EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 November 2016
EMA/128306/2016
Human Medicines Research & Development Support Division

EMA workshop on qualification and reporting of physiologically-based pharmacokinetic (PBPK) modelling and simulation

Programme

21 November 2016
European Medicines Agency, London, United Kingdom

Meeting **room 3A**

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
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Objectives of the workshop

A growing number of regulatory submissions include Physiologically Based Pharmacokinetic (PBPK) models. An overview of PBPK modelling in regulatory decision making at the European Medicines Agency has recently been published. Presently, the main purposes of PBPK models in regulatory submissions are to qualitatively and quantitatively predict drug interactions and support initial dose in paediatric and first in human trials. However, it is expected that the extent of use will expand as new scientific data are generated and the confidence in PBPK modelling increases.

PBPK models are complex, with the majority of PBPK regulatory submissions involving the use of a commercially available specialized PBPK platform. The PBPK platform therefore needs to be qualified for the intended use and the predictive performance of included drug models needs to be evaluated.

EMA launched a public consultation on the 'guideline on the qualification and reporting of PBPK Modelling and Simulation' in July 2016. The public consultation will end 31 January 2017. The intent of this guideline is to provide detailed advice on what to include in a PBPK analysis report to allow assessment of the predictive performance of the drug model. In addition, it is intended to clarify what supportive data are expected to be shown in order to qualify a PBPK platform for the intended purpose.

This workshop is aimed at providing an opportunity to disseminate the key messages in the guideline and to provide details on qualification procedures and evaluation of drug models. It is also aimed at communicating EMA's current thinking on the utility of PBPK with stakeholders from other regulatory agencies, pharmaceutical industry, academia, patient representatives and PBPK platform developers.

Programme overview

Sessions

Session 1: Introduction and setting the scene to the draft PBPK guideline

Session 2: Qualification of the PBPK platform for the intended purpose

Session 3: Reporting and Evaluation of predictive performance of the PBPK model

Session 4: Further discussions

Organising Committee

List of speakers:

Jan Welink

Anna Nordmark

Efthymios Manolis

Neil Parrott

Amy Cheung

Viera Lukacova

Masoud Jamei

Michael Block

Rolf Burghaus

Susan Cole

Ping Zhao

Leon Aarons

Ine Skottheim Rusten

Eva Gil-Berglund

EMA:

Enrica Alteri

Kevin Blake

Jane O'Sullivan

Monica Simeoni

Programme details

08:30–9:00 Registration

The workshop will be held in room 3A. Badges must be collected at the reception on the ground floor.

Day Chair **Jan Welink**, Dutch Medicines Evaluation Board (MEB), Chair of the Pharmacokinetic Working Party, European Medicines Agency (EMA)

09:00-09:10 Welcome and Opening

Enrica Alteri, Head of Medicines Evaluation Division, EMA

09:10-09:30 Session 1: Introduction and setting the scene to the draft PBPK Guideline

Anna Nordmark, Medical Products Agency (MPA)

Introduction of the PBPK Guideline and expectations of the day.

09:30-13:00 Session 2: Qualification of the PBPK platform for the Intended Purpose

Particular points for discussion include views of PBPK platforms companies and pharmaceutical industry interest groups on how qualification can be done in a more systematic way and with learnings from using PBPK for assessing DDI potential, predicting PK in paediatrics and evaluating biopharmaceutics.

09:30-09:45 **Efthymios Manolis**, EMA

CHMP qualification procedure on novel methodologies and how can it be used for qualification of the intended use.

09:45–10:05 **Neil Parrott**, IQ Group representative

10:05–10:25 **Amy Cheung**, EFPIA representative

10:25–10:40 **Viera Lukacova**, Gastroplus representative

10:40-10:55 Coffee Break

10:55–11:10 **Masoud Jamei**, SimCYP representative

11:10–11:25 **Michael Block**, PKSim representative

11:25–11:45 **Rolf Burghaus**, Bayer representative

11:45–12:15 Clarifying Questions to Speakers

12:15–13:00 **Discussion**

Panel: Joseph Grillo, Food and Drug Administration (FDA), Eva Gil-Berglund (MPA), Anna Nordmark (MPA), Efthymios Manolis (EMA), Jan Snoeys (Janssen), Xavier Pepin (AstraZeneca), Vikram Sinha (Merck), Alexandra Galetin (University of Manchester), Erik Sjögren (Uppsala University) Frank Bretz (Novartis)

13:00-14:00 **Lunch break**

14:00-15:55 **Session 3: Reporting and Evaluation of predictive performance of the PBPK model**

Particular points for discussion are what to include in the reporting and evaluation of the PBPK drug model from EU and US regulators, sensitivity analysis and uncertainty evaluation

14:00–14:15 **Susan Cole**, Medicines and Healthcare Products Regulatory Agency (MHRA)

Aspects from the draft guideline regarding reporting and evaluation of predictive performance - what is missing in submissions today?

14:15–14:30 **Ping Zhao,** FDA

Application of PBPK modelling to support dosing recommendations – the US FDA experience.

14:30–14:45 **Leon Aarons**, (University of Manchester)

Sensitivity analysis and uncertainty evaluation in the PBPK setting.

14:45–14:55 **Ine Skottheim Rusten**, Norwegian Medicines Agency (NoMA), Chair of the Modelling and Simulation Working Group (MSWG), EMA

Uncertainty quantification.

14:55-15:10 **Clarifying Questions to the Speakers**

15:10–15:55: **Discussion**

Panel: Ping Zhao (FDA), Ine Skottheim Rusten (NoMA), Andrew Thomson (EMA), Kevin Blake (EMA), François Bouzom (UCB), Mohamad Shebley (AbbVie), Leon Aarons (University of Manchester), Wilhelm Huisinga (University of Potsdam)

15:55-16:10 **Coffee Break**

16:10-17:00 **Session 4: Further discussions**

16:10-16:25 **Eva Gil-Berglund**, MPA

Overview of comments on the guideline received so far and a summary of major areas that require attention.

16:25–16:50: **Discussion**

Panel: Eva Gil-Berglund (MPA), Anna Nordmark (MPA), Susan Cole (MHRA), Ine Skottheim Rusten (NoMA), Ping Zhao (FDA), Joseph Grillo (FDA), Andrew Thomson (EMA), Kevin Blake (EMA), Efthymios Manolis (EMA)

16:50-17:00 **Closing remarks**

Travel and Accommodation

Participants must possess valid travel documents and, where relevant, a visa for entry into the United Kingdom. Should you require an official letter of invitation, please contact PKWP@ema.europa.eu.

Recording and Photography

The Agency records or broadcasts a number of its meetings, including some virtual meetings. This is part of the Agency's commitment to the principle of transparency as enshrined in the Treaty on the European Union. The conference will be recorded. By attending these events you consent to any photographing, recording, broadcast and publication of presentations on the EMA website.

WiFi access

WiFi is available throughout the EMA. Login details can be found on the back of your EMA access pass.

Restaurant facilities

Restaurant, deli bar and coffee bar are available (located on 4th floor) - please note you will need to have either £10.00 or €10.00 minimum cash in order to purchase a pre-paid canteen card

There are also many cafes and restaurants in the Canary Wharf area. More information can be found in the Canary Wharf area guide (restaurants, shops, etc.):

www.allinlondon.co.uk/regions/canary-wharf

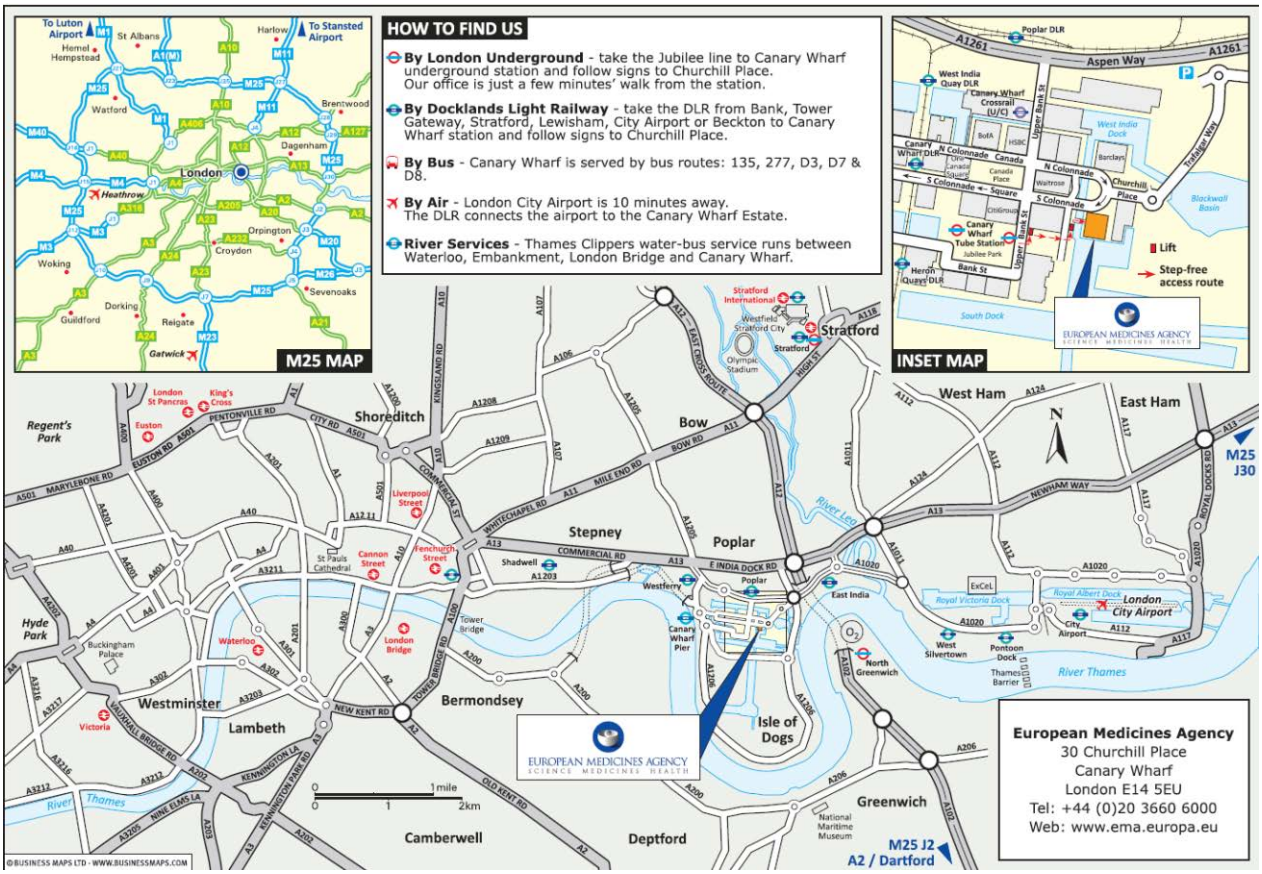
http://www.canarywharf.com/workwithus/The-Estate/Estate-Map/

Getting to Canary Wharf

The EMA is located in Canary Wharf, a business district in the east of London.

Please find below the public transport options for travelling to Canary Wharf together with the approximate journey times and the map of the area.

Directions to European Medicines Agency and map of the area



By Docklands Light Railway (DLR)

Both venues are a short walk from Canary Wharf or Heron Quays station on the DLR. Services run from Bank, Tower Gateway, Lewisham, Stratford, King George V and Beckton.

By Underground

The nearest stop for both venues is Canary Wharf station on the Jubilee Line. From East exit (NB. This is the closest exit to 30 Churchill Place): exit the station and turn left into Upper Bank Street, turn right at Canada Square and continue straight into Churchill Place.

By Bus

Canary Wharf is serviced by local bus numbers D3, D7, D8, 135 and 277.

River services

River services run between Embankment, London Bridge and Canary Wharf throughout the day. Canary Wharf pier is roughly a 15-minute walk from the European Medicines Agency.

From London City Airport

Take DLR City Airport to Canary Wharf (journey time is around 20 minutes).

From Gatwick Airport

Take a mainline train to London Bridge, then the Jubilee Line to Canary Wharf (journey time around 50 minutes).

From Heathrow Airport

Take the London underground Piccadilly Line to Green Park, change to the Jubilee Line to Canary Wharf (journey time around 1hr 20 minutes).

Alternatively, take the Heathrow Express train to Paddington, then the Circle or Bakerloo line to Baker Street, then the Jubilee Line to Canary Wharf (journey time around 1hr 20 minutes).

Alternatively, you can take the Heathrow Express train to Paddington, then the District or Circle Line to Tower Hill then the Docklands Light Railway (DLR) to Canary Wharf (journey time around 1hr 30 minutes).

From Stansted Airport

Take the Stansted Express to London Liverpool Street then the Circle Line to Tower Hill and change onto the DLR to Canary Wharf (journey time around 70 minutes).

From Luton Airport

Take a first Capital Connect train to London Bridge then the Jubilee Line to Canary Wharf (journey time around 60 minutes).

From St Pancras International train station

Take the Northern Line to London Bridge then the Jubilee Line to Canary Wharf (journey time around 45 minutes).

Contact

Should you have any questions, please contact Monica Simeoni or Kevin Blake via PKWPS@ema.europa.eu

Useful links

http://www.tfl.gov.uk/

National Rail

Gatwick Express

Heathorw Express

Stansted Express

Eurostar

Heathrow airport

Gatwick airport

London City

London Stansted

Hillgate travel