINES

- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
- Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.
- Directive 2004/28/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/82/EC on the Community code relating to veterinary medicinal products.
- Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use.
- Directive 2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.
- Detailed guidance on the European clinical trials database (EUDRACT Database)
- Detailed guidance on the collection, verification and presentation of adverse reaction clinical trials on medical products for human use.
- Detailed guidance on the European database of Suspected Unexpected Serious Adverse Reactions (Eudravigilance – Clinical Trial Module)
- Detailed guidance on the application format and documentation to be submitted in an Ethics Committee opinion on the clinical trial on medical products for human use.
- Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial.
- Updating the Notice to Applicants – Part 1A application form, Chapters 1, 2,3 and 5, Volume 2B, Common Technical Document (CTD)
- A revised version of the 'Questions and answers' document related to the CTD was published 26 April 2004.
- CPMP/EWP/558/95 Note for Guidance on Evaluation of Medicinal Products Indicated for Treatment of bacterial Infections (CPMP adopted April 2004)
- CPMP/SWP/1094/04 Guideline on the Evaluation of Control Samples for Toxicokinetic Parameters in Toxicology Studies: Checking for Contamination with the Test Substance (Released for consultation March 2004) Corrigendum
- CPMP/QWP/1529/04 CPMP Guideline on Control of Impurities of Substances (adopted for implementation, April 2004)
- CPMP/QWP/227/02 (EMEA/CVMP/134/04) Note for Guidance on European Drug Master File procedure (Adopted by CPMP, January 2004)
- CPMP/BWP/2758/02 Guideline on Pharmaceutical aspects of product information for human vaccine. Effective June 2004.

PRODUCT AUTHORISATION SCHEDULE (SPC) GUIDANCE

Applicants' attention is drawn to the publication of a revised Schedule template under the Human Medicines Publications section of the IMB website **www.imb.ie**. Please note the addition also of supporting guidance notes on the formatting conventions to be followed. We would request applicants for all new national applications and new applications submitted under the Mutual Recognition procedure to use this template. All new applications currently under assessment will be issued using this format.

For the Summary of Product Characteristics section of the Schedule, information should be presented in accordance with the *Guideline on Summary of Product Characteristics* published on the EU Commission website (note: this guideline is included in The Rules Governing Medicinal Products in the European Union, Volume 2C: Notice to Applicants - Regulatory Guidelines).

Further useful guidance may be found in the EMEA *QRD Product Information Template with Explanatory Notes* which was updated last January. Please also refer to the EMEA website for the *QRD table of non-standard abbreviations* to be used in the Schedule, labelling and package leaflet.

ARTICLE 61(3) NOTIFICATIONS UNDER DIRECTIVE 2001/83/EC

Applicants' attention is drawn to the publication of a new IMB application form for Article 61(3) Notifications under Directive 2001/83/EC, on the Human Medicines Publications section of the IMB website **www.imb.ie**. Please note these notifications are for changes to labels and/or patient information leaflets not connected with changes to the SPC, in accordance with the Directive 2001/83/EC. Please note applications not using this form received after 15 September 2004 will not be validated.

NOTICE TO HOLDERS OF PRODUCT AUTHORISATIONS FOR HUMAN VACCINES

All batches of human vaccines marketed in Ireland are required to be subject to prior Official Control Authority Batch Release in accordance with Article 114.1 of Directive 2001/83/EC. A statement of this requirement appears in Part I of the Product Authorisation schedules issued by the IMB for all human vaccines.

The IMB requires that, for all batches of human vaccine proposed to be placed on the market in Ireland (with the exception of centrally authorised vaccines), the Product Authorisation holder shall have *transmitted* to the IMB the following documentation not less than eight working days before the proposed date of release of the batch on to the Irish market:

- A covering letter
- A copy of the Marketing Information Form, signed and dated by the qualified person within the company
- A copy of the OMCL Batch Release Certificate (or, in the special case of Poliomyelitis Vaccine (Oral), the certificate of approval for each monovalent bulk used to manufacture the batch of vaccine proposed to be released).

These notifications may be submitted:

- Via e-mail to **controlauthoritycerts@imb.ie**
- Via letter to Control Authority Certificates, Licensing Section, Irish Medicines Board, Earlsfort Centre, Dublin 2, Ireland.

Copies of the original forms should be retained by the company and made available to the IMB on request.

Product Authorisation holders must comply with the requirements to provide such notifications on an on-going basis to the IMB, commencing no later than 31 July 2004.

NOTICE TO HOLDERS OF PRODUCT AUTHORISATIONS FOR PLASMA DERIVED MEDICINAL PRODUCTS

All batches of plasma derived medicinal products marketed in Ireland are required to be subject to prior Official Control Authority Batch Release in accordance with Article 114.2 of Directive 2001/83/EC. A statement of this requirement appears in Part I of the Product Authorisation schedules issued by the IMB for all plasma derived medicinal products.

Notice is given that the IMB requires that, for all batches of plasma derived medicinal product proposed to be placed on the market in Ireland (with the exception of centrally authorised plasma derived medicinal products), the Product Authorisation holder shall have transmitted to the IMB, the following documentation, not less than eight working days before the proposed date of release of the batch on to the Irish market:

- A covering letter
- A copy of the Marketing Information Form, signed and dated by the qualified person within the company
- A copy of the OMCL Batch Release Certificate
- A copy of the OMCL batch release certificate of approval for the plasma pool used in the manufacture of the plasma derived medicinal product.

Notifications may be submitted:

- Via e-mail to **controlauthoritycerts@imb.ie**
- Via letter to Control Authority Certificates, Licensing Section, Irish Medicines Board, Earlsfort Centre, Dublin 2, Ireland,

Copies of the original Forms should be retained by the company and made available to the IMB on request.

Product Authorisation holders must comply with the requirements to provide such notifications on an on-going basis to the IMB, commencing no later than 31 July 2004.

IMPLEMENTATION OF THE CTD IN MR PROCEDURES

The date for implementation of the CTD format for dossiers in MR procedures (MRPs) has been put back from 1 January 2005 to 1 May 2005.

This means that old-format dossiers submitted to the RMS for the national authorisation before 1 July 2003 may be submitted in the same format for an MR procedure up to 30 April 2005. The MRP must have completed the validation phase by 30 April 2005.

Where the MRP does not start until 1 May 2005 or after, or where an old-format dossier was submitted to

the RMS for the national authorisation after 1 July 2003, the dossier must be re-formatted into the CTD format for the MRP.

NEW COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE REPRESENTATIVE

Since 1 May, each Member State is represented on the CHMP by one member , plus an alternate. The IMB is pleased to announce that Dr. David Lyons is the Irish member, and Dr. Patrick Salmon, the alternate.

PARALLEL PRODUCT AUTHORISATIONS

Updated Guide to Parallel Product Authorisations for Medicinal Products

The European Commission has recently issued an updated Communication on parallel imports, which is available from their website. The Communication provides guidance on the practical application of European Court of Justice rulings on parallel import cases and their application to national measures for dealing with parallel imports. One of the main new requirements for applicants and competent authorities relates to the expansion of the EU on 1 May.

In the Accession treaties with the Czech Republic, Estonia, Latvia, Lithuania, Hungary, Poland, Slovakia and Slovenia, there is a specific Intellectual Property Transitional Mechanism which affects parallel importation. Under this mechanism, a patent holder or the holder of a Supplementary Protection Certificate can rely on existing rights in the EU to prevent the importation and marketing of his product in a new or old Member State if the product was originally placed on the market in one of the eight countries listed above, irrespective of the country from which the importation occurs. If applicants wish to import medicinal products which were first placed on the market in these countries, they must give one month's notice to the patent or PA holder of their intention and confirm that they have done so in the application form. The notification must given the patent or PA holder sufficient information to adequately identify the product concerned.

The IMB's Guide to Parallel Product Authorisations for Medicinal Products for Human Use as been updated in line with the Commission Communication and the application forms for new applications and for applications to add additional sources have been updated to require applicants to provide the necessary confirmation as outlined above. These documents can be found on the IMB website.

PPAs and Generic MAHs: updating product information

Parallel importers and generic product marketing authorisation holders are reminded of their obligation to maintain and update their SPCs, package leaflets and labelling in line with those of the relevant originator products. This is of particular significance with respect to safety issues.

IR TO IE - CHANGE IN THE ABBREVIATION FOR IRELAND USED IN APPLICATION FORMS

Applicants should note that the two-letter abbreviation for Ireland used in application forms for marketing authorisations is being changed from IR to IE. IE is the correct ISO two-letter abbreviation for the country. This change has already been made in the EU variation form and will be included in the next versions of the Part IA application form and the EU renewal form.

RENEWALS

Applicants are reminded that the IMB National Additional Requirements Form requires details of the site of importation/distribution in Ireland. Any site listed in the application form is required to hold an appropriate Wholesaler's Licence as defined in the *Guidance note on the wholesaling of medicinal products for human use in Ireland*, available on the IMB Website at **http://www.imb.ie/uploads/publications/3431307_IND-001-01x.doc**

PROCEDURAL GUIDANCE FOR VARIATIONS/NOTIFICATIONS

Submission of notification and variation applications

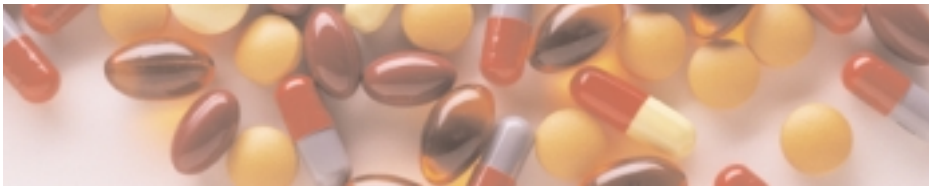
- Type IA and IB notification applications and Type II variation applications should be submitted separately in order to expedite the assessment process.
- Where the same variation is submitted by a company for a number of products or a number of product ranges, this should be clearly stated in the cover letter accompanying the variation. This applies even where the variations are not submitted at the same time.
- When a change is made to any manufacturing site, all current manufacturers and the site functions listed in Part I, Section 5 of the PA licence should be stated in the 'Present' and 'Proposed' sections of the application form. The same requirement also applies when changing drug substance manufacturer(s).

Labels/package leaflet changes

- When updating product labelling in line with guideline 'Excipients in the Label and Package Leaflet of Medicinal Products for Human Use' (Eudralex 3BI7a), both the labels and the package leaflets must be updated.
- When a variation is submitted to introduce any change to the labels and/or package leaflets, both the current and proposed labels/leaflets must be submitted in support of the variation.

Endorsements to schedule

- On approval of a variation, the IMB issues a revised schedule where applicable. PA holders should check the schedule at the earliest opportunity and if corrections are needed, send the annotated schedule to the IMB by return.



PRODUCT LABELLING

Use of the word 'New'

'New' may be used on product labelling in order to alert healthcare professionals and/or patients to a change to an existing product. In these cases, 'new' must be followed by the property that has changed, e.g., 'New markings', 'New formulation'.

Presentation of the product name

In line with the *Guideline on the Readability of the Label and Package Leaflet of Medicinal Products for Human Use*, the name of a medicinal product should consist of the invented name, strength and pharmaceutical form. The product name should appear as an integrated, cohesive unit in the same field of vision on the inner and outer labelling and the legibility of the name should not be adversely affected as a result of the application of company livery styles or logos.

Use of colour

An appropriate use of colour can aid clarity and identification of essential information on the outer and inner label. Due to the potentially critical impact of colour on clarity, final decisions cannot be made on labelling until full colour mock-ups are submitted.

TECHNICAL LEAFLETS

In response to a request for clarification on IMB requirements for technical leaflets supplied with medicinal products, we have adopted the following policy.

Technical leaflets or technical information may be provided either as:

- the full SPC, in the same document as the patient information leaflet or as a separate document, or
- practical information for preparation and/or handling of the product for medical and healthcare professionals (i.e. appropriate information from sections 4.2 and 6.6 of the SPC). This may be provided as a separate document or at the end of the patient information leaflet, with the heading, 'Information for the Healthcare Professional'.

Where either the full SPC or the preparation/handling information is provided in the same document as the leaflet, it may be presented as a tear-off section.

TRANSFER APPLICATIONS

A change has been made to the fees for transfer applications. Until now, no fee was charged for transfers before authorisation. The IMB has now decided to charge a small administrative fee of €120 to cover the costs involved in processing these applications. The Guide to Transfer of Product Authorisations has been amended to reflect this change and is available on our website.

NUMBER OF COPIES FOR CENTRALISED APPLICATIONS

For all centralised applications please send only one copy to the Receipts and Validations Department.

CORRECTIONS TO LICENCES

Companies should ensure that they notify the IMB, within 30 days of receipt of a licence (as a result of new, renewal or variation application) of any amendments or corrections required to the document. Notifications after the 30 day limit will require a variation application and relevant fee.

CLINICAL TRIALS

The requirements of Directive 2001/20/EC on clinical trials come into effect in Ireland on 1 May through the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004 (S.I. No. 190 of 2004). The IMB has issued a number of guidance documents and a new application form to be used with the EU application form:

- Guide to clinical trial applications
- Guidance on the investigational medicinal product dossier
- Guidance on EU clinical trial application form
- Guidance on clinical trial labelling requirements
- Form for additional national requirements for a clinical trial authorisation

These documents are available from our website.

Applications from 1 May 2004 must be in line with the requirements set out in the regulations and in the above guidance documents. Applications must include both the EU application form and the IMB form for additional national requirements. Before making an application, sponsors must obtain a EudraCT number by logging onto **http://eudract.emea.eu.int** and following the instructions to obtain a security code and to apply for the EudraCT number. This number, and the email confirmation of the number, must be included on the application. Applications which do not comply with the new requirements will not be validated.

Until the approval system of the Department of Health and Children for ethics committees is fully operational, the IMB will accept clinical trial applications without identification of the ethics committee in the application form, provided this information is notified to us when it is available.

Applicants should note that the current system of Clinical Trial Subcommittee meetings and cut-off dates still apply to applications received after 1 May.

Clinical trials authorised under the Control of Clinical Trials Act

Permissions for category 2 and 3 studies issued under the Clinical Trials Acts 1987 and 1990 state the following:

'In pursuance of section 11(1) (b) of the Act, the Irish Medicines Board hereby requests that a report on the progress of the trial shall be made to him on the expiry of this permission or not later than six months from the date of completion or cancellation of the trial.'

The IMB is attempting to close off those clinical trials on the clinical trials database that are listed as authorised but have had no regulatory activity for over 2 years.

A representative from the IMB will be in contact with clinical trial permission holders over the coming months by phone, or by letter, to determine the status of these clinical trials. It would be appreciated if per-

mission holders, in the meantime, could check the status of all clinical trials that have been authorised to determine if the relevant report on the progress of the trial has been submitted to the IMB. If no notification has been submitted, it would be appreciated if this report could be provided at the earliest convenience.

Notifications should be marked for the attention of the Clinical Trials Unit.

Transitional arrangements for trials under the Control of Clinical Trials Act

Clinical trials for which applications were under assessment on 1 May 2004

Applicants will need to update their applications in line with the Regulations. These updated applications will then be processed according to the timelines in the Regulations.

Clinical trials for which approval/permission was granted on 1 May 2004

Applicants should make any amendments under the Control of Clinical Trials Act and use the appropriate variation forms on the IMB website.

Clinical trials for which the permission is due to expire after 1 May 2004

Expiry dates on current permission no longer apply but applicants will have to re-apply under the Regulations if the trial continues past 1 May 2006.

For all on-going trials under the Control of Clinical Trials Act, annual safety reports must be provided, as required by Regulation 32(3) of he European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004 (S.I. No. 190 of 2004). The annual safety report should be submitted within 60 days of the end of the reporting year. The reporting year ends on the anniversary date of the first authorisation of the clinical trial. For information on the content of these reports, please consult the Guide to Clinical Trial Applications which is available on the IMB website.

ELECTRONIC ADR REPORTING

Further to previous newsletter articles, companies are reminded that the IMB continues to actively test electronic submission of ICSRs in order to meet the obligation for implementation of electronic reporting. A number of companies are now transmitting XML files to the IMB via the ESTRI gateway in accordance with the guidance detailed in the previous articles on this topic.

Additional companies interested in initiating electronic submission of ICSRs to the IMB should contact Ms. Shirley Mulvey at **smulvey@imb.ie** for further information and testing details.

Companies are reminded that in order to allow the IMB to comply with ICH E2B requirements, those who continue to submit paper copies of ADR reports as of May 2004 are requested to provide details of the *primary source reporter*. At a minimum the reporter's profession/occupation should be specified on the ADR report, eg, GP, dentist, pharmacist etc.

HOMEOPATHIC MEDICINES

Information Day

An information day was held at the Hilton Hotel, Dublin, on 27 January 2004. There were 78 participants including manufacturers and distributors of homeopathic medicinal products (HMPs) on the Irish market. In addition, representatives of the various organisations with an interest in homeopathic medicines, both national and international, as well as IMB staff, were in attendance.

The meeting opened with a welcome and introduction to the IMB by Mr. Pat O'Mahony CEO of the IMB. This was followed by a presentation on 'EU and Irish Legislation, pertaining to Homeopathic Medicines', by Mr. Tom McGuinn, Chief Pharmacist of the Department of Health and Children. The third presentation on the Simplified Registration Scheme (SRS) was given by Dr. Gwen Glasgow, Homeopathic Medicines Coordinator, IMB.

The second session included a presentation on the 'Industry's Perspective' given by Mr. Jonathan Griffith of Weleda Ireland, on behalf of the Irish Health Trade Association. The final presentation by Ms. Felicity Lee of the Homeopathic Expert Committee of the MHRA, gave an overview of the operation of the SRS in the UK.

The formal presentations were followed by a 'Questions and Answers' session with a panel composed of the speakers as well as a representative of the Inspectorate Department, IMB: This session was chaired by Dr. Mike Morris, Technical Director, IMB.

Presentations can be viewed on the IMB web site **www.imb.ie**.

Industry expressed their support for the registration scheme as launched by the IMB and their willingness to submit applications for the registrations of their products.

This process is currently underway for mineral product registrations and continues with the recent launch of phase 2 of the SRS, the call for plant registration applications (see notice at the end of this section, which appeared in the Irish Times 29 March 2003).

A number of issues relating to homeopathic medicinal products [HMP] on the Irish market, which need to be addressed, were acknowledged during the information day, these include:

1. HMPs with therapeutic indications currently available on the Irish market.

Only HMPs without indications qualify for the SRS in accordance with the EU Directive 2001/83/EC and S.I. No. 142 of 1998. In many of the Member States of the EU, (i.e. pre-1992) product licences exist, allowing HMPs carrying therapeutic claims to remain on their markets. Constraints of both EU and Irish legislation governing the SRS were highlighted at the information day.

After consultation on this issue it was agreed that the situation in other Member States would be examined, in particular the new national rules being implemented in the UK would be considered. Following this, consultation will take place with the Department of Health and Children and the IMB will revert back to industry on the issue in due course.

2. HMPs with invented names, currently on the Irish market.

There are a number of HMP on the

Irish market with invented names. In accordance with EU Directive 2001/83/EC and S.I. No. 142 of 1998, only HMPs with the scientific name of the stock(s) used are currently eligible for the SRS. Many of these products, with invented names, fall into the category of complex products (more than one stock), and these are in the final category of HMPs due for assessment (2004 - 2005).

In his presentation, Mr. Tom McGuinn pointed out that a common position to allow the use of invented names has been taken at EU level; this would apply where more than one stock has been used in the preparation of a HMP. This is due to come into effect in 2005. It was agreed that this would be taken into consideration, in particular when finalising the date for submission of complex product registration applications.

Notice in *Irish Times* 29 March 2004

LAUNCH OF THE SECOND PHASE OF THE SIMPLIFIED REGISTRATION SCHEME FOR HMP.

Medicinal Products (Licensing and Sale) Regulations, Statutory Instrument Number 142 of 1998: Simplified Registration Scheme for Homeopathic Medicinal Products for Human use.

Companies who wish to market Homeopathic Medicinal Products of plant origin, which qualify for the Simplified Registration Scheme, as provided for in the above regulations and in accordance with EU Directives for Human Medicines, 92/73/EEC and 2001/83/EC; are hereby notified that applications for such registration can be submitted to the Irish Medicines Board with effect from the 1st of April 2004.

All applications for products containing single plant substances, in homeopathic dilution, must be submitted to the IMB between 1/4/2004 and 30/9/2004, in order that such products may lawfully remain on the market.

Any product in the single plant category for which an application has not been submitted by the date above must be removed from the market by 31/12/2004.

Guidance Notes and Application Forms for the scheme are available directly from the IMB or on the web site at **www.imb.ie**.

VETERINARY MEDICINES

VETERINARY PHARMACOVIGILANCE ISSUES – 2003

The IMB received 78 national reports of suspected adverse reactions (SARs) to veterinary medicinal products (VMPs) for the period 1 January to 31 December 2003. Fifty-nine reports were received from marketing authorisation holders (MAHs), 13 directly from veterinary surgeons in practice, three from veterinary surgeons in regional veterinary laboratories and three directly from animal owners.

Of the total number of SARs reported, 65 involved veterinary pharmaceutical products and 17 concerned vaccines. The majority of SAR reports (n=75) related to single VMPs, with two or more VMPs identified in three reports. Suspected adverse drug reactions were reported in the following species: human (three reports), cattle (23), horses (five), sheep (23), pigs (five), dogs (14) and cats (five). Al 3 human SARs associated with the use of VMPs related to inadvertent self-injection.

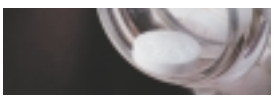
Lack of expected efficacy was reported for 25 VMPs. These included 13 reports relating to the use of triclabendazole for the treatment of Fasciola hepatica in sheep.

Of the remaining reports (n=53), the product(s) used was considered to have been probably or possibly associated with the observed reaction in 29 cases. In a further 19 cases there was insufficient information on which to base a conclusion relating to causality and in the remaining 5 cases it was concluded that the VMP(s) was definitely not the cause of the observed reaction.

A more detailed report on veterinary pharmacovigilance issues for 2003 is posted on the IMB website.

NEW COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS REPRESENTATIVE

Since 1 May, each Member State is represented on the CVMP by one member, plus an alternate. The IMB is pleased to announce that Dr. Gabriel Beechinor is the Irish member, and Mr Rory Breathnach, the alternate.



AVAILABILITY OF VETERINARY MEDICINES IN IRELAND

The IMB is concerned to ensure that there is an adequate range of authorised veterinary medicinal products available in this country. Initiatives to support this objective which have been made in recent years include:

- maintenance of a cost-effective, predictable and speedy authorisation system for veterinary medicinal products in this country;
- participation by IMB personnel in the development of EMEA policy on extrapolation of maximum residue limits from major food species to minor species, as well as the elaboration of minor use, minor species product development guidelines and elaboration of the provision for free advice on such products;
- the development of an informal harmonisation system for products marketed jointly in the UK and Ireland;
- support for applicants wishing to have dual labelling with other member states;
- support for applicants wishing to

harmonise renewal dates for national applications which are also authorised in other Member States;
- contributions to discussion at national and international fora on this subject.

The Director of Veterinary Medicines delivered a presentation on the 10 March on this subject to the Working Group on Medicines and Welfare of the Farm Animal Welfare Advisory Council established by the Minister for Agriculture and Food. IMB personnel have also met with other stakeholders in an attempt to improve the availability of medicines for minor uses in this country. As there are many challenges to this issue, including political, legal, financial, regulatory and logistical aspects, the IMB recognises that it cannot solve the dilemma on its own. However, in an effort to further contribute to the solution in a tangible way, the IMB has decided to:
- meet with applicant companies which might have or have been identified by stakeholders as having a product authorised in another EU Member State for a minor use indication to see if they would be interested in making application for such products in Ireland, and
- revise its criteria for the allocation of products as eligible for a much-reduced authorisation fee as a 'service item' (see separate article regarding the definition of such products).

Companies interested in this initiative are requested to contact Dr. J.G. Beechinor, Director of Veterinary Medicines, on + 353 1 676 4971 ext 3318/9.

CHANGE IN THE ABBREVIATION FOR IRELAND USED IN APPLICATION FORMS

VPA holders and applicants should note that the two-letter abbreviation for Ireland used in application forms for marketing authorisations is being changed from IR to IE. IE is the correct ISO two-letter abbreviation for the country. This change has already been made in the EU variation form and will be included in the next versions of the Part IA application form and the EU renewal form.

CRITERIA FOR ELIGIBILITY OF VETERINARY MEDICINAL PRODUCTS FOR SERVICE ITEM FEE

The Service Item fee category allows applicants to apply for a marketing authorisation for a veterinary medicinal product at a fraction of the cost to the IMB in providing the service. It therefore represents a significant commitment by the IMB to the provision of veterinary medicinal products for minor use indications in order to avoid animal suffering and safeguard public health. As the IMB Act requires the IMB to recover the costs of its activities, it is apparent that the 'Service Item' category is to be used exceptionally, in the interests of animal welfare and public health, to assist applicants in bringing applications to Ireland where the normal commercial returns from the market would not be expected to cover the applicable new product application fees.

Applications for consideration under this category will be judged on a case-by-case basis. However, the following general rules apply:

1. There is no alternative veterinary medicine currently authorised in Ireland.
2. There is a need for the product for the treatment or prevention of disease in animals or for the maintenance of animal welfare or public health.
3. Revenue from the sale of the product is limited and would not be expected to cover the applicable standard fee.
4. The IMB will recoup the difference between the Service Item fee and the applicable standard fee in those cases where an applicant wishes to make an application for mutual recognition of the Irish authorisation at a future date or in those cases where the returns from the market significantly exceed the expected revenues.
5. In the light of uptake of this category and the available IMB resource, the IMB reserves the right to alter any of the conditions. The IMB has committed to accept up to four products for the service item fee category for the current year and will review it position again in 2005 in the light of its budget for that year.

FEE INCREASE

The new Veterinary Fees were implemented on 10 March 2004. A letter was sent from our Accounts Department to all VPA Holders informing them of these new fees. The new Veterinary Medicines Fee Application Form and Guide To Fees For Veterinary Medicines can be viewed on our website www.imb.ie.

FUNDING OF THE VETERINARY SERVICE OF THE IMB

As discussed with stakeholders in 2003, the IMB intends to carry out a review of fees each year as part of its annual business cycle. As stakeholders will be aware, the IMB is obliged under the IMB Act 1995 to ensure that its income meets the costs of the provision of its services. The Veterinary Department had a deficit of 180,000 on its 2003 budget. The revised fees for 2004 for applications for veterinary medicinal products came into effect on 10 March, more than two months later than planned. The Board of the IMB has taken a decision that the Veterinary Department should recover the full costs of providing its services at the earliest opportunity. With this in mind, discussions on the framing of the fees for 2005 will commence early in summer with a view to their implementation on 1 January 2005.

IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCTS (IVMPS)

Proposed changes in the supply routes of IVMPs

The Department of Agriculture and Food (DAF) has proposed a number of significant changes to the Animal Remedies Regulations, including changes in the method of supply of IVMPs. One of the proposed changes which will impact on a number of IVMPs is the removal of the POM(E) supply category. On adoption of the legislative changes, the marketing authorisations for IVMPs with a sup-

ply route of POM(E) will need to be altered. The new supply route will be decided upon following an assessment of the risk:benefit profile of the product in accordance with a revised policy on the supply of IVMPs which has been adopted following consultation with DAF. This policy differs from previous IMB policy which was predominantly species-based and is based on a scientific evaluation of the risk:benefit profile of the product on a case-by-case basis. This revised policy has been implemented for all new and review product applications on 1 April 2004 (excluding those authorisations already issued by the DAF on or before that date). It is possible that the conditions for supply as stated in the product authorisation document in respect of the other authorised IVMPs may also need to be changed depending on the final legislative position. As stated previously, all such alterations will need to be made by way of a variation application together with the appropriate fee.

While awaiting the proposed legislative changes, the IMB is prepared to amend the marketing authorisation for products bearing a POM(E) supply route to the new route free of charge, if licence documents are being re-issued as a consequence of an application for a variation or a renewal. The IMB is adopting this approach in order to avoid unnecessary administration and packaging costs for the industry. However, it must be emphasised that authorisation holders are not obliged to alter supply routes at this time and may wish to wait until the proposed changes to the supply of animal remedies have been enacted.

Variations to IVMPs currently licensed under the Therapeutic Substances Act 1932.

In the past, IMB policy has been that variations to, or transfers of, products licensed under the Therapeutic Substances Act 1932 would be processed free of charge if the IMB had not started or was in the early stages of the review assessment. In the light of experience and in the knowledge of the financial constraints on the Veterinary Department this policy has now changed. The IMB has no option but to charge for all regulatory activities relating to review products, irrespective of their licence status. For information on the appropriate fee, please consult the IMB 'Guide to Fees'.

Diluents/solvents

The IMB would like to inform industry that it is prepared to accept separate applications for marketing authorisations for diluents (solvents) which are used to either reconstitute or dilute immunological active substances.

The IMB has adopted this approach as this licensing practice offers many advantages to authorisation holders e.g. for companion animal vaccines where the end-user has the option to reconstitute/dilute the active substance with either a liquid immunological or the solvent, supplying the immunological to the veterinarian without a solvent may reduce cost in terms of both solvent supply and disposal of unused solvent. In addition to this economic benefit, a reduction in waste disposal is of environmental benefit. Furthermore, as the same solvent may be recommended for reconstitution/dilution with a number of different immunologicals, a separate licence for the solvent may reduce packaging costs. As cost plays an important role in the availability of medicines, particularly for immunologicals which have a relatively small market, the IMB sees a reduction in unnecessary costs to be of great importance.

For further information please contact Pearl Healy on 676 4971 ext 3318 or by e-mail at **pearl.healy@imb.ie.**

LEGISLATION AND GUIDELINES

- List of Species and breeds revised after public consultation (EMEA/CVMP/553/03-CONSULTATION-Rev.1).
- Guideline on Causality Assessment revised after public consultation and comments received (EMEA/CVMP/552/03-CONSULTATION-Rev.1) The current document has been updated following consultation and adopted by CVMP, and comes into effect in October 2004.
- Revision of the Guideline for Fixed Combination Products (EMEA/CVMP/384/04).
- Joint CVMP/CPMP draft Guideline on stability testing for applications for variations to a marketing authorisation (EMEA/CVMP/373/04). October 2004.

These documents are available on the EMEA web site: **www.emea.eu.int**

PROPOSED AMENDMENTS TO THE ANIMAL REMEDIES REGULATIONS

The Department of Agriculture and Food has proposed a number of significant changes to the Animal Remedies Regulations. These changes are expected to have effects on several authorisations for veterinary medicinal products in Ireland including:

- Provision that veterinary medicines prescribed by a veterinary surgeon may in future, with certain exceptions, be supplied by Licensed Merchant outlets (with appropriately trained personnel) as well as by pharmacies and veterinarians.
- The removal of the 'Prescription only – Exempt' category from the sales categories provided for in the legislation.
- Designation of the IMB as competent authority for immunological veterinary medicinal products.

The department has consulted with the IMB and other bodies in relation to these and other proposed changes. It is expected that the department will finalise the legislation in early summer. Marketing authorisation holders who will need to amend the stated method of supply of their products to meet the new legislative requirements will be expected to submit applications for variation and pay the appropriate fee.

SIMPLIFIED REGISTRATION PROCEDURE FOR HOMEOPATHIC VETERINARY MEDICINAL PRODUCTS

Homeopathic products for use in pet animals are not subject to the usual full authorisation procedure for veterinary medicines but must be registered by the IMB according to a

simplified procedure. Currently this simplified system does not apply to homeopathic products for food producing species where the conventional standards of quality, safety and efficacy apply, although this may change following the introduction of revised EU and national legislation within the next two years.

Requirements for applications for pet animals are similar to those of human homeopathic products and similar to the requirements in other Member States for hamoepathic products for human use. The requirements are available on the IMB website in the relevant human medicines section. The pharmaceutical quality and manufacturing requirements are equivalent to those required for full authorisation. However in view of the nature of such products, no safety studies are required as long as there is a sufficient degree of dilution. Under the simplified procedure, no therapeutic indications or claims are permitted on product or promotional literature and so there is no requirement for efficacy studies. One application can cover a series of products derived from the same stock; fees are the same as for similar applications for human homeopathic products.

On receipt of an application, the IMB will allocate an individual product registration number (HoVR number). On approval of the application and of labelling mock-ups, a certificate of registration will be issued. The HoVR number and certain other text must be shown on the label.

The IMB will discuss any proposals for these applications with potential applicants. Please contact Emily Hassett on 676 4971 ext 3320 or by email **emily.hassett@imb.ie**.

STAFF CHANGES IN VETERINARY DEPARTMENT

Ms. Anita Moriarty, who has recently joined the Veterinary Department from the Human Medicines Department, has taken over responsibility for licence renewals and variations. Ms. Sinead Murphy has joined the Human Medicines Department after four years service in the Veterinary Department and we would like to express our thanks and wish her all the best in her new post.

Dr. Joanne Gallagher, Immunological Assessor and Mr. Bryan Kavanagh, Technical Officer, will join the Veterinary Department on the 1 June, 2004.

INSPECTORATE

NEW IMB GUIDANCE NOTE ON PRODUCT RECALLS – FOR COMMENT

The IMB is pleased to announce the publication for comment of a draft *Guidance Note For Product Authorisation Holders, Irish Manufacturers And Irish Wholesalers In Relation To The Recall Of Medicinal Products For Human And Veterinary Use*

This draft document is available in the News Section of our website **www.imb.ie**, so that stakeholders and other interested parties may review and comment on the provisions of the document prior to its finalisation, which is expected during August 2004.

Any comments on the provisions of this guidance note should be sent in writing, by email or by fax no later than 14 August 2004 to Kevin O'Donnell; **kevinodonnell@imb.ie** or by fax (01) 676 4061. Please clearly state your name and organisation, if any, when submitting. We will endeavour to take them into account when finalising the guidance note.

INFORMATION DAY ON SUPPLY AND DISTRIBUTION

The Inspectorate Department held an Information Day on the Supply and Distribution of Medicinal Products at Clontarf Castle, Dublin, on 14 April 2004. The Information Day focused on the supply by wholesalers to the grocery trade, and on the retail sale to the public by the larger grocery retail outlets.

The topics covered at the Information Day included:

- a review of medicinal product legislation;
- advice on what may and may not be sold in a non-pharmacy retail outlet;
- a brief on the common infringements found to occur in this supply line;
- the requirements for holding and maintaining a Wholesalers Licence;
- a review of the recall procedure for medicinal products.

It is hoped that this presentation will help those whose main business function is in food distribution and supply to be aware of the requirements of the medicinal products legislation, and to comply with the legislation in order to ensure the continued safeguarding of public health and safety.

DRAFT CHANGES TO THE EU GMPS – FOR COMMENT

Two sets of changes are currently proposed to the EU GMPs

Product Quality Review - Addition to Chapter 1 to the *EU Guide to Good Manufacturing Practice* and *Ongoing Stability - Addition to Chapter 6 to the EU Guide to good Manufacturing Practice*

The drafts can be viewed at **http://pharmacos.eudra.org/F2/eudralex/vol-4/home.htm** and the documents were open for comment until 15 June.

IMPORTATION OF MEDICINAL PRODUCTS

Companies are reminded that all medicinal products which are imported into the European Economic Area (EEA) must be formally released by a Qualified Person. Where a Mutual Recognition Agreement is not in place and operational

with the country of origin, the batches must be retested within the EEA before release. This requirement relates to a retest rather than an original test. Thus, the product should be tested at the site of manufacture in the originating country and also within the EEA for the purposes of batch release.

In late 2003, the European Commission published on its website a Guidance Note on this issue, providing a clear interpretation of the EU legislation governing the importation of human and veterinary medicinal products from third countries. Interested parties should go to the GMP section of the website, at **http://pharmacos.eudra.org/F2/pharmacos/gmp_doc.htm** for access to this guidance note, *Note to the Members of the GMP Inspectors group – Interpretation of Articles 51(1)b of Directive 2001/83/EC and 55(1)b of Directive 2001/82/EC*, dated 19 December 2003.

EMEA STATEMENT ON QP DISCRETION IN BATCH CERTIFICATION ACTIONS

On 27 January 2004, the EMEA published a statement on the subject of QP Discretion in Batch Certification Actions. The EMEA paper is available for review at **http://www.emea.eu.int/Inspections/docs/004704en.pdf.pdf**.

The statement includes reference to the QP notifying the Supervisory Authority of batches of medicinal products which failed to fully meet the requirements defined in the marketing authorisation and where the QP is considering certifying such batches for release. However it should be noted that, for products authorised for marketing in Ireland, the Batch Specific Request procedure operated by IMB specifically precludes the presentation of out-of-specification batches for consideration under that procedure.

Human New Product Authorisations Issued (January–April 2004)

PA Number	Product Name	PA Number	Product Name
PA0021/052/001	ALKA RAPID CRYSTALS	PPA0465/091/006A	SERETIDE EVOHALER
PA0022/088/001	MELIANE	PPA0465/105/001A	COMBIVENT METERED
PA0022/088/002	MELIANE ED	PPA0465/105/002A	COMBIVENT UDVS
PA0043/025/002	STREPSILS INTENSIVE SUGAR FREE ORANGE	PPA0465/106/001A	COZAAR
		PPA0465/109/001A	COZAAR-COMP
PA0281/106/001	DICLO 75 RETARD	PPA0465/111/001A	SINGULAIR
PA0290/075/001	PHYSIOTEARS	PPA0465/112/001A	MOBIC
PA0320/005/003	COLGATE TOTAL PLUS WHITENING	PPA0465/112/002A	MOBIC
PA0437/016/008	GENTAMICIN INJECTION BP	PPA0465/114/001A	ARTHROTEC
PA0476/015/001	AMOCLAV	PPA0465/114/002A	ARTHROTEC
PA0577/034/002	GERMENTIN	PPA0465/116/001A	ATACAND
PA0577/034/003	GERMENTIN	PPA0465/116/002A	ATACAND
PA0690/009/001	INDIUM (111IN) DTPA	PPA0465/117/001A	ATACAND PLUS
PA0748/003/013	RISPERDAL QUICKLET	PPA0465/118/001A	CELEBREX
PA0748/003/014	RISPERDAL QUICKLET	PPA0465/118/002A	CELEBREX
PA0748/003/015	RISPERDAL QUICKLET	PPA0465/119/001A	CORDARONE X
PA0934/001/001	NALTREXONE 50 mg Film-coated Tablets	PPA0465/121/001A	SELECTOL
		PPA0465/121/002A	SELECTOL
PA0934/002/001	ETHYLEX	PPA0465/123/001A	ZINNAT
PA1077/097/004	SEROXAT	PPA0465/127/001A	SEREVENT INHALER
PPA0465/091/004A	SERETIDE EVOHALER	PPA1151/001/001A	SINEMET CR
PPA0465/091/005A	SERETIDE EVOHALER		

Human New Product Authorisations Withdrawn (January–April2004)

PA Number	Product Name	PA Number	Product Name
PA0006/011/004	Soframycin Skin	PA0013/079/001	Diovan
PA0013/070/004	Estraderm MX	PA0013/079/002	Diovan
PA0013/070/005	Estraderm MX	PA0013/087/009	Voltarol Ophtha
PA0013/070/006	Estraderm MX	PA0013/098/001	Riamet

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Human New Product Authorisations Withdrawn (January–April2004)

PA Number	Product Name
PA0013/108/001	Penciclovir Intravenous
PA0013/108/002	Penciclovir Intravenous
PA0016/024/004	DEPO-PROVERA
PA0016/054/002	VERYL
PA0017/055/001	Vasoxine
PA0019/013/005	VIBRAMYCIN-D
PA0019/013/008	VIBRAMYCIN
PA0019/013/009	VIBRAMYCIN
PA0019/024/004	FELDENE
PA0019/024/006	FELDENE DISPERSIBLE
PA0019/024/007	FELDENE DISPERSIBLE
PA0019/024/009	FELDENE IM
PA0019/024/011	FELDENE MELT
PA0019/024/012	FELDENE MELT
PA0019/044/003	DIFLUCAN
PA0022/020/001	Mucaine
PA0035/042/001	MEFOXIN
PA0035/042/002	MEFOXIN
PA0035/044/005	Blocadren
PA0035/046/001	Cogentin
PA0035/051/001	Aldomet
PA0035/070/003	TIENAM I.V. 13ML
PA0035/077/001	NOROXIN
PA0037/023/010	METHOTREXATE
PA0038/016/001	HARMOGEN
PA0038/086/001	NIAR
PA0043/034/001	EMZOL
PA0044/009/002	Ceporex
PA0044/009/003	Ceporex
PA0046/035/001	Minihep Syringes
PA0050/143/001	Berocca
PA0060/042/001	ERVEVAX
PA0062/026/011	Flemoxin Solutabs
PA0062/026/012	Flemoxin Solutabs
PA0062/026/013	Flemoxin Solutabs
PA0062/026/014	Flemoxin Solutabs
PA0062/026/015	Flemoxin Solutabs
PA0062/026/016	Flemoxin Solutabs
PA0073/138/001	FEMPLAN - MA .
PA0077/002/001	DANOL
PA0077/002/002	DANOL
PA0077/003/002	Hexopal Forte
PA0077/046/001	PYROGASTRONE
PA0077/117/001	Ossopan 800
PA0126/025/002	MELZINE
PA0126/025/004	MELZINE

PA Number	Product Name
PA0126/028/001	Tiperal
PA0167/037/013	Mannitol
PA0167/037/014	Mannitol
PA0167/042/001	Dianeal With Glucose 1.36 %
PA0167/043/001	Dianeal 130/Glucose 1.36 % w/v/ 13.6 mg/ml
PA0167/044/001	Dianeal/Glucose 3.86%
PA0167/045/001	Dianeal 130/Glucose 1.36%/Potassi-um 2.5mmol/l
PA0172/004/004	Soluble Anadin
PA0172/027/001	Axid AP
PA0172/036/001	Infra-Rub Pain Relieving
PA0172/036/002	Infra-Rub
PA0206/011/001	BELLADONNA POROUS PLASTER ON RED FLANNELETTE
PA0212/003/004	Gammabulin Lyophilised
PA0218/025/002	ACTRAPID PENFILL
PA0218/026/002	INSULATARD PENFILL
PA0218/026/003	INSULATARD NOVOLET
PA0218/029/002	MIXTARD 30 PENFILL 1.5 ML
PA0218/029/003	MIXTARD 30 NOVOLET 1.5 ML
PA0218/033/002	MIXTARD 10 PENFILL
PA0218/034/002	MIXTARD 20 PENFILL 1.5 ML
PA0218/035/002	MIXTARD 40 PENFILL 1.5ML
PA0218/036/002	MIXTARD 50 PENFILL 1.5ML
PA0236/013/004	CISPLATIN
PA0236/013/006	CISPLATIN
PA0257/012/001	Top C
PA0261/002/001	HUMEGON
PA0261/002/002	HUMEGON
PA0281/026/001	Primacine
PA0281/028/003	Naprex Enteric Coated
PA0281/028/004	Naprex Enteric Coated
PA0281/036/001	Pinamox
PA0281/036/002	Pinamox
PA0281/044/001	Pinalgesic
PA0281/060/001	Temazine
PA0281/060/002	Temazine
PA0281/084/001	Tenchlor
PA0281/084/002	Tenchlor
PA0281/092/003	Pinamet
PA0281/104/001	Azathioprine
PA0290/001/001	Isopto Frin
PA0290/003/001	Isopto Carbachol
PA0290/004/001	Isopto Atropine
PA0290/005/001	BSS (Balanced Salt Solution)

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Human New Product Authorisations Withdrawn (January–April2004)

PA Number	Product Name
PA0408/023/001	Compound Magnesium Trisilicate
PA0436/012/001	CIMETIDINE
PA0436/012/002	CIMETIDINE
PA0436/012/003	CIMETIDINE
PA0437/018/001	Methylprednisolone Sodium Succinate
PA0437/018/002	Methylprednisolone Sodium Succinate
PA0506/018/001	METANIUM
PA0540/074/003	SUPREFACT DEPOT 3 MONTHS
PA0549/006/001	ETHYPHARM PARACETAMOL
PA0549/006/002	ETHYPHARM PARACETAMOL
PA0549/006/003	ETHYPHARM PARACETAMOL
PA0549/008/001	ETIPROFEN SR
PA0549/012/001	TOPFEN
PA0549/012/002	TOPFEN CR
PA0549/012/003	TOPFEN CR
PA0566/011/001	Vamin 9
PA0566/011/002	Vamin 9
PA0590/011/001	ERYACNE 2
PA0590/011/002	ERYACNE 4
PA0677/004/001	HEMATOCIS Kit for labelling red blood cells
PA0677/011/001	Thallium Chloride
PA0677/014/001	PHYTACIS
PA0711/021/001	CEC
PA0711/021/002	CEC
PA0711/022/004	Tamox
PA0751/005/001	Peritoneal Dialysis COD 55
PA0751/005/002	Peritoneal Dialysis COD 55
PA0751/005/003	Peritoneal Dialysis COD AA
PA0751/005/004	Peritoneal Dialysis COD AA
PA0751/005/005	Peritoneal Dialysis COD AC
PA0751/005/006	Peritoneal Dialysis COD AC
PA0793/001/001	ISOFLURANE MEDEVA EUROPE
PA0819/009/001	Lisinopril-ratio
PA0819/009/002	Lisinopril-ratio
PA0819/009/003	Lisinopril-ratio
PA0819/009/004	Lisinopril-ratio
PA0822/001/007	LUSTRAL
PA0872/003/001	CORLOPAM
PA0907/001/001	LANSINOH FOR BREASTFEEDING MOTHERS
PA0970/036/005	Bricanyl Spacer Inhaler
PA0970/039/001	Entocort CR
PA0970/055/001	XYLOCARD
PA0970/058/001	ROSUVASTATIN ASTRAZENECA
PA0970/058/002	ROSUVASTATIN ASTRAZENECA
PA0970/058/003	ROSUVASTATIN ASTRAZENECA
PA1046/006/002	TRAMADOL HYDROCHLORIDE
PA1077/045/001	Respirontin Nebules
PA1077/051/001	Alkeran
PA1077/051/003	Alkeran
PA1077/065/002	Leukeran
PA1077/070/001	Myleran
PA1077/096/001	PENBRITIN
PA1077/096/002	PENBRITIN
PPA0465/008/001B	AMOXIL
PPA0465/068/003A	CIPRAMIL
PPA0465/068/003B	CIPRAMIL
PPA0465/092/001A	LAMICTAL
PPA0465/092/002A	LAMICTAL
PPA0465/092/003A	LAMICTAL

Human New Product Authorisations (Mutual Recognition) (January–April 2004)

PA Number	Product Name
PA0877/003/001	Rabipur
PA0013/112/001	RESCULA
PA0050/138/002	TRANSIPEG
PA0167/101/004	PHYSIONEAL 35 GLUCOSE
PA0167/101/005	PHYSIONEAL 35 GLUCOSE
PA0167/101/006	PHYSIONEAL 35 GLUCOSE
PA0365/083/001	EQUASYM
PA0365/083/002	EQUASYM
PA0365/083/003	EQUASYM
PA0566/006/004	GLAMIN
PA0566/031/001	Glucose 5% w/v Intravenous Infusion BP
PA0566/031/002	Glucose Intravenous Infusion BP 5%,
PA0566/031/003	Glucose 5% w/v Intravenous Infusion BP
PA0566/031/004	Glucose 5% w/v Intravenous Infusion
PA0566/031/005	Glucose 10 % w/v Intravenous Infusion BP
PA0566/031/006	Glucose 10 % w/v Intravenous Infusion BP
PA0566/031/007	Glucose 10 % w/v Intravenous Infusion BP
PA0566/031/008	Glucose 10 % w/v Intravenous Infusion BP
PA0577/050/001	PAXT
PA0577/050/002	PAXT

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Human New Product Authorisations (Mutual Recognition) (January–April 2004)

PA Number	Product Name	PA Number	Product Name
PA0711/051/001	Lispril-Hydrochlorothiazide	PA0654/015/001	FemSeven Conti
PA0711/051/002	Lispril-Hydrochlorothiazide	PA0736/018/003	PROPOFOL-LIPURO 2%
PA1129/001/001	RUPAFIN	PA0819/027/001	LISINOPRIL Hydrochlorothiazide
PA1130/001/001	Simator	PA0819/027/002	LISINOPRIL Hydrochlorothiazide
PA1130/001/002	Simator	PA0865/002/003	KERAL
PA1130/001/003	Simator	PA0876/006/001	SIMVASTATIN
PA1130/001/004	Simator	PA0876/006/002	SIMVASTATIN
PA0007/063/001	MUCOANGIN	PA0876/006/003	SIMVASTATIN
PA0012/095/001	ANGELIQ	PA0876/006/004	SIMVASTATIN
PA0012/096/001	ALLURENE	PA0901/001/003	ENANTYUM
PA0035/085/005	SINGULAIR ALLERGY	PA0970/027/003	NEXIUM
PA0281/118/001	LOSEPINE	PA0970/047/009	NAROPIN
PA0281/118/002	LOSEPINE	PA0979/011/006	GAVISCON ADVANCE Peppermint
PA0437/051/001	IRINOTECAN HYDROCHLORIDE	PA0979/011/007	GAVISCON ADVANCE - PEPPERMINT
PA0540/018/002	SYNERCID	PA1014/001/002	COPAXONE
PA0540/078/001	TELFAST	PA1070/003/001	DOXORUBICIN
PA0544/039/001	POLIOMYELITIS VACCINE (Inactivated)	PA1126/001/001	Tiritek Allergy
PA0573/006/001	COLOSOL	PA1139/001/001	OLUX
PA0577/054/001	SIMVASTATIN	PA1147/001/001	PAROSER
PA0577/054/002	SIMVASTATIN	PA1165/001/001	Niaspan
PA0577/054/003	SIMVASTATIN	PA1165/001/002	Niaspan
PA0577/054/004	SIMVASTATIN	PA1165/001/003	Niaspan
PA0585/012/001	PRESINEX	PA1165/001/004	Niaspan

Veterinary New Product Authorisations Issued (January–April 2004)

VPA Number	Product Name	VPA Number	Product Name
10990/038/001	TRAMAZOLE DRENCH	10019/063/003	RIMADYL TABLETS 100 MG
10990/038/002	TRAMAZOLE DRENCH	10966/028/001	MARBOCYL P
10960/052/001	MAXIMEC HORSE	10966/028/002	MARBOCYL P
10019/079/001	RIMADYL PALATABLE	10966/028/003	MARBOCYL P
10019/079/002	RIMADYL PALATABLE	10859/012/001	FATROMECTIN CATTLE 0.5 % POUR-ON SOLUTION
10019/079/003	RIMADYL PALATABLE		

Veterinary New Authorisations Issued (Mutual Recognition) (January–April 2004)

VPA Number	Product Name	VPA Number	Product Name
10832/001/001	HIPPOTWIN	10021/047/003	ADVANTIX SPOT-ON SOLUTION FOR DOGS > 10 UP TO 25KG
10836/002/001	DALMARELIN 25 MICROGRAM/ML SOLUTION FOR INJECTION	10021/047/004	ADVANTIX SPOT -ON SOLUTION FOR DOGS OVER 25KG
10021/047/001	ADVANTIX SPOT-ON SOLUTION FOR DOGS UP TO 4KG	10825/002/001	JOHNSON FORFLEAS DOG COLLAR
10021/047/002	ADVANTIX SPOT-ON SOLUTION FOR DOGS > 4 UP TO 10KG	10955/013/001	HYPERCARD 10MG COATED TABLETS

Veterinary Product Authorisations Withdrawn (January–April 2004)

VPA Number	Product Name	VPA Number	Product Name
10019/004/001	TERRAMYCIN SOLUBLE	10950/002/001	LEVAVERM
10019/005/001	TERRAMYCIN SOLUBLE CONCENTRATE	10950/003/001	FENAVET WORM DRENCH
10857/024/001	IVOMEC SR BOLUS FOR CATTLE	10966/018/001	CEFASEPTIN MITE
10910/003/001	ARNOVERM	10988/057/001	FORAMIN PLUS

Veterinary Immunological New Authorisations Issued (January–April 2004)

VPA Number	Product Name	VPA Number	Product Name
10857/059/001	Gallivac SE	10996/179/001	Porcilis Glässer
10861/083/001	Poulvac IBBM + Ark		

Veterinary Immunological Review Authorisations Issued (January–April 2004)

VPA Number	Product Name	VPA Number	Product Name
10277/067/001	SCABIVAX	10861/060/001	POULVAC BURSINE 2
10277/064/001	FOOTVAX	10996/167/001	NOBIVAC PARVO C10996/137/1 Nobilis Marek THV lyo
10996/171/001	NOBIVAC TRICAT	10996/177/1	Nobivac Solven
10861/058/001	POULVAC IBMM		
10996/169/001	NOBIVAC LEPTO 2		