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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.



Pharmaceutical Development and GXP Inspections

A concept paper on the use of transgenic animals in the manufacture of biologics for human use was released on 24 July 2009 ([EMEA/CHMP/BWP/134153/2009](#)). It outlines the planned revisions of the guideline to adapt the quality guidance already in place for other production systems to the special case of transgenic animal systems.

A concept paper on pharmaceutical aspects of the product information for human vaccines was released on 24 July 2009 ([EMEA/CHMP/BWP/290688/2009](#)). The guideline will be revised to take into account developments in both regulatory and scientific fields.

The 'Questions & Answers' webpage developed by the CHMP/CVMP Quality Working Party addresses a number of questions raised by marketing authorisation holders and authorities on matters related to the quality of medicinal products. It provides an EU harmonised position on issues that can be subject to different interpretation or require clarification. The document was updated to include information on calculation of thresholds for impurities ([Link](#)).

A new version of the EudraGMP database ([EudraGMP 2.0](#)) has been released on 4 August 2009. The database now provides public access to information about manufacturing, importation authorisations and Good Manufacturing Practice (GMP) certificates. The European regulators have decided to give the general public access to the information contained in the database, with the exception of commercial and personal information ([Press release](#)).

'Questions and Answers' documents relating to 'ICH Topic Q8, Q9 and Q10 Note for guidance on Pharmaceutical Development/Quality Risk Management/Pharmaceutical Quality System' were released for information in June 2009 ([EMEA/CHMP/ICH/265145/2009](#)).

The following annexes to ICH Q4B (Guidance on Regulatory Acceptance of Analytical Procedures and/or Acceptance Criteria) were released:

- ICH Q4B Annex 5 to Note for evaluation and recommendation of pharmacopoeial texts for use in the ICH regions on disintegration test general chapter ([EMEA/CHMP/ICH/308895/2008](#)). It will come into effect in December 2009.
- ICH Q4B Annex 8 to Note for evaluation and recommendation of pharmacopoeial texts for use in the ICH regions on sterility test general chapter ([EMEA/CHMP/ICH/645592/2008](#)). It will come into effect in December 2009.
- Draft ICH Q4B Annex 9 Step 3 Tablet Friability General Chapter ([EMEA/CHMP/ICH/379801/2009](#)).
- Draft ICH Q 4 B Annex 10 Step 3 Polyacrylamide Gel Electrophoresis ([EMEA/CHMP/ICH/381133/2009](#)).

Advanced Therapies

Commission Directive 2009/120/EC amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to advanced therapy medicinal products was published in September 2009 ([Link](#)). The document is a revised technical annex to Directive 2001/83/EC which updates the definitions and pharmaceutical, non-clinical and clinical requirements for the authorisation of gene, cell and tissue engineered products.

A European Commission regulation on the certification of quality and non-clinical data relating to advanced therapy medicinal products developed by SMEs was published in July 2009 ([Link](#)). The new procedure will allow SMEs developing gene, cell and tissue engineered medicinal products to certify their quality and non-clinical data with a view to support the development of such products. Further draft procedural guidance is available in the following documents ([EMEA/CAT/418458/2008](#); [EMEA/CAT/486831/2008](#)). SME companies developing gene, cell or tissue engineered products interested in this new EMEA service are advised to contact the SME Office.

An ICH paper on considerations and general principles to address virus and vector shedding was released on 29 July 2009 ([EMEA/CHMP/ICH/449035/2009](#)). It provides guidance for designing non-clinical and clinical shedding studies, including information on analytical assays for detection, considerations for the sampling profiles and schedules in both non-clinical and clinical studies.

Non-clinical Safety Guidance

An updated ICH guidance [ICH M 3 (R2)] on non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals was published on 29 June 2009 ([CPMP/ICH/286/95](#)). The revised document recommends international standards for the harmonisation of the non-clinical safety studies to support human clinical trials as well as marketing authorization for pharmaceuticals. It will help to reduce the differences between regions, facilitate the conduct of clinical trials and reduce the use of animals. It will come into effect in December 2009.

Efficacy Guidance

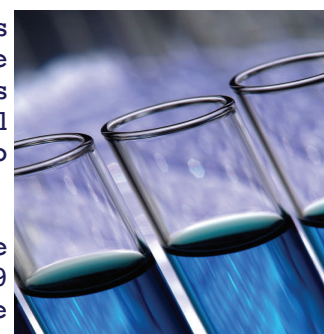
A reflection paper on non-clinical and clinical development of similar medicinal products containing recombinant interferon alpha was released on 29 June 2009 ([EMEA/CHMP/BMWP/102046/2006](#)). It presents the current view on the data needed to demonstrate comparability of two recombinant, non-pegylated, interferon alfa containing medicinal products.

A draft guideline on non-clinical and clinical development of biosimilar erythropoietins was released on 15 September 2009 ([EMEA/CHMP/BMWP/301636/2008](#)). It outlines the non-clinical and clinical requirements for erythropoietin containing medicinal products claiming to be similar to another already marketed. Criteria for extrapolation of clinical data to other indications approved for the reference medicinal product are also discussed. It is released for consultation until January 2010.

An updated 'Questions & Answers: Positions on specific questions addressed to the EWP therapeutic subgroup on Pharmacokinetics' was released on 30 July 2009 ([EMEA/618604/2008 Rev. 1](#)). It was updated to include information on bioequivalence studies for generic products containing clopidogrel.

A revised CHMP guideline on the clinical evaluation of diagnostic agents was adopted on 23 July 2009 ([CPMP/EWP/1119/98/Rev. 1](#)). It was revised to better define the steps needed in the development of diagnostic agents, and the assessment of benefits and risks. The Appendix on the development of imaging agents was also reviewed. It will come into effect in February 2010.

An draft ICH guidance (ICH E 16) on genomic biomarkers related to drug response: context, structure and format of qualification submissions ([EMEA/CHMP/ICH/380636/2009](#)) was released on 29 June 2009.



Scientific Advice

Procedural announcement for electronic-only applications of EMEA Scientific Advice applications

As of October 2009, the EMEA will only accept electronic submissions for new and follow-ups Scientific Advice, Protocol Assistance and Qualification of novel methodologies requests ([Link](#)). Further information about Scientific Advice and the new Qualification Scientific Advice is available [here](#).

Regulatory Guidance

Updated regulatory guidance on paediatric requirements was published on the 'Medicines for Children' webpage:

- Revised priority list for studies of off-patent paediatric medicinal products ([EMEA/414936/2009 Rev. 2009](#)). The Paediatric Regulation includes provisions for funding of studies of off-patent medicinal products (currently through EU Framework Programmes) with a view to submission of a Paediatric Use Marketing Authorisation (PUMA). The revised list provides the basis for the Fourth Call of the 7th EU Framework Programme (FP) and ensures that funds are directed into the research of medicines with the highest needs in the paediatric population.
- New Standard Operating Procedure (SOP) on 'Handling of applications for paediatric investigation plan (PIP) and/or waiver from pre-submission to PDCO opinion' ([SOP/H/3207](#))
- Consolidated EMEA decision on the list of class waivers 2009 ([EMEA/225021/2009-P/65/2009](#))
- Information on annual reports of deferrals ([Link](#))

Updated EMEA, EC Pre- and post authorisation regulatory guidance was published relating to:

- Community Vaccine/Plasma Master File certification system and Eudravigilance ([Link](#))
- Dossier requirements for post-authorisation submissions in the centralised procedure ([EMEA/300339/2008](#))
- 'E-submissions/ICH M2/Questions and Answers on the Common Technical Document for the Registration of Pharmaceuticals for Human Use' ([Link](#))
- Clinical trials guidelines/EudraLex Volume 10/Questions and Answers ([Link](#))
- Explanatory note on fees payable to the EMEA ([EMEA/405816/2009](#))
- Updated guidance on Summary of Product Characteristics (SmPC)/Notice to Applicants/Volume 2C ([Link](#))
- Updated XML forms on Electronic Common Technical Document (eCTD) submissions- Notice to Applicants Volume 2B ([Link](#)).

News from the European Commission

The European Commission released in July 2009 an update of the guidance on 'Borderline products, drug-delivery products and medical devices incorporating, as integral part, an ancillary medicinal substance or an ancillary human blood derivative/MEDDEV 2.1/3 rev.3' ([Link](#)). The document further clarifies cases where a given product is a medical device, an in vitro diagnostic or a medicinal product. Further information on EMEA regulatory advice on classification matters is available under [Link](#), and for advanced therapies under [Link](#).

The European Commission published on 3 July 2009 a summary of the outcome of the public consultation of two draft implementing guidelines required by Commission Regulation (EC) No 1234/2008 of 24 of November 2008 (The 'Variation Regulation') ([Link](#)). The 'Variation Regulation' introduces major changes to the operation of variations procedures to streamline variations approval for human and veterinary medicines authorised through the mutual recognition, decentralised or centralised systems. The guidelines provide details on the work sharing procedure (i.e. NCA evaluating variations on behalf of other NCAs), the notification system (immediate or delayed notification of type IA variations) and the changes to the variations classification (Type IA, IA(IN), IB, II). The 'Variation Regulation' will come into force in January 2010.

Directive 2009/53/EC of the European Parliament and of the Council amending Directive 2001/82/EC and Directive 2001/83/EC was published on 30 June 2009 ([Link](#)). It intends to harmonise variations to marketing authorisations granted under purely national procedures. This Directive is part of a global revision of the legal framework on variations to make the overall system clearer, simpler and more flexible.

The European Commission published on 30 July 2009 several calls for proposals of FP7 including three calls under the 'Health' title, with priorities on adverse drug reaction research included in call 'FP7-HEALTH-2010-single-stage' ([Link](#)). The European Medicines Agency released on 7 August 2009 information to support researchers in developing proposals that meet the needs of the selected research areas ([Link](#)). Further information on FP7 is available to SMEs through the Network of [SMEs National Contact Points](#).

Veterinary Medicines

The European Commission released on 29 June 2009 new guidance on the assessment of environmental risks of veterinary medicines ([Link](#)). The document included in Volume 6C/Notice to Applicants offers guidance on environmental considerations in the benefit/risk assessment of veterinary medicines, and related data requirements.

A new regulation on Maximum Residue Limits entered into force on 8 July 2009 ([Link](#)). It lays down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin. It repeals Council Regulation (EEC) No 2377/90 and amends Directive 2001/82/EC and Regulation (EC) No 726/2004 of the European Parliament and of the Council.

The European Commission released in July and September 2009 updates of the Notice to Applicants – Veterinary Medicinal Products - Volume 6A-Chapter 7 and Volume 6 including updated Member States requirements and electronic dossier requirements ([Link](#))

The European Commission released on 13 July 2009 a guideline on electronic submissions for veterinary medicinal products dossiers ([Link](#)). It intends to assist applicants and regulators with submissions of dossiers in electronic format and specifies the basic parameters required for an acceptable electronic submission.

A 'Policy document on the classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited markets' was published on 6 August ([EMEA/429080/2009](#)). Regulation (EC) No 726/2004 requires the EMEA to introduce measures to assist companies developing products in this area. The document provides a comprehensive reference source on the definition and classification of such products, as well as procedural details on how to apply for such classification. The document was drafted considering the SMEs operating in this field.

Meetings

The following meetings have been announced:

- A SME workshop for micro, small and medium sized enterprises (SMEs) focusing on "Paediatric Medicines" to be held on 23 October 2009 ([Link](#)).
- A workshop on 'In vitro Cytokine release assays to predict Cytokine release syndrome: The current state-of-the-science' to be held on 19 November 2009 ([Link](#)).
- An EMEA-TOPRA meeting on regulatory affairs to be held on 1-2 December 2009 ([Link](#)).

The reports and presentations from the following meeting were released on the EMEA website:

- 'EMEA/EFPIA Workshop on Integrating Pharmacogenomics Early into Drug Development: PK as a working example' held on 19 December 2008 ([Link](#)).
- Ad-hoc expert group on nanomedicines held on 29 April 2009 ([Link](#))
- Veterinary e-submission workshop held on 7 May 2009 ([Link](#))
- EMEA workshop on Monoclonal Antibodies held on 2 July 2009 ([Link](#))



SME companies registered with the EMEA

434 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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