

Fit-for-Purpose Initiative Overview

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Disclaimer

- Views expressed in this presentation are those of the speaker and do not necessarily represent an official FDA position
- I do not have any financial disclosures regarding pharmaceutical drug products

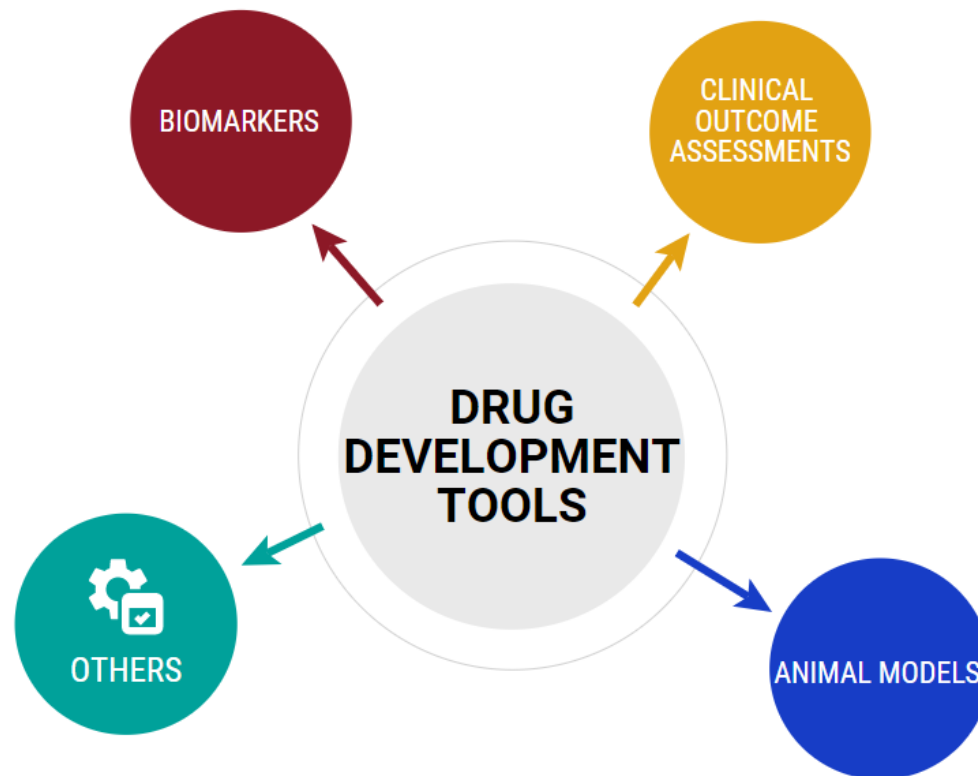
Objectives

- Background
- Process
- Submission Criteria
- Tools deemed “fit-for-purpose” to date
- Impact

Background

- In 2004, FDA published a whitepaper entitled, ***“Innovation or Stagnation: Challenge and Opportunity on the Critical Path to Medical Products”***
- FDA launched the Critical Path Initiative (CPI) to encourage powerful scientific and technical innovations for more efficient drug development

Drug Development Tools (DDTs)



Fit-for-Purpose Initiative

- Includes methodologies, in silico disease models
- Tool is deemed “fit-for-purpose” based on regulatory evaluation, and made available on FDA.gov for public use

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REVIEW PROCESS

How to
Reach Us

Drug Development Tools: Fit-for-Purpose Initiative

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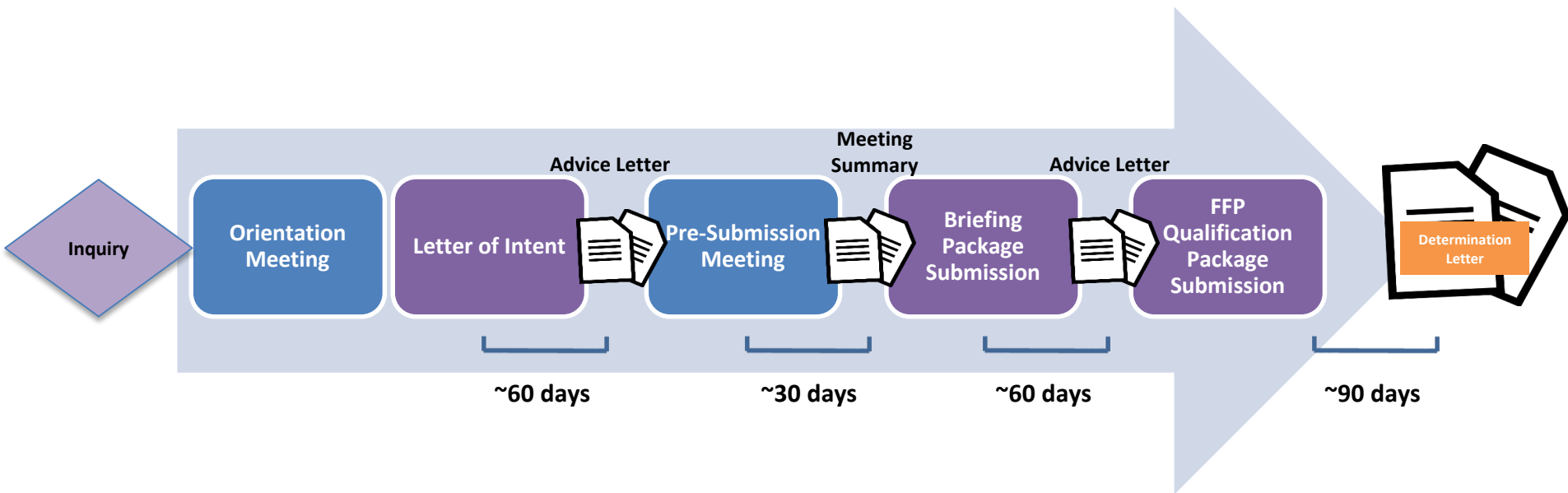
Background

The Fit-for-Purpose (FFP) Initiative provides a pathway for regulatory acceptance of dynamic tools for use in drug development programs. Due to the evolving nature of these types of drug development tools (DDTs) and the inability to provide formal qualification, a designation of 'fit-for-purpose' (FFP) has been established. A DDT is deemed FFP based on the acceptance of the proposed tool following a thorough evaluation of the information provided. The FFP determination is made publicly available in an effort to facilitate greater utilization of these tools in drug development programs.

Contact Us

~~For more information about the FFP Initiative, please contact~~
DrugDevelopmentTools@fda.hhs.gov

Fit-for-Purpose Review Timeline



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SUBMISSION CRITERIA

Letter of Intent

- Describes context of use (COU)
- Summarizes content of the briefing document
- Describes intent of submission
 - To obtain consultation and advice on the COU and/or data and modeling plan
- Provide any other information may guide our review
 - Description of the tool and how it relates to the previously accepted model
 - What intended elements will be built in this model
 - What will be submitted within the package and if it invokes specific software for review
 - *Any specific questions that necessitate our response*

Additional Considerations

- State the key issue that this tool will address in drug development
- Define data integration approach
- Describe all data sets used to inform the model
- Validate read-outs from other clinical trials (e.g., published in literature) to validate model predictions/test the robustness of the model
- Use a subset of the database for model validation purposes; provide a plan for creating this subset

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TOOLS DETERMINED TO DATE

Fit-For-Purpose Tools and Supporting Information:

Disease Area	Submitter	Tool	Trial Component	Issuance Date and Supporting Information
Alzheimer's disease	The Coalition Against Major Diseases (CAMD)	Disease Model: Placebo/Disease Progression	Demographics, Drop-out	Issued June 12, 2013 <ul style="list-style-type: none"> Determination Letter The tool is freely available at: https://bitbucket.org/metrumrg/alzheimers-disease-progression-model-adascog/wiki/Home
Multiple	Janssen Pharmaceuticals and Novartis Pharmaceuticals	Statistical Method: MCP-Mod	Dose-Finding	Issued May 26, 2016 <ul style="list-style-type: none"> Determination Letter Statistical Review Pharmacometric Review

Determination Letter

Please refer to your submission, provided on behalf of the Coalition Against Major Diseases (CAMD), which contains a package intended to support the utility of a trial simulation tool for planning certain clinical trials involving patients with mild to moderate dementia of the Alzheimer's type.

We have completed our review of your submission and have determined it is fit-for-purpose in the contexts, and with the caveats and constraints, outlined in this letter.

Goal and Intended Applications

The goal of the proposed simulation tool is to serve as a public resource for sponsors designing trials of new therapies for Alzheimer's disease (AD). CAMD intends that this simulation tool will provide quantitative support in the design and planning of clinical trials involving subjects with mild to moderate AD. The submission further suggests that the proposed tool could be used during all clinical stages of AD drug development, including proof-of-concept, dose-ranging, and confirmatory trial design and could encompass various types of treatment mechanisms (e.g. symptomatic and disease-modifying).

The submission outlines several intended applications of the proposed tool:

- Sample size calculations
- Determination of optimal trial durations and treatment effect measurement times
- Comparison of the sensitivity of competing trial designs to assumptions about the types of expected treatment effects (time to maximal effect, effects that increase or decrease over time)
- Determination of the most appropriate data analytic methods for novel trial designs

FDA Assessment

Quantitative disease-drug-trial models are potentially useful tools to represent the time course of clinical outcomes, placebo effects, drug pharmacologic effects and trial execution characteristics. The CAMD quantitative AD model was developed based on patient-level and summary data to support the design of future drug development studies in patients with mild to moderate AD. Different data resources (e.g., derived from literature, the AD Neuroimaging Initiative (ADNI), and CAMD database) were used to build up the current model and describe longitudinal changes

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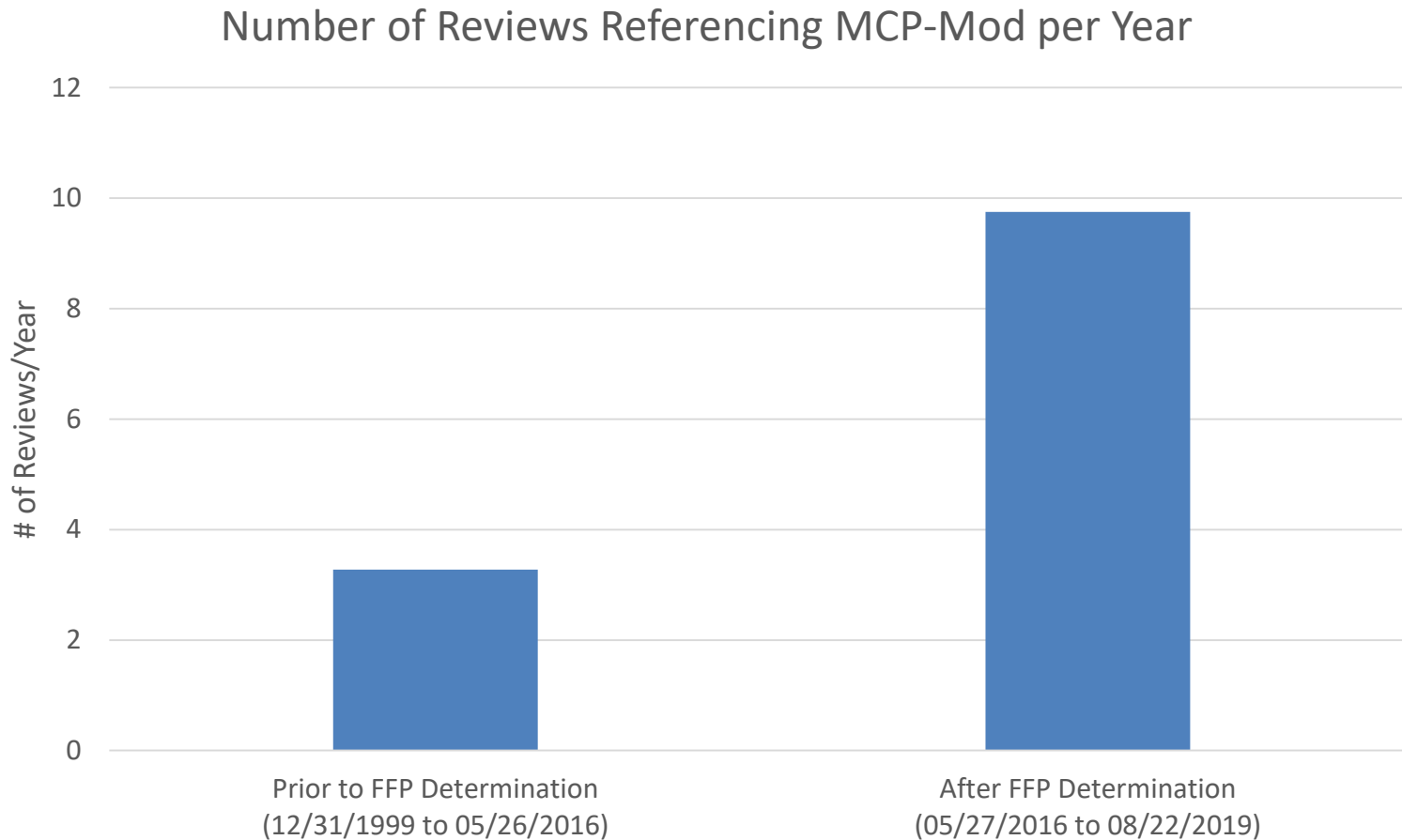
IMPACT

MCP-Mod

- Statistical methodology for model-based design and analysis of Phase II dose finding studies under model uncertainty
- Serves as a principled strategy to explore and identify adequate doses for drug development

MCP-Mod

Utilization before and after FFP determination



Data Sharing

- Tools made publicly available on FDA.gov
- Contingent on data sharing
- Data sharing is encouraged

Useful Links

- CDER's DDT Programs and Initiatives -
<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm426815.htm>
- CDER's Fit-for-Purpose Initiative -
<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm505485.htm>

Acknowledgements

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