IRISH MEDICINES BOARD

news MEDICINAL PRODUCTS LETTER

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GENERAL

STAFF CHANGES

Paul Scannell and *Orla Goggin* were appointed Technical Officers in the Medical Devices Department.

Rosann Deegan was appointed Pharmaceutical Assessor in the Human Medicines Department.

Sarah Walsh was appointed Scientific Officer in the Human Medicines Department.

Susan Reid was appointed Immunological Assessor in the Veterinary Medicines Department.

Donal O'Donnell and *James McKenna* were appointed Veterinary Assessors in the Veterinary Medicines Department.

HUMAN MEDICINES

LEGISLATION AND GUIDELINES

CHMP/EWP/40326/06 Questions & Answers on the Bioavailability and Bioequivalence Guideline

EMEA/214301/06 EMEA Pandemic Influenza crisis management plan for the evaluation and maintenance of Pandemic Influenza vaccines and antivirals

Annex I – EU influenza pandemic process map

EMEA/CHMP/VWP/263499/06 Guideline on dossier structure and content of Marketing Authorisation applications for Influenza vaccines with avian strains with a pandemic potential for use outside of the core dossier context (Released for consultation July 2006)

EMEA/341972/2006 CHMP SWP Reflection Paper on PPARs (Perosisome Proliferator Activated Receptors)

EMEA/129510/06 Practical guidance on the extension of Commission Decision Annexes in the new Accession Country languages

GMP DECLARATIONS FOR ACTIVE SUBSTANCE MANUFACTURERS

In accordance with Article 46(f) of Directive 2004/27/EC, manufacturing authorisation holders are required to use as starting materials only active substances which have been manufactured in accordance with the detailed guidelines on the Good Manufacturing Practice for starting materials as adopted by the Community.

Confirmation of compliance with the above requirement is now required for all applications for new marketing authorisations, renewals and variation applications (detailed below) where a change to the registered manufacturers is proposed.

New Applications/Renewals

As the QP responsible for batch release takes overall responsibility for each batch, a declaration of compliance with Article 46(f) is required from the QP at each of the registered batch release sites for the finished product. In addition, this declaration is also required from the QP at all manufacturing sites that use the active substance as the starting material.

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Where multiple manufacturing/batch release sites are registered, a single declaration may be submitted provided that:

- The declaration makes it clear that it is signed on behalf of all the involved QPs.
- The arrangements are underpinned by a technical agreement as described in Chapter 7 of the GMP Guide and the QP providing the declaration is the one identified in the agreement as taking specific responsibility for the GMP compliance of the active substance manufacturer(s). Note: these arrangements are subject to inspection by the competent authorities.

Variations

QP declarations in relation to the GMP status of active substance manufacturers are required for variations in which a change is proposed to the manufacturer of the active substance, manufacturer of the finished product or manufacturer responsible for the batch release of the finished product. The *Guideline on Dossier Requirements for Type 1A and Type 1B Notifications* (June 2006) clearly sets out the requirements for Type 1 notifications.

For Type II variations companies are requested to note that the requirements for GMP declarations in relation to active substance manufacturers are identical to those outlined in the documentation requirements for the corresponding Type 1 Notification, e.g. for a Type II variation to add a new manufacturer of an active substance (e.g. where the new active substance manufacturer uses an EDMF), the same declarations are required as outlined in documentation requirement 6 for a Type 1B No. 14(b) notification.

If multiple manufacturing/batch release sites are involved, a single declaration may be submitted provided that the conditions previously outlined for new applications/renewals are fulfilled.

Declaration

The declaration regarding the GMP status of the active substance manufacturer(s) must be unambiguous. Details of the basis on which this declaration can be provided are available on the EMEA website at the following address: **http://www.emea.eu.int/Inspections/GMPfaqAS.html**

Companies are requested to note that a declaration from the relevant QP(s) is required even if a valid GMP certificate for the active substance manufacturer issued by a competent authority or a CEP issued by the EDQM is available.

The following is a suggested wording for the declaration:

I, the undersigned, confirm that *the name of active substance(s)* manufactured at *name of active substance manufacturer(s)* used in the manufacture of *name of the finished product(s)* is manufactured in accordance with the detailed guidelines on Good Manufacturing Practice for starting materials as adopted by the Community.

Where only a single declaration is provided for a number of different manufacturing sites:

This declaration is signed on behalf of the following QPs:

Name of QP(s), Name of manufacturing site(s)

The submission of this single declaration on behalf of the named QPs is underpinned by a technical agreement as described in Chapter 7 of the GMP Guide and I confirm that I am the QP identified in the agreement as taking specific responsibility for the GMP compliance of the active substance manufacturer(s).

Signature: _____ Date: ____

Qualified Person

Name of manufacturing site

Companies are encouraged to use the above wording in order to expedite the assessment process.

UPDATE ON ELECTRONIC REPORTING OF NON-IRISH ADVERSE REACTIONS

The IMB would like to take this opportunity to highlight a change in the national reporting requirements of adverse reactions occurring outside Ireland.

Companies and sponsors are advised that with immediate effect there will no longer be a requirement to submit non-Irish adverse reaction cases in paper format where these are reported electronically. However, prior to submitting non-Irish reports electronically, companies are requested to notify the IMB via e-mail to **imbpharmacovigilance@imb.ie** of their intention to do so. Please note that acknowledgement or IMB reference numbers are not issued for non-Irish reports, including those received electronically (i.e. XML acknowledgement will not be issued).

In addition to the local reporting requirements, companies and sponsors are reminded that all non-Irish reports should continue to be submitted directly to the EudraVigilance database located at the EMEA in the usual way.

For detailed information and guidance please see the updated IMB 'Guide to Electronic Submission of ICSRs and SUSARs Associated with Use of Human Medicines' which can be found in the Pharmacovigilance section of the IMB website at **www.imb.ie**, under 'Electronic Reporting'.

INFORMATION SEARCHES

The IMB provides a search facility for information on authorised products containing certain active ingredients. A fee is payable for this service and requests for searches concerning medicinal products for human use must be sent to the Post Licensing Section by:

- E-mail to **hm_searches@imb.ie**
- Fax to 01- 6762517
- Letter to Human Medicines Searches, Post Licensing Section, Irish Medicines Board, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland.

VETERINARY MEDICINES

LEGISLATION AND GUIDELINES

EMEA/CVMP/EWP/117899/04 Guideline on Efficacy and Target Animal Safety Data Requirements for Veterinary Medicinal Products intended for Minor Uses or Minor Species(Adopted by CVMP 20 July 06)

EMEA/32995/06 Guideline on the Procedure for Accelerated Assessment Pursuant to Article 39 (8) of Regulation (EC) No 726/2004 (CVMP adopted May 2006)

EMEA/CVMP/QWP/339588/2005 Guideline on Parametric Release (Veterinary) (CVMP adopted October 2006) The guideline will come into effect 1 January 2007.

CVMP/128710/04 Quality Data Requirements for Veterinary Medicinal Products intended for Minor Uses or Minor Species (CVMP adopted 20 July 2006)

EMEA/CVMP/66781/05 Guideline on Safety and Residue Data Requirements for Veterinary Medicinal Products intended for Minor Uses or Minor Species (Adopted by CVMP 20 July 2006)

CHANGE IN MEMBERSHIP OF ADVISORY COMMITTEE FOR VETERINARY MEDICINES

Mr. John McManus, pharmacist, resigned from the ACVM on 1 August 2006. It is expected that the Minister for Health and Children will make a new appointment over the coming months.

CHANGES IN METHOD OF SUPPLY OF INTRAMAMMARY ANTIBIOTICS

As already announced in the April IMB Newsletter (issue no. 24) the IMB would like to remind relevant applicant companies that, (they must submit all relevant applications before 31 March 2007) in order to ensure that all amendment applications are evaluated and approved in time to achieve compliance with the designation of 'prescription only medicine' before the deadline of 1 July 2007. The IMB understands that the Department of Agriculture and Food (DAF) has agreed a period of six months from 1 July 2007 after which time any products which are not compliant with the required method of supply will be uplifted from the market. The IMB will advise the DAF of progress in the receipt and approval of amendments relating to this task so that any non-compliant products may be uplifted from retailers.

REQUESTS FOR CLASSIFICATION – UPDATE

The IMB website has been updated to replace the link 'out of scope' with 'classifications'. This link is still accessed via Veterinary Medicines Publications/application forms. We hope the change of terminology will make it easier for those seeking information about borderline products to find the relevant documents, which have also been updated. The application form for an IMB opinion has been redesigned and renamed as 'Request for Classification of a Borderline Product For Animal Use'. The ' Guide to the Definition of an Animal Remedy and the Classification Process' now includes up-to-date references to the current legislation.

The IMB has also reviewed its internal procedures for dealing with requests for classifications. Decisions on such requests are made by IMB veterinary assessors with appropriate internal consultation, and advised to applicants by an administrative officer. Any applicant wishing to appeal a decision must do so within 14 days. Appeals will be considered by the Management Committee of the IMB; technical issues will be referred as necessary to the IMB Advisory Committee for Veterinary Medicines.

CRITERIA FOR EXEMPTION OF CERTAIN VETERINARY MEDICINES FOR FOOD-PRODUCING ANIMALS FROM THE REQUIREMENTS FOR PRESCRIPTION CONTROL

The IMB welcomes the announcement by the Minister for Agriculture and Food on 11 October that her Department was satisfied that the exemption criteria mean that current off-prescription veterinary medicines will not have to be reclassified as prescription only. The IMB is in discussion with the DAF regarding the proposed amendments needed to the Animal Remedies legislation to give effect to the directive and will keep stakeholders informed of significant developments which impact on the supply of authorised medicines.

IMB GENERAL GUIDANCE ON SUBMISSION OF TYPE IA AND IB NOTIFICATIONS FOR NATIONAL APPLICATIONS

All national Type IA, Type IB and Type II variation applications must be submitted in accordance with Commission *Guideline on Dossier requirements for Type IA and Type IB notifications*, July 2003. Such applications must satisfy all the relevant conditions and must be accompanied by all relevant documentation as detailed in the guideline.

The IMB has been accepting Type IA and IB notifications in the new format for some time but has found that a large percentage are still not being submitted correctly.

The most common errors in the application for Type IA/IB notifications include:

a) The application form not signed and dated. Please note that it is a legal document and must be signed and dated.

b) Incorrect classification of notifications type.

c) The relevant page from the guideline not included or the relevant boxes not ticked
d) 'Present' and 'Proposed' sections of the application form not filled out or not filled out correctly. It should be noted that these sections are relevant to all changes and not just to SPC/labelling changes.
e) The exact documentation that is required not submitted
f) Extra changes made in addition to notification applied for e.g. used opportunity to update the leaflet.
g) The package leaflet and labelling are not submitted, where relevant.

Please be advised that timelines applicable to mutual recognition variations will not apply to national variation applications at this time. Companies must therefore await IMB notification before implementation of the change(s).

Each notification application must be submitted separately and full documentation must be included with each application.

The following must accompany Type IA and Type IB notifications:

1. Covering letter
2. Appropriate fee
3. Application form
4. A copy of the relevant page(s) from the Commission Guideline on Dossier requirements for Type IA and Type IB notifications, July 2003
5. Relevant documentation

Information to be included in each section above:

1. *Covering letter*
The covering letter should clearly state the type of notification i.e. Type IA or Type IB. In addition the covering letter should state any additional information relevant to the application e.g. whether other applications are being submitted in parallel.

2. *Appropriate fee.* For guidance, see the Veterinary Medicines Fee Application Form.

3. *Application form*
The application form is available from the IMB web site (EU Variation Application Form). For all Type I notifications, all sections for changes that are not relevant to the application should be deleted. The rest of the application form must be completed in full, signed and dated. All sections must be completed and all relevant boxes checked.

4. *Copy of the relevant page(s)* of the Commission *Guideline on Dossier requirements for Type IA and Type IB notifications*.
The inclusion of a copy of the relevant page from the guideline is a requirement of the application form and must therefore be attached directly to the form. The applicant must tick the boxes in front of each condition and required documentation. It would be preferable to make cross-reference to the location of each document in the submitted documentation as Appendix 1, Appendix 2 etc.
Please note that all required conditions must be fulfilled for each notification.

5. *Relevant documentation*
Only documentation required should be submitted.
In addition, if the change(s) affect the summary of product characteristics (SPC), labels or package leaflet, a revised SPC and full colour mock ups of the labels and package leaflet (signed and dated on each page) must be submitted. Only those label/leaflet amendments that are described in the application form will be approved and no other changes to any other aspect of content, layout or design will be considered. It should be noted that the marketing authorisation holder has a legal obligation to ensure that the labelling and package leaflet are correct and comply with the relevant requirements.

Please note that consequential changes are regarded as changes which are unavoidable and a direct result of the 'main change' and not simply a change that occurs at the same time. Type IA notifications can only have Type IA consequential change(s), Type IB notifications can have both Type IA and Type IB consequential changes.

Overall the applicant is responsible for the correct submission of the notification.

IMB Procedure for scientific check/assessment:

For Type IA and IB notifications the applicant will be informed of any deficiencies and will have **30 days** to submit any additional data. If the application is incorrectly classified (e.g. Type 1B submitted as a Type IA or Type II submitted as a Type 1B) the applicant will be informed and will have **30 days** to submit an amended application form and any additional data required.

All Type IA and IB notifications should be sent to the Receipts and Validation Section, IMB.

VARIATIONS INVOLVING DMF'S

The procedure outlined below should be followed when submitting variation applications which involve assessment of a DMF.

The open and closed sections of the DMF along with a letter of access and expert report (or scientific overview if in CTD format) must be submitted *by the DMF holder* to the IMB. On receipt of these the DMF holder will be issued with an IMB reference number.

The applicant must obtain this number from the DMF holder and submit it and a copy of the *same version* of the open section of the DMF with the variation application form.

The application cannot be assessed unless all sections of the DMF are submitted by the DMF holder and the versions submitted by the applicant and the DMF holder are the same.

Once the assessment process has started all correspondence should be addressed to the relevant assessor.

IMB INFO DAY 2007 – PRELIMINARY ANNOUNCEMENT

The Veterinary Medicines Department of the IMB is planning to hold its next Info Day in November 2007. We should be pleased to receive

ideas for topics that might be included in the programme. Comments should be sent to sinead.barron@imb.ie.

ACCESS TO IMB DATA ON AUTHORISED ANIMAL REMEDIES

Further to representations made over recent months, the IMB is pleased to report that it is in a position in principle to provide external access to information contained within its database of authorised animal remedies. For reasons of security, the IMB does not allow direct access to its internal systems at this time, but can provide a copy of the required data elements which can subsequently be used by service providers to populate data fields for veterinary prescriptions and for product comparison purposes.

In order to avail of this service a number of conditions must be satisfied, as follows:-

1. The IMB product listing is dynamic and follows ongoing decisions on licensing. Accordingly any listing made available must acknowledge this fact and contain an appropriate IMB disclaimer.
2. The information will be provided in a manner and time to be agreed with the IMB, e.g. monthly updates.
3. The IMB will not engage in an exclusive contract for this service with any one body.
4. The cost of provision of the service should be met by the organisation requesting the information.

For further information on this service, please contact Kevin Horan (kevin.horan@imb.ie), Programme Manager, Information Technology & Change Management Department.

PLANNED ORGANISATIONAL CHANGES IN THE VETERINARY MEDICINES DEPARTMENT

A review of the organisational arrangements within the Veterinary Medicines Department was undertaken in Q3 in the context of the impact of the revised legislation and of changing service requirements. The Board of the IMB at their meeting on 25 October 2006 approved an increase in the level of resources by three to enable the department to be more technically focussed and capable of a wider range of activities. A new management structure based on a predominantly skills based model has also been agreed. The implementation plan for the realisation of the new structure is in preparation, with the new model expected to be in place in Q2, 2007.

PRODUCT LITERATURE IN ELECTRONIC FORMAT

The Veterinary Medicines Department is currently undertaking a pilot project relating to electronic signing and storing of product literature. Applicants are therefore encouraged to submit final mock-ups electronically rather than in hard copy. These may be provided in PDF format via normal e-mail or Eudralink. Password protection or other forms of security cannot be applied to the electronic documents submitted.

It is anticipated that this system will simplify the process for both the applicant and the IMB and improve our efficiency in processing and accessing product literature.

REFORMATTED SPCS FOR PHARMACEUTICAL VETERINARY MEDICINAL PRODUCTS

Since November 2005 most issued SPCs have been re-formatted in line with Directive 2001/82/EC as amended by Directive 2004/28/EC. This re-formatted SPC includes a qualitative list of all excipients present in the product formulation. This information is being taken directly from section 4 of the Product Specific Details of the approved licence document, although the quantities of excipients in the formulation are not included in the SPC.

The remaining sections of the SPC are re-formatted in line with the updated Directive but do not include any information additional to that currently present in the SPC.

To date the IMB has, as a courtesy, forwarded a copy of the reformatted SPC to the applicant for comment prior to issue and publication on the IMB website. In order to streamline procedures, as of from 1 January 2007, this practice will be discontinued and the reformatted SPC will be issued directly following completion of the relevant variation/renewal. In line with our current practices the SPCs present on the IMB website will be updated on a regular basis as amendments to them are issued.

THE ALIGNMENT OF THE SPCS FOR IMMUNOLOGICAL 'REVIEW' PRODUCTS BETWEEN THE UK AND IRELAND

In June 2006, the IMB raised with the Veterinary Medicines Directorate (VMD), the issue of the potential loss of 'review' veterinary immunological medicinal products (IVMPs) to the Irish market due to the requirement for Irish and British specific packaging for IVMPs available in both countries. As a result of these discussions, the IMB and VMD met on the 5th September to discuss ways in which product loss could be prevented. Harmonisation of the Summary of Product Characteristics (SPCs) between the UK and Ireland represents the best means of securing products to the Irish market. However, the industry has suggested significant modifications to the existing harmonisation procedure to make it attractive to the immunological SPCs. Accordingly, the IMB and VMD have modified the existing harmonisation procedure for 'review' immunologicals. This revised harmonisation procedure is referred to as the 'Alignment procedure' to help distinguish this new IVMP specific procedure from the existing harmonisation procedure. A copy of the minutes of this meeting plus action points/decisions and the revised procedural document have been forwarded to all meeting participants. These documents are also available on the IMB website. For further details on the alignment procedure please contact Dr. Una Moore, Senior Immunological Assessor on 00 353 1 6343319 or via e-mail at una.moore@imb.ie.

PROCEDURE FOR JOINT IMB/VMD ASSESSMENT OF PACKAGING FOR PRODUCTS AUTHORISED THROUGH THE MUTUAL RECOGNITION OR DECENTRALISED PROCEDURES.

As part of the discussions on the 'alignment' procedure, the issue of joint Irish and UK packaging for products licensed through the mutual recognition (MR) and decentralised procedures (DCP) was raised. Industry stated that a more coordinated approach from the IMB and VMD with respect to approval of mock-ups would help them reduce the time taken for new IVMPs to be introduced to the Irish market. It was indicated that as the current procedure and timelines used by the IMB and VMD differ, in some cases, this prohibits the use of joint UK/ Irish packaging. In some instances, due to financial constraints, the resulting requirement for Irish specific packaging may result in products never reaching the Irish market. The IMB and VMD responded to this issue immediately and where possible, are currently jointly assessing packaging for new IVMPs going through either the MRP or DCP. A procedural document is currently in development and should be released to industry in the New Year for comment. This procedure was initially developed for IVMPs, however, it is also proposed to use this procedure, for a trial period, for the joint assessment of packaging for new pharmaceutical products. A copy of the procedural document will be placed on the IMB website when completed. For further details on the joint packaging assessment procedure please contact Ms. Susan Reid, Immunological Assessor on 00 353 1 6343319 or via e-mail at susan.reid@imb.ie.

COMPLIANCE

GOOD MANUFACTURING AND MARKET COMPLIANCE INFORMATION DAY

9 November 2006

The Good Manufacturing Practice (GMP) and Market Compliance Information Day was hosted by the Compliance Department on the 9 November 2006 in the Crowne Plaza Hotel in Santry. The main purposes of the seminar were to provide an update on the latest developments in legislation and guidelines relating to the manufacture of medicinal products and to outline the IMB's approach to their implementation and evaluation.

The programme opened with an address by the Chief Executive of the Irish Medicines Board, Mr Pat O'Mahony, who welcomed the 222 delegates and provided an overview of the objectives for the seminar.

A number of presentations were given by IMB GMP and GDP Inspectors and Market Compliance section on the following topics:

- New legislation – what the changes mean for manufacturers
- Inspection of laboratories and ongoing stability testing
- Storage of medicinal products
- Training
- Annex 19 – Reference and retention samples
- Annex 1 update
- Engineering Inspections
- Market Compliance Section and regulatory compliance inspections
- Product quality reviews / deviations / QP discretion

The presentations were followed by an active question and answer session on a wide range of GMP related issues. The questions were answered by the panel which included the IMB GMP and GDP Inspectors, IMB Enforcement Officers, Market Compliance Officers and a representative from the IMB Human Medicines Department.

To view the presentations visit the IMB's website www.imb.ie

CONTROLLED DRUGS INFORMATION SEMINAR

8 November 2006

An information seminar covering various regulatory aspects relating to controlled drugs was hosted by the Compliance Department on the 8 November 2006 in the Crowne Plaza Hotel in Santry. The purpose of the seminar was to provide an update on developments in transferring the controlled drug functions to the IMB, given that this process will be formally commenced in early 2007.

The seminar attracted interest from a wide range of stakeholders, and the IMB was pleased with the large attendance, which included manufacturers, wholesalers, industry representatives, regulatory consultants, various public bodies and other interested parties.

The programme commenced with an opening address by the Chief Executive of the IMB, Mr Pat O'Mahony, who welcomed the delegates, and provided an overview of the objectives for the seminar.

In transferring the controlled drug functions, the IMB has worked in partnership with various stakeholder groups including the Department of Health and Children and An Garda Siochána. The seminar included presentations given by both of these parties outlining their role in this process. The first was given by Ms Mary O'Reilly from the Social Inclusion Unit of Department of Health and Children, and provided an update on the legislative amendments that will enable the transfer of the controlled drug functions to the IMB, including the IMB Miscellaneous Provisions Act 2006 and other regulations currently under development. The second presentation was given by Inspector Gerard Carroll from the Garda National Crime

Prevention Office, and provided an overview of crime prevention measures.

A number of presentations were given by IMB Controlled Drugs Inspectors and staff on the following topics:

- Overview of controlled drug inspection Programme 2005
- Precursor chemicals
- Statistical reporting for controlled drugs
- Exportation of waste for incineration
- IT developments – the extranet applications systems

The seminar concluded with an interactive question and answer session, which covered a wide range of regulatory and compliance requirements for controlled drugs

Copies of all of the presentations given at the seminar are currently available on the IMB's website at **www.imb.ie**.

ONLINE LICENCE APPLICATION FOR CONTROLLED DRUGS

The commencement of the various provisions relating to controlled drugs set out under the IMB (Miscellaneous Provisions) Act 2006 is scheduled to take place in early 2007. From this time the IMB will formally undertake the role of issuing licences and other authorities for controlled drugs and substances.

The IMB intends to launch this new role primarily on the basis of online licence application and processing. This will provide significant enhancements in the efficiency of these processes to the various stakeholder groups.

Pharmatrust is the system developed by the IMB for management of online licence application. The system facilitates application for primary licences, import and export licences and estimate management. Appropriate measures have been taken to secure both access and the application processes.

Pharmatrust is now available for access to all licence holders. In preparation for undertaking the role of issuing controlled drug licences the IMB would like to invite all current controlled drug licence holders to register their companies to access *Pharmatrust*. Registration can be completed online under the Compliance section of the website at **www.imb.ie**

Once the licence holder has requested to access the system, the IMB will put into place the necessary security features.

It is advisable that registration is completed as soon as possible as licence holders will also need to familiarise themselves with the use of the system. The IMB will assist with training needs that may arise in the roll-out of the use of the application.

Further information on the registration process can be obtained by e-mailing **pharmatrust@imb.ie** or contacting the Licensing Section of the Compliance Department.

REQUIREMENTS TO AUDIT API SITES

Since 30 October 2005, manufacturers of medicinal products for human and veterinary use are required to use only active substances which have been manufactured in accordance with GMP (Part II of the EC Guide to GMP). A declaration to this effect is required to be included in applications for marketing authorisations and in relevant variations. The overall responsibility for this lies with the QP certifying the finished product batch before release to market or before export.

There is no legal requirement across the EU for licensing of active substance manufacturers but the competent authorities do carry out inspections of active substance manufacturers in accordance with the EU Compilation of Procedures. Where the outcome of such an inspection determines that the site operates in accordance with the principles and guidelines of GMP for active substances (Part II of the EC guide to GMP) then the competent authority may issue a GMP certificate which may be restricted to certain operations or manufacture of particular substances at the site.

While possession of a current GMP Certificate by the active substance manufacturer may be taken into account in the overall assessment of a site, the manufacturer of the medicinal product must itself verify by audit that it is satisfied with the site, its quality system and the application of this system in relation to the active substance supplied from the site. An audit of an active substance manufacturer may be carried out by a third party. However, any such arrangement with a party from outside the licensed finished product manufacturing site should be described in a technical agreement. This agreement should address the matters of competence and independence of the party performing the audit on behalf of the manufacturer. The position as stated above is in line with statements which have been made by the EMEA in relation to the auditing of active substance manufacturers.

For further information, see the EMEA website at **www.emea.eu.int**

GMP ANNEX 3 'MANUFACTURE OF RADIOPHARMACEUTICALS': DRAFT REVISION FOR PUBLIC CONSULTATION.

The annex has been revised in the light of new GMP requirements for actives substances used as starting materials (GMP Part II). It includes application of Part II of the EU GMP Guide to the manufacture of radiopharmaceuticals. Public comments should be sent to **entr-gmp@ec.europa.eu** and **david.cockburn@emea.europa.eu** by 30 March 2007

Further information is available at **http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/new.htm**

Human New Product Authorisations Issued (August – November 2006)

PA Number	Product Name
PA0068/015/001	LOCABIOTAL PRESSURISED
PA0074/061/001	Risperidone
PA0108/025/005	Creon
PA0678/106/001	Beechams Cold & Flu Hot Lemon
PA0678/106/002	Beechams Cold & Flu Hot Blackcurrant
PA0678/106/003	Beechams Cold & Flu Hot Lemon with Honey
PA0678/107/001	Panadil
PA0688/006/001	Risperidone
PA0688/006/002	Risperidone
PA0688/006/003	Risperidone
PA0688/006/004	Risperidone
PA0688/006/005	Risperidone
PA0688/006/006	Risperidone
PA0688/006/007	Risperidone
PA0754/009/001	Cytarabine Ebewe
PA0754/009/002	Cytarabine Ebewe
PA0754/009/003	Cytarabine Ebewe
PA0899/017/002	BECLO-RHINO ALLERGY
PA1017/004/001	CIFOX
PA1017/004/002	CIFOX
PA1017/004/003	CIFOX
PA1063/024/001	Napamide PR
PA1077/093/009	Augmentin ES
PA1080/019/001	Losartan
PA1080/019/002	Losartan
PA1080/019/003	Losartan
PA1080/019/004	Losartan
PA1080/019/005	Losartan
PA1140/003/003	Midalozam
PA1140/003/004	Midalozam
PPA0465/073/003	Flixotide Nebules
PPA0465/073/004	Flixotide Nebules
PPA0465/090/003	Lescol XL
PPA0465/177/001	Locoid
PPA0465/178/001	Pharmaton
PPA0465/180/001	Diovan
PPA0465/181/001	Solpadeine Soluble
PPA0465/182/001	Xanax
PPA0465/182/002	Xanax
PPA0465/182/003	Xanax
PPA0465/183/001	Ursofalk
PPA0465/184/001	Non Drowsy Sinutab
PPA0465/185/001	Difene
PPA0465/187/001	Nicorette
PPA0465/187/002	Nicorette
PPA0465/187/003	Nicorette Mint
PPA0465/187/004	Nicorette Mint

PA Number	Product Name
PPA0465/189/001	Zydol
PPA0465/192/001	Solian
PPA1151/003/003	Zoton FasTab
PPA1151/003/005	Zoton FasTab
PPA1151/004/003	Lipostat
PPA1151/007/001	Losec MUPS
PPA1151/008/001	Zimovane
PPA1151/009/001	Zantac
PPA1151/010/001	Istin
PPA1151/010/002	Istin
PPA1151/011/001	Lipitor
PPA1151/011/002	Lipitor
PPA1151/012/001	Nu-Seals
PPA1151/015/001	Fosamax Once Weekly
PPA1151/016/001	Protium
PPA1151/016/002	Protium
PPA1151/017/001	Nexium
PPA1151/017/002	Nexium
PPA1151/018/001	Spiriva
PPA1328/001/001	Protium
PPA1328/003/001	Mobic
PPA1328/004/001	Zinnat
PPA1328/005/001	Zomig
PPA1328/006/001	Livial
PPA1328/007/001	Tegretol
PPA1328/008/001	Zydol
PPA1328/009/001	Imdur
PPA1328/010/002	Diamicron MR
PPA1328/011/001	Nasonex
PPA1328/013/001	Cardicor
PPA1328/013/002	Cardicor
PPA1328/013/003	Cardicor
PPA1328/013/004	Cardicor
PPA1328/013/005	Cardicor
PPA1328/014/001	Klacid LA
PPA1328/017/001	Actonel
PPA1328/018/001	Atacand
PPA1328/018/002	Atacand
PPA1328/018/003	ATACAND
PPA1328/019/001	Beconase Aqueous
PPA1328/020/001	Betaloc
PPA1328/021/001	Cipramil
PPA1328/021/002	Cipramil
PPA1328/022/001	Coversyl
PPA1328/022/002	Coversyl
PPA1328/023/001	Dovonex
PPA1328/023/002	DOVONEX
PPA1328/024/001	Fucidin

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Human New Product Authorisations Issued (cont) (August – November 2006)

PA Number	Product Name
PPA1328/025/001	Ikorel
PPA1328/026/001	Lipostat
PPA1328/027/001	Movicol
PPA1328/028/001	Neurontin
PPA1328/028/002	NEURONTIN
PPA1328/029/001	Nexium
PPA1328/030/001	Nizoral Shampoo
PPA1328/031/001	Phyllocontin Continus
PPA1328/033/001	Scheriproct
PPA1328/034/001	Serc
PPA1328/035/001	SERETIDE DISKUS
PPA1328/036/001	Serevent Inhaler
PPA1328/037/001	Sinemet Plus
PPA1328/038/001	Symbicort Turbohaler 100/6 Inhalation Powder
PPA1328/039/001	Topamax
PPA1328/039/002	Topamax
PPA1328/039/003	Topamax
PPA1328/040/001	Salamol CFC-Free Inhaler
PPA1328/041/001	Ventolin Evohaler
PPA1328/041/002	Ventolin
PPA1328/042/001	Zanidip
PPA1328/043/001	Zimovane
PPA1328/044/001	Accolate
PPA1328/045/001	Accupro
PPA1328/046/001	Activelle
PPA1328/047/001	Adalat LA
PPA1328/047/002	Adalat LA
PPA1328/047/003	Adalat LA
PPA1328/047/004	Adalat Retard
PPA1328/048/001	Amaryl
PPA1328/048/002	Amaryl
PPA1328/052/001	Atacand Plus
PPA1328/053/001	Betaloc
PPA1328/056/001	CAPOTEN
PPA1328/056/002	CAPOTEN
PPA1328/056/003	CAPOTEN
PPA1328/057/001	CELEBREX
PPA1328/059/001	Crestor
PPA1328/060/001	DAONIL
PPA1328/061/001	DETRUSITOL
PPA1328/061/002	DETRUSITOL
PPA1328/062/001	SOLARAZE

Human New Product Authorisations (Mutual Recognition) (August – November 2006)

PA Number	Product Name
PA0021/085/001	Gamunex 10%, 100mg/ml solution for Infusion
PA0030/044/003	Lamisil Once
PA0030/056/001	Lamisil AT
PA0050/053/005	Roaccutane
PA0126/162/001	Cantaxel
PA0126/163/001	Ramitace
PA0126/163/002	Ramitace
PA0126/163/003	Ramitace
PA0148/059/002	Celluvisc
PA0281/125/001	Ketopine
PA0298/015/001	Amlodipine
PA0298/015/002	Amlodipine
PA0372/007/001	Cefuroxime Sodium
PA0372/007/002	Cefuroxime Sodium
PA0372/007/003	Cefuroxime Sodium
PA0408/063/001	Clarithromycin
PA0408/063/002	Clarithromycin
PA0437/055/001	Vinorelbine
PA0437/056/001	Oxaliplatin Mayne
PA0577/079/001	Xatger
PA0577/079/002	Xatger
PA0577/083/001	Emizof
PA0577/083/002	Emizof
PA0577/083/003	Emizof
PA0577/086/001	Fostepor
PA0577/086/002	Fostepor Once Weekly
PA0585/023/001	Imitag
PA0585/023/002	Imitag
PA0711/101/001	Cefuroxime
PA0711/101/002	Cefuroxime
PA0711/101/003	Cefuroxime
PA0711/106/001	Rispone
PA0711/111/001	Topit
PA0711/111/002	Topit
PA0711/111/003	Topit
PA0711/111/004	Topit
PA0736/020/001	Venfundin
PA0736/020/002	Venfundin
PA0736/020/003	Venfundin
PA0748/025/012	Eprex
PA0749/011/001	Co-Amoxiclav
PA0749/011/002	Co-Amoxiclav
PA0749/012/001	Cefotaxime

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Human New Product Authorisations (Mutual Recognition) (cont.) (August – November 2006)

PA Number	Product Name
PA0749/012/002	Cefotaxime
PA0749/012/003	Cefotaxime
PA0749/018/001	Modafinil Teva
PA0749/020/001	Lamotrigine Teva
PA0749/020/002	Lamotrigine Teva
PA0749/020/003	Lamotrigine Teva
PA0749/020/004	Lamotrigine Teva
PA0891/003/003	Xyzal
PA0941/002/001	Inflexal V
PA0966/003/002	By-Madol SR
PA0966/003/003	By-Madol SR
PA0966/003/004	By-Madol SR
PA0966/003/005	By-Madol SR
PA0966/016/001	Bymot Dispersible Tablets
PA0966/016/002	Bymot Dispersible Tablets
PA0966/016/003	Bymot Dispersible Tablets
PA0966/016/004	Bymot Dispersible Tablets
PA0966/016/005	Bymot Dispersible Tablets
PA0966/016/006	Bymot Dispersible Tablets
PA1025/002/001	Protamine sulphate LEO Pharma anti-heparin
PA1049/004/001	Rectogesic
PA1049/005/001	Tostran

PA Number	Product Name
PA1077/047/005	Serevent Evohaler
PA1077/113/001	Salmeterol
PA1135/003/001	Beneprav 10 mg Tablets
PA1135/003/002	Beneprav 20 mg Tablets
PA1135/003/003	Beneprav 40 mg Tablets
PA1135/004/001	Pravalo 10 mg Tablets
PA1135/004/002	Pravalo 20 mg Tablets
PA1135/004/003	Pravalo 40 mg Tablets
PA1245/001/001	Lotemax
PA1255/001/001	Alutard Avanz
PA1255/001/002	Alutard Avanz
PA1255/001/003	Alutard Avanz
PA1255/002/001	EpiPen Junior
PA1255/002/002	EpiPen
PA1255/004/001	Grazax
PA1286/006/002	Cosopt Preservative-Free
PA1302/001/001	Matrifen
PA1302/001/002	Matrifen
PA1302/001/003	Matrifen
PA1302/001/004	Matrifen
PA1302/001/005	Matrifen
PA1325/001/001	Erdotin

Human New Product Authorisations Withdrawn (August – November 2006)

PA Number	Product Name
PA0002/007/001	Mycostatin
PA0002/057/011	VIDEX
PA0002/057/012	VIDEX
PA0002/057/013	VIDEX
PA0002/057/014	VIDEX
PA0002/057/015	VIDEX
PA0002/078/001	Pravagettes
PA0006/003/001	Cidomycin Intrathecal
PA0006/033/001	IBUPROFEN
PA0006/033/003	IBUPROFEN
PA0006/038/001	ALLOPURINOL
PA0006/038/002	ALLOPURINOL
PA0007/004/003	TRANXENE
PA0012/081/001	Curandron
PA0018/004/001	Intal
PA0021/073/002	REDOXON DOUBLE ACTION
PA0030/024/001	Mu-Cron
PA0030/037/001	BRADOSOL PLUS
PA0035/073/001	ZOCOR
PA0037/045/001	CALCIUM LEUCOVORIN
PA0038/083/001	Froben SR

PA Number	Product Name
PA0038/083/005	Froben
PA0038/083/006	Froben
PA0040/003/005	FLAGYL
PA0040/021/003	Neulactil
PA0043/028/001	BALNEUM
PA0043/030/001	BALNEUM PLUS
PA0043/032/001	Unguentum M
PA0043/033/001	Aknemycin
PA0044/009/004	CEPOREX
PA0044/009/005	CEPOREX
PA0044/023/002	BETNOVATE N
PA0046/062/001	Bocatriol
PA0046/062/002	Bocatriol
PA0046/063/001	Heparin Sodium
PA0046/063/002	Heparin Sodium
PA0057/009/001	Hiprex
PA0057/069/001	Epaq
PA0060/006/002	Tagamet
PA0060/006/005	Tagamet
PA0060/046/002	Algitec
PA0072/006/001	Delsym

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Human New Product Authorisations Withdrawn (cont.) (August – November 2006)

PA Number	Product Name
PA0077/127/001	Skelid
PA0102/025/001	Norgalax
PA0126/082/003	DICLOMEL SR
PA0126/111/001	Gliclazide
PA0172/014/001	Freezone
PA0172/020/001	Junior Paracetamol
PA0172/031/001	GEVRAL INSTANT PROTEIN ORANGE FLAVOUR
PA0172/031/002	GEVRAL INSTANT PROTEIN STRAW BERRY FLAVOUR
PA0172/031/003	GEVRAL INSTANT PROTEIN CUSTARD FLAVOUR
PA0172/031/004	GEVRAL INSTANT PROTEIN CHOCO LATE FLAVOUR
PA0271/010/002	Tylex
PA0282/086/001	Hay-Rite 10mg Tablets
PA0282/087/001	Flucazol
PA0282/087/002	Flucazol
PA0282/087/003	Flucazol
PA0329/001/002	Eludril
PA0329/008/001	Primalan
PA0436/022/002	Cromogen Inhaler
PA0436/022/003	Cromogen Easi-Breathe Inhaler
PA0437/003/003	Dopamine 160 mg/ml Sterile Concentrate
PA0441/026/001	Vicks Coldcare
PA0476/005/002	Atenolol
PA0476/005/003	Atenolol
PA0522/005/001	Sure-Lax Senna
PA0540/016/003	Suprax
PA0540/019/003	MERBENTYL
PA0540/036/001	Cidomycin Adult
PA0540/036/002	Cidomycin Adult
PA0540/049/001	IDARAC
PA0540/075/001	Surgam SA
PA0565/003/001	Nifedipine
PA0565/003/002	Nifedipine
PA0610/015/001	ELECTROLADE BANANA
PA0610/015/002	ELECTROLADE MELON
PA0610/015/003	Electrolade Blackcurrant
PA0610/015/004	Electrolade Orange
PA0678/042/001	ACTIPROFEN
PA0678/071/004	NiQuitin
PA0678/071/005	NiQuitin
PA0678/071/006	NiQuitin
PA0678/085/001	SETLERS WIND-EZE
PA0688/001/001	Paracetamol
PA0711/034/001	Solol
PA0711/034/002	Solol
PA0711/048/001	Citalopram
PA0735/007/012	Imagopaque
PA0735/007/014	Imagopaque
PA0735/007/015	Imagopaque
PA0771/004/003	RECOFOL
PA0775/003/001	FAVINT
PA0800/002/001	HAEMATE P
PA0819/001/001	FLUOXETINE
PA0862/001/001	SMART DOSE
PA0894/002/001	R.B.C.
PA0936/031/001	SOLEXA
PA0936/031/002	SOLEXA
PA0970/018/005	Seroquel 4-day starter pack
PA0970/019/001	TENORMIN INJECTION
PA0970/035/001	BRICANYL EXPECTORANT
PA0970/036/001	BRICANYL INHALER
PA0970/036/006	BRICANYL
PA0970/037/001	Bricanyl SA
PA0979/016/001	Senokot 7.5 mg/5ml Oral Solution
PA0979/019/001	Disprin Extra
PA0987/001/001	Solvazinc
PA0997/002/001	Hypaque 25%
PA0997/002/002	Hypaque
PA0997/002/003	Hypaque
PA0997/003/001	Hypaque 45%
PA1022/009/001	NIOPAM 200
PA1022/010/001	NIOPAM 300
PA1022/012/001	NIOPAM 370
PA1077/096/004	Penbritin
PA1077/096/005	PENBRITIN
PA1175/002/009	BETADINE VAGINAL
PA1175/002/016	Betadine Antiseptic Swab
PA1175/002/017	Betadine Swabsticks
PA1175/002/018	Betadine Mistette
PA1175/004/001	EPADERM
PA1175/013/001	Ster-Zac

Veterinary New Product Authorisations Issued (August – November 2006)

VPA Number	Product Name
10799/002/001	Somulose Solution for Injection
10859/014/001	Ecomectin 18.7 mg/g Oral paste for Horses
10960/063/001	ECTOFLITS Summer and Winter Sheep Dip, 60% w/w Dip
10960/064/001	Trimectin Injection
10960/065/001	Bovimec Injection for cattle
10960/066/001	Porcimec Injection for Pigs

Veterinary New Authorisations Issued (Mutual Recognition) (August – November 2006)

VPA Number	Product Name
10021/050/001	Bayer Flumethrin Bee Hive Strips 3.6 mg
10796/001/001	Solubenol 100 mg/g Oral Emulsion
10989/052/001	Forthyron 200 microgram Tablets
10989/052/002	Forthyron 400 microgram Tablets
10989/053/001	Domidine 10 Mg/Ml. Solution for Injection
10996/202/001	Zitac vet 50mg tablets for dogs
10996/202/002	Zitac vet 100mg tablets for dogs
10996/202/003	Zitac vet 200mg tablets for dogs

Veterinary Product Authorisations Withdrawn (August – November 2006)

VPA Number	Product Name
10016/039/001	Kaogel V
10019/053/003	Copporal
10019/056/001	Liquid Lectade
10021/015/001	Rompun 2% Solution
10021/028/001H	Bayvarol Strips
10277/017/001	Cepramycin Milking Cow
10484/005/001	Con-Plas
10484/006/001	Con-Orf Cutaneous Spray Solution
10484/008/001	Conamycin-CH Cutaneous Spray Solution
10484/013/001	Breatheze
10830/005/001	Flukinex 3
10835/031/001	Program Oral for Cats
10857/014/001	Ketofen 1% Injection (20 ml)
10881/014/001	Bob Martin Flea & Tick Collar for Dogs
10934/001/001	Sarafin 100% w/w Premix for Med.Feedstuffs
10956/003/001	B V P Calcium 20 Plus
10966/014/001	Keelogane Pour-on
10966/022/001	Peroxyderm
10983/025/001	Electydral
10988/041/001	Lactolyte
10989/019/001	Euthaject
10995/016/001	Vetrimoxin
10996/039/001	Dystosel
10996/164/001	Mectacur

Veterinary Immunological New Authorisations Issued (Mutual Recognition) (August – November 2006)

VPA Number	Product Name
10019/105/001	Rispoval RS+Pi3 Intranasal
10996/200/001	Bovilis IBR Marker inac

Veterinary Immunological Review Authorisations Issued (August – November 2006)

VPA Number	Product Name
10861/062/001	Poulvac MD Vac CA
10996/135/001	Nobilis IB H120

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