OPTIMIZING OINDP REGULATORY PATHS WITH MODEL MASTER FILES

While there is universal consensus on the value of streamlining and speeding up the drug development process, the pharmaceutical industry continues to face challenges in aligning all parties on the path to this important destination.

For example, great promise is encapsulated in the shift to "quantitative medicine" and the development of sophisticated digital solutions to simulate biological processes and outcomes.

However, points of friction still exist around legacy regulatory frameworks, which place burdensome and sometimes avoidable requirements on the companies pioneering these technologies. A case in point is the need to repeatedly provide validation and verification details for the same simulation model when supporting multiple submissions from multiple applicants.

In this context, a Model Master File (MMF) plays a crucial role in helping unlock the emerging potential of the quantitative medicine landscape. MMFs are effectively repositories for validated models, enabling regulatory submission and review to be streamlined where these models are reused. The premise is similar to that of a Drug Master File (DMF), which provide the means to repeatedly reference detailed 'master' information without the need for it to be resubmitted multiple times. And, just as is the case with DMFs, MMFs are entirely confidential, thus safeguarding the intellectual property of the companies who are responsible for developing the technology in the first place.

The dynamics surrounding the use of MMFs, and their increasing significance to modern drug development, is discussed in depth in a recent paper co-authored by (among others) Dr. Will Ganley, Nanopharm's Manager, Computational Pharmaceutics, and Dr. Jan de Backer, CEO of Fluidda, a key Nanopharm partner.

Published in *Pharmaceutical Research*,[1] an official journal of the American Association of Pharmaceutical Scientists, the piece provides a comprehensive overview of the benefits of MMFs for technology providers like Nanopharm and Fluidda as FDA-acknowledged vehicles for confidential sharing of validated computational models as part of a regulatory review. More broadly, it highlights how MMFs can be seen as a linchpin for connecting technology companies and regulators, facilitating more productive ongoing

[1] https://link.springer.com/article/10.1007/s11095-025-03833-3

communication between the two parties and, over time, supporting more effective use of modelling and simulation as “trusted tools in the drug development process”.

Bringing theory to life, the piece includes five case studies that demonstrate important applications of the MMF. This includes discussion of Nanopharm’s SmartTrack™ platform and its use of Computational Fluid Dynamics (CFD) and Physiologically based pharmacokinetic (PBPK) modelling to demonstrate alternative bioequivalence in Orally Inhaled and Nasal Drug Products (OINDPs).

The capability of SmartTrack™ to accurately predict biological outcomes delivers clear advantages for derisking clinical trial design and optimising candidate batch selection. Indeed, this use of modelling was referenced in a series of updated Product Specific Guidances (PSGs) published by the FDA in 2024, indicating the regulator’s support for the use of alternatives to Clinical Endpoint Studies in an abbreviated new drug application (ANDA).

As noted in the case study, both CFD and PBPK models within the SmartTrack™ platform are validated in accordance with the V&V40 standard.[2] Current practice would dictate that the documentation and some data generation must, therefore, be completed separately for each new application of the model. The use of an MMF in this context would prevent the need for much of this repetitive work, simplifying and accelerating the process.

Furthermore, while an MMF must be referenced under a closely defined application scenario, there is scope for its contents to be expanded over time, laying ever stronger and broader foundations for future implementation. In the case of OINDPs, for example, an MMF could be broadened out to support multiple inhaler types, aerosol particle sizes or flow dynamics.

But, as the article’s authors indicate, for MMFs to fulfil this future potential, clear guidelines will be essential for defining acceptable practices for model modifications and the scope of verification required for use in different contexts. Only then can credibility and reliability be assured.

Additionally, there is an imperative to address the existing framework supporting the relationship between technology companies and the FDA, which is arguably not currently fit for purpose. Good work has been

[2] https://www.asme.org/codes-standards/find-codes-standards/assessing-credibility-of-computational-modeling-through-verification-and-validation-application-to-medical-devices

done by the Quantitative Medicine Center of Excellence (QM CoE) and the Center for Research on Complex Generics (CRCG) to facilitate discussions around modelling and simulation between the two parties, but any direct dialogue is typically focused on individual drug applications or sometimes research grants. Interactions are almost exclusively limited to specific NDA and ANDA submissions, where information is relayed via the intermediary of the submitting organisation.

So, while much of the promise of MMFs is encapsulated in sophisticated simulation technologies, collaboration will be essential in unlocking its full potential. By improving understanding and communication between technology companies and regulators, computational models can be integrated more closely into regulatory frameworks, helping usher in the age of qualitative medicine and promoting a more efficient pathway for the development of safe and effective drugs.

To read the article in full, please follow this link, and for more information about MMFs and modelling technologies, including Nanopharm's SmartTrack™ platform, contact our team today.