



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Challenges in moving to a circuit/mechanism-based approach such as RDoC from an EMA perspective

Definition of conditions and endpoints

17th Annual ISCTM Conference

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Disclaimer

The views expressed in this presentation are the personal opinion of the author and should not be understood as being made on behalf of or reflecting the position of the EMA or one of its committees or working parties.



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- Ontology of mental illnesses
- Selection of population
- Measurement of the effect



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What are mental illnesses?

“RDoC framework conceptualizes mental illnesses as brain disorders”¹

“RDoC is [...] agnostic about the mechanistic and causal relationships between psychology and biology and [...] advocates rigorous integration of the two domains”²

“Mental disorders are best characterized in terms of the interaction between different components in a psychopathology network [...] connected through a myriad of biological, psychological and societal mechanisms”³

¹ Insel, T. et al, 2010 Am J Psychiatry 167:7, July 2010

² Lake, J.I. et al. 2017 Zeitschrift für Psychologie, 225(3), 170–174

³ Borsboom, D., 2017 World Psychiatry, 16(1)



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How would a good way to select patients look like?

It should be **reproducible**, select rather **homogeneous populations**, and identify groups **likely to benefit** from a certain treatment.



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DSM-V entity	kappa
Schizophrenia	0.46
MDD	0.28

¹

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¹ Regier, D.A., 2013. J Am. Psych, 170(1), 59-70.



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In a sample of 1566 patients, DSM-IV MDD criteria were met in 170 different ways²

¹ Regier, D.A., 2013. J Am. Psych, 170(1), 59-70.

² Zimmerman, M., 2015. Compr. Psych, 56, 29-34.



Where do we go from here?

While the limitations of the available systems (especially for some of the diagnoses) are acknowledged, there is no current alternative gold standard.

Extensive interactions between academics, developers and regulators are encouraged.

The European Medicines Agency has a scheme for the [Qualification of Novel Methodologies](#), giving advice early on in the development and publishing the outcome of final qualifications. Earlier – preliminary interactions are encouraged with the [Innovation Task Force](#).



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26 July 2018
CHMP/EWP/566/98 Rev.3
Committee for medicinal products for human use (CHMP)

Guideline on clinical investigation of medicinal products in the treatment of epileptic disorders

Draft



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26 July 2018
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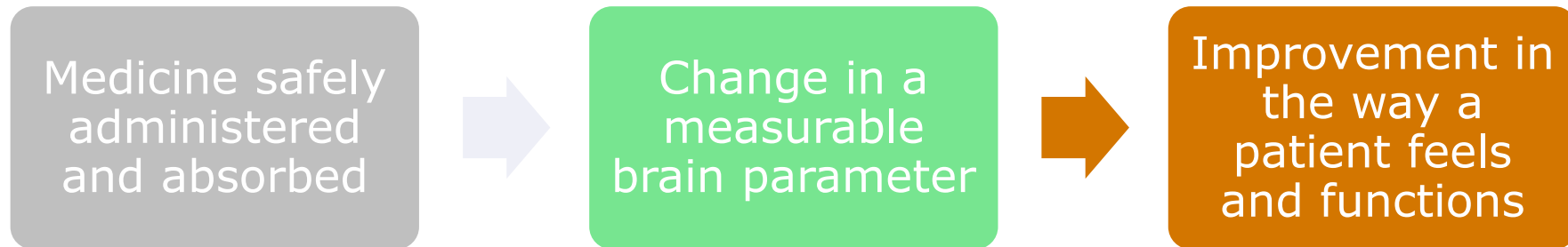
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26 March 2015
EMA/CHMP/771815/2011, Rev. 2
Committee for Medicinal Products for Human Use (CHMP)

Guideline on clinical investigation of medicinal products
for the treatment of Multiple Sclerosis

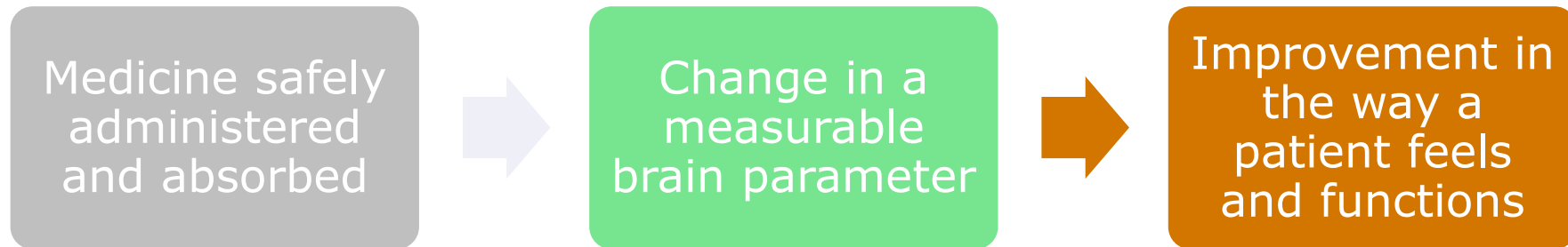


An hypothesis-driven drug development





An hypothesis-driven drug development



FIH and PK studies

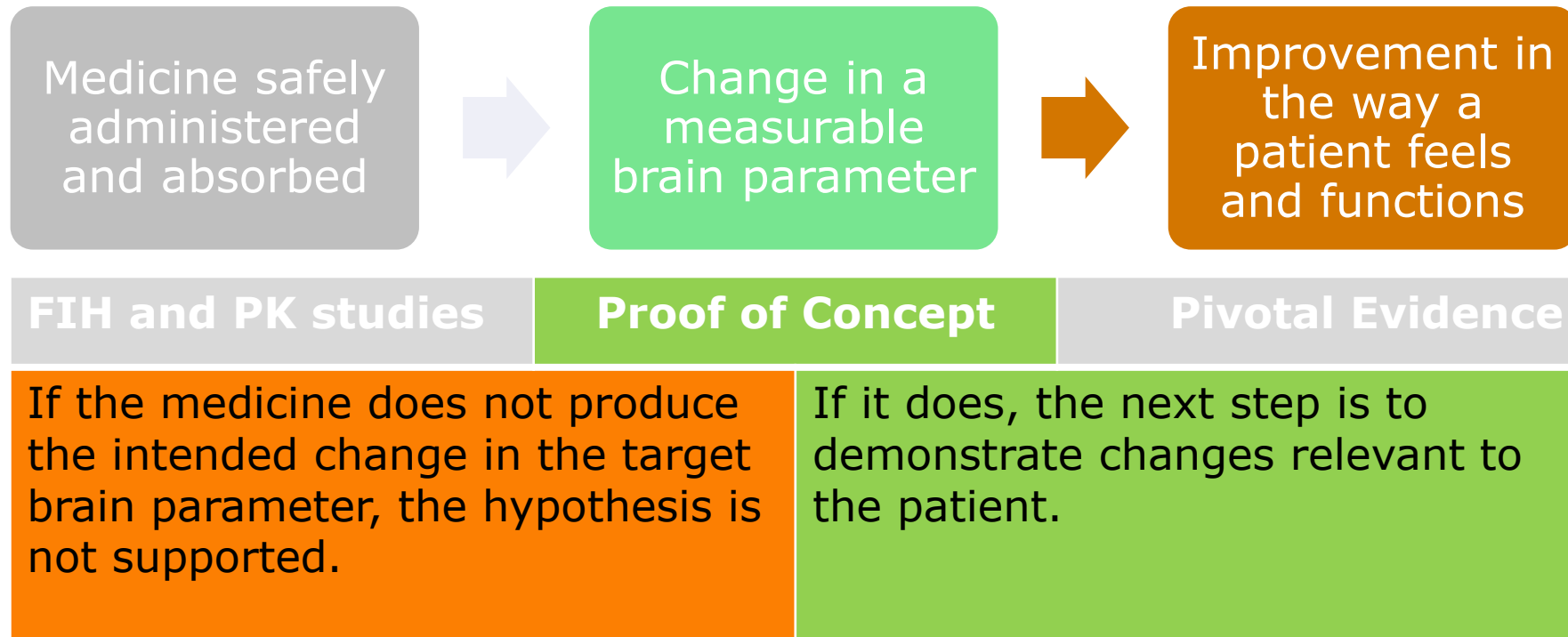
Proof of Concept

Pivotal Evidence

In addition to the usual safety and pharmacokinetics parameters, hypothesis-specific early Proof of Principle might be generated.

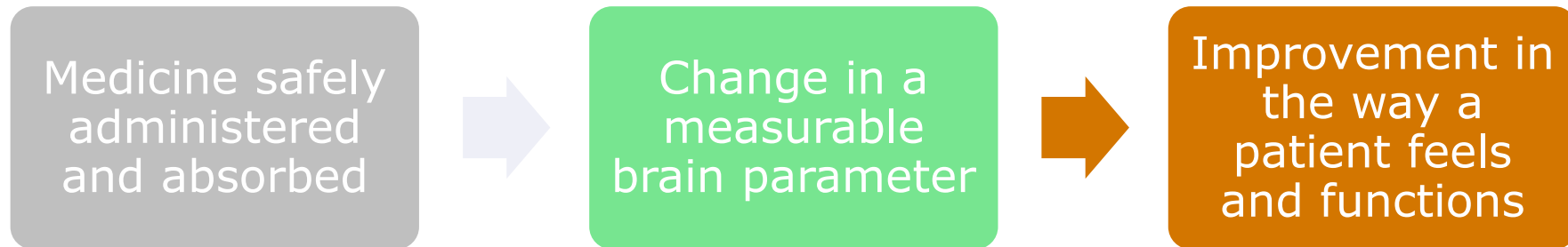


An hypothesis-driven drug development





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FIH and PK studies

Proof of Concept

Pivotal Evidence

A clinically relevant benefit – to weight against the risks - needs to be established and quantified. Biomarkers are unlikely to be sufficient. The currently available outcome measurement tools are far from ideal- engagement with regulators on other ways to measure such outcomes are encouraged.



What is the matter with you?



~~What is the matter with you?~~

What matters to you?¹

¹ Berwick, D.M., 2016. JAMA, 315(13), 1329-1330.



Any questions?

Further information

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