News from the EMA

More information can be found on the Agency's website: www.ema.europa.eu.

The articles included in this section are a selection from the European Medicines Agency's news and press release archive for April 2016 to July 2016.

Listening to the public's views on the safety of medicines

PRAC adopts rules of procedure on public hearings on selected safety reviews

April 15, 2016 – The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has adopted the final rules of procedure for public hearings to be held by the Committee. The rules of procedure describe the process and practical arrangements for the preparation, conduct, and follow-up of public hearings.

As part of the implementation of these rules, the European Medicines Agency (EMA) will now organise an internal dry run exercise in order to test the process and procedures of public hearings. The dry run is scheduled to take place at the PRAC meeting in July 2016. Public hearings could take place as early as the fourth quarter of 2016, as soon as a relevant topic is identified.

Public hearings are a new tool for EMA to engage European Union (EU) citizens in the supervision of medicines and to listen to their views and experiences. The pharmacovigilance legislation has given the PRAC the possibility to hold public hearings as part of certain safety reviews of medicines, particularly in relation to their therapeutic effects and available therapeutic alternatives, as well as the feasibility and acceptance of proposed risk management and minimisation activities.

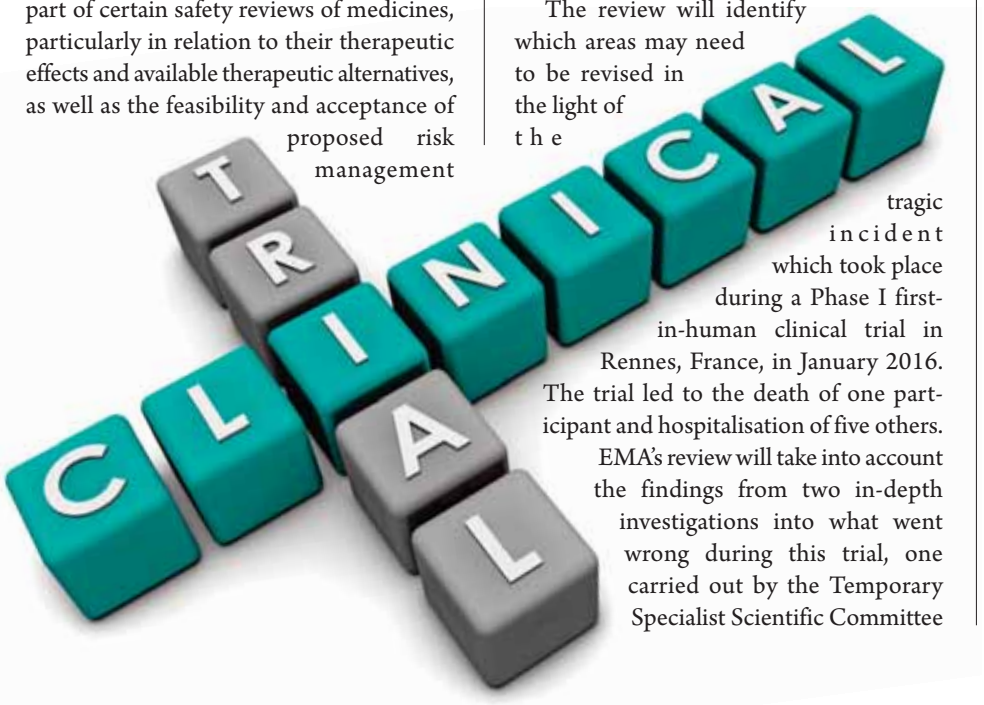
Contributions made by the public during a public hearing will be considered by the PRAC and inform the Committee's decision-making. Public hearings will be held on a case-by-case basis, where the Committee determines that collecting the views of the public would bring added value to its review. More details are outlined in the rules of procedure document.

Draft rules of procedure were published by the Agency for comments in July 2014 and drew 200 comments from 22 stakeholder contributions representing 25 organisations. The rules were updated and revised in light of the comments received.

Improving safety of first-in-human clinical trials

EMA starts EU-wide reflection on necessary changes to best practices

May 27, 2016 – The EMA has started a review of the guidelines that describe first-in-human clinical trials and the data needed to enable their appropriate design and allow initiation. This is being done in cooperation with the European Commission and the Member States of the EU.



The review will identify which areas may need to be revised in the light of the tragic incident which took place during a Phase I first-in-human clinical trial in Rennes, France, in January 2016. The trial led to the death of one participant and hospitalisation of five others. EMA's review will take into account the findings from two in-depth investigations into what went wrong during this trial, one carried out by the Temporary Specialist Scientific Committee (TSSC) set up by the French medicines agency ANSM, and the other by the Inspection Générale Des Affaires Sociales (IGAS), the inspectorate for socia,l affairs in France.

Both reports include a series of recommendations regarding the requirements for authorisation and conduct of first-in-human clinical trials for further examination by the international regulatory and public health community.

EMA's work will focus on best practices and guidance. The aim is to agree a concept paper by July identifying areas for change and proposals to further minimise the risk of similar accidents. The concept paper will form the basis for an EU-wide review of the guidelines. This process will include targeted discussions with stakeholders and a public consultation on proposed changes later in 2016.

The EMA review has started with two groups of experts who are carrying out preparatory work. One group is looking at pre-clinical aspects and the data needed from laboratory tests or animal studies to safely initiate first tests in humans. The other group is looking at clinical aspects of the design of first-in-human trials and how these could be improved to better ensure the safety of human volunteers taking part in these trials. This will lead into one EU-wide expert group discussion

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on revision of guidelines.

Clinical trials are essential for the development of medicines and without them patients cannot gain access to new potentially life-saving medicines. In the EU, the approval and conduct of clinical trials is within the remit of the relevant authorities of the European Member States.

EU guidelines are in place to ensure that these clinical trials are conducted as safely as possible. These guidelines include the requirement for extensive studies, including in animals, to gather information about a medicine before it is given to humans.

Severe adverse reactions in healthy volunteers such as those observed in the trial in Rennes are extremely rare during clinical trials. Since 2005, approximately 14,700 phase I clinical trials (with participation of 305,000 subjects) have been conducted in the EU, including 3,100 first-in-human studies. Only one other severe incident has been previously reported in that time in the EU.

Single, central platform now mandatory for all periodic safety update reports

PSUR repository facilitates information exchange on the safety of human medicines authorised in the EU

June 10, 2016 – As of June 13, 2016, all periodic safety update reports (PSURs) for human medicines authorised in the EU must be submitted to the PSUR repository, which has been developed by the EMA in close collaboration with EU Member States and the industry.

The PSUR repository is a single, central platform for PSURs and related documents to be used by all regulatory authorities and pharmaceutical companies in the EU. It was introduced by the EU pharmacovigilance legislation to facilitate the exchange of information on the safety of authorised medicines between regulators and pharmaceutical companies.

Marketing authorisation holders must now use the repository as a single point for all submissions and should no longer submit their PSURs to national competent authorities. The eSubmission Gateway is available on the eSubmission website.

The PSUR repository provides an important simplification for marketing authorisation holders allowing them to send all PSURs to a single recipient. It also facilitates the assessment of the reports by ensuring that national competent authorities, EMA and its scientific committees have timely and secure access to all relevant documents.

In June 2015, EMA's Management Board gave the green light for the use of the repository following an independent audit that confirmed that the tool meets the agreed functional specifications. Since the initial release of the PSUR repository in January 2015, EMA has been supporting companies and national competent authorities to ensure they are ready to use this new tool. The system has been implemented

Regulation of advanced therapy medicines

Report details concrete proposals to encourage development and authorisation of advanced therapy medicinal products (ATMPs) in the EU

June 3, 2016 – The EMA today published a report from a multi-stakeholder expert meeting held on May 27, 2016 to explore possible ways to foster the development of ATMPs in Europe and expand patients' access to these new treatments.

ATMPs comprise gene therapies, tissue engineered products and somatic cell therapies. These medicines have the potential to reshape the treatment of a wide range of conditions, particularly in disease areas where conventional approaches are inadequate. However, eight years since EU legislation on ATMPs entered into force in 2008, only five ATMPs are currently authorised. At the same time clinical trials investigating ATMPs appear to represent a fast-growing field of interest, underlining the need to better support innovation through a coherent and appropriate regulatory environment.

The meeting brought together leading academics and researchers, representatives from patients' and healthcare professionals' organisations, small and large pharmaceutical companies, the investment community, incubators and consortium organisations, health technology assessment (HTA) bodies, national competent authorities and the European Commission. In their discussions they focused on four key areas:

- Facilitating research and development
- Optimising regulatory processes for ATMPs
- Moving from hospital exemption to marketing authorisation
- Improving funding, investment and patient access

Ideas and solutions proposed by the different stakeholders are summarised in the meeting report published today. Some of the recurring themes include the need for early interaction and guidance from regulators, more transparency and information sharing, greater harmonisation between Member States on various aspects of the ATMP legislative framework and measures to tackle inequalities in patient access to ATMP treatments.

EMA and its scientific committees, together with the European Commission and the national competent authorities, have started discussing the proposals made during the meeting. Concrete actions will be determined over the next few months and shared with stakeholders.

Notes

- Although a total of seven ATMPs have received a marketing authorisation since 2009, only five ATMPs are currently authorised. One marketing authorisation for an ATMP was withdrawn by the marketing authorisation holder and the authorisation for another ATMP is currently suspended.
- For a recent analysis on clinical trials with ATMPs see Hanna E, Remuzat C, Auquier P, Toumi M. Advanced therapy medicinal products: current and future perspectives. J Mark Access Health Policy 2016;4.

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using a phased approach and feedback from users has been taken into account to improve the system. Guidance, interactive training sessions and links to all relevant documents have been made available on EMA's eSubmission website.

PSURs are reports providing an evaluation of the benefit-risk balance of a medicine. Marketing authorisation holders must submit PSURs at defined time points following a medicine's authorisation. PSURs include the results of all studies carried out with this medicine, both in its authorised and unauthorised uses.

EMA uses the information in PSURs to determine if there are new risks identified for a medicine or whether the balance of benefits and risks of a medicine has changed. It can then decide if further investigations need to be carried out or can take action to protect the public from the risks identified, for example by updating the information provided for healthcare professionals and patients.

EMA goes electronic for PDCO opinions and subsequent EMA decisions

PDCO opinions and subsequent EMA decisions will be transmitted to applicants electronically only

July 6, 2016 – From August 1, 2016 the EMA will transmit the opinions of the Paediatric Committee (PDCO) and subsequent EMA decisions to applicants in electronic format only. Applicants will no longer receive paper versions.

PDCO opinions and subsequent EMA decisions will be sent to applicants as a PDF via EudraLink – the European medicines regulatory network's secure file-transfer system. EMA decisions, as well as PDCO opinions will no longer contain a signature.

The date when the EudraLink message is opened by applicants for the first time will be considered as the day of the receipt of the document attached to the EudraLink message, for the purpose of calculating procedural timelines in accordance with Regulation (EC) No. 1901/2006. EudraLink automatically records this date as "access by".

Applicants should download and archive the attached documents upon receipt, as Eudralink preserves file attachments only for up to 90 days. EMA will retain a read-only version of the electronic documents in its electronic archives. Further information can be found on Paediatric investigation plans: questions and answers, under the section "Applying for a Paediatric Investigational Plan waiver or deferral". Applicants will be offered the possibility to opt-out and receive documents as hard copy instead.

The move from printouts to electronic documents responds to stakeholders' feedback collected over the years. Among the benefits of this change are: accelerated delivery of documents, more convenient receipt of documents as well as a shift towards greener solutions in line with EMA's environmental policy.

EMA statement on the outcome of the UK referendum

EMA's procedures and work streams continue as usual

July 6, 2016 – The EMA acknowledges the outcome of the referendum of June 23, 2016. A majority voted against United Kingdom's (UK) continued membership of the EU and it is now up to the UK government to decide how to act upon the outcome of the referendum.

EMA would like to underline that its procedures and work streams are not affected by the outcome of the referendum. The Agency will continue its operations as usual, in accordance with the timelines set by its rules and regulations.

No Member State has ever decided to leave the EU, so there is no precedent for this situation. The implications for the seat and operations of EMA depend on the future relationship between the UK and the EU. This is unknown at present and therefore we will not engage in any speculations.

EMA welcomes the interest expressed by some Member States to host the Agency in future. The decision on the seat of the Agency will however not be taken by EMA, but will be decided by common agreement among the representatives of the Member States.

The European Regulatory Network as a whole is a very strong and flexible system that is able to adapt to changes without jeopardising the quality and effectiveness of its work. The Agency is in close contact with the EU institutions. As soon as concrete information will become available, EMA will share it with its stakeholders.