News bulletin for small and medium-sized enterprises

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

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

Advanced Therapies

On 15-16 January 2009, the European Medicines Agency (EMEA) held the first meeting of the new Committee for Advanced Therapies (CAT). The CAT is a multidisciplinary committee gathering the best available expertise in Europe in the field of advanced therapy medicinal products (Gene, cell and tissue engineering products). It was established in accordance with Regulation (EC) No 1394/2007 on advanced therapy medicinal products. Further information is available in Press release, Questions and answers.

A guideline on safety and efficacy follow-up/risk management of advanced therapy medicinal products was published on 2 December 2008 (EMEA/149995/2008). It describes specific aspects relating to pharmacovigilance, risk management planning, safety and efficacy follow-up of authorised advanced therapy medicinal products. It applies as of 1 January 2009.

An ICH document on oncolytic viruses was published on 11 December 2008 (EMEA/CHMP/GTWP/607698/2008). It identifies general principles to be applied for the clinical development of oncolytic viruses irrespective of their classification in each ICH region.

A guideline on xenogeneic cell-based medicinal products was released for consultation on 27 February 2009 (EMEA/CHMP/CPWP/83508/2009). It addresses issues such as sourcing and testing of animals, manufacture, quality control, non-clinical and clinical development, surveillance, animal health and welfare in the sourcing of materials. Once finalised it will replace the points to consider document on xenogeneic cell-therapy medicinal products (CPMP/1199/02) and will be annexed to the guideline on cell-based medicinal products (EMEA/CHMP/410869/2006). The

Pharmaceutical Development

A concept paper on the revision of the CHMP guideline on parametric release was released on 5 December 2008 (EMEA/CHMP/QWP/569959/2008). It updates the CHMP note for guidance on parametric release adopted in February 2001 to include the replacement of sterility testing and review its content in light of the new ICH Q8, Q9 and Q10 guidelines.

Annexes to ICH Quality topics were released in December 2008 and will come into effect in June 2009:

- ICH Topic Q8 Annex Pharmaceutical Development (EMEA/CHMP/ICH/518819/2007)

The annex clarifies key concepts from the core guideline and describes the principles of Quality by Design. It is not intended to establish new regulatory requirements but shows how concepts and tools (e.g. design space) outlined in the core Q8 guideline could be put into practice by applicants.

The following Annexes to ICH Quality topics relating to the official pharmacopoeial texts (Ph.Eur, JP, USP) recommend that the following tests can be used interchangeably in the ICH regions:

- ICH Topic Q4B Annex 4A Micrological examination of non-sterile products: micrological enumeration tests (EMEA/CHMP/ICH/308671/2008)
- ICH Topic Q4B Annex 4B Micrological examination of non-sterile products: tests for specified micro-organisms (EMEA/CHMP/ICH/308817/2008)
- ICH Topic Q4B Annex 4C Micrological examination of non-sterile products: acceptance criteria for pharmaceutical preparations and substances for pharmaceutical use (EMEA/CHMP/ICH/308867/2008)
- ICH Topic Q4B Annex 6 Uniformity of dosage units (EMEA/CHMP/ICH/645408/2008)
- ICH Topic Q4B Annex 7 Dissolution test (EMEA/CHMP/ICH/645469/2008)
- ICH Topic Q4B Annex 8 Sterility test (EMEA/CHMP/ICH/645592/2008)

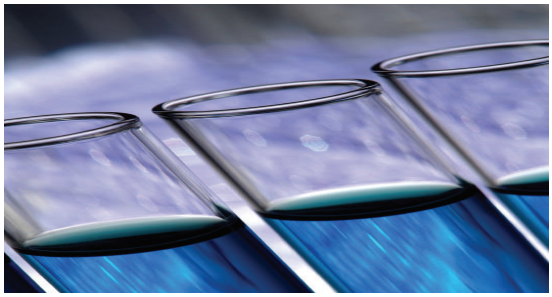
A concept paper on the need for a CHMP guideline on the validation of bioanalytical methods was released for consultation on 20 January 2009 (EMEA/CHMP/EWP/531305/2008). The new guideline to be developed will include general and specific (e.g. actual analysis of study samples) recommendations for the validation of bioanalytical methods.

Annex 14 of the GMP Guide (Manufacture of medicinal products derived from human blood or plasma) was released for consultation on 13 February 2009 (Link). It was revised in the light of Directive 2002/98/EC and its implementing directives setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components. The deadline for comments is 31 July 2009.

A draft note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products was released 27 February 2009 (EMEA/410/01 – Rev. 4). It includes revisions to consider the advancement of science in the area of transmissible encephalopathies and the evolving situation regarding Bovine Spongiform Encepalopathy (BSE) across the world. It is released for consultation until 30 June 2009.

Non-Clinical Development

A draft ICH (International Conference on Harmonization) guideline on the non-clinical evaluation for anticancer pharmaceuticals was released on 19 December 2008 (EMEA/CHMP/ICH/646107/2008). It provides guidance on the design of an appropriate program of non-clinical studies for the development of anticancer pharmaceuticals, and aims at facilitating their development while ensuring the protection of patients from unnecessary adverse effects and avoiding unnecessary use of animals. The deadline for comments is 31 March 2009.



Clinical Development

The EMEA published on 12 February 2009 its strategy in relation to the acceptance in marketing-authorisation applications of clinical trials conducted in third countries. The purpose is to reinforce the EMEA's contribution to ensure that trials carried out in third countries were conducted in accordance with good-clinical-practice and ethical standards (EMEA strategy paper). In this respect a reflection paper on the extrapolation of results from clinical studies conducted outside Europe to the EU-population was also released in 27 February 2009 (EMEA/CHMP/EWP/692702/2008). The paper should be regarded as a complement to the ICH E5 when deciding whether certain clinical trials conducted in a specific area of the world would be relevant to the EU setting or if there are reasons to perform additional clinical trials within the EU.

A European Commission communication including guidance on paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the EudraCT information to be made public by the EMEA was published on 4 February 2009 (Link). One of the aims of the 'Paediatric Regulation' (Regulation (EC) No 1901/2006) is to increase the availability of information on the use of medicinal products in children and to avoid repetition of studies. The document sets out the nature of the information to be entered into EudraCT, the information to be made accessible to the public, the paediatric clinical trial results to be submitted and made public and the responsibilities of the EMEA.

A 'questions and answers' document on pharmacokinetics topics was published on 6 March 2009 (EMEA/618604/2008). It aims to address specific questions in relation to pharmacokinetic evaluations and in particular requirements for bioequivalence studies and their assessment.

Orphan Medicines

A discussion paper including recommendations on the elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation was released on 21 January 2009 (EMEA/COMP/15893/2009). It is based on the experience accumulated over recent years with hundreds of orphan drug designation applications, most of which include a discussion on significant benefit.

A public statement on supplementary fee incentives for designated orphan medicinal products developed by SMEs was announced on 6 February 2009. With effect as of 1 February 2009, the fee reduction policy for designated orphan medicinal products has been revised to reinforce support to micro, small and medium-sized enterprise (SME). Detailed information is available in the published document (EMEA/63200/2009).

A subsidy scheme offering support to SMEs developing orphan medicines has been launched in January 2009 in the Netherlands. The subsidy scheme is an initiative of the Dutch Steering Committee for Orphan Drugs which is an independent organisation set up by the Dutch Minister of Health. Its members are representatives of patients, healthcare professionals, industry organisations, regulators with the mission to encourage the development of orphan drugs. The scheme will offer Dutch pharmaceutical SMEs a subsidy (up to 7200€) for the costs of writing and submitting orphan drug designation applications to the EMEA. Further information is available from the EMEA SME Office.

(e)CTD

A Questions and Answers document on the International Conference on Harmonization (ICH): M 2 - Common Technical Documents for the Registration of Pharmaceuticals for Human Use was released in December 2008 (CPMP/ICH/820/03).

The EMEA announced in December 2008 its plans to mandate the use of the Electronic Common Technical Document (eCTD) format for electronic-only submissions in the centralised procedure as of 1 January 2010. From 1 July 2009 until 1 January 2010, the EMEA will continue to accept non-eCTD electronic-only submissions (eCTD is however, the recommended format). Further information can be found in the following documents:

- EMEA implementation of electronic-only submissions and mandatory eCTD submissions in the centralised procedure: Statement of Intent (EMEA/572459/2008)
- EMEA implementation of electronic-only submissions and mandatory eCTD submissions in the centralised procedure: Statement of Intent relating to Non-eCTD submissions (EMEA/577842/2008)
- EMEA implementation of electronic-only submissions eCTD submission: Practical guidelines relating to Non-eCDT submissions (EMEA/633919/2008v1.0)
- EMEA implementation of electronic-only submissions eCTD submission: Questions and Answers relating to practical and technical aspects of the implementation (EMEA/596881/2007v0.5)

Technical and procedural assistance on eCTD applications produced by SMEs may be offered by the EMEA e.g. technical eCTD validation, testing of eCTD submissions.

Regulatory Guidance

Guidance on the EMEA Scientific Advice procedure and the new biomarker qualification procedure were released in February 2009 as follows:

- EMEA Guidance for companies requesting scientific advice or protocol assistance (EMEA-H-4260-01-Rev. 5)
- Qualification of novel methodologies for drug development: Guidance to applicants (EMEA/CHMP/SAWP/72894/2008)

Updated guidance for the preparation of applications for a paediatric investigation plan and/or waiver was released in December 2008 (EMEA/651100/2008).

A new section of the EMEA website has been created to provide information on the work the EMEA is doing in the area of medicines for older adults (Medicines for the elderly).

New Legislative Proposals

The European Commission released on 10 December 2008 a communication on the future of the pharmaceutical sector and three new legislative proposals to strengthen the current legislation with respect to the following:

- Access to reliable information on medicines by EU citizens
- Strengthening of the EU pharmacovigilance system
- Improvement of legislation relating to counterfeit medicines

Further detailed information is available on the European Commission website (Link).

The European Commission published on 12 December 2008 Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (Link). The regulation is part of a global revision of the legal framework on variations to make the overall system clearer, simpler and more flexible for marketing authorisations holders. A public consultation paper on the implementation of the regulation was released for consultation on 20 March 2009 (Link). It includes details of the various categories of variations, guidance on the operation of the procedures laid down in Chapters II, III and IV of the regulation and on the documentation to be submitted pursuant to these procedures. Contributions from SMEs are particularly welcomed by 18 May 2009.

Meetings

- The 1st EMEA Workshop on Advanced Therapy Medicinal Products (ATMPs) will take place on 3 April 2009 at the EMEA (Agenda)
- The 2nd EMEA/EFPIA workshop on Adaptive Design in Confirmatory Trials will take place on 2 April 2009 at the EMEA (Agenda)

For further information see Link.

SME companies registered with the EMEA

357 companies currently have SME status assigned by the EMEA. The list of companies is published on the EMEA 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:
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