EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 March 2017
EMA/849195/2016
Human Medicines Research and Development Support Division

FP7 Small-population research methods projects and regulatory application workshop

29-30 March 2017, meeting room 3A-3M

asterix

IDeAl Integrated DEsign and AnaLysis of small population group trials

InSPiRe Innovative methodology for small populations research

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
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Item	Agenda of 29 March 2017	Presenters and speaker	Time
	Welcome	Enrica Alteri	10:00
1	**Session 1 – Setting the scene** Chaired by Cécile Ollivier and Frank Pétavy		
1.1	Overview on Asterix: Advances in Small Trials dEsign for Regulatory Innovation and eXcellence	Kit Roes	10:10
1.2	Overview on IDeAl: DEsign and AnaLysis of clinical trials in small sample population groups	Ralf-Dieter Hilgers	10:30
1.3	Overview on InSPiRe: Innovative methodology for Small Populations Research	Nigel Stallard	10:50
1.4	Regulatory pathways for supporting novel methodologies and opportunities for interactions with regulators	Anja Schiel Ine Skottheim Rusten	11:10
1.5	Patients' perspective	Christine Lavery	11:30
	Discussion	All	11:40
	Short break		11:50
2	**Session 2 - Evidence synthesis** Chaired by Ralf-Dieter Hilgers and Norbert Benda		
2.1	Presentation of work package results	Tim Friede Kit Roes Armin Koch & Kristina Weber Stephen Senn	12:00
2.2	Discussion: • How to deal with potential heterogeneity in evidence synthesis / meta-analysis of small population clinical trials. • New approaches to include historical controls and/or prior clinical trial data into design and analysis of small population trials. • Sharing clinical trial data.	Ségolène Aymé Dirk Mentzer	12:45
2.3	Wrap-up of session 2	Chairs	13:20
	Lunch break	Chairs	13:30
3	**Session 3 – Extrapolation** Chaired by Tim Friede and Cécile Ollivier		
3.1	Presentation of work package results	Sarah Zohar Franz König Holger Dette	14:30
3.2	Discussion: • Extrapolation of dose response information: Design and Analysis. • Adapting the significance level for clinical trials in vulnerable, small populations, based on prior evidence of larger populations. • Confirmatory design and analysis allowing adaptive design modifications, such as selection of a more promising subgroup	Dirk Mentzer Andrew Thomson Heinz Schmidli	15:15

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3.3	Wrap-up of session 3		15:50
	Coffee break	Chairs	16:00
4	**Session 4 - Level of evidence and decision theoretic aspects** Chaired by Kit Roes and Frank Pétavy		
4.1	Presentation of work package results	Nigel Stallard Carl-Fredrik Burman Ralf-Dieter Hilgers Martin Posch	16:30
4.2	Discussion • Value, performance and implications of different randomization methods in small size trials. • Decision-theoretic and value-of-information models (taking patient horizon into account) for clinical trials in small populations. • Decision theoretic approaches for targeted therapies with special focus on societal in contrast to commercial sponsor's perspective. • Adapting the “usual” level of evidence.	Anja Schiel Aaron Dane	17:15
4.3	Wrap-up of session 4		17:50
	End of Day 1		18:00

Item	Agenda of 30 March 2017	Presenters and speaker	Time
	Start of Day 2		
5	**Session 5 - Study Endpoints and statistical analysis** Chaired by Martin Posch and Armin Koch		
5.1	Presentation of work package results	Geert Molenberghs Hanneke van der Lee Susanne Urach Robin Ristl	08:30
5.2	Discussion: • Improving value and potentially efficiency (statistically and in terms of recruitment) of trials with patient centric outcomes. • Surrogate endpoints: Assessing, validation • Leveraging multiple endpoints in small trial size setting.	Norbert Benda Bernd Jilma	09:15
5.3	Wrap-up of session 5	Chairs	09:50
	Coffee break		10:00
6	**Session 6 - Innovative designs, Pharmacometrics, modelling and optimal designs** Chaired by Nigel Stallard and Bernd Jilma		
6.1	Presentation of work package results	France Mentré Stephen Senn Mats Karlsson Moreno Ursino Stavros Nikolakopoulos	10:30
6.2	Discussion: • Multi-armed trial, with adaptive features, in small populations. • PtC for N-of-1 trials, Cross over trials, • Pharmacometrical modelling and design considerations of NLMEM • Optimal sequential designs and sample size reassessment in small populations (with large prior uncertainty). • Dose-finding including PK and dose limiting toxicities.	Joseph Standing	11:15
6.3	Wrap-up of session 6	Chairs	11:50
7	**Session 7: Wrap-up and next steps** Chaired by Anja Schiel		
	• Feedback from sessions 2 to 6 • Way forward and collaboration between InSPiRe, IDeAl and Asterix • Summary EMA	Session Chairs Frank Pétavy	12:00
8	Discussion		12:30
	Final wrap-up and conclusions		
	End of Day 2 and of the workshop		13:00

Coordinating committee

Norbert Benda, Bundesinstitut für Arzneimittel und Medizinprodukte

Kit C.B. Roes, University Medical Center Utrecht

Ralf-Dieter Hilgers, Universitaetsklinikum Aachen

Armin Koch, Medizinische Hochschule Hannover

Franz König, Medizinische Universität Wien

Martin Posch, Medizinische Universität Wien

Nigel Stallard, University of Warwick

Ferrán Torres, Hospital Clinic de Barcelona

Cécile Ollivier, European Medicines Agency

Frank Pétavy, European Medicines Agency

List of speakers

Enrica Alteri, European Medicines Agency

Cécile Ollivier, European Medicines Agency

Frank Pétavy, European Medicines Agency

Kit C.B. Roes, University Medical Center Utrecht

Ralf-Dieter Hilgers, Universitaetsklinikum Aachen

Nigel Stallard, University of Warwick

Anja Schiel, Statens legemiddelverk

Ine Skottheim Rusten, Statens legemiddelverk

Christine Lavery, Eurordis

Tim Friede, University Medical Center Göttingen

Armin Koch, Medizinische Hochschule Hannover

Kristina Weber, Medizinische Hochschule Hannover

Stephen Senn, Luxembourg Institute of Health

Ségolène Aymé, INSERM

Dirk Mentzer, Paul-Ehrlich-Institut

Sarah Zohar, INSERM

Franz König, Medizinische Universität Wien

Holger Dette, Ruhr-University Bochum

Andrew Thomson, European Medicines Agency

Heinz Schmidli, Novartis

Carl-Fredrik Burman, AstraZeneca

Martin Posch, Medizinische Universität Wien

Aaron Dane, DaneStat

Geert Molenberghs, Universiteit Hasselt

Hanneke van der Lee, Woman-Child Center, AMC

Susanne Urach, Medical University of Vienna

Robin Ristl, Medizinische Universität Wien

Bernd Jilma, Medizinische Universität Wien

Norbert Benda, Bundesinstitut für Arzneimittel und Medizinprodukte

France Mentré, INSERM

Mats Karlsson, Uppsala University

Stavros Nikolakopoulos, UMC Utrecht

Moreno Ursino, INSERM

Joseph Standing, University College London

Practical information

Arrival at the Agency

On arriving for your meeting at 30 Churchill Place, please report to reception where you will be issued with an access pass. This pass will allow you to access our industry lounge, which you are welcome to utilise during your visit. The industry lounge is located through the sliding doors to the right of the reception desk past the security turnstiles. Your EMA contact point will meet you here.

The Agency requires all visitors to provide a **valid photo ID** on arrival, such as a passport, an identity card or driving licence.

Physical disability

Let us know if you would like any specific help or information that would make your stay more comfortable. We will be very happy to help.

Registration

We strongly advise you to arrive 40 to 50 minutes before the start of the workshop, to allow you time for registration and settling down.

Meeting room

The plenary meeting will take place in the room 03-A.

Wi-Fi access & Laptop computers

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

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. This workshop will be broadcast and recorded. By attending this event you consent to any photographing, recording, broadcast and publication of presentations on the EMA website.

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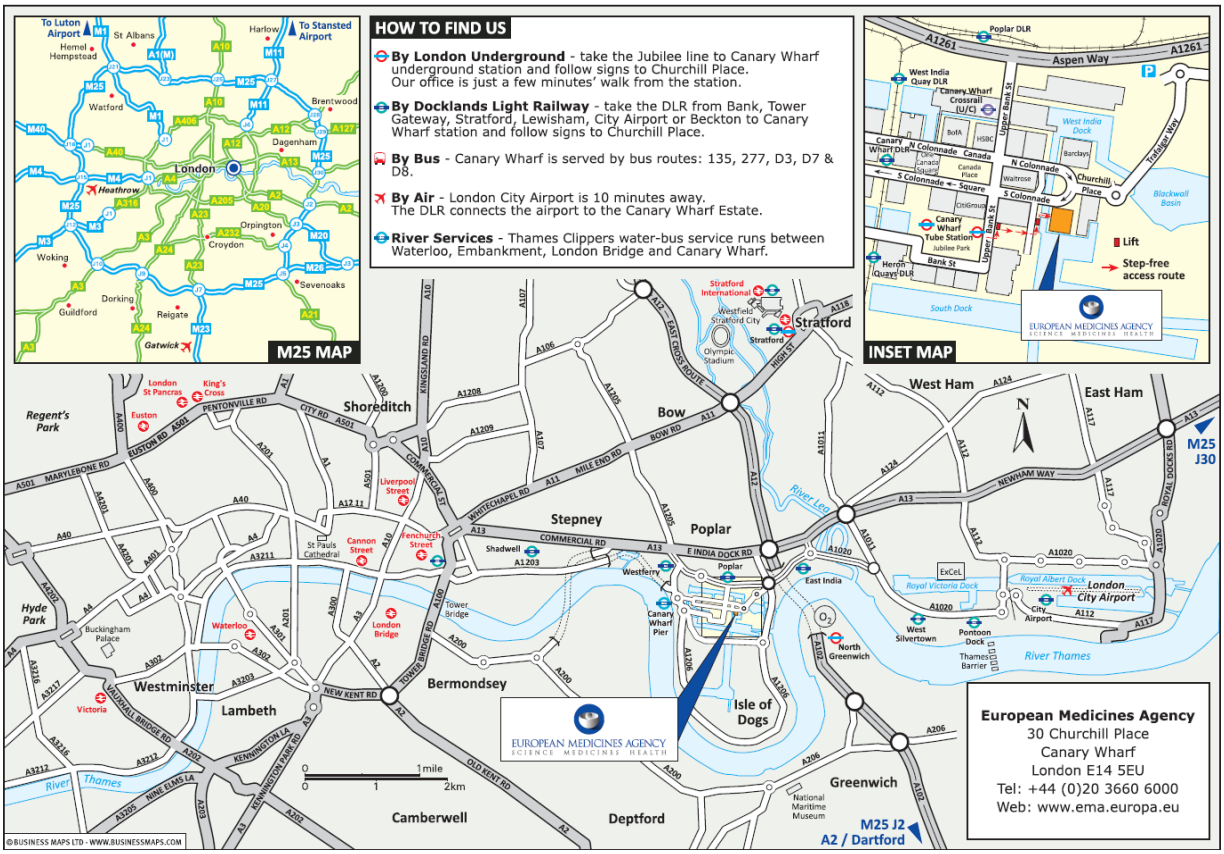
Contact

Should you have any questions, please contact PMEworkshops@ema.europa.eu

Directions to European Medicines Agency and map of the area

European Medicines Agency
30 Churchill Place, Canary Wharf
London E14 5EU, United Kingdom



By Underground

The nearest stop for Churchill Place 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 Docklands Light Railway (DLR)

The Agency is a short walk from Canary Wharf station on the DLR. Services run from Bank, Tower Gateway, Lewisham, Stratford, King George V and Beckton. Exit into The South Colonnade, turn left towards Canada Square continuing 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.

From Heathrow Airport

Take the London underground Piccadilly Line to Green Park, change to the Jubilee Line to Canary Wharf.

Alternatively, take the Heathrow Express train to Paddington. From Paddington you can take the Circle or Bakerloo line to Baker Street, then the Jubilee Line to Canary Wharf.

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.

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.

From Luton Airport

Take a first Capital Connect train to London Bridge then the Jubilee Line to Canary Wharf.

From St Pancras International train station

Take the Northern Line to London Bridge then the Jubilee Line to Canary Wharf.

Plan your journey: https://tfl.gov.uk/plan-a-journey/ and http://www.nationalrail.co.uk/

By car

There are no parking facilities at 30 Churchill Place and it is recommended that you take public transport. However, four nearby public car parks are operated by Canary Wharf. Rates and further information can be found on the Canary Wharf website: http://www.canarywharf.com/aboutus/The-Estate/Travel-/Roads--Parking/