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# European Medicines Agency Modelling and Simulation Working Group plan 2014

## 1. Meetings

A total of 11 meetings in parallel with the scientific advice working party (SAWP) meetings, of which, two will be organised as face-to-face meetings. Nine will be organised as virtual meetings.

## 2. Product-related issues

Contribution on relevant Modelling and Simulation (M&S) aspects to:

**CHMP**: providing support to the Committee for Medicinal Products for Human Use (CHMP) on dossier evaluation, to facilitate consistency of assessments and the coherence of CHMP opinions

**PDCO**: providing support to the Paediatric Committee (PDCO) on PIP evaluation, to facilitate consistency of assessments and the coherence of PDCO opinions

**Scientific Advice**, Protocol Assistance and Qualification of novel methodologies at request of the Scientific Advice Working Party

Other requests received via the CHMP from other EMA Committees and Working Parties. For example, it is envisaged that collaboration with **EMA Extrapolation Group** (for M&S application to extrapolation from adults to the paediatric population) and **Geriatric Expert Group** (for M&S application to extrapolation from the clinical trial population to older adults) would be particularly helpful.

## 3. CHMP guidelines and related documents

In addition to the substantive support to SAWP and PDCO and potentially growing support to CHMP, objectives for the group will be also the drafting of M&S Regulatory Guidelines/Concept Papers. Based on experience in SAWP and PDCO procedures in 2013 and the EMA/EFPIA Workshop on Modelling and Simulation held at the end of 2011, the following guidelines and related documents were identified as pivotal to facilitate appropriate regulatory application of modelling and simulation to reduce uncertainty in the benefit/risk decisions for new medicines:

- **Guideline on extrapolation** (2H2014). In collaboration with the **Extrapolation Working Group**. An overarching concept paper has been written by the Extrapolation Working Group.

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PKPD modelling is one of the most common tools utilised in extrapolation across populations and therefore has high regulatory impact requiring clear guidance on regulatory standards for methodology and documentation.

- **Concept paper on development and reporting of physiologically based pharmacokinetic (PBPK) models (2H2014).** In collaboration with **PKWP**. Because of their mechanistic basis, these models have great value to predict drug-drug interactions, PK in the paediatric population and impact of organ impairment and aging. Given their complexity, however, careful consideration of an appropriate qualification of models, particularly as applied to individual molecules is needed. Also, as the generic models included in commercially available software are continually evolving, there is a unique challenge of continuous system validation.
- Contribution to update of **Points to consider on pharmacokinetics and pharmacodynamics in the development of antibacterial medicinal products (1H2014)**. In collaboration with **IDWP**.
- **Guidance (could be a Q&A document) on how to best use and incorporate modelling and simulation in regulatory submissions (2H2014).** This was identified as a barrier to companies explaining the modelling basis of their drug development decisions in the submitted dossiers. As this type of modelling integrates data across studies and potentially from preclinical to clinical studies, including pharmacological and clinical endpoints, it can be an invaluable "chain of evidence" to reduce uncertainty in benefit/risk decisions and inform and strengthen the RMP.
- **M&S Template for assessors.** This will help streamline the regulatory approach on M&S.

In general, the priority list of guidelines/concept papers will be updated based on the experience from product related discussions. As Guidelines in specific therapeutic fields are updated, it is envisaged that the Working Group will provide useful expertise on methodological issues.

# 4. Training and Workshops

- As one of the objectives of the M&S working group is to enhance the collective competence and capacity to provide scientific advice and assessment of modelling and simulation in marketing authorisation applications and PIPs, a regular programme of assessor training is envisaged. To support development where establishment of agreed regulatory standards will have the most impact, one workshop is planned together with SAWP and BSWP on **dose finding**.

- As part of the longer term objective for competence development in the EU regulatory system a basic level assessors training on M&S will be organised.

# 5. Activities with external parties

- It is envisaged that continued collaboration with **US FDA and MHLW/PMDA** would help the working group to achieve their objectives. Regulatory input to selected EU framework projects would help in the alignment of European regulatory needs with developing approaches in drug development. Additionally, it is envisaged that the M&S working group could make valuable contributions **to ad-hoc briefing meetings and qualification procedures on methodological topics with external parties** (pharmaceutical companies, academia, public/private partnership or patients' associations).