



## News bulletin for small and medium-sized enterprises

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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.



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### Non-clinical and clinical guidance

A guideline on the treatment of premenstrual dysphoric disorder (PMDD) was adopted on 21 July 2011 ([EMA/CHMP/607022/2009](#)). The scope of the document is to provide guidance on the identification of the target population, study duration and efficacy/safety endpoints. It will come into effect in February 2012.

Four concept papers were released in July 2011 and are open for comments until 30 September 2011:

1. Revision of the guideline on *Multiple Sclerosis* ([EMA/CHMP/CNSWP/257565/2011](#)). The guideline will be updated with respect to target population, trial design, choice of endpoints and paediatric requirements;
2. Development of a guideline on *Duchenne and Becker Muscular Dystrophy* (8 July 2011; [EMA/CHMP/CNSWP/236981/2011](#));
3. Revision of the guideline on low-molecular-weight heparins ([EMA/CHMP/BMWP/522386/2011](#)). It discusses the need to revise the current requirement for a comparative clinical trial demonstrating similar efficacy and safety of the biosimilar versus the reference low-molecular-weight heparin in the prevention of venous thromboembolism in patients undergoing major orthopaedic surgery;
4. Revision of the guideline on biosimilar recombinant human (short-acting) insulins ([EMA/CHMP/BMWP/506470/2011](#)). It discusses the need to revise the guideline to extend its scope to include insulin analogues and long-acting human insulin preparations. The need for non-clinical studies and the development of clinical sections relating the pivotal PD/clamp study, the PK assessment, the patient population and the size of the clinical safety study are also discussed.

## Non-clinical and clinical guidance continued

A draft reflection paper on methodological issues associated with *pharmacogenomic biomarkers* (BM) was published on 12 July 2011 ([EMA/446337/2011](#)). It highlights key principles in relation to patient selection and trial methodology applicable to the development and validation of a marker through the lifecycle of a medicinal product i.e. pre-authorisation and post-marketing stages; many principles are also applicable to prognosis and some of these may also apply to non-genomic BMs and surrogate biomarkers in the context of drug development. The paper is open for comments until 25 November 2011.

A 'questions and answers' document on '*ICH Topic M 3 (R2) Non-Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals*' was published on 25 July 2011 ([EMA/CHMP/ICH/507008/2011](#)). It clarifies several points of the ICH M3 guideline including e.g. the 50-fold clinical exposure margin, the assessment of reversibility and the characterization and evaluation of the toxicity of metabolites.

A draft reflection paper on the data requirements for intravenous liposomal products developed with reference to an innovator product ([EMA/CHMP/806058/2009](#)) was released for consultation on 27 July 2011. It provides guidance on the generation of quality, non-clinical and clinical data to support a marketing authorisation of intravenous liposomal products developed with reference to an innovator liposomal product. The principles outlined in the paper can also be considered applicable to other novel types of 'liposome-like' and vesicular products including those to be administered by routes other than intravenous administration. The paper is open for comments until 31 January 2012.

A revised guideline on plasma-derived medicinal products was adopted on 29 July 2011 ([EMA/CHMP/BWP/706271/2010](#)). The amendments relate to:

- The collection and testing of starting material, including reference to the PMF guideline;
- The detection of HCV RNA by Nucleic Acid Amplification Technology, which became a mandatory European Pharmacopoeia (Ph. Eur.) requirement for plasma pool testing;
- The deleted requirement for ALT testing which has been removed from the Ph. Eur. Monograph "Human plasma for fractionation";
- The inclusion of the '*Guideline on Assessing the Risk for Virus Transmission - CPMP/BWP/5180/03*' into the guideline;
- The reference to the guideline on the replacement of rabbit pyrogen testing by an alternative test for plasma-derived medicinal products (EMA/CHMP/BWP/452081/2007).

## Pharmaceutical development guidance

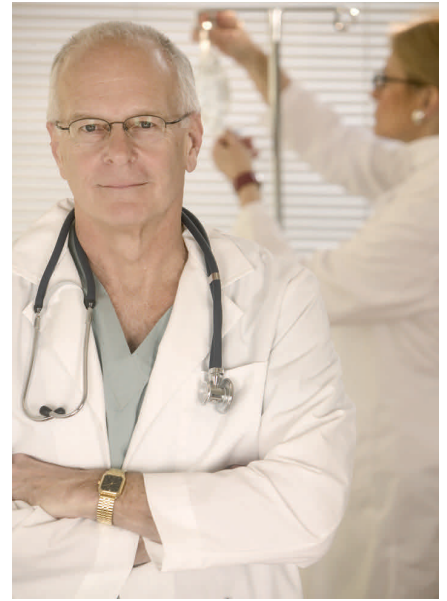
A draft guideline on stability testing requirements for variations to a marketing authorisation was released on 26 July ([EMA/CHMP/CVMP/QWP/441071/2011](#)). It outlines the stability data which have to be generated by type of variation. It applies to chemical active substances and related finished products, herbal drugs, herbal drug preparations and related herbal medicinal products; it is not applicable to radiopharmaceuticals, biologicals and products derived from biotechnology. It is released for consultation until 31 January 2012.



## Good clinical practice (GCP) standards

A draft reflection paper on risk-based quality management in clinical trials was published on 5 August 2011 ([EMA/INS/GCP/394194/2011](#)). It aims at facilitating the development of a more systematic, risk-based approach to the quality management of clinical trials. The current way quality management systems are implemented in clinical trials are costly and time-consuming. A proportionate approach is recommended in order to cover the needs of academic researchers, SMEs and large multinational pharmaceutical companies. The paper is open for consultation until 15 February 2012 and SMEs are particularly invited to provide comments.

A draft reflection paper on the use of interactive response technologies in clinical trials was released on 11 August ([EMA/INS/GCP/600788/2011](#)). Interactive voice response systems utilising telephones and web-based systems facilitate overall drug management in clinical trials e.g. assistance with dose titration, unblinding and expiry date update. The paper intends to provide guidance to sponsors and service providers. It is open for consultation until 15 February 2012.



## Pharmacovigilance

Guidance on the 'electronic submission of information on medicinal products for human use by marketing authorisation holders to the European Medicines Agency in accordance with Article 57(2), second subparagraph of Regulation (EC) No. 726/2004' was published on 1 July 2011 ([EMA/399691/2011](#); [EMA/505633/2011](#)). It details the format in which pharmaceutical companies need to submit information on all medicines authorised or registered in the European Union by the legal deadline of 2 July 2012. This information will help to create a list of all medicines authorised and registered in the EU, including medicines authorised centrally via the Agency and medicines authorised by regulatory authorities in the Member States. It will also identify medicines accurately, especially medicines included in the reports of suspected adverse reactions.

The electronic submission of this information can be achieved by companies in two ways:

1. develop tools to initiate the electronic submission via the EudraVigilance Gateway to the Agency;
2. use the data entry tools provided by the Agency specifically developed for SMEs;

A training program is currently being developed by the Agency. Further information will be announced on the EMA and EudraVigilance website.



## Veterinary guidance

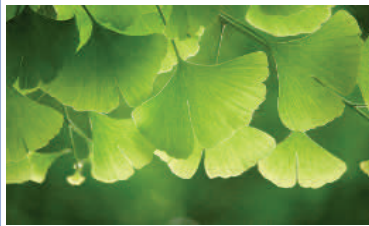
The updated 'List of changes to the combined VeDDRA list of clinical terms' for the reporting of suspected adverse reactions in animal and humans to veterinary medicinal products ([EMA/CVMP/PhVWP/380221/2011](#); guidance [EMA/CVMP/PhVWP/288284/2007-Rev.4](#)) was adopted on 30 June 2011.

Two 'questions and answers' documents were published on 20 July 2011 relating to the:

- Implementation of the CVMP guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 (phase I) and GL38 (phase II) ([EMA/CVMP/ERA/172074/2008-Rev.3](#)). This will be of interest to marketing authorisation holders when preparing environmental assessment reports for their applications.
- CVMP guideline on the summary of product characteristics for antimicrobial products ([EMA/CVMP/414812/2011](#)).



## Scientific advice on herbal medicinal products



A draft guidance for companies seeking scientific advice on traditional herbal medicinal products was published on 20 July 2011 ([EMA/HMPC/127670/2011](#)). It was developed for companies which consider seeking support from the Committee on Herbal Medicinal Products (HMPC) on traditional herbal medicinal products. It provides an outline of the procedure available and clarifies its scope. It is released for comments until 15 November 2011.

## New European legislation on falsified medicines

The new legislation on falsified medicines was published on 1 July 2011 in the Official Journal of the European Union ([Directive 2011/62/EU](#)). It aims at preventing falsified medicines entering the legal supply chain and reaching patients. Harmonised safety and strengthened control measures will be introduced across Europe, including:

- obligatory features on the outer packaging of medicines to demonstrate that they are authentic;
- strengthened requirements for the inspection of the manufacturers of pharmaceutical ingredients;
- the obligation for manufacturers and distributors to report any suspicion of falsified medicines;
- an obligatory logo that must be placed on the websites of legally operating online pharmacies, with a link to official national registers.

The new legislation will apply as of 2 January 2013.

## Meetings

- A workshop on advanced therapies will take place on 27 October 2011 in Brighton, UK. The workshop organised by the European Medicines Agency's (CAT) will be of interest to stakeholders involved in research and development of gene and cell therapy products. It is hosted by the European Society for Gene and Cell Therapy (ESGCT) as part of its annual congress. Further information is available [here](#).
- A Joint DIA/EFGCP/EMA paediatric forum will take place 26-27 September 2011 in London, UK ([Link](#)). This year's conference has the EMA as official co-organizer of the conference and will take place 5 years after the introduction of the paediatric regulation. Reduced registration fees are available for small to medium-sized enterprises (contact DIA at [diaeurope@diaeurope.org](mailto:diaeurope@diaeurope.org))
- A Joint DIA/EMA/FDA orphan drug designation workshop will take place on 10-11 November 2011 in London, UK ([Link](#)). It aims to provide regulatory assistance to sponsors developing orphan drug designation applications intended for regulatory submissions. Reduced registration fees are also available for small to medium-sized enterprises (contact DIA at [diaeurope@diaeurope.org](mailto:diaeurope@diaeurope.org))
- Information on the workshops of the European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA) is available under [Link](#). Enpr-EMA is a 'network' of research networks, investigators and centres with recognised expertise in performing clinical studies in children. It aims to foster high-quality ethical research on medicines for children and one of its tasks is to facilitate the access of the pharmaceutical industry to paediatric clinical study centres and experts.

## SME companies registered with the Agency

576 companies currently have SME status assigned by the Agency. The companies are published in the Agency's public SME registry at: <http://fmapps.emea.europa.eu/SME/>

## 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 or queries on this news bulletin can be forwarded to the SME Office:

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