# Exposure-response modeling for dose selection under model uncertainty: Extending the MCP-Mod approach

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Abstract

Poor dose-regimen selection resulting from insufficient knowledge of the dose-exposure-response relationship remains one of the key challenges in clinical drug development, believed to be associated with the high attrition rates observed in confirmatory trials. Different methods have been proposed to improve on the conventional, inefficient paradigm of pairwise testing of active doses versus placebo, among them MCPMod. This approach has the appealing feature of combining well-established aspects of hypothesis testing and modeling, implementing dose-response estimation and dose selection under model uncertainty. MCPMod has recently received a positive Qualification Opinion from CHMP/EMA, as well as a Fit-for-Purpose denomination from the U.S. FDA. The original formulation and extensions to date of MCPMod have been restricted to dose-response modeling and testing of dose-response signal, under a wide range of response types (e.g., continuous, binary, time to event, etc.). This talk describes an extension of the MCPMod methodology to exposure-response modeling (and signal testing) under model uncertainty. Examples and simulations will be presented to illustrate the use of the proposed approach, using the current implementation of MCPMod in the DoseFinding R package.

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