IRISH MEDICINES BOARD

news LETTER

MEDICINAL PRODUCTS

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GENERAL

Chief Executive of Irish Medicines Board moves to Pharmaceutical Industry

The Irish Medicines Board (IMB) announced that Professor Frank Hallinan resigned as Chief Executive a position he held since 1998. Professor Hallinan is joining Wyeth Biopharma as Director of Quality.

The Chairman of the Board, Mr. Pat O'Mahony thanked Professor Hallinan for his immense contribution to the IMB during his four-year term. *"Professor Hallinan oversaw extensive organisational and managerial changes in the Irish Medicines Board which provided huge benefits for the efficient and smooth running of the IMB during a very challenging period. On behalf of the Board, I wish him well in his new position."*

Irish Medicines Board Appoints New Chief Executive

The Board of the IMB is pleased to announce the appointment of Mr. Pat O'Mahony, MVB, MVM, MBA, MRCVS as Chief Executive Officer of the IMB. He took up his new position on 9 December 2002. As CEO, Mr. O'Mahony will advise the Board on policy and strategic direction of the organisation. He will be responsible for the management of the day to day activities of the IMB, with the assistance of the senior executive team and expert committees and sub-committees. He will also represent the IMB to industry, statutory bodies, the EU and the general public.

Mr. Pat O'Mahony, MVB, MVM, MBA, MRCVS the new Chief Executive Officer of the IMB.

Mr. O'Mahony joins the IMB from the Food Safety Authority of Ireland where he was Director of Consumer Protection. He has 12 years experience in the food safety sector and worked as a Technical Manager in the pharmaceutical industry in Ireland and the UK. As a qualified veterinary surgeon, he spent a number of years in private veterinary practice. Mr. O'Mahony also holds a Masters Degree in Veterinary Medicine and an MBA degree from the Michael Smurfit Graduate School of Business, UCD.

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2002 IMB Information Days

INSPECTORATE INFORMATION DAY

An Inspectorate Department Information Day took place in the Citywest Hotel, Saggart, Co. Dublin on Friday, 27 September 2002. The purpose of the event was to provide industry and other interested parties with an update on Inspectorate thinking and on current requirements. The meeting also provided companies with an opportunity to meet the staff of the Inspectorate, and presented an opportunity for Inspectorate staff to receive industry feedback and comments. This was the third Inspectorate Information Day, and the large number of attendees (220) demonstrated that there is considerable interest from industry in IMB events such as these.

Dr Joan Gilvarry, IMB's Medical Director, opened the meeting, and presentations were then given by several Inspectorate staff members, as well as from industry and MCA. The topics covered were:

- A Validation Approach to setting up a New Drug Product Manufacturing Facility (Dr. Bettina Krausenbaum, Pfizer Ireland Pharmaceuticals)
- Post-Marketing Compliance Monitoring (Ms. Muireann Lydon, Senior Inspector & Inspectorate Quality Manager, IMB)
- Sampling (Mr. Paul Sexton, Inspector, IMB)
- GMP Deficiencies (Mr. Victor Garvin, Inspector, IMB)
- Current Inspectorate Issues - Pharmacovigilance, Manufacturer's Licences, Marketing Authorisations, Technical Agreements, Site Master files, Sterile Manufacturing, Self-Inspection Reports (Mr. Stan O'Neill, Senior Inspector, IMB)
- Inspection Experience with Isolators (Dr. Ian Thrussell, Senior Inspector, Medicines Control Agency, UK)
- Enforcement Update (Mr. Hugo Bonar, IMB)
- PIC/S & The International Medicinal Inspectorate (Mr. Brendan Casey, Senior Inspector, IMB)
- Update on Legislation and Other Topical Issues (Mr. John Lynch, Director of Inspection, IMB)

There was a Question & Answer session at the end of the day, and a number of interesting questions were put forward for discussion.

Copies of the IMB presentations may be obtained by telephoning the Inspectorate Department on 01-6764971.

CONTROLLED DRUGS PROJECT INFORMATION MEETING

An information meeting on the transfer of the controlled drug licensing and regulation functions from the Department of Health and Children to the IMB took place on the 6 November 2002 in Dublin.

The Department of Health and Children and the IMB jointly hosted the meeting. Presentations were given by Mr Tom McGuinn, Chief Pharmacist, and Ms Louise Kenny Assistant Principal, both from the Department of Health and Children, and Dr Lorraine Nolan, Controlled Drugs Project Manager, IMB. The presentations gave an overview of the key aspects of the project which include the arrangements for control currently provided by the Department of Health and Children, the proposed amendments to legislation necessary for the IMB to undertake these functions, and new developments once the transfer to the IMB has been completed.

Attendees were present from a range of sectors including the pharmaceutical and chemical industries, healthcare sector and others. The IMB and the Department of Health and Children would like to express their thanks to all attendees at what was considered an informative and beneficial meeting.

Updates on the development of this project and its progression towards the stage of transfer will regularly be available through the IMB website and also through the IMB Newsletter.

NEW IMB WEBSITE

The IMB launched a new version of its website www.imb.ie at the end of 2002. The new site aims to provide ease of navigation across the various activities carried out by the IMB, together with a simple mechanism to find and download relevant guidance, publications and application forms.

In 2003 further improvements to the site will occur with enhanced 'on-line' functionality for both health care professionals and industry users. Further information will be published in the IMB newsletters.

We welcome feedback on the style and content of our site and would ask you to send any suggestions to us at imb@imb.ie

UPDATES

Please consult our website at www.imb.ie as updates are regularly made to it. In addition, you can also check out any vacancies within the IMB.

Staff Changes at the IMB

NEW STAFF APPOINTMENTS

- *Dr Patrick Costello* was appointed in September 2002 to the position of GMP Inspector for Blood and Biologicals.

Dr. Orla Conaghey, *Dr. Marie Louise Nolan* and *Ms Una Mockler* have recently taken up Pharmaceutical Assessor posts.

HUMAN MEDICINES

LEGISLATION AND GUIDELINES

Medicinal Products (Prescription and Control of Supply) (Amendment) Regulations 2002 (S.I. No. 627 of 2002)

The Medicinal Products (Prescription and Control of Supply) (Amendment) Regulations, 2002 were signed by the Minister for Health and Children on 18 December, 2002. The amendment updates the controls on prescription and supply of medicinal products to the public.

New or revised exemptions from prescription control are introduced for the following substances: diclofenac sodium, flurbiprofen, fluticasone propionate, ibuprofen, lodoxamide trometamol and terbinafine hydrochloride.

The regulations list certain homoeopathic medicinal products which may be supplied without a medical prescription and in non-pharmacy outlets. They also allow the supply of herbal medicinal products containing *Ginkgo biloba* L. or *Hypericum perforatum* L. without a prescription when extemporaneously supplied in certain limited circumstances.

An amendment to the Medicinal Products (Control of Paracetamol) Regulations, 2001 is also introduced, in which the reference to 'paediatric use' in the current regulations is amended to 'use in children under six years of age'.

ADOPTED NOTES FOR GUIDANCE

- CPMP/EWP/612/00 Note For Guidance on the Clinical Investigation of Medicinal Products for Treatment of Nociceptive Pain (CPMP adopted November 2002)
- CPMP/EWP/2922/00 Note for Guidance on the Clinical Investigation of Medicinal Products in the treatment of Asthma (CPMP adopted November 2002)
- CPMP/EWP/205/95 *Revision 2* Note for Guidance on Evaluation of Anticancer Medicinal Products in Man (CPMP adopted September 2002)

  see also CPMP/EWP/569/02 *draft* Addendum on Paediatric Oncology (CVMP released for consultation September 2002)
- Topic Q3(M) Step 4 Note for Guidance on Impurities: Residual Solvents – Permissible Daily Exposure (TDE) for Tetrahydrofuran and N. Methylpyyrolidone (CPMP/ICH/1940/00 – CPMP Adopted September 2002)

ADOPTED POSITION PAPERS

- EMEA/22314/02 Position Paper on Re-establishment of Working Seeds and Working Cell Banks using TSE compliant materials.

LABEL AND LEAFLET MOCK UPS

Where possible, we would appreciate it if applicants could submit mock ups of labels and leaflets on A4 paper. This will facilitate the scanning of mock ups into our database. Mock ups on larger paper sizes should only be submitted if they are too large to fit on A4 paper at their actual market size.

ADDITIONAL INFORMATION ON THE LABEL AND IN THE PACKAGE LEAFLET

We have received requests recently for approval to add information to the label and the package leaflet which is additional to the items provided for in Directive 2001/83, Articles 54 to 69. Article 62 of the Directive states that the outer packaging or package leaflet may include '...symbols or pictograms designed to clarify certain information mentioned in Articles 54 or 59(1) or other information compatible with the summary of product characteristics which is useful for health education, to the exclusion of any element of a promotional nature'. IMB policy on some of the additional information requests we have been receiving is given below.

- **General information on the medical condition**

  Information on the condition for which the product has been prescribed may be included in the leaflet, provided it is in line with the requirements of Article 62 of Directive 2001/83.

- **Websites**

  Website addresses are not permitted on the label or leaflet, whether they are sites related to the PA holder or to the particular product. References to other websites, such as those for patient organisations or for medical conditions are not acceptable, as we are not in a position to continuously monitor the content of these sites to ensure that they are not promotional. This decision will be re-visited if a clear consensus is reached among EU regulatory authorities and the European Commission that references to such websites is acceptable.

- **Telephone numbers and email addresses**

  Telephone numbers or email addresses for the PA holder are acceptable on the label and/or leaflet. They can also be included in the printed version of the SPC used by the PA holder but will not be included in the SPC which is part of the PA schedule.

- **Accreditation logos**

  Accreditation logos or statements, e.g. 'organic', 'Kosher', 'Halal', 'Guaranteed Irish', are not acceptable on the label or leaflet, with the sole exception of the recycling symbol which may be used on the label or leaflet in line with EU requirements for recovery and recycling of packaging waste under directive 94/62/EC.

- **Patient registration forms**

  Forms in the package leaflet or coupons which request patients to send their details to the PA holder for further information are considered promotional and are not acceptable.

- **Patient organisation details**

  Contact details for independent patient organisations may be included in package leaflets.

PRODUCT NAMES AND GMS REIMBURSEMENT

The Medicinal Products (Prescription and Control of Supply) Regulations, 1996, SI No. 256 of 1996, allow the OTC sale of prescription products under certain defined conditions.

Where PA holders have obtained authorisation for both prescription and OTC sale on one PA and under one product name, this has led to difficulties in obtaining reimbursement approval for the prescription version of the product. This is because the General Medical Services (GMS) Board cannot approve the prescription product for reimbursement if it is also advertised as an OTC product, in accordance with the requirements of directive 89/105/EEC and Department of Health and Children criteria for approving reimbursement of medicinal products. (The only exception is nicotine replacement products.)

To avoid this problem, companies should obtain two PAs, one for the prescription version and one for the OTC version. This is also the IMB's preference, as the two versions have different labels and leaflets. The products must have different names, though the difference need only be slight and the root brand name can be kept if wished. Examples of names which have been accepted by the GMS Board are:

Prescription-Only Product
Zovirax Cream
Pepcid
Feldene Gel

OTC Product
Zovirax Cold Sore Cream
Pepcid AC
Feldene Topigel

Note that when both prescription and OTC supply is requested in the one MR application and two PAs are granted, both PAs are considered to be within the MR procedure for future variation and renewal applications.

If the PA holder chooses not to advertise the OTC version, a single PA for both versions may be acceptable to the GMS, however the PA holder should check with the GMS Board beforehand.

In order to comply with the requirements of the Medical Preparations (Advertising) Regulations 1993 – 1996, the method of sales promotion for the OTC version in the PA schedule will be to the health professionals only.

VARIATIONS

Variations to change the name and /or address of the PA holder

Variations to change the name and/or address of the PA holder are Type I variations where the legal entity of the holder remains the same. In order to improve the handling of these variations, the following points should be noted.

As the name and/or address change affects the entire range of products, the variation application must cover all the PA holders authorised products.

- Variations to all products licensed by the national procedure in the range should be submitted directly to the IMB.
- Variations to products licensed by the MR procedure should be submitted through MR, within three months of submission of the national variations and, where possible, for all MR products together.

Applications should be made solely for the name and/or address changes. Any consequential variations relating to the same legal entity should be submitted at the same time on separate forms to facilitate processing.

Where the name of the PA holder is changed, the application should be accompanied by proof that the legal entity remains the same, e.g. a certificate of incorporation. A statement from the PA holder is not sufficient.

The application should consist of one copy of the variation application form, an attached list of all authorised products in the PA range, and a certificate of incorporation if applicable. The present and proposed sections of the variation form should show the present and proposed declarations of the name and/or address on the labels and package leaflet. If there is a change in the company logo, the present and proposed version should be stated. The position and size of the present and proposed logos should be similar. Revised SPCs, labels and leaflets are not required. Any other change to the labels and leaflet, such as colour, design, layout, text, etc. must be applied for as a separate variation.

No fee is charged for address changes. Changes to the name of the PA holder are charged at the following maximum rate: up to 50 PAs €6349; greater than 50 PAs €12,697.

Endorsements to the schedule are not issued for these variations. PA holders will receive a letter of approval stating that the change will be reflected in the relevant section of the next endorsement to be issued or into the next renewal schedule.

The name and/or address change should be implemented within 12 months, i.e., batches released 12 months after approval of the variation must carry the revised text. If a longer period is required for some products, this should be indicated and justified in the covering letter.

Please note that applications to change the name of the PA holder as a result of a change in the legal entity do not comply with the condition for Type I, no. 3 variations. They are dealt with as transfer applications, which are purely national procedures, even for products approved through MR. A Guide to Transfer Applications and transfer application forms are available from the 1MB website, in the Human Medicines, Publication section.

Variations to both quality and clinical data

Where a single variation application is submitted for both quality and clinical changes, the application will be assessed by both a pharmaceutical and a medical assessor. Each assessor reviews and approves only the changes that are relevant to them. PA holders should wait for approval from each assessor before implementing the changes.

Incorporation of new safety data in product information

The procedure agreed by the IMB and IPHA on incorporation of new safety data (including shelf-life and storage conditions) into product information (SPC/PILs) following variation is available from the IMB's website (www.imb.ie), under Human medicines – Publications – Variations.

This procedure outlines three categories of such changes and specifies timescales for full implementation of revised documentation. The classification of changes are categorised as follows:

Category 1 – Urgent Safety Information e.g. important, new data that would normally involve circulation of a 'Dear Healthcare Professional' letter. The aim is to have updated PILs incorporated in all stock at wholesale level as soon as possible, but at the latest within one month of receipt of approval of the variation.

Category 2 – Other Significant Safety (Including Quality) Information – includes changes which provide significant information for both healthcare professionals and patients, but would not normally involve circulation of a 'Dear Healthcare Professional' letter, e.g. items covered in the IMB's Drug Safety Newsletter. The aim is to have updated PILs in all stock at wholesale level as soon as possible, but at the latest within three months of receipt of approval of the variation.

Category 3 – Other Information – includes all other data (not previously specified), incorporated either at the request of the PA holder or the IMB, e.g. following review of a PSUR. The aim is to have updated PILs incorporated in all stock at wholesale level as soon as possible, but at the latest within six months of receipt of approval of the variation.

Marketing authorisation holders are reminded to consult this document when relevant variations are submitted or requested and to grade variation applications accordingly. Issues arising with logistical difficulties will be considered on a case by case basis. Implementation will be monitored by the IMB Inspectorate.

Changes in distributors

A change in the primary distributor of a product should no longer be submitted to the IMB as a variation to the PA. However, as this information is vital to the IMB's Inspectorate for their handling of batch recalls and product defect issues, PA holders are requested to notify the Inspectorate Department (*yvonne.maloney@imb.ie*) of the primary distributors for their products and any changes to them. The notification should include the name and address of the distributor, and office and 24-hour contact details. For full details, please see the item titled '*Notification of Distributors to the IMB Inspectorate*' in the Inspectorate section of this newsletter.

STYLISTIC MATTERS

We would like to bring the following stylistic matters to the attention of applicants:

- The correct abbreviation for the European Pharmacopoeia is Ph. Eur.; the abbreviations EP stands for the European Parliament.
- The correct title for the marketing authorisation holder in Ireland is Product Authorisation holder or PA holder. The term product licence is a UK term for UK marketing authorisation holders. For joint Irish/UK packs, the following terms are acceptable: Product authorisation licence holder, PA/PL holder, MA holder, marketing authorisation holder.
- Where reference is made to company addresses in the SPC, label and leaflet, all addresses outside Ireland should include the country (addresses within Ireland need not include the country).

CLEANING REQUIREMENTS FOR CFC-FREE INHALERS

The switch from CFC to CFC-free metered dose inhalers is well advanced throughout Europe and generally agreed to be fulfilling its aim of a 'seamless transition'. There are however, a number of minor differences in the new formulations which are attributable to the CFC-Free propellants (hydrofluoroalkanes, HFAs), of which health professionals should be aware in order to provide appropriate patient counselling.

Cleaning : HFAs are more hygroscopic than CFCs and this may lead to a greater potential for the spray hole in the actuator to become progressively blocked-up due to excessive drug deposition. The IMB has become aware of a somewhat higher level of complaints involving apparent device failure with the new HFA inhalers than with the older CFC inhalers. Regular cleaning of the actuator has always been a recommendation in patient information leaflets but whereas it may not have been adhered to rigorously by users of CFC inhalers, it assumes a much greater importance in the case of the HFA inhalers. Cleaning instructions, involving the removal, washing and drying of the plastic actuator at specified intervals, are contained in each product patient information leaflet and should be emphasised to the patient at time of dispensing. Investigations of complaints of faulty devices made to companies reveal that following cleaning in line with the Patient Information Leaflet, the vast majority of inhalers were stated to be restored to normal operation.

Patient perception : Patients may perceive a difference in taste between the CFC and HFA products due to the propellants. This is referred to in the leaflet also. Occasionally, patients notice a lower pressure on inhalation, which they may incorrectly assume to be a 'faulty' inhaler. This is due generally to the lower volumes dispensed by the valves of HFA products and the smaller diameter of the spray exit hole. Patients should be reassured that none of these effects is of consequence to the performance of their inhaler.

Measures are currently being considered by the IMB, in conjunction with the companies marketing these CFC-Free inhalers, to highlight the importance of adherence to the cleaning recommendations in the leaflet. Pharmacists have also been urged to report all complaints concerning problems in operation of these inhalers to the IMB.

COMMON TECHNICAL DOCUMENT

Applicants are reminded that the Common Technical Document (CTD) format for applications will be mandatory from 1 July 2003. This format will be required for all new and variation applications made from that date.

- New stand-alone applications: all sections of the application must be in CTD format.
- Line extension applications: Modules 1 and 2 must be in CTD format, while reference can be made to already-submitted and approved old formats of the safety and efficacy data, only if no new additional data is re-submitted for these sections.
- Generic applications: Modules 1 and 2 must be submitted; cross-reference can be made to the non-clinical and clinical data in the originator's product dossier.
- Mutual-recognition applications: initial applications after 1 July to the RMS for the first national authorisation must be in CTD format. If the initial application to the RMS was made before 1 July 2003 in the old format, this format will be accepted by CMS until 31 December 2004.
- Variation applications: New data must be in CTD format. Cross-references to data in the old format are acceptable.

Further details of the requirements for different types of applications can be found in the Questions and Answers document on the Commission's website (*http://pharmacos.eudra.org/F2/eudralex/vol-2/B/ctdqa_au2002.pdf*). Please note that this document is due to be updated shortly with further questions and answers.

MALTESE TWINNING PROJECT

The IMB has contributed substantially to the development of the European system and intends to continue to be a leading player in its operation and further development following on from EU expansion. In 2002, an IMB and MCA consortium, with Ireland as the lead partner, was awarded the twinning project to assist the Maltese Government establish a competent authority, namely the Medicines Authority.

The EU-funded twinning projects within the accession countries aim to develop modern and efficient administrations which can implement the community's legislation (acquis communautaire) to the same standard as Member States. The main aim of this project is to provide advice and expertise to the authority so that medicines placed on the local market can be regulated in compliance with EU requirements.

The Project Leaders are Dr. Joan Gilvarry, Director of the Medical Department, IMB and Ms. Lilian Wismayer, Director of the Medicines Regulatory Unit, Malta. The Pre-Accession Advisor (PAA), Ms. Anne Gray, has been seconded to Malta for the duration of the project (18 months). She will be supplemented by carefully planned and timed missions of other specialists to hold training events and co-ordinate awareness raising visits, etc to accompany the reform process towards the targeted result.

For the IMB twinning has wide benefits: it provides a useful tool for building long lasting partnerships with accession countries in the field of medicines regulation, meets wider Government objectives to support the enlargement of the European Union and offers development opportunities to IMB staff.

WEBSITE CHANGES – HUMAN MEDICINES

The following guides and application forms have been updated on our website at www.imb.ie

- Guide to Parallel Product Authorisations for Medicinal Products for Human Use, and application forms
- Guide to Transfer of Product Authorisations for Medicinal Products for Human Use, and application forms

PHARMACOVIGILANCE NEWS

Implementation of Electronic Reporting of Individual Case Safety Reports (ICSRs) to the IMB

In order to meet the requirements for electronic reporting, the IMB wishes to inform companies that we are in a position to accept ICHE2B reports as xml files as of 1 February 2003.

It is a prerequisite that your company has a profile on the EMEA EudraVigilance gateway. If you do not already have one, please contact the EMEA.

The IT system of the IMB only supports ICH ICSR DTD Version 2.1. Please make sure that your files match this standard.

In order to facilitate the process, the following criteria should be applied:

- Please submit separate files for
  - Irish cases
  - Cases where Ireland is the Rapporteur/Reference Member State
  - All other cases
- Please note that an individual *xml* file is not required for each report, but reports can be grouped together according to the three types described above. However, all files submitted should be clearly identified according to type in the accompanying covering note.
- In the case of follow-up reports for Irish cases, the IMB case reference number assigned should be provided on the covering note.
- For an initial trial period, paper copies of these cases are also requested.
- The contact point for queries regarding the above, initiating testing and obtaining the gateway address is smulvey@imb.ie

HERBAL MEDICINES

HERBAL MEDICINES PROJECT

At the end of 2002, comment from the Minister for Health and Children was still awaited on the IMB Herbal Medicines Project r report and on the report on the IMB Herbal Medicines Seminar held in May 2002.

EU DIRECTIVE ON TRADITIONAL HERBAL MEDICINAL PRODUCTS

The Danish Presidency held the second Council Working Group meeting on the proposed Directive on 16 October 2002. Two of the key issues raised were the scope of the Directive and the proposed definition of 'traditional use', which relies exclusively on the product having been available for 30 years on the European market with a derogation to 15 years for products from outside the EU. It was suggested that the proposed transitional period between agreement on the Directive and full compliance would facilitate many products in terms of their time on the market. It was also suggested that it might be possible that the proposed Committee on Herbal Medicinal Products (CHMP) could review individual products that did not satisfy the 30/15 years of use.

In parallel to the work of the Council Working Group, the European Parliament Committee for the Environment, Public Health and Consumer Policy has proposed a number of amendments to the Directive, which were presented to the plenary session of the European Parliament on 6 November 2002. Twenty eight of these amendments were agreed by the Parliament and will now be considered by the European Commission.

The Parliament amendments and the European Commission response will form the basis for discussion on the proposed Directive at the next Council Working Group, date to be confirmed.

MEDICINAL PRODUCTS (PRESCRIPTION AND CONTROL OF SUPPLY) (AMENDMENT) REGULATIONS 2002 (S.I. NO. 627 OF 2002)

The Department of Health and Children has published an amendment to the Medicinal Products (Prescription and Control of Supply) Regulations 1996 (S.I. No. 256 of 1996) as detailed on page 3.

Following consultation with the IMB a number of amendments relating to herbal substances were agreed. These include a general exemption allowing herbal practitioners to extemporaneously dispense *Hypericum perforatum* L. and *Ginkgo biloba* L. for the treatment of individual patients under their care as part of an individual consultation. In addition, *Hypericum perforatum* L. has been listed in Schedule 3 Part 2 allowing non-prescription controlled products containing this herbal substance to be sold in non-pharmacy retail outlets. Finally, all herbal substances in the schedules to this Regulation will now be listed according to their scientific names (i.e. genus, species, variety, author) rather than their common names as previously.

VETERINARY MEDICINES

LEGISLATION AND GUIDELINES

Adopted guidelines

The following guidelines have been adopted by the CVMP:

- Guideline on the SPC for antimicrobial products (EMEA/CVMP /612/01).
- Guideline on the Demonstration of efficacy for veterinary medicinal products containing antimicriobial substances (EMEA/CVMP /627/01).

Position Papers

The following position papers have been adopted by CVMP:

- Establishment of MRLs for milk in relation to the daily intake by children (EMEA/CVMP/391/02).
- Re-establishment of Working Seeds and Working Cell Banks using TSE compliant materials (EMEA/22314/02).
- Maximum In-Use Shelf-Life for Medicated Drinking Water (EMEA/CVMP/1090/02).

VICH Guidelines

The Committee adopted the following guidelines following the close of the consultation period:

- VICH GL28: Safety of Veterinary Drugs in Human Food: Carcinogenicity Testing (CVMP/VICH /645/01).
- VICH GL31: Safety of Veterinary Drugs in Human Food: Repeat-Dose (90 days) Toxicity Testing (CVMP/VICH/484/02).
- VICH GL32: Safety of Veterinary Drugs in Human Food: Developmental Toxicity Testing (CVMP /VICH/485/02).
- VICH GL33: Safety of Veterinary Drugs in Human Food: General approach to testing (CVMP /VICH/486/02).

The guidelines will come into effect by 1 October 2003.

BORDERLINE PRODUCTS BETWEEN VETERINARY MEDICINAL PRODUCTS AND BIOCIDES

The Advisory Committee for Veterinary Medicines (ACVM) is aware of an EU Commission Guidance document on biocidal products which ▼

classifies certain products as being regulated under the Biocides, rather than the Veterinary Medicines, legislation. The IMB has requested a meeting with the appropriate authority within the Department of Agriculture & Food to clarify whether the established IMB Guide to the Definition of an Animal Remedy requires amendment. It is expected that a meeting will take place during January 2003, following which further advice will be given by the IMB. In the interim, the existing policy, as stated the IMB Guide, remains valid.

VARIATION/RENEWAL APPLICATIONS

The IMB wishes to remind applicants that from 31 January 2003, colour mock-ups are required for variation and renewal applications which result in changes to the product literature. At time of application, hand amended mock-ups are acceptable. Final mock-ups are required prior to authorisation of the requested variation or renewal.

NEW IMB WEBSITE

The Veterinary Department would like to take this opportunity to invite you to visit the updated IMB website (www.imb.ie), which was launched in November 2002. The current site contains more information and is more user-friendly than its predecessor. The IMB is committed to keeping the structure and content of its website under review and would welcome comment from users of the site. If you identify any errors, experience any problems with navigation or have any suggestions for improvement or additional content, we would be delighted to hear from you. Any comments on the veterinary section of the site should be forwarded to vetinfo@imb.ie.

INSPECTORATE

WHOLESALING

Licensed wholesalers are required not to supply medicinal products to persons not entitled to receive such products. A licensee may not supply medicinal products to an unauthorised wholesaler. In this regard, attention is drawn to the general conditions of the Wholesaler's licence issued by the Inspectorate Department, in particular, the licence conditions referring to the provisions of Article 7 of the Medical Preparations (Wholesale Licences) Regulations, 1993.

To ensure compliance with these regulations, the Responsible Person should ensure that the necessary controls are in place to assure that the sales and marketing departments of wholesalers are aware of and are trained in these requirements, and that orders are not taken from, and processed for, persons not entitled to receive medicinal products.

Internal training and documented procedures should also address the provision of promotional (free) samples in accordance with the Medical Preparations (Advertising) Regulations, 1993.

NOTIFICATION OF DISTRIBUTORS TO THE IMB INSPECTORATE

The IMB Inspectorate will shortly be contacting all licensed wholesalers to request that, where applicable, they submit a variation to amend their licenses to include details of medicinal products and PA Holders for which they act as a primary distributor. No fee will be charged for these variations. **A primary distributor is considered to be the distributor who first places the medicinal product on the Irish market. This includes all wholesalers who first receive a medicinal product for distribution in Ireland and who distribute the product to other Irish wholesalers or directly to retailers.**

In cases where the primary distributor is **not** located in Ireland, (i.e. where a medicinal product is distributed directly to retailers in Ireland by a licensed wholesaler located in another member state of the EU), the IMB is requesting all PA holders for such products to provide the IMB Inspectorate with the following information:

- PA number of each product for which the primary distributor is located outside Ireland
- Name and address of the primary distributor for each product
- Names of two contact person(s) at the primary distributor, together with their office and 24 hour telephone numbers

This information is required to ensure the ability of the IMB Inspectorate to perform an immediate and effective recall of medicinal products in an emergency situation.

PA holders are requested to send the above details to Ms. Yvonne Maloney, Senior Administrator, Inspectorate, Irish Medicines Board, Earlsfort Centre, Earlsfort Terrace, Dublin 2. There will be no charge for the provision of such information by PA holders.

LICENCES

Revised application forms have been issued by the Inspectorate. They are as follows:

- Application for a new Licence – Veterinary and Human Product Manufacturers
- Application for renewal of Manufacturer's / Wholesaler's Licence
- Application for a variation to Manufacturer's / Wholesaler's Licence

All forms can be located on the IMB website – Inspectorate Section – Publications Section

Companies should note the following when applying for a variation to a Manufacturer's Licence or a Wholesaler's Licence:

- all applications should include a

present and a proposed form of the licence;

- applications to include a new Qualified Person on a Human Medicinal Product Manufacturer's licence or on a Veterinary Medicinal Product Manufacturer's licence must have attached a Curriculum Vitae and the training records for the proposed Qualified Person;
- applications to include new personnel on a licence, other than Qualified Persons, must have Curriculum Vitae attached for the proposed personnel.

The format of Inspectorate Manufacturing and Wholesaling licences is set to change shortly. For manufacturing licences, the EU format of a manufacturing licence, as defined in the Revised Compilation of Community Procedures, published in May 2001, will be adopted. As a result, a variation to amend an existing manufacturing licence will be required. Companies holding manufacturing licences will shortly be notified in writing of this requirement. No variation fee will apply to these variations.

RESPONSES TO INSPECTION REPORTS

- When responding to Inspection Reports from the Inspectorate, companies are invited to include a comment on each deficiency noted, if the company considers such a comment necessary. In some cases some companies have interpreted this invitation as a request, which is not the intention of the statement. Please note that comments should only be included if the company feels this is necessary.
- When responding to Inspection Reports, it is generally unnecessary to provide copies of amended documents such as SOPs. If such documents are required, they will be requested by the Inspector in follow up correspondence. Where supporting documentation which has not been requested is provided to the Inspectorate of the IMB, the documentation will be returned to the company without review.

MUTUAL RECOGNITION AGREEMENTS

The latest updates are available from www.emea.eu.int/pdfs/technical/mra

Human New Product Authorisations Issued (September - December 2002)

PA Number	Product Name
PA0004/058/002	PARACETAMOL
PA0004/059/001	DIAREZE LOPERAMIDE HYDROCHLORIDE
PA0017/047/004	ALKERAN
PA0050/109/001	DELSYM
PA0126/113/001	MAXILIEF
PA0144/043/001	STIEFEL SUNBLOCK LOTION
PA0176/071/001	SIMVASTATIN
PA0176/071/002	SIMVASTATIN
PA0176/071/003	SIMVASTATIN
PA0618/019/001	ASILONE ANTACID LIQUID
PA0618/019/002	ASILONE
PA0618/019/003	ASILONE ANTACID
PA0711/007/003	ACC
PA0748/003/010	RISPERDAL CONSTA
PA0748/003/011	RISPERDAL CONSTA
PA0748/003/012	RISPERDAL CONSTA
PA0789/005/001	FLUOROURACIL "EBEWE"
PA0848/002/001	SIMVASTATIN REAL
PA0848/002/002	SIMVASTATIN REAL
PA0848/002/003	SIMVASTATIN REAL
PA0848/002/004	SIMVASTATIN REAL
PA0913/022/006	OXYCONTIN TABLETS
PA0995/002/001	SIMVASTATIN PHARMA
PA0995/002/002	SIMVASTATIN PHARMA
PA0995/002/003	SIMVASTATIN PHARMA
PA1078/001/001	SIMVASTATIN
PA1078/001/002	SIMVASTATIN
PA1078/001/003	SIMVASTATIN
PA1079/001/001	SIMVASTATIN
PA1079/001/002	SIMVASTATIN
PA1079/001/003	SIMVASTATIN
PA1080/001/001	SIMSTAT
PA1080/001/002	SIMSTAT
PA1080/001/003	SIMSTAT
PA1080/001/004	SIMSTAT
PA1081/001/001	SIMVASTATIN CT
PA1081/001/002	SIMVASTATIN CT
PA1081/001/003	SIMVASTATIN CT
PA1081/001/004	SIMVASTATIN CT
PA1082/001/001	SIMVASTATIN
PA1082/001/002	SIMVASTATIN
PA1082/001/003	SIMVASTATIN
PA1082/001/004	SIMVASTATIN
PPA0465/087/001	EMCOR
PPA0465/087/002	EMCOR
PPA0465/089/001	ZYBAN
PPA0465/090/001	LESCOL
PPA0465/090/002	LESCOL
PPA1071/002/001	ZESTRIL
PPA1071/002/002	ZESTRIL
PPA1071/003/001	COVERSYL
PPA1071/004/001	SEREVENT INHALER
PPA1071/005/001	IMDUR

Human New Product Authorisations Issued (Mutual Recognition) (September - December 2002)

PA Number	Product Name
PA0035/094/001	ARCOXIA
PA0035/094/002	ARCOXIA
PA0035/094/003	ARCOXIA
PA0050/150/001	VALCYTE
PA0111/005/001	CEFOTAXIME
PA0111/005/002	CEFOTAXIME
PA0111/005/003	CEFOTAXIME
PA0167/111/001	BAXTER PROPOFOL
PA0167/111/002	BAXTER PROPOFOL
PA0218/025/007	ACTRAPID FLEXPEN
PA0218/026/007	INSULATARD FLEXPEN
PA0218/029/007	MIXTARD 30 FLEXPEN
PA0593/035/001	OMEPRAZOLE
PA0678/071/007	NIQUITIN CQ CLEAR
PA0678/071/008	NIQUITIN CQ CLEAR
PA0678/071/009	NIQUITIN CQ CLEAR
PA0711/042/001	LUVASED MONO
PA0740/007/001	BISOPROLOL HEMIFUMARATE GENTHON
PA0740/007/002	BISOPROLOL HEMIFUMARATE GENTHON
PA0748/049/001	CONCERTA XL
PA0748/049/002	CONCERTA XL
PA0748/049/003	CONCERTA XL
PA0805/002/001	LEXAPRO
PA0805/002/002	LEXAPRO
PA0805/002/003	LEXAPRO
PA0805/002/004	LEXAPRO
PA0819/014/001	RANITIDINE-RATIOPHARM
PA0819/014/002	RANITIDINE-RATIOPHARM
PA0823/027/002	VEGANIN
PA0833/004/001	ZOLGEN
PA0833/004/002	ZOLGEN
PA0854/001/002	CLINOLEIC

Human New Product Authorisations Issued (Mutual Recognition) (September - December 2002) (Cont)

PA Number	Product Name	PA Number	Product Name
PA0876/005/001	FLUTAMIDE MACO PHARMA POTASSIUM	PA1020/001/001	FOMEPIZOLE OPI 5MG/ML
PA0931/005/001	CHLORIDE AND SODIUM CHLORIDE	PA1037/001/001	BARICOL
PA0970/018/006	SEROQUEL	PA1049/001/001	ZINDACLIN
PA0970/018/007	SEROQUEL 300	PA1057/001/001	DIABACT UB

Human Centralised Product Authorisations Issued (September - December 2002)

PA Number	Product Name	PA Number	Product Name
EU/1/02/226/001	INDUCTOS	EU/1/02/231/1-25	MIXTARD

Human Product Authorisations Withdrawn (September - December 2002)

PA Number	Product Name	PA Number	Product Name
PA0002/072/004	CARACE	PA0037/026/001	LEDERFEN
PA0002/072/005	CARACE	PA0037/026/002	LEDERFEN
PA0007/034/001	DUOVENT MDI	PA0038/002/007	ERYTHROCIN
PA0013/097/001	MENOREST	PA0038/002/008	ERYTHROCIN
PA0013/097/002	MENOREST	PA0046/004/006	FUCIDIN INTERTULLE
PA0013/097/003	MENOREST	PA0046/016/008	BURINEX
PA0013/097/004	MENOREST	PA0046/024/005	ONE-ALPHA
PA0016/012/001	NEO-CORTEF	PA0046/039/001	UNIHEP LEO 1000
PA0016/012/002	NEO-CORTEF	PA0046/039/002	UNIHEP LEO 5000
PA0016/020/002	MEDRONE	PA0046/039/003	UNIHEP LEO 10000
PA0016/020/003	MEDRONE	PA0046/039/004	UNIHEP LEO
PA0016/047/001	CYTARABINE	PA0057/051/001	SUPER PLENAMINS
PA0016/047/003	CYTARABINE	PA0060/036/001	RIMEVAX
PA0016/054/001	VERYL	PA0062/022/002	DE-NOLTAB
PA0016/054/003	VERYL	PA0073/007/001	CHENOFALK
PA0021/001/001	TRASYLOL	PA0077/050/001	FERGON
PA0021/001/002	TRASYLOL	PA0077/092/001	GASTRON
PA0022/013/001	OVRAN 30	PA0077/142/001	ASPEGIC 100
PA0037/023/001	METHOTREXATE	PA0077/142/002	ASPEGIC 500
PA0037/023/002	METHOTREXATE	PA0077/142/003	ASPEGIC 1000
PA0037/023/004	METHOTREXATE	PA0108/012/001	DUVADILAN RETARD
PA0037/023/005	METHOTREXATE	PA0108/013/003	YUTOPAR
PA0037/023/006	METHOTREXATE	PA0126/012/003	MELFEN
PA0037/023/007	METHOTREXATE	PA0148/023/001	CHLOROPTIC
PA0037/023/008	METHOTREXATE	PA0148/030/001	OPHTHETIC STERILE OPTHALMIC
PA0037/023/009	METHOTREXATE	PA0148/042/001	OCUFEN LIQUIFILM OPHTHALMIC
PA0037/023/012	METHOTREXATE	PA0179/009/008	WATER FOR INJECTION
PA0037/023/013	METHOTREXATE	PA0179/032/002	METRONIDAZOLE
PA0037/023/014	METHOTREXATE	PA0187/013/002	KABIKINASE
PA0037/023/016	METHOTREXATE	PA0187/013/004	KABIKINASE IV MI

Human Product Authorisations Withdrawn (September - December 2002) (Cont)

PA Number	Product Name
PA0187/013/005	KABIKINASE IV MI
PA0199/004/002	CONRAY 325
PA0236/013/001	CISPLATIN
PA0236/013/002	CISPLATIN VIALS
PA0236/013/003	CISPLATIN
PA0236/020/001	OLBETAM
PA0271/004/001	PHASONIT 5
PA0271/004/002	PHASONIT 10
PA0290/058/001	ISOPTO CARPINE 0.5%
PA0290/058/004	ISOPTO CARPINE 3.0%
PA0303/027/001	BUSORIL
PA0303/027/002	BUSORIL
PA0303/034/001	ELDOPAR
PA0303/034/002	ELDOPAR
PA0337/006/001	KIDDI PHARMATON
PA0363/008/001	ANTABUSE EFFERVESCENT
PA0372/003/001	LUGACIN
PA0372/003/002	LUGACIN PAEDIATRIC
PA0437/005/011	METHOTREXATE
PA0437/005/012	METHOTREXATE
PA0437/005/013	METHOTREXATE
PA0484/011/001	SURGICAL SPIRIT
PA0488/005/001	BARATOL
PA0488/005/002	BARATOL
PA0488/007/001	ISORDIL
PA0488/007/002	ISORDIL
PA0488/009/001	EXPULIN CHESTY COUGH LINCTUS
PA0516/010/002	NAPRELAN
PA0516/022/001	ERYMIN
PA0516/023/001	UNIVER
PA0516/023/002	UNIVER
PA0540/073/001	SUPRECUR DEPOT
PA0577/027/001	MEFENAMIC ACID
PA0678/006/001	EOLARIX VACCINE
PA0697/005/001	ENFLURANE
PA0711/002/005	CAPTOR
PA0711/006/001	FRUDEX
PA0711/015/001	TERFEN
PA0711/018/001	BROMOX
PA0711/018/002	BROMOX
PA0711/018/003	BROMOX
PA0711/018/003	BROMOX
PA0711/019/001	TIMOLOL MALEATE OPHTHALMIC
PA0711/019/002	TIMOLOL MALEATE OPHTHALMIC
PA0711/019/003	TIMOLOL MALEATE OPHTHALMIC
PA0711/026/001	ATE-NIFE
PA0711/044/003	CEDINE
PA0748/014/002	PANCREASE HI LIPASE
PA0748/037/002	PEVARYL
PA0773/001/001	HESPAN
PA0828/006/001	BENPERIDOL
PA0872/005/002	FEMATRIX 80
PA0936/001/002	CYKLO Q
PA0936/007/001	KAOPECTATE
PA0936/030/002	REHIDRAT ORANGE
PA1001/001/001	ADSORBED DIPHTHERIA & TETANUS VACCINE
PA1001/001/002	ADSORBED DIPHTHERIA & TETANUS VACCINE
PA1001/002/001	ADSORBED TETANUS VACCINE BP
PA1001/002/002	ADSORBED TETANUS VACCINE
PA1001/003/001	ADSORBED DIPHTHERIA VACCINE BP (CHILD)
PA1001/004/001	ARILVAX YELLOW FEVER VACCINE LIVE B.P.
PA1001/006/001	TUBERCULIN PPD
PA1001/007/001	BCG VACCINE INTRADERMAL
PA1009/002/001	CARBEX
PA1009/006/004	PENTASA
PA1009/010/001	GHRH FERRING
PPA0465/011/001	ALDOMET
PPA0465/011/002	ALDOMET
PPA0465/012/004	ADALAT RETARD
PPA0465/029/002	CALPOL SIX PLUS
PPA0465/036/001	OPTICROM
PPA0465/037/001	FELDENE DISPERSIBLE
PPA0465/037/002	FELDENE DISPERSIBLE
PPA0465/039/002	LOSEC
PPA0465/041/003	BECOTIDE ROTACAPS
PPA0465/063/001	CARDURA
PPA0465/063/003	CARDURA

Veterinary New Product Authorisations Issued (September-December 2002)

PA Number	Product Name	PA Number	Product Name
10019/78/1	Rimadyl-Cattle 50 mg/ml Solution for Injection	10881/10/1	Bob Martin Flea Spray
10960/45/1	Teat Seal Non Antibiotic	10948/2/1	C-DIP
10987/57/1	Provid P Paste.	10987/58/1	Triclaben 5% Oral Suspension for Sheep
10999/83/1	Noroclav Injection.	10987/59/1	Triclaben 10% Oral Suspension for Cattle
10999/93/1	Noromectin Injection for Pigs		

Veterinary Mutual Recognition Authorisations Issued (September-December 2002)

PA Number	Product Name	PA Number	Product Name
10021/44/1	BAYCOX 5% Oral Suspension	10850/4/1	VIRBAMEC Pour On Solution For Cattle 5 mg/ml
10827/2/1	Blockade	10995/17/3	SELGIAN 40KG

Veterinary Product Authorisations Withdrawn (September-December 2002)

PA Number	Product Name	PA Number	Product Name
10019/045/001	CLAMOXYL ORAL MULTIDOSER	10954/001/001	STIMOVAR 5000 I.U.
10028/038/001	NUVAN TOP	10954/001/003	STIMOVAR
10046/011/001	OXYTOCIN LEO	10954/001/004	STIMOVER
10046/020/001	LEO YELLOW TEAT DIP/SPRAY	10962/028/001	VITENIUM
10046/021/001	LEO YELLOW SUPER TEAT DIP/SPRAY	10962/042/001	DEPOSEL
10046/021/002	LEO YELLOW SUPER (READY TOUSE)	10962/057/001	SCORDEX
10277/035/001	STREPTOPEN MILKING COW	10981/003/001	PENI L.A.
10277/036/001	STREPTOPEN DRY COW	10996/020/001	SESORAL
10835/014/001	TOPCLIP GOLD SHIELD	10996/069/001	DEPOMYCIN
10951/001/001	CAHLVERM WORM DRENCH	10997/001/001	PHARMACILLIN LA

Veterinary Immunological Authorisations Issued (September-December 2002)

PA Number	Product Name	PA Number	Product Name
10839/003/001	ALPHA JECT 3000	10974/019/001	FUROGEN 2 INJECTION VACCINE

Veterinary Immunological Authorisations Issued (Mutual Recognition) (September-December 2002)

PA Number	Product Name	PA Number	Product Name
10857/052/001	AVINEW	10861/081/001	SUVAXYN PARVO/E
10019/077/001	STELLAMUNE ONCE	10996/172/001	BOVILIS IBR MARKER
10277/087/001	M+PAC		