IRISH MEDICINES BOARD
Bord Leigheasra na hÉireann

IMB NEWSLETTER

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Correspondence/Comments should be marked for the attention of: Publications Officer, Irish Medicines Board, Earlsfort Centre, Earlsfort Terrace, Dublin 2.

Tel: +353 1 676 4971
Fax: +353 1 676 7836
Email: foi@imb.ie
Internet: http://www.imb.ie

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GENERAL

2002 IMB Information Days

The IMB is pleased to announce that during 2002, it plans to hold five Information Days for authorisation holders, applicants and other interested parties in the areas of Human Medicines (one day), Veterinary Medicines (one day), Pharmaceutical Manufacturers (one day) and Medical Devices (two days).

The following are the available schedules for these Information Days:

Human Medicines Information Day

The next Human Medicines Information Day will be held on Monday 15 April 2002, in the Citywest Hotel, Saggart, Co Dublin. The morning session will focus on labels and patient information leaflets, including a presentation on the IMB's new policy with regard to mock-ups, which is announced elsewhere in this newsletter. Invited speakers include Professor Patricia Wright from Cardiff University on package leaflet design and Mr Tim Delaney, MPSI, from The Adelaide and Meath Hospital on practical issues with currently-marketed labels. The afternoon session will focus on current topics of interest, including the IMB's views on the Commission's proposals for the review of the legislation. As with previous meetings, it is envisaged that the day will provide opportunities for formal and informal exchanges of information between the IMB, PA holders and interested bodies. The fee is €250 (including meeting documentation, refreshments and lunch) and should be paid before Friday 22 March, 2002. A copy of the agenda and the registration form are included at the end of the newsletter (Appendixes I and II) and are also available on the IMB website at **http://www.imb.ie**

Veterinary Medicines Information Day

The IMB Veterinary Information Day will be held on Friday 14 June, 2002 in the Great Southern Hotel, Dublin Airport. Invited speakers include Ms. Avril Doyle, MEP (European Parliament Rapporteur on availability of veterinary medicines), Mr. Philip Kirwan, Dept of Agriculture, Food and Rural Development and Mr. Jo Vanhemelrijck, FEDESA who will address the subject of medicines availability, the Review of the Directive 2001/82/EC and the precautionary principle in the product authorisation procedure. Updates on IMB activities on national procedures in relation to veterinary medicines and vaccines will also be provided. The fee is €250 (including meeting documentation, refreshments and lunch) and should be paid before 31 May, 2002. Full details and booking forms will be available shortly from the IMB website at **http://www.imb.ie** or from Ms. Simona Bordean ***(simona.bordean@imb.ie)***.

Medical Devices Information Day

Two Information Days will be held for the Medical Device sector in 2002. The first is aimed at Dental Technicians and Dental Laboratories and will take place at Citywest Hotel on Saturday 18 May, 2002. The presentations will include an overview of the Medical Devices Department of the IMB and an overview on how to meet the essential requirements of the Directives. It is envisaged that the new guidance note on Meeting the Essential Requirements of Legislation will be launched at that meeting. Further details will follow on the IMB website at **http://www.imb.ie** or from ***medicaldevices@imb.ie***. The second meeting will take place in October which will target the general medical device and *in-vitro* diagnostic medical device sectors. Details will follow on the venue and agenda in the next newsletter.

IMB adopts IT Strategic Plan

The Board of the IMB approved a new IT Strategic Plan for the organisation at its January meeting. It is a comprehensive and exciting initiative for the IMB, requiring major investment. The complete programme of projects, encompassing both business redesign and technology, will take approx three years to complete.

The Plan is the result of several month's work with external consultants, staff and the senior management team of the IMB. A questionnaire to industry provided vital feedback to the process, highlighting the need for a new approach to licensing activities with a strong emphasis on customer service.

Record of meetings with IMB personnel

In order to maximise the efficient utilisation of time and to capture correctly the outcome of discussions between applicant companies and personnel from the IMB, the IMB will in the future request applicants to submit a detailed agenda and list of attendees prior to any meeting. The IMB will also co-operate in the production of an agreed record of the outcome and conclusions of all key meetings. The conclusions of such meetings will be communicated in writing or by email to the applicant company following the meeting, for agreement and comments. It is expected that these conclusions will serve as the official record of the outcome of the meeting.

Adoption of the Codification Directives

Two codifying Directives on the Community Codes relating to medicinal products for veterinary (2001/82/EC) and human use (2001/83/EC) have now been fully adopted and were published in the Official Journal no. L 311 of 28.11.2001. They can be obtained from the European Commission website at **http://dg3.eudra.org/F2/pharmacos/docs.htm#news**. These Directives supersede the earlier directives and are intended to make EU pharmaceutical law more accessible for all involved parties by consolidating requirements into single legal references for both categories of medicinal product. It should also be noted that the Commission's review of European legislation will be based on these codified texts.

These directives do not require any modifications as such, of existing requirements. However, the IMB will be amending our documentation to cross-refer to the new directives and we will gradually introduce these changes in 2002. The following tables summarise these changes for human and veterinary medicines, respectively:

The following is a reference to the earlier human medicines directives and their various amendments, which are replaced by the Codification Directive (2001/83/EC):

- Council Directive 65/65/EEC of January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products, as amended by:

  Council Directive 66/454/EEC
  Council Directive 75/319/EEC
  Council Directive 83/570/EEC
  Council Directive 87/21/EEC
  Council Directive 89/341/EEC
  Council Directive 92/27/EEC
  Council Directive 93/39/EEC

- Council Directive 75/318/EEC of the laws of Member States relating to analytical, pharmacotoxological and clinical standards and protocols in respect of the testing of medicinal products, as amended by:

  Council Directive 83/570/EEC
  Council Directive 87/19/EEC
  Council Directive 89/341/EEC
  Commission Directive 91/507/EEC
  Council Directive 93/39/EEC
  Commission Directive 1999/82/EC
  Commission Directive 1999/83/EC

- Council Directive 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products, as amended by:

  Council Directive 78/420/EEC
  Council Directive 83/570/EEC
  Council Directive 89/341/EEC
  Council Directive 92/27/EEC
  Council Directive 93/39/EEC
  Commission Directive 2000/38 /EC

- Council Directive 89/342/EEC of 3 May 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions of immunological medicinal products consisting of vaccines, toxins or serums and allergens.

- Council Directive 89/343/EEC of 3 May 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for radiopharmaceuticals.

- Council Directive 89/381/EEC of 14 June 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products and laying down special provisions for medicinal products derived from human blood or human plasma.

- Council Directive 92/25/EEC of 31 March 1992 on the wholesale distribution of medicinal products for human use.

- Council Directive 92/27/EEC of 31 March 1992 on the labelling of medicinal products for human use and on package leaflets.

- Council Directive 92/28/EEC of 31 March on the advertising of medicinal products for human use.

- Council Directive 92/73/EEC of 22 September 1992 widening the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products and laying down additional provisions on homeopathic medicinal products.

The following is a reference to the Directives, which are replaced by the Veterinary Codification Directive (2001/82/EC):

- Council Directive 81/851/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to veterinary medicinal products.
- Council Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to analytical, pharmacotoxological and clinical standards and protocols in respect of the testing of veterinary medicinal products.
- Council Directive 90/677/EEC of 13 December 1990 extending the scope of Directive 81/851/EEC on the approximation of the laws of the Member States relating to veterinary medicinal products and laying down additional provisions for immunological veterinary medicinal products.
- Council directive 92/74/EEC of 22 September 1992 widening the scope of Directive 81/851/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to veterinary medicinal products and laying down additional provisions on homeopathic veterinary medicinal products.

Payment of Fees

All fees should accompany applications made to the Irish Medicines Board and cheques, drafts etc., should be made payable to the Irish Medicines Board.

All payments must be made in Euro.

Cheque/bank drafts must be drawn on an Irish Bank or payment made by credit transfer/electronic fund transfer (E.F.T) to:

Bank Name: Allied Irish Bank
1/3 Lower Baggot Street
Dublin 2
Ireland

Account Name: Irish Medicines Board

Account Number: 33712185

Sort Code Number: 93-10-12

Fees must be paid in full, associated bank charges are for your own account.

When paying fees by credit transfer / EFT, please forward a copy of the bank's advice note with the application. Please ensure that the relevant product authorisation number / application type is stated on the bank's advice note.

Applications received without details of payment will be delayed in terms of evaluation / assessment.

If the EFT system that you use cannot give application details, please fax details of the application to 00353 1 6614764.

European Pharmacopoeia 2002

The fourth edition of the European Pharmacopoeia came into force on 1 January 2002. Monographs of the European Pharmacopoeia are legally binding throughout all European countries including Ireland, which is a signatory to the European Pharmacopoeia convention.

Website Updates

Please consult our website at **http://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

- Lisa-Ann Byrne, Drug Safety Associate has joined the Medical Department with specific responsibility in the area of clinical trials.
- Maria Carleton, Medical Device Auditor and Andrea Hanson, Medical Device Vigilance Co-ordinator have recently taken up duty in the Medical Device Department.
- In February, Susann Bradley will join the Pharmaceutical Department as Pharmaceutical Assessor and Dr Gwen Glasgow will take up duty as Homeopathic Project Co-ordinator.

- Celine Creighton will join the staff of the Inspectorate as Good Clinical Practice Inspector.

Staff changes:

- Dr. Victor Garvin has recently been appointed as a GMP inspector. Dr. Garvin was previously employed by the IMB as a Pharmaceutical Assessor.
- Ms. Maggie Gething has recently joined the Veterinary Unit as a full-time Veterinary Assessor.
- Ms. Mary O'Grady and Ms. Eibhlin Prendergast have recently been appointed as Senior Pharmaceutical Assessors.
- Dr. Karen Quigley, Pharmaceutical Assessor, has joined the European Medicines Evaluation Agency as a National Expert for a one year period.

HUMAN MEDICINES

Legislation and Guidelines

Adopted Notes for Guidance

- CPMP/QWP/158/01 (CVMP/115/01) Note For Guidance on Quality of Water for Pharmaceutical Use (CPMP/CVMP adopted Nov. 01)

Please see also Adoption of the Codification Directives under the General section.

Guidance for the Submission to the IMB of Mock-ups of Packaging and Package Leaflets

In accordance with Article 8.3 of Directive 2001/83 the IMB requires a mock-up of the outer and immediate packaging of a medicinal product together with the package leaflet as part of the approval process for human medicinal products. Enclosed with this newsletter **(Appendix III)** is a copy of a guidance document for industry entitled 'Guidance for the Submission to the IMB of Mock-ups of Packaging and Package Leaflets'.

From 1 May 2002, the IMB will require mock-ups of the outer and immediate packaging of a medicinal product together with the package leaflet as outlined below:

- New applications: on application or during assessment.
- Renewals and relevant variations: on application.

In the case of variation applications these should be accompanied by the existing mock-ups with the proposed changes highlighted.

It should also be noted that licences will not be issued for new products or renewals, nor relevant variations approved until final mock-ups have been submitted and approved.

This outline and the accompanying Guidance document may be viewed on the IMB website at **http://www.imb.ie**

New Requirements for receipt of data and files From 1 January 2002

In recognition of the increased volumes of data being produced, we are seeking to reduce the numbers of copies of data submitted to the IMB. We believe that this will be both beneficial for companies and for the IMB. Where only one copy of data is requested, applicants should keep a second copy for their own files.

1. **National New Products**

Part I	3 copies
Parts II to IV	2 copies

2. **Mutual Recognition (MR) applications where Ireland is a Concerned Member State**

Part I	3 copies
Parts II to IV	1 copy

3. **National Variations**

Application form	2 copies
Supporting data	1 copy

4. **MR variations where Ireland is a Concerned Member State**

Application form	2 copies
Supporting data	1 copy

5. **Renewals**

Application form	2 copies
SPC, labels and leaflet	2 copies
Supporting data	1 copy

Named Patient / Use of Unauthorised Medicines

From the 1 January 2002, the IMB is not accepting notification of use of unauthorised medicines. This decision has been made in conjunction with the Department of Health & Children.

This does not alter the legislative position where the requirement that a medical preparation be authorised is waived in the case of 'the importation or sale of a medical preparation by or to the order of a registered medical practitioner or registered dentist for the treatment of a patient under his care' (Article 4b, Medicinal Products (Licensing and Sale) Regulations 1998.)

Prescribers therefore continue to take the responsibility of prescribing unauthorised medicines they consider appropriate and necessary but the IMB should not be informed.

Dual labelling of aspirin–containing products or products with known interactions with aspirin

The European Commission has decided that the name 'aspirin' cannot be used in package leaflets of products authorised through the centralised procedure. This means that where there are potential interactions between a centrally-authorised product and aspirin, the information given to the patient will not mention aspirin but only 'acetylsalicylic acid, a substance present in many medicinal products used to relieve pain and lower fever'.

Some products authorised nationally in Ireland are labelled only with the name aspirin and so patients may not be aware that the active substance is also called acetylsalicylic acid. Consequently, references to acetylsalicylic acid in patient leaflets of centrally-authorised products may well be ignored by the patient as not relevant to them, resulting in the risk of serious adverse drug interactions occurring.

Following consultation with industry representatives, the IMB has contacted companies who hold PAs for aspirin-containing products, regarding the need to update product labelling and literature to ensure :

- The common name of the active substance, where it follows the brand name, is stated as 'acetylsalicylic acid (aspirin)' or 'aspirin (acetylsalicylic acid)'
- For the primary quantitative declaration, the recommended text is '… contains x mg of acetylsalicylic acid (also known as aspirin)…'
- Other references to aspirin throughout the label and package leaflet do not need to also refer to acetylsalicylic acid.

All product placed on the market after 1 October 2002, must comply with the above. Where changes have to be made to the label or leaflet, PA holders have been asked to submit variations by 29 March 2002.

Dual declarations will also be required in the package leaflets of other products which refer to interactions with aspirin. PA holders are asked to review their product leaflets and amend the declaration where necessary. Revised leaflets should be submitted as part of a change to other clinical sections of the leaflet or no later than the time of next renewal.

Variations

Change in name or name and address of the Product Authorisation Holder

Product Authorisation Holders are reminded that if there is a change to the company name or a change to the name and address, a bulk variation should be submitted for all the products in the range. If there is a consequential change in name of the manufacturer this should also be included in the variation application.

A Certificate of Incorporation for a name change should accompany this application.

Change in address only of the Product Authorisation Holder

Please note that there is no fee charged for a change in address. This change should be submitted as a notification to the Variations Section and should apply to all products in the range.

PA holders will be notified by letter stating that the above changes have been approved and will be incorporated at time of next renewal or endorsement.

If you have any queries on the above please contact the Variations Section.

Variation Approval Letters

In order for the IMB to issue approval letters which clearly identify the variations being approved, applicants are asked to include a short reference to the variation at the top of the application's covering letter, e.g. 'Extension of shelf life', revision to 4.2 of the SPC'. This reference will then be used in the approval letter, along with the IMB variation procedure number, to notify approval of the variation.

Pharmacovigilance News

Update on EU Human and Veterinary Pharmacovigilance Legislation

The IMB wishes to remind readers that in accordance with Article 106 of Directive 2001/83/EC and Article 77 of Directive 2001/82/EC, a new Volume (Volume 9) of *The Rules Governing Medicinal products in the European Union on Pharmacovigilance for Human and Veterinary Medicinal Products* was published by the European Commission on 5 December, 2001. This volume was prepared in close consultation with the European Agency for the Evaluation of Medicinal Products (EMEA), member states and interested parties. It brings together, for the first time, general guidance on the requirements, procedures, roles and activities in pharmacovigilance, for both industry and regulators of medicinal products. It also incorporates international agreements reached within the framework of the International Conference on Harmonisation (ICH) and makes specific reference to the international terminology, MedDRA.

This publication coincides with the date on which Member States have to comply with Directives 2000/37/EC and 2000/38/EC which amended the pharmacovigilance chapters of Directives 75/319/EEC and 81/851/EEC respectively. These amendments are now integrated into the two codifying Directives on the Community Codes relating to medicinal products for veterinary and human use referred to above.

The principal changes arising from Commission Directive 2000/37/EC and 2000/38/EC may be summarised as follows:

- Expansion and revision of pharmacovigilance definitions
- A requirement for Marketing Authorisation Holders (MAHs) to provide to the competent authorities, all information relevant to the evaluation of the benefits and risks of a medicinal product, including information arising from post-authorisation safety studies.
- Revision of reporting requirements for MAH's.
- Establishment of a data processing network to facilitate exchange of pharmacovigilance data regarding medicinal products authorised in the community.

Compliance with Regulatory Pharmacovigilance Obligations

Further to a previous newsletter item (September 2001), on the European Concept Paper on Company Compliance with pharmacovigilance regulatory obligations, it should be noted that a revised version of the document, taking account of feedback from industry and other interested parties, has become effective from 1 January 2002. The concept paper, which was compiled by the Pharmacovigilance Working Party (PhVWP) of the CPMP, was subsequently adopted by the CPMP and endorsed by the Heads of Agencies. It sets out the legal basis for pharmacovigilance obligations, how compliance should be monitored in the EU and the types of regulatory action which may be considered by competent authorities in the event of non-compliance.

New fax number for Human Pharmacovigilance Unit

Please note that a new fax number has been assigned to the Pharmacovigilance Unit. The number is +353-1-6762517 and this number should be used for submission of ADE/ADR reports and other faxes intended for the staff of the Pharmacovigilance Unit.

Herbal Medicines

Herbal Medicines Project Complete

The IMB is very pleased to announce that the Herbal Medicines Project has been successfully completed and the final report has now been submitted to the Minister for Health and Children for consideration. The work of the project and of the *ad hoc* Scientific Committee on Herbal Medicinal Products (SCHMP) is detailed below.

1. Herbal Medicines Project Final Report

Following the seventh meeting of the SCHMP held on 25 September 2001, the final report was agreed. The report was endorsed by the Expert Sub-Committee of the Advisory Committee on Human Medicines (ACHM), the ACHM and the Board before being placed on the IMB website for public comment.

The final report was released for public consultation on 1 November 2001 through the IMB website for a period of eight weeks (closing date 27 December). A total of 92 responses to the report were submitted to the IMB during the consultation period.

Comments received as part of this consultation process were reviewed by the IMB and the ad hoc SCHMP at a meeting on 9 January 2002. A review document detailing proposed corrections, amendments and clarifications was agreed and is now available on the IMB web site **(http://www.imb.ie)** along with the final version of the Herbal Medicines Project Report.

2. Establishment of a Traditional Medicinal Products Database

The traditional medicinal products information database is now also complete and includes a total of 2246 products. Two thousand and three (2003) of these are products for which information has been supplied by manufacturers and wholesalers to the IMB through the Herbal Medicines Project. The remainder are products currently on the IMB product authorisation database that could also fall within the scope of the proposed interim national scheme.

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

3. European Developments

The European Commission has agreed the latest draft of the proposed Directive on Traditional Herbal Medicinal Products (17 January 2002). It will now be sent to the European Parliament and the Council. For further information see the European Commission website at **http://pharmacos.eudra.org/**. The IMB is pleased to note that the Herbal Medicines Project proposal for an interim national licensing scheme for traditional medicinal products is very much in line with this latest EU draft.

VETERINARY MEDICINES

Legislation and Guidelines

The following guidelines and position papers have been adopted by the CVMP from September 2001 to December 2001:

Notes for Guidance:

- Guideline on the Requirements and Controls applied to Bovine Serum used in the Production of Immunological Veterinary Medicinal Products (EMEA/CVMP/743/00-FINAL).
- Guideline on the Quality of Water for Pharmaceutical Use (EMEA/CVMP/115/01 – FINAL).
- Guideline on Statistical Principles for Veterinary Clinical Trials (EMEA/CVMP/816/00 – FINAL).
- Guideline for the Conduct of Efficacy Studies for Non-Steroidal Anti-inflammatory Drugs (EMEA/CVMP/237/01 – FINAL).

VICH Guidelines:

- Efficacy of anthelmintics: Specific recommendations for equines (Step 7) (CVMP/VICH/833/99).
- Efficacy of anthelmintics: Specific recommendations for porcines (Step 7) (CVMP/VICH/834/99).

- Efficacy of anthelmintics: Specific recommendations for canines (Step 7) (CVMP/VICH/835/99).
- Efficacy of anthelmintics: Specific recommendations for felines (Step 7) (CVMP/VICH/545/00).
- Efficacy of anthelmintics: Specific recommendations for poultry (Step 7) (CVMP/VICH/546/00).

Harmonisation of product labelling between the UK and Ireland

The IMB notes with some regret that there has been only limited uptake by applicant companies of the opportunity for harmonisation of product labelling between the UK and Ireland in respect of well-established veterinary medicines. Among the practical difficulties encountered and notified to the IMB is that some products are under assessment for renewal of the marketing authorisation in the UK, and therefore the harmonised label cannot be agreed in the interim. In a further effort to assist in the availability of an adequate range of veterinary medicines in Ireland, the IMB will accept renewal applications for existing authorisations for veterinary medicines ahead of their Irish renewal date, in order to derive a common renewal date with the UK. Thus, even where the labels of existing products may differ, the fact that the IMB will accept the necessary renewal data at the same time as the Veterinary Medicines Directorate in the UK should assist animal health companies in addressing the demands for data by both authorities with a similar data set. The IMB will charge a standard Type I variation fee of €305 per product application for the administrative work necessitated by such requests for the synchronisation of renewal dates.

Provision of Periodic Safety Update Reports (PSURs)

Applicants are reminded that for all new product authorisations, unless other requirements have been laid down as a condition of the authorisation, Periodic Safety Update Reports must be submitted every six months for the first two years after authorisation, annually for the subsequent two years and thereafter at time of renewal of the authorisation (Article 75 point 5 of Directive 2001/82/EC - Directive 81/851/EEC as amended). For immunological products that have been or are in the process of being assessed as part of the immunological review, PSURs need only be submitted at each five year renewal.

Mutual Recognition with Ireland as Reference Member State (RMS)

The IMB would like to emphasise once again the protocol for applicants who wish to use Ireland as RMS for veterinary medicinal product applications, under the Mutual Recognition (MR) procedure. The protocol is as follows:

- Notification in writing to Ms. Sinead Barron ***(sinead.barron@imb.ie)*** of a request for the IMB to act as RMS at least six months ahead of the expected procedure start.
- Meeting between the applicant and the IMB to review state of the file, need for any updates, expected delivery date of updated dossier (if necessary) or date of issue of the veterinary product authorisation, list of Concerned Member States (CMSs), available IMB resources, notification of application to CMSs and expected date for commencement of the mutual recognition procedure.
- At least 90 days before the intended commencement date for the MR procedure, the IMB must be in a position to issue or amend the product marketing authorisation. Failure by applicants to meet the IMB requirements, including where necessary the submission of an updated dossier and the correct fee, will therefore result in the MR procedure being delayed.
- The IMB will allocate a Project Manager from its secretarial section to liaise with the applicant and ensure the timely progress of the application through to completion.
- The IMB must notify CMSs by electronic mail of the anticipated application at least 90 days before the commencement of the procedure.
- In common with other agencies, the IMB wishes to ensure an even distribution of work during the year. Therefore, the IMB will generally not be in a position to

act as RMS for more than two applications in any given month. Thus applicants need to ensure that every effort is made at the time of the original meeting with the IMB to set realistic targets for the commencement of the procedure. Deadlines which are missed may result in the reallocation of the MR slot to alternative applications and the application being delayed to the next available slot.

Disclosure of new information on veterinary medicines authorised in Ireland and elsewhere

Veterinary product authorisations are subject to the provisions of the Animal Remedies Regulations, 1996 (S.I. No. 179 of 1996) and the conditions set out in Part I of the Authorisation Schedule. Applicants are expected be familiar with all of the conditions of product authorisation and, in particular, the requirement on disclosure of new information on the product or change in the status of the authorisation elsewhere in the European Union. Any new information which affects the validity of the data underpinning the authorisation or which alters the quality, safety or efficacy of the product or affects the Summary of Product Characteristics and other literature, whether or not the data were generated from studies conducted at the request of the IMB should be disclosed to the IMB. Clause 4 of Part I of the authorisation Schedule of issued by the IMB states:

The authorisation holder shall forthwith inform the Board of any information received by him which may alter the validity of the data which was contained in, or furnished in connection with, the application for the product authorisation for the purpose of being taken into account in assessing the quality, safety or efficacy of the veterinary medicinal product to which the authorisation relates.

The authorisation holders shall forthwith inform the Board of any prohibition or restriction imposed by the competent authority of any other State in which the veterinary medicinal product to which the authorisation is marketed.

Index of authorised veterinary medicines

The IMB will shortly be publishing on its website **(http://www.imb.ie)** a list of authorised veterinary medicines including both pharmaceutical veterinary medicines, which are authorised by the IMB, as well as immunological veterinary medicines (vaccines), which are authorised by the Department of Agriculture, Food and Rural Development. This list will reflect the status at the time of last update and will be subject to change without notice over time. The publication of the list is in accordance with the promise of the IMB given at the IMB Veterinary Information Day in October 2000 to make available a listing of authorised products as soon as existing work backlogs had been eliminated.

Advertising of Veterinary Medicinal Products Prior to Authorisation

The IMB has noted that some companies have advertised products in national journals in advance of the product being authorised in this country. This practice is contrary to the Animal Remedies Regulations, 1996 which states that *"a person shall not sell or supply an animal remedy save under and in accordance with an animal remedies authorisation for the time being in force"*. The term "sell" is defined in the Animal Remedies Act, 1993 as including "offer, expose or keep for sale, invite an offer to buy". Similarly, the IMB believes that applicant companies cannot lawfully place mock-ups of products which are not yet authorised in this country on display in trade exhibitions or similar. If the IMB becomes aware of such activities, it will inform the Department of Agriculture, Food and Rural Development accordingly so that enforcement action may be undertaken.

New appointment to the IMB's Veterinary Advisory Committee

Dr. Kevin O'Farrell, MVB, MRCVS, PhD, Fermoy, Co. Cork has been appointed by the Minister for Health & Children Mr. Micheal Martin, to the Veterinary Advisory Committee of the Irish Medicines Board. His appointment

follows the resignation of Dr. Iona Pratt of the Health and Safety Authority.

Veterinary Pharmaceuticals

Submission to the IMB of Mock-ups of Packaging and Package Inserts for Veterinary Pharmaceutical Products

In accordance with Article 12 of Directive 2001/82/EC (Directive 81/851/EEC as amended), the IMB requires a mock-up of the label and outer packaging of a veterinary medicinal product, together with the package insert, as part of the approval process for veterinary pharmaceutical products (including applications for renewal as well as variations and new applications). These requirements will not, at present, apply to veterinary immunological products, which are authorised by the Department of Agriculture, Food and Rural Development. From 1 May 2002, the IMB will require mock-ups of the label and outer packaging of a veterinary pharmaceutical product together with the package insert as outlined below:

- New applications

  Proposed mock-ups should be provided on submission or during assessment. Changes may be required to these mock-ups during the assessment and a request for final mock-ups will be forwarded by the relevant assessor prior to licensing.

- Renewals

  Mock-ups should be provided on submission. If changes to these mock-ups are requested during the assessment, a request for final mock-ups will be forwarded by the relevant assessor prior to licensing.

- Variations

  For a variation application where changes are proposed which necessitate changes to the label and/or package insert, the application should be accompanied by the existing mock-ups with proposed changes highlighted. Following assessment the relevant assessor will request the final mock-ups, prior to approval.

It should be noted that failure to provide final mock-ups will delay issue of product authorisations for new products and renewals, and approval of relevant variations.

The requirements for mock-ups and other literature and an accompanying guidance document may be viewed on the IMB website at **http://www.imb.ie**

Residual solvents – Application to existing active substances and products

The VICH residual solvent guideline (CVMP/VICH/502/99) came into effect in June 2001 for new applications for veterinary pharmaceuticals containing a new active substance. A timetable for application of this guideline to new applications for veterinary pharmaceutical products containing an established active substance and to existing veterinary pharmaceutical products (EMEA/CVMP/423/01) has been adopted by CVMP. By January 2002 all new Marketing Authorisation applications should comply with the guideline. All existing veterinary pharmaceutical products, other than those administered by topical application, must also comply with respect to class 1 solvent limits by the same date. Where necessary, VPA holders should submit Type I or Type II variations as detailed below:

- No action is required when the product does not contain a class 1 solvent or is administered topically.
- Type I variation is required when a solvent is changed in order to comply with the guideline and the residual levels are within the limits.
- Type II standard variation is required when a solvent is changed in order to comply with the guideline and this change impacts on the physio-chemical properties of the active substance or the product.
- Type II complex variation is required, with toxicological justification, when residual levels of a solvent cannot meet the relevant guideline limits.

Continued use of class 1 solvents must be justified in all relevant variations. In the absence of a variation, it is assumed that the product complies with the guideline. A section has been added to IMB renewal application form

in which VPA holders are requested to indicate the status of each product. This section of the renewal form is intended only to confirm compliance; no data will be accepted as part of the renewal procedure.

Changes to National Authorisations resulting from Mutual Recognition

For products that are originally authorised by the IMB and subsequently enter the Mutual Recognition (MR) procedure, changes to the current authorisation in Ireland may be necessary in order for mutual recognition to take place. Where such changes are necessary, the applicant will introduce these using either of the following national procedures:

- By submitting a variation application to bring the Irish labelling and Summary of Product Characteristics (SPC) into line with those adopted on day 90 of the MR procedure, or
- By making a voluntary application for renewal of the Market Authorisation dating from day 90 of the Mutual Recognition procedure. No supporting documentation will be required for this renewal. The advantage of following this procedure is that the Marketing Authorisation in the Concerned Member States will have the same approximate renewal date and this will facilitate the preparation of Periodic Safety Update Reports (PSURs) for all Member States.

Whether you choose to vary or renew the authorisation, you are requested to submit amended labels, inserts and other packaging to comply with the SPC agreed on day 90 of the procedure.

Outstanding variations to veterinary pharmaceutical products

In order to ensure that IMB records are fully up-to-date ahead of the project to electronically scan all applications for product authorisation and to update our tracking system, we would welcome any queries regarding outstanding variation applications. If Veterinary Product Authorisation Holders have any concerns, they are requested to provide name of the product and VPA number, date of submission and type of application to Ms. Simona Bordean ***(simona.bordean@imb.ie)***.

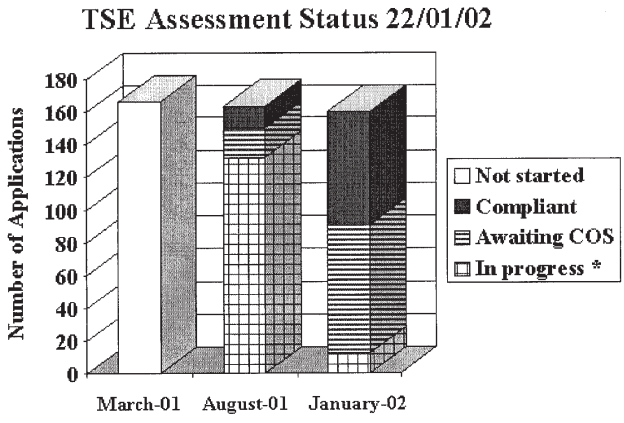
New Delivery Systems for OP Concentrates

The IMB is aware that new standards in delivery systems have been developed, or are currently under development, by a number of companies involved in marketing organophosphate (OP) concentrates in Ireland. This issue was discussed at a recent meeting of the Advisory Committee for Veterinary Medicines of the IMB and it was concluded that, for all relevant products on the Irish market, new closed delivery systems, or similar, aimed at reducing operator exposure to the concentrate must be in place before 31 October 2002 and any product not in compliance with the new standard at that date should be recalled from the market.

Veterinary Immunologicals

Transmissable Spongiform Encephalopathy (TSE) – Assessment status of Immunological Veterinary Medicinal Products.

Excellent progress has been made in this area over the last five months, see figure below.



*Note that 9 of the 12 assessments in progress are being conducted through the MR procedure and as such, the timetable for completion of these is outside the control of the IMB.

As it remains the IMB's intention to complete the TSE project as soon as possible, it is necessary that European Pharmacopoeia Certificates of Suitability (COS) be forwarded to the IMB as soon as they are available. The IMB also urges companies or applicants who have TSE queries outstanding to make every effort to resolve them. If assistance is required, please contact the Immunological Assessor responsible for the TSE evaluation. If there are problems in obtaining information from suppliers of starting materials, this should be made known to the IMB, as this information will be passed on to the Department of Agriculture, Food and Rural Development.

The IMB notes with satisfaction the progress on this project and the excellent cooperation and considerable effort of the applicant companies involved.

INSPECTORATE

Legislation and Guidelines

A number of updates to legislation and guidelines have been recently made and can be accessed from the following website:

http://pharmacos.eudra.org/F2/pharmacos/docs.htm

To summarise, the legislation and guideline changes are as follows:

- Annex 13 *Manufacture of investigational medicinal products* has been revised in order to implement the 'Detailed Guidelines' for the manufacture and the labelling of investigational medicinal products as provided for in Directive 2001/20/EC relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. Draft 1 is released for a six months consultation period. Comments are expected before 1 May 2002.
- An updated compilation of administrative procedures for GMP inspections has been prepared and is available on the European Commission's website at **http://pharmacos.eudra.org.** This compilation updates and replaces document III/5698/94, which had been prepared within the ad hoc group of inspectors and published by the Commission. It includes guidance for inspectors on rapid alerts, exchange of information between inspectorates, batch certificates and a format for a community inspection report.
- Paragraph 42 of Annex 1 to Volume 4 of *The Rules Governing Medicinal Products in the European Union* has been revised to take account of current practices.

PIC/S

The press release in relation to the PIC/S committee meeting in November 2001 is available at the following website:

http://www.picscheme.org/pubs/press/prnov01.htm

Of particular interest in the press release is reference to the draft PIC/S Guidance on Best Practices for Computerised Systems in Regulated 'GxP' Environments. This document is scheduled to be made available for industry comments by early 2002 for a period of six months. The revised draft recommendation will be made available on the PIC/S website.

Mutual Recognition Agreements

The latest status from the EMEA is available from:

http://www.emea.eu.int/pdfs/technical/mra/003301en.pdf

Australia

In place for human and veterinary medicinal products. The agreement is based on the exchange of certificates of GMP compliance for manufacturers and batch certificates.

Canada

There is no new date for the start of the operational phase.

New Zealand

The agreement is in place for human medicinal products. The operational phase for veterinary medicinal products is expected to start by the beginning of 2002.

United States
The transitional period has expired and the United Kingdom was the only Member State which was evaluated. A time plan needs to be agreed before a formal extension of the transitional MRA can be considered.

Switzerland
The MRA is awaiting ratification. A new tentative date is May/June 2002.

Japan
The commencement date of the 18 month preparatory work is 1 January 2002. The MRA is for human medicinal products only.

GMP Observations

Internal Audits - IMB expectations concerning frequency and viewing audit reports

The IMB expects to see a programme of audits such that all GMP areas are covered at least once per annum. A review of the programmes will include the mechanics of the audit process, the training and experience of auditors, the extent to which departmental heads are involved, and a log of internal audits carried out. Reports of internal audits are not normally reviewed.

The IMB differentiates internal audits and audits of suppliers. Reports of supplier audits can be reviewed. This includes a corporate audit of a sister company where that sister company is supplying a partially complete or finished medicinal product to the Irish site which is being inspected and which is responsible for final batch release.

The IMB is aware that there may be difficulty in gaining access to carry out supplier audits where the medicinal product manufacturer purchases very small quantities from a supplier. Sharing of audit reports of such suppliers is acceptable provided that any contract auditor was appropriately trained and experienced and that the scope of any audit covered the material/product is relevant to the contract giver.

HUMAN NEW PRODUCT AUTHORISATIONS ISSUED SEPTEMBER – DECEMBER 2001

PA Number	Product Name
PA0017/099/010	LAMICTAL DISPERSIBLE
PA0035/082/003	COZAAR
PA0037/069/004	ZOTON FASTAB
PA0037/069/005	ZOTON FASTAB
PA0043/006/004	NUROFEN
PA0043/037/001	CROOKES IBUPROFEN LIQUID
PA0047/077/005	PROZAC WEEKLY
PA0050/141/001	REDOXON DOUBLE ACTION
PA0050/141/002	REDOXON DOUBLE ACTION
PA0141/026/002	VIDISIC SDU
PA0144/038/001	STIEPROX
PA0282/077/001	PAROXETINE
PA0282/077/002	PAROXETINE
PA0361/014/001	STERILE CONCENTRATE FOR CARDIOPLEGIA INFUSION
PA0476/013/001	CIPROFLOXACIN
PA0476/013/002	CIPROFLOXACIN
PA0476/013/003	CIPROFLOXACIN
PA0476/013/004	CIPROFLOXACIN
PA0544/016/001	MENOMUNE A/C/Y/W-135
PA0677/003/001	PULMOCIS
PA0678/039/010	PANADOL EXTRA SOLUBLE
PA0678/039/012	PANADOL ACTIFAST
PA0678/071/004	NIQUITIN
PA0678/071/005	NIQUITIN
PA0678/071/006	NIQUITIN
PA0690/014/001	TECHNESCAN HSA
PA0711/016/001	VERAP
PA0711/016/002	VERAP
PA0711/016/003	VERAP
PA0711/016/004	VERAP RETARD
PA0711/016/005	VERAP RETARD
PA0711/029/004	TRADOL INJECTION
PA0740/003/001	SIMVASTATIN FILM COATED TABLETS
PA0740/003/002	SIMVASTATIN FILM COATED TABLETS
PA0740/003/003	SIMVASTATIN FILM COATED TABLETS
PA0740/003/004	SIMVASTATIN FILM COATED TABLETS
PA0740/004/001	SIMVASTATIN SY FILM COATED TABLETS
PA0740/004/002	SIMVASTATIN SY FILM COATED TABLETS
PA0740/004/003	SIMVASTATIN SY FILM COATED TABLETS
PA0740/004/004	SIMVASTATIN SY FILM COATED TABLETS
PA0740/005/001	SIMVASTATIN SH COATED TABLETS
PA0740/005/002	SIMVASTATIN SH COATED TABLETS
PA0740/005/003	SIMVASTATIN SH COATED TABLETS
PA0740/005/004	SIMVASTATIN SH COATED TABLETS
PA0740/006/001	SIMVASTATIN GENTHON COATED TABLETS
PA0740/006/002	SIMVASTATIN GENTHON COATED TABLETS
PA0740/006/003	SIMVASTATIN GENTHON COATED TABLETS
PA0740/006/004	SIMVASTATIN GENTHON COATED TABLETS
PA0735/007/012	IMAGOPAQUE
PA0735/007/014	IMAGOPAQUE
PA0735/007/015	IMAGOPAQUE
PA0798/002/001	BCG VACCINE SSI
PA0810/001/004	LIPANTIL MICRO CAPSULE
PA0810/001/005	LIPANTIL MICRO CAPSULE
PA0849/002/001	HUMAN ALBUMIN GRIFOLS
PA0979/009/003	FYBOGEL ZEST
PA0979/022/001	PARACETAMOL FROM THE MAKERS OF DISPRIN
PA0979/023/001	IBUPROFEN FROM THE MAKERS OF DISPRIN
PPA0465/012/005	ADALAT LA
PPA0465/012/006	ADALAT LA
PPA0465/038/004	ZOVIRAX
PPA0465/062/001	LUSTRAL
PPA0465/062/002	LUSTRAL
PPA0465/069/001	PREMARIN
PPA0465/069/002	PREMARIN
PPA0465/073/001	FLIXOTIDE EVOHALER
PPA0465/073/002	FLIXOTIDE EVOHALER
PPA0465/077/001	IMURAN
PPA0465/077/002	IMURAN
PPA0465/078/001	RISPERDAL
PPA0465/078/002	RISPERDAL
PPA0465/078/003	RISPERDAL
PPA0465/078/004	RISPERDAL
PPA0465/078/005	RISPERDAL
PPA0465/079/001	CATAFLAM
PPA0465/080/001	DETRUSITOL
PPA0465/080/002	DETRUSITOL
PPA0465/081/001	LIVIAL

HUMAN NEW PRODUCT AUTHORISATIONS WITHDRAWN SEPTEMBER – DECEMBER 2001

PA Number	Product Name
PA0006/014/001	DECORTISYL
PA0006/014/002	DECORTISYL
PA0006/017/001	PRECORTISYL
PA0006/017/002	PRECORTISYL
PA0006/031/001	CHLORAMPHENICOL
PA0006/032/001	ATROPINE
PA0006/034/001	DIAZEPAM
PA0006/034/002	DIAZEPAM
PA0006/034/003	DIAZEPAM
PA0006/037/001	OXPRENOLOL
PA0006/037/002	OXPRENOLOL
PA0006/037/003	OXPRENOLOL
PA0006/037/004	OXPRENOLOL
PA0006/041/001	HYPROMELLOSE
PA0006/045/001	CEFROM
PA0006/045/002	CEFROM
PA0006/045/003	CEFROM
PA0006/045/004	CEFROM
PA0006/045/005	CEFROM POWDER
PA0006/045/006	CEFROM POWDER
PA0007/002/006	ATROVENT AUTOHALER
PA0007/034/005	DUOVENT AUTOHALER
PA0009/034/002	RHINOCORT AQUA
PA0013/052/001	CLIMACTOL
PA0013/052/002	CLIMACTOL
PA0017/067/001	ANGISED
PA0023/008/006	LASIX
PA0023/008/007	LASIX
PA0030/033/001	TRIOGESIC ELIXIR
PA0030/033/002	TRIOGESIC
PA0030/034/001	TRIOMINIC
PA0030/034/002	TRIOMINIC
PA0030/036/001	ALLEREZE PLUS
PA0040/018/004	LARGACTIL
PA0040/018/005	LARGACTIL
PA0040/026/004	STEMETIL
PA0040/027/004	SURMONTIL
PA0040/027/005	SURMONTIL
PA0041/026/002	TRILUDAN
PA0041/031/001	LURSELLE
PA0060/014/001	STELABID
PA0074/047/002	CALAMINE
PA0077/039/001	LINGRAINE
PA0086/011/001	DIMOTAPP
PA0086/011/003	DIMOTAPP PAEDIATRIC
PA0086/012/001	DIMOTAPP L.A.
PA0090/009/001	PANCREX V
PA0090/009/002	PANCREX V FORTE
PA0090/009/003	PANCREX V
PA0090/009/004	PANCREX V
PA0090/009/005	PANCREX
PA0100/034/001	LASMA SUSTAINED RELEASE
PA0126/025/001	MELZINE
PA0167/085/001	NUTRINEAL PD2 1.1%
PA0240/002/001	DICOPAC (TWO CAPSULES + ONE SOL. FOR INJ.)
PA0261/024/001	CORDIUM
PA0261/024/002	CORDIUM
PA0261/024/003	CORDIUM
PA0261/041/001	RIMEXEL
PA0281/065/001	COTENT 50
PA0281/065/002	COTENT 100
PA0300/005/001	LABOSEPT
PA0303/033/001	DIVINA
PA0436/022/001	CROMOGEN INHALER
PA0437/022/002	FLUPHENAZINE DECANOATE
PA0437/022/004	FLUPHENAZINE DECANOATE
PA0468/019/001	AAA MOUTH & THROAT
PA0544/023/001	H-B-VAX II PAEDIATRIC
PA0544/023/002	H-B-VAX II
PA0644/002/001	RONICOL
PA0743/001/001	ERYCAPS ERYTHROMYCIN
PA0757/006/001	NARDIL
PA0776/001/003	CIPRAMIL
PA0798/001/001	TUBERCULIN PPD RT23 SSI
PA0798/001/003	TUBERCULIN PPD RT23 SSI
PA0815/002/001	TIMONIL RETARD
PA0815/002/002	TIMONIL RETARD
PA0855/003/004	LASIX
PA0855/004/002	TOPISOLON
PA0855/004/003	TOPISOLON
PA0855/005/001	HOSTACYCLINE
PA0855/006/001	LASIKAL
PA0855/009/001	RASTINON
PA0855/011/001	DANERAL SA
PA0855/015/001	ARELIX
PA0855/015/002	ARELIX
PA0855/019/001	TARIVID IV INFUSION
PA0855/019/004	TARIVID
PA0863/004/001	DERMAZOLE
PA0914/001/001	TIMOLOL CIBA VISION
PA0914/001/002	TIMOLOL CIBA VISION
PA0936/001/001	CYKLO-F
PA0946/002/001	ACTINAC
PA0979/009/001	FYBOGEL CITRUS
PA1009/012/001	TESTOTOP 10
PA1009/012/002	TESTOTOP 15
PA1009/013/001	TESTOSTERONE FERRING

HUMAN PRODUCT AUTHORISATIONS WITHDRAWN SEPTEMBER – DECEMBER 2001 (contd)

PA Number	Product Name	PA Number	Product Name
PPA0465/007/001	INDOCID	PPA0465/016/001	NATRILIX
PPA0465/007/002	INDOCID	PPA0465/019/001	VENTOLIN INHALER
PPA0465/007/003	INDOCID R	PPA0465/034/001	PERSANTIN
PPA0465/012/002	ADALAT	PPA0465/034/002	PERSANTIN
PPA0465/013/001	VOLTAROL	PPA0465/035/001	MINOCIN
PPA0465/013/002	VOLTAROL	PPA0465/035/002	MINOCIN
PPA0465/014/001	ALDACTONE	PPA0465/039/003	LOSEC
PPA0465/014/002	ALDACTONE		

HUMAN NEW PRODUCT AUTHORISATIONS (MUTUAL RECOGNITION) SEPTEMBER – DECEMBER 2001

PA Number	Product Name	PA Number	Product Name
PA0013/079/003	DIOVAN	PA0408/055/001	RANBAXY FLUOXETINE
PA0013/079/004	DIOVAN	PA0566/021/003	FRESENIUS PROPOFOL 2%
PA0013/092/004	TRILEPTAL	PA0819/017/001	ZOLPIDEM-RATIOPHARM
PA0013/109/001	TAREG	PA0819/017/002	ZOLPIDEM-RATIOPHARM
PA0013/109/002	TAREG	PA0822/006/001	RELPAX
PA0016/064/001	REBOXETINE	PA0822/006/002	RELPAX
PA0016/064/002	REBOXETINE	PA0891/003/001	XYZAL
PA0126/103/005	CLAVAMEL	PA0931/004/001	MACO PHARMA SODIUM CHLORIDE AND GLUCOSE
PA0167/109/001	OLICLINOMEL N4-550		
PA0167/109/002	OLICLINOMEL N4-550E	PA0936/010/001	XALACOM
PA0167/109/003	OLICLINOMEL N5-800	PA0961/001/001	LIQUI-CHAR
PA0167/109/004	OLICLINOMEL N-800E	PA0992/001/001	BICAFLAC BUFFER SOLUTION
PA0167/109/005	OLICLINOMEL N6-900	PA0992/002/001	BECAFLAC ELECTROLYTE SOLUTION WITHOUT POTASSIUM
PA0167/109/006	OLICLINOMEL N6-900E		
PA0566/021/004	FRESENIUS PROPOFOL 2%	PA0992/003/001	BICAFLAC ELECTROLYTE SOLUTION WITH
PA0568/008/001	PRETERAX		
PA0700/016/001	VIASPAN	PA0998/001/001	DR. SCHEFFLER VITAMIN C
PA0789/002/005	CISPLATIN “EBEWE”	PA1009/018/001	GONAPEPTYL DEPOT
PA0167/109/007	OLICLINOMEL N7-1000	PA1014/001/001	COPAXONE
PA0167/109/008	OLICLINOMEL N7-1000E	PA1026/001/007	NEUPOGEN SINGLEJECT
PA0289/002/003	GLUCOPHAGE	PA1026/001/008	NEUPOGEN SINGLEJECT
PA0289/009/001	DIABEX		

HUMAN CENTRALISED PRODUCT AUTHORISATIONS ISSUED SEPTEMBER – DECEMBER 2001

PA Number	Product Name	PA Number	Product Name
EU/1/01/196/001	CASPOFUNGIN MSD	EU/1/01/197/002	FOSCAN
EU/1/01/196/002	CASPOFUNGIN MSD	EU/1/99/110/005	SUSTIVA
EU/1/01/196/003	CASPOFUNGIN MSD	EU/1/99/111/005	STOCRIN
EU/1/01/197/001	FOSCAN		

VETERINARY NEW PRODUCT AUTHORISATIONS ISSUED SEPTEMBER – DECEMBER 2001

PA Number	Product Name	PA Number	Product Name
10277/085/001	COOPERS ECTOFORCE SHEEP DIP	10996/053/001	METRICURE
10881/014/001	BOB MARTIN FLEA & TICK COLLAR FOR DOGS	10996/127/002	VIVITONIN 100
		10996/157/001	UNISOLVE
10960/044/001	DUO-TABS	10996/165/001	BOVIVAC S
10983/038/001	AURIZON	10999/092/001	NOROMECTIN PREMIX FOR SWINE
10988/018/003	RILEXINE 600		

VETERINARY PRODUCT AUTHORISATIONS WITHDRAWN SEPTEMBER – DECEMBER 2001

PA Number	Product Name	PA Number	Product Name
10021/034/001	BINIXIN	10965/001/001	HARTZ 2 IN 1 FLEA & TICK FOR DOGS
10126/008/001	PROCILLIN L A		
10484/016/001	BLOAT TREATMENT	10965/009/001	HARTZ 2 IN 1 FLEA & TICK FOR CATS
10857/013/001	COPACAPS EWE/CALF		
10857/025/001	PANOMEC PASTE FOR HORSES	10965/012/001	HARTZ RID FLEA SPRAY FOR DOGS
10857/042/001	COPACAPS CATTLE		
10932/001/001	WATER FOR INJECTION	10989/003/001	AMOXYCILLIN 15%

APPENDIX I

IMB Human Medicines Information Day

April 15, 2002 - Citywest Hotel and Conference Centre, Saggart, Co Dublin

9.00 **Registration**

9.30 **Welcome**
Professor Frank Hallinan, Chief Executive Officer, IMB

Session 1 **Labels and leaflets: meeting the needs of the user**
Chair Dr Joan Gilvarry, Medical Director, IMB

9.45 **Patient leaflets: content and comprehension, a regulatory perspective**
Dr Sheila Killalea, Medical Officer, IMB

Approaches to readability
Dr Caitríona Fisher, Senior Pharmaceutical Assessor, IMB

Evidence-based leaflet design
Professor Patricia Wright, School of Psychology, Cardiff University

Discussion

11.15 **Coffee**

11.45 **Can the pharmaceutical industry learn from packaging related errors?**
Mr Tim Delaney MPSI, Head of Pharmacy and Director of Accreditation, Adelaide and Meath Hospital

IMB guidance for submission of labels and leaflets
Mr Edward Bourke, Senior Pharmaceutical Assessor, IMB

Discussion

13.00 **Lunch**

Session 2 **Current issues**
Chair Mr Tom McGuinn, Chief Pharmacist, Department of Health and Children

14.30 **IMB view of Commission's proposals for legislative change**
Professor Frank Hallinan, Chief Executive Officer, IMB

Company compliance with pharmacovigilance obligations
Ms Niamh Arthur, Pharmacovigilance Co-ordinator, IMB

Update on TSE issues
Ms Kathleen O'Neill, Senior Pharmaceutical Assessor, IMB

IT Strategic Plan
Ms Suzanne McDonald, IT Manager, IMB

15.30 **Questions and answers**

16.00 **Close of meeting**

APPENDIX II

Irish Medicines Board

Human Medicines Information Day 15 April, 2002

Citywest Hotel, Saggart, Co Dublin

Registration Form

Company Name _____

Payment details _____

Fee Euro 250 per delegate Cheques to be made payable to the Irish Medicines Board

Name	Position in company	Phone, fax and e-mail contact details

Please return no later than Friday 22 March, 2002 to:

Ms Margaret Miley
Irish Medicines Board
Earlsfort Centre
Earlsfort Terrace
Dublin 2

APPENDIX III

GUIDANCE FOR THE SUBMISSION OF MOCK-UPS OF PACKAGING AND PACKAGE LEAFLETS

Introduction

Following review of its current procedures regarding the receipt and approval of labels and leaflets for human medicinal products, the IMB now seeks to inform product authorisation holders of updated requirements in this regard. In so doing, it is reaffirmed that the approval of product labels and leaflets is an intrinsic part of the product licensing process. The product labels and leaflet play an essential part in the safe and effective use of the medicine by both the patient and healthcare professionals.

Directive 2001/83/EC on the *Community code relating to medicinal products for human use*, article 8.3 requires that:

'…the application shall be accompanied by one or more specimens or mock-ups of the outer packaging and the immediate packaging of the medicinal product, together with a package leaflet.'

The definition of a mock-up for the purpose of this guidance is that used in the current EU Guideline on the *Readability of the Label and Package Leaflet of Medicinal Products for Human Use*, which specifies:

'A flat art-work design in full colour, presented so that, (following cutting and folding where necessary), it provides a replica of both the outer and immediate packaging and of the leaflet and clearly demonstrates the three dimensional presentation of the label text and of the leaflet text.'

IMB Requirements

From 1 May 2002, the IMB will require mock-ups of the outer and immediate packaging of a medicinal product together with the package leaflet as outlined below:

i. New applications: on application or during assessment.
ii. Renewals and relevant variations: on application.
In the case of variation applications these should be accompanied by the existing approved packaging and leaflet artwork with the proposed changes highlighted.

Where a range of pack sizes are proposed for marketing, only a mock-up of the minimum and maximum pack sizes for each strength and dosage form need be presented. It is understood that these mock-ups will also be representative of intermediate pack sizes with the sole exception of a statement regarding pack size/number of units.

It should be noted that during assessment, labels and leaflets will (as currently applies) be agreed with the individual medical and pharmaceutical assessors. Any changes requested and agreed during assessment should then be incorporated into the final mock-ups of the packaging and package leaflet and one copy submitted to the IMB (refer to Submission of Final Mock-ups). It should be noted that no other changes to any aspect of content, layout or design should be included other than those agreed during the assessment.

Each mock-up of the final packaging and leaflet must be dated and signed by the applicant. The final mock-ups will be retained at the IMB as the approved market pack and leaflet. It should be noted that licences will not be issued for new products or renewals, nor relevant variations approved until final mock-ups have been submitted and approved.

Submission of Final Mock-ups

Please note that only one copy of the final mock-ups should be submitted to the IMB as outlined below:

1. New product applications and renewals

In the case of a new product application or renewal final mock-ups will be requested by the relevant administration section when the draft schedule is forwarded for comment, prior to licensing.

2. Variations

With respect to relevant variations the following points should be noted:

i. For a variation where changes to the medical and pharmaceutical information are proposed which necessitate changes to the labels and leaflet, a request for final mock-ups will be made by the relevant administration section prior to approval.

ii. For a variation where changes to either the medical or pharmaceutical information are proposed which necessitate changes to the label and leaflet, the assessor concerned will request the final mock-ups, prior to approval.

It is essential that the final mock-ups returned to the relevant administration section or assessor, be signed and dated, and include all changes / modifications agreed during assessment. If this is not the case further requests for the agreed mock-ups will be made, with subsequent delays in licensing or approval.