

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

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EMA workshop on qualification and reporting of physiologically-based pharmacokinetic (PBPK) modelling and simulation, EMA 2016-11-21

Please provide written comments!

- Deadline for comments Jan 31st, 2017
- Use specific form and be as clear and constructive as possible

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2016/10/event_detail_001331.jsp&mxxxid=WC0b01ac058004d5c3

• We provide a response to each comment in a tabular format



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17 November 2016

<Name of committee (Committee abbreviation)>

Overview of comments received on '<document title>' (EMA/.../...)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	
2	
3	



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IQ Consortium

International Consortium for Innovation and Quality in Pharmaceutical Development



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Selection of General comments from IQ

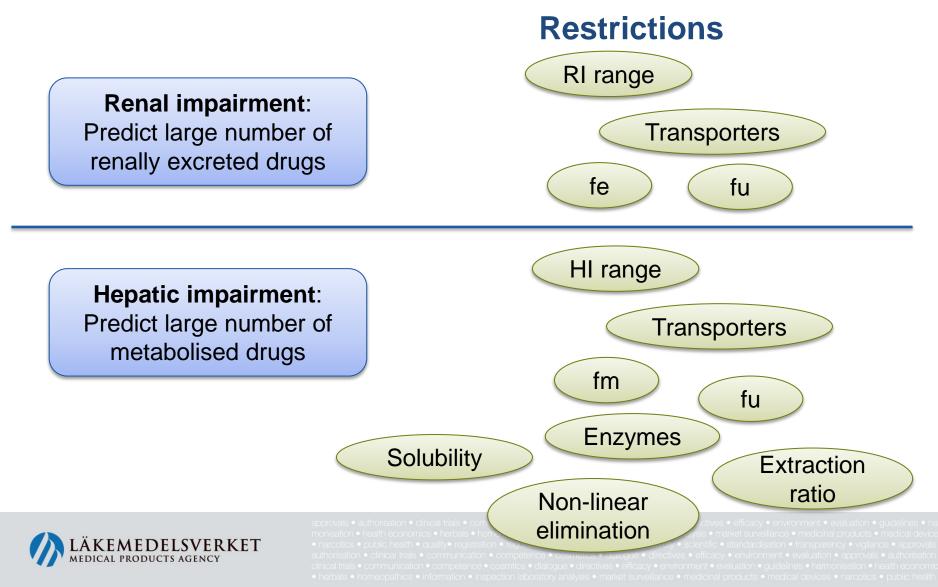
• Include other areas than DDI, such as mechanistic absorption issues (PPI DDIs, food-effect), hepatic and renal impairment, multiple-dose pharmacokinetics, induction, etc

Qualification needed before this may be accepted

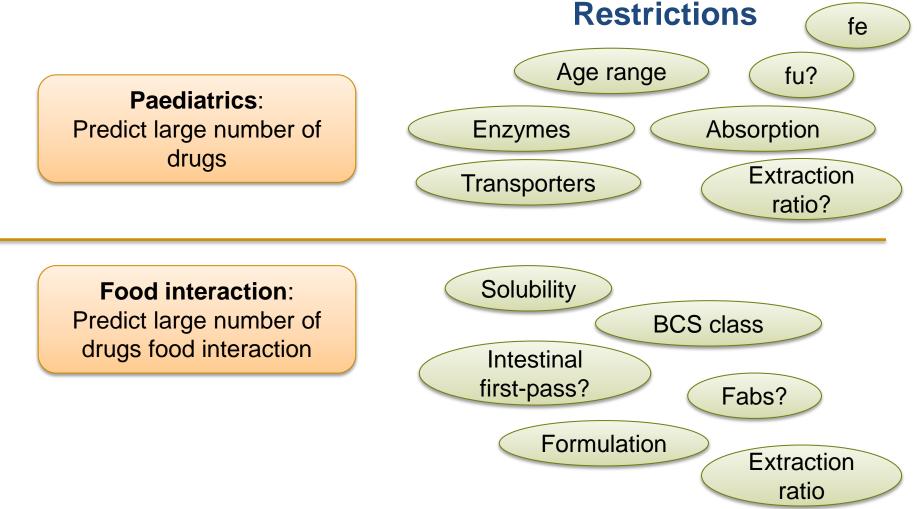


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Backup slide: Translating qualification dataset requirements



Backup slide: Translating qualification dataset requirements





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General comments

- Is i.v. data mandatory? (indicated by the GL text)
- Clearer separation between drug and system
- Need to re-perform all submitted PBPK simulations using the latest (qualified) version?

The version used needs to be qualified. If old but qualified - discuss consequences.



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Specific comments

- How will the CHMP qualifications be listed at the Ema web? Can this be a source to what components are qualified?
- Are all papers included in peer reviewed journals considered qualified as long as enough detail is provided?
- Version control: Full qualification or bridging dataset?

Depends on alterations. Full dataset is default.



Specific comments

- Qualification dataset: clarify selection criteria with regards to PK characteristics. Give examples for perpetrator and victim.
- What does qualified "scenario" mean? Could massbalance data or DDI with perpetrator be a limiting condition?
- Requirements for in-house vs commercial platform?
 What differences? (encouraged to seek central advice)
- Concentration at site of enzyme how?
- Guidance on sensitivity analysis



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Examples of questions to take home

- How do we streamline the qualification process to allow for it to be as fast as possible?
- For the qualification what is adequate precision?
- When we apply a qualification having a certain precision, how do we take the uncertainty into account?
- Clarify qualification requirement for low impact and possible consider high ethical impact (supporting study design paediatrics)
- Clarify how to select parameters which should be subject to SA
- Which qualification requirements should be set for situations where parts of the platform behaviour has been qualificed before through the CHMP procedure.



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further

- Learned societies qualification: details
- Possibility to retract qualifications?



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The secret of getting ahead is getting started

-Mark Twain



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