EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

News bulletin for small and medium-sized enterprises

ISSUE 12 JUNE 2010

This news bulletin is published four times a year by the SME Office of the European Medicines Agency.

The news bulletin aims to bring to the attention of SMEs, and their stakeholders, documents and activities related to the European regulatory environment.

IN THIS ISSUE:

Veterinary medicines

Pharmaceutical development guidance

A reflection paper on controls of the active substance in the finished product for immunological veterinary medicinal products was adopted on 18 March 2010 (EMA/CVMP/IWP/582970/2009). It discusses the different methods currently used, the difficulties associated with the validation of these tests, the problems arising from the use of *in vivo* tests and the possibility of an alternative *in vitro* approach for the batch testing.

A guideline on data requirements to support in-use stability claims for veterinary vaccines was adopted on 18 March 2010 (EMA/CVMP/IWP/250147/2008). It provides a framework which will enable applicants to maintain a consistent approach when generating data to support an appropriate in-use shelf-life of a veterinary vaccine. It will come into effect on 1 October 2010.

A VICH guidance 'GL45: Bracketing and matrixing designs for stability testing of new veterinary drug substances and medicinal products' was adopted on 28 May 2010 (EMA/CVMP/VICH/581467/2007). It provides guidance on such designs and outlines situations where bracketing or matrixing can be applied. It will come into effect in April 2011.

A VICH guidance 'GL18: Residual solvents in new veterinary medicinal products, active substances and excipients' was adopted on 28 May 2010 (EMA/CVMP/VICH/502/1999-Rev.1). It recommends acceptable amounts for residual solvents in pharmaceuticals for the safety of the target animal as well as for the safety of residues in products derived from treated food producing animals. It recommends the use of less toxic solvents and describes levels considered to be toxicologically acceptable for some residual solvents. It is released for consultation until 31 October 2010.

Safety and efficacy guidance

A guideline on data requirements for multi-strain dossiers for inactivated vaccines against Avian Influenza, Blue Tongue and Foot and Mouth Disease was adopted on 18 March 2010 (EMA/CVMP/IWP/105506/2007). Vaccines against these diseases represent a special case for vaccines licenses in terms of rapid and frequent changes in the strains included in the vaccines. The advantage of the multi-strain dossier approach is to allow only one dossier to be submitted and maintained which can cover a wide range of vaccine strains. The guidance details the analytical, safety and efficacy requirements of these types of dossiers. Further information is available under EMA/43283/2010. It will come into effect on 1 July 2010.

Veterinary medicines

A guideline on user safety for pharmaceutical veterinary medicinal products was adopted on 18 March 2010 (EMA/CVMP/543/03-Rev.1). Pharmaceutical legislation requires that applications for veterinary medicinal products must provide safety documentation relating to the potential risks which may result from the exposure of human beings to the veterinary medicinal product, for example during its administration to the animal. The document provides guidance and advice on user safety and conducting user safety risk assessments. It replaces the guideline that came into effect on 13 July 2005 (EMEA/CVMP/543/03-FINAL). It will come into effect on 1 October 2010.

A reflection paper on the demonstration of a possible impact of maternally derived antibodies on vaccine efficacy in young animals was adopted on 18 March 2010 (EMA/CVMP/IWP/439467/2007). Veterinary pharmaceutical legislation requires that the influence of passively acquired and maternally derived antibodies on the efficacy of a vaccine is adequately evaluated. If vaccination is recommended in animals at an age at which maternally acquired immunity may still be present and interfere with active immunity development, studies to determine whether such interference occurs should be performed. The document aims to provide guidance on how to demonstrate to which extent maternally derived antibodies may have an impact on the efficacy of vaccines when administered to animals at an age at which maternally acquired immunity is still present.

A guideline on data requirements for immunological veterinary medicinal products intended for minor use or minor species came into effect on 1 May 2010 (EMA/CVMP/IWP/123243/2006-Rev.2). As part of a series of efforts to support the development of such products, a guideline has been developed to define acceptable data requirements for the demonstration of quality, safety and efficacy for immunological veterinary medicinal products intended for minor uses. A non-exhaustive list of minor uses/limited markets of immunological veterinary medicinal products is also included in the guidance.

Advanced therapies

A draft reflection paper on stem cell-based medicinal products was released on 30 March 2010 (EMA/CAT/571134/2009). Existing guidance on cell-based medicinal products covers the general aspects of all cell-based products including stem cell-based ones. Stem cell-based medicinal products may include terminally differentiated cells derived from stem-cells, from pluripotent stem cells or even from a mixture of cells with varying differentiation profile. The document is also relevant to all medicinal products using stem cells as starting material. It has been developed to communicate the current status of discussions and to invite comments in the area of stem cell based medicinal product development, where scientific knowledge is fast evolving and regulatory experience is limited. It is released for consultation until 30 June 2010.

Information on products classified as advanced therapy (gene therapy, cell therapy and tissue engineering products) medicinal products by the Committee on Advanced Therapies has been updated (Link). SMEs developing such products are advised to refer to the information published and seek classification of their products if needed. Further information can be requested from the SME Office.

A reflection paper on in-vitro cultured chondrocyte containing products for cartilage repair of the knee was adopted on 18 May 2010 (EMA/CAT/CPWP/568181/2009). It addresses specific points related to medicinal products containing in vitro cultured autologous chondrocytes intended for the repair of cartilage lesions of the knee.

The Committee for Advanced Therapies adopted during its May meeting its first opinion on the certification for an advanced therapy medicinal product (EMA/CAT/328191/2010). The certification is a new procedure introduced to support the development of gene, cell and tissue-engineering products by small and medium-sized enterprises. Its aims at facilitating the dialogue with the regulatory authorities early in drug development with a view to certifying experimental data's compliance with regulatory requirements.

Preclinical and clinical guidance

A guideline on repeated dose toxicity of active substances intended for human use was released on 29 March 2010 (CPMP/SWP/1042/99 Rev 1). It includes guidance on the choice of animal species, the size of groups and animal husbandry, selection of the dose regimen, duration and route of administration. Guidance is also included on the parameters to be monitored during the in-life phase and special studies which may be needed in case of special activity of a certain medicinal product. It will come into effect on 1 September 2010.

A draft guideline on investigation of drug interactions was released on 30 April 2010 (CPMP/EWP/560/95/Rev. 1 – Corr.*). It provides recommendations on how to evaluate the potential for drug-food and drug-drug interactions for medicinal products and herbal medicinal products and how to translate results of these evaluations into treatment recommendations. It is released for consultation until 31 October 2010.

A draft guideline on the use of pharmacogenetic methodologies in the pharmacokinetic evaluation of medicinal products was released on 6 May 2010 (EMA/CHMP/37646/2009). It addresses the influence of pharmacogenetics on drug pharmacokinetics and considerations for the design and conduct of investigations during drug development. Specific guidance is also given on studies recommended at different phases of drug development to ensure that adequate efficacy and safety data in pharmacogenetic subpopulations that have variable systemic exposure of active substances are generated. It is released for consultation until 31 October 2010.

Good Clinical Practice (GCP) guidance

A draft *'Reflection paper on ethical and GCP aspects of clinical trials of medicinal products for human use conducted in third countries and submitted in marketing authorisation applications to the European Medicines Agency'* was released on 28 May 2010 (EMA/712397/2009). Revisions to the pharmaceutical legislation which came into force in 2004 emphasize the ethical standards required for clinical trials conducted outside the European Economic Area (EEA) and included in European Marketing Authorisation Applications for medicinal products for human use. The number of patients recruited in countries outside of the EEA is substantial (http://www.ema.europa.eu/Inspections/GCPgeneral.html). Some clinical trials are conducted across several regions, including Europe, whereas many others are conducted solely outside of the EEA. The document highlights the need for cooperation between Regulatory Authorities involved in the supervision of clinical trials and the need to extend and link the networks to support these activities. It is released for consultation until 30 September 2010.

SME registration, application fees and orphan medicines

Documentation requirements for seeking and renewing SME status have been simplified by the SME Office. Companies can now submit an electronic copy of the declaration form and supporting documentation to the SME Office via e-mail and send the required signed original of the declaration form via post. For all of the other supporting documentation, an electronic copy via e-mail will be sufficient. Further details are available here.

Information on new fees applicable as of 1 April 2010 were published (EMA/MB/818152/2009; EMA/818151/2009). Further information is available under Link.

A note for guidance on the format and content of the annual report for orphan medicinal products was published on 21 April 2010 (EMA/COMP/189/2001 Rev. 2). Regulation (EC) No 141/2000 on Orphan Medicinal Products requires sponsors to submit annual reports to the European Medicines Agency on the state of development of their designated medicinal products. The guidance is intended to provide advice on the preparation of these reports.

News from the European Commission

A public consultation on the *'Notice to Applicants – Veterinary Medicinal Products - Volume 6B'* was launched by the European Commission on 3 March 2010 (Link). The document's content and format have been updated in accordance with the new Annex I published in Directive 2009/9/EC. Additionally, certain terms and legal references have been adapted. The deadline for providing comments to the public consultation is 15 May 2010.

A public consultation on the legal framework for veterinary medicinal products was launched by the European Commission on 13 April 2010 (Link). Its objective is to receive stakeholders' views on the strengths and weaknesses of the current framework and how it could be improved. SMEs are particularly welcome to provide comments to the public consultation which is open until 15 July 2010.

A revised *'Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial'* was published on 3 March 2010 (2010/C 82/01). The following related documents were also released:

- A revised 'Questions & Answers' document applying to clinical trials
- Annex VI to Guidance for the conduct of GCP inspections - Record keeping and archiving of documents.
- Substantial Amendment Notification Form
- Declaration of the End of Trial Form

The guidance was revised following the introduction of paediatrics and advanced therapies legislation and also include the following changes:

- Definition of the 'Member State concerned' (i.e. Member State where the clinical trial is to be performed)
- Timelines for clinical trial authorisation ('as rapidly as possible and may not exceed 60 calendar days') and timelines for handling of invalid applications
- Notion of 'amendment' and 'substantial' in relation to assessment by the national competent authorities of the Member State concerned (not the Ethics Committee) and notification requirements of amendments
- Deletion of tables detailing the national requirements that were included in previous versions

All revised documents are now available in Volume 10 of Eudralex-Volume 10 Clinical trials guidelines on the European Commission's website (Link).

A document summarising the principles and procedures that are applied to requests for duplicate marketing authorisation applications under Article 82(1) of Regulation (EC) No 726/2004 was published by the European Commission (Link) on 7 April 2010.

A public consultation on Annex 2 of the good manufacturing practices (GMP) laying down the guidelines for the manufacture of biological medicinal substances and products for human use was launched on 19 April 2010 (Link). Annex 2 is proposed to be revised as a result of the restructuring of the GMP guide, the increased breadth of biological products to include several new product types such as transgenic derived products and advanced therapy medicinal products. The deadline for providing comments to the public consultation is until 15 July 2010.

Meetings

Reports and presentations from the following meetings were published:

- European Medicines Agency/IFAH-Europe info day – 'Latest developments in scientific review, legislation and marketing authorisation procedures' (Link).
- '10 years of orphan regulation in Europe' conference (Link)
- Workshop on medicines for bees (Link)
- Workshop on in vitro cytokine release assays (Link)
- Workshop on stem cell-based therapies (Link)

The workshop on nanomedicines originally planned on 26-27 April 2010 is now due to be held 2-3 September 2010. Invitation and registration forms are available here.

The presentations of the SME workshop which took place on 28 May 2010 will be available in the following link.

SME companies registered with the Agency

448 companies currently have SME status assigned by the Agency. The list of companies is published on the Agency's website at: http://www.emea.europa.eu/pdfs/SME/registeredcompanies.pdf

Contact the SME Office

The SME Office has been set up within the Agency to address the particular needs of smaller companies. The Office aims to facilitate communication with SMEs through dedicated personnel who will respond to practical or procedural enquiries, monitor applications, and organise workshops and training sessions for SMEs. Any comments on this news bulletin can be forwarded to the SME Office:

E-mail: smeoffice@ema.europa.eu

Direct telephone: +44 (0)20 7418 8575/8463

Fax: +44 (0)20 7523 7040