EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 February 2018
EMA/710355/2017
Product Development Scientific Support Department

Work plan for the Modelling and Simulation Working Group (MSWG) for 2018

Chairperson: Ine Skottheim Rusten

The activities outlined in the work plan for 2018 have been agreed considering the respective business priorities, as well as the Agency's relocation as a result of the UK's exit from the EU and its impact on the Agency's business continuity, and may be subject to further review and reprioritisation in accordance with the business continuity plan of the Agency

1. Meetings scheduled for 2018

Face-to-face meetings are planned for the following dates:

- 29-30 November

10 monthly virtual meetings/web sharing will be planned to accommodate scientific input to products scientific advice and evaluation.

The above mentioned dates may be modified as needed. Additional virtual meetings may be organised ad-hoc to respond to time-sensitive requests on products and to progress guidelines, as required.

2. Guidelines

2.1. New EU Guidelines

Action: Specialised input

Guideline on qualification and reporting of physiologically-based pharmacokinetics modelling and analyses, EMA/CHMP/458101/2016.

Leading group Pharmacokinetics Working Party (PKWP)

Target date Final guideline to be released Q4 2018

Comments Comments received from **public** consultation that ended in 2017 will be incorporated into the final guideline.

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Reflection paper on extrapolation of efficacy and safety in medicine development, EMA/199678/2016

Leading group Extrapolation Working Group

Target date Final reflection paper to be published in 2018

Comments Draft reflection paper was published in April 2016. Contribution to the development of this reflection paper.

Reflection paper on investigation of pharmacokinetics and pharmacodynamics in the obese population, EMA/CHMP/PKWP/535116/2016.

Leading group Pharmacokinetics Working Party (PKWP)

Target date Final reflection paper to be released Q4 2018.

Comments In collaboration with PKWP. Public consultation of the draft reflection paper to end in the first half of 2018

2.2. EU Guidelines under revision

Action: Lead

Note for guidance on the role of pharmacokinetics in the development of medicinal products in the paediatric population, EMEA/CHMP/EWP/147013/2004.

Target date Draft for public consultation to be finalised Q2 2018.

Comments Joint work with the Pharmacokinetics Working Party (PKWP) with PDCO input. Comments received from public consultation on the associated concept paper that ended in 2017 will be incorporated into the draft guideline.

Action: Specialised input

Guideline on the investigation of drug interactions, CHMP/EWP/147013/04.

Leading group Pharmacokinetics Working Party (PKWP)

Target date Draft to be released for public consultation by Q4 2018.

Comments Comments received from public consultation on the associated concept paper that ended in 2017 will be incorporated into the draft guideline. The need to work on a list of substrates/inhibitors/inducers has also been identified.

Appendix 1 of the guideline on the pharmacokinetic and clinical evaluation of modified release dosage forms, EMA/CPMP/EWP/280/96 Corr1.

Leading group Pharmacokinetics Working Party (PKWP)

Target date Draft to be released for public consultation by Q4 2018.

Comments Proposal under discussion on whether there is a need to have a formal revision of the appendix only (this would include a concept paper) or whether the proposed changes could be reflected in a Q & A.

2.3. ICH Guidelines

E11A Paediatric extrapolation

Target date Step 2 is planned in 2020.

Comments Support to the expert working group in this work that follows the publication of ICH E11(R1), the revised guideline on clinical investigation of medicinal products in the paediatric population and of the EMA Reflection paper on extrapolation of efficacy and safety in paediatric medicine development.

3. Medicinal Products-specific activities

3.1. Pre-Authorisation activities

- Contribution on relevant M&S aspects to Scientific Advice and protocol assistance upon request from the Scientific Advice Working Party
- Contribution on relevant M&S aspects to PIPs upon request from the PDCO
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3.2. Evaluation and supervision activities

- Contribution to product-related assessment following specific CHMP request
- M&S issues upon request from CMDh
- Pharmacovigilance issues upon request from the CHMP and PRAC
- Other requests received from EMA Committees and Working Parties, e.g. Quality Working Party, PWKP, Biologics Working Party, Biostatistics Working Party

4. Input in European activities

4.1. Training for the network and knowledge building

- Assessor training on the Extrapolation. Format to be defined
- Assessor training on the new PBPK guideline. Format to be defined
- Assessor training on the Exposure Response Analysis. Format to be defined
- Software-specific trainings. Format to be defined

4.2. Other input in European activities

- Questions and Answers document on methodological aspects of using M&S in paediatric drug development
  Document will be initially developed for internal purposes, i.e. standardisation of practice across the regulatory network.
- Modelling and Simulation in PIP Summary Reports and in the key binding elements in the PIP opinions
  Update, in collaboration with the PDCO, the required information on Modelling and Simulation in PIP Summary Reports and in the key binding elements in the PIP opinions. Define criteria for MSWG involvement (in reviewing modelling and simulation studies) and translation into a PIP Opinion key binding element measure.
- Questions and Answers document on methodological aspects of using exposure response analysis in regulatory review.
  Document will be initially developed for internal purposes, i.e. standardisation of practice across the regulatory network.
- Questions and Answers document on methodological aspects of using c-QTC analysis for cardiac risk assessment
  Document will be initially developed for internal purposes, i.e. standardisation of practice across the regulatory network.

5. Input in International activities (beyond ICH guidelines)

International regulatory cluster on M&S with participation of EMA, US-FDA, MHLW/PMDA and Health Canada - 4 Cluster TCs are planned.

6. Contribution to dialogue and engagement with stakeholders and external parties

6.1. Workshops

Technical stakeholder workshop on qualification of PBPK models with contributors to the public consultation on the Guideline on qualification and reporting of physiologically-based pharmacokinetics modelling and analyses (Q2 2018). PKWP and SAWP also involved.

6.2. Other activities with stakeholders and external parties

- Regulatory Presentation at PAGE meeting 2018 and ACOP meeting 2018 and other fora.
- The MSWG will continue to encourage industry and academia led activities (such as ddmore, MID3, PMX interest group) towards better standardisation and utilisation of M&S.
- Interact with consortia developing QSP models or in silico trial frameworks through ITF meetings and Qualification procedures.