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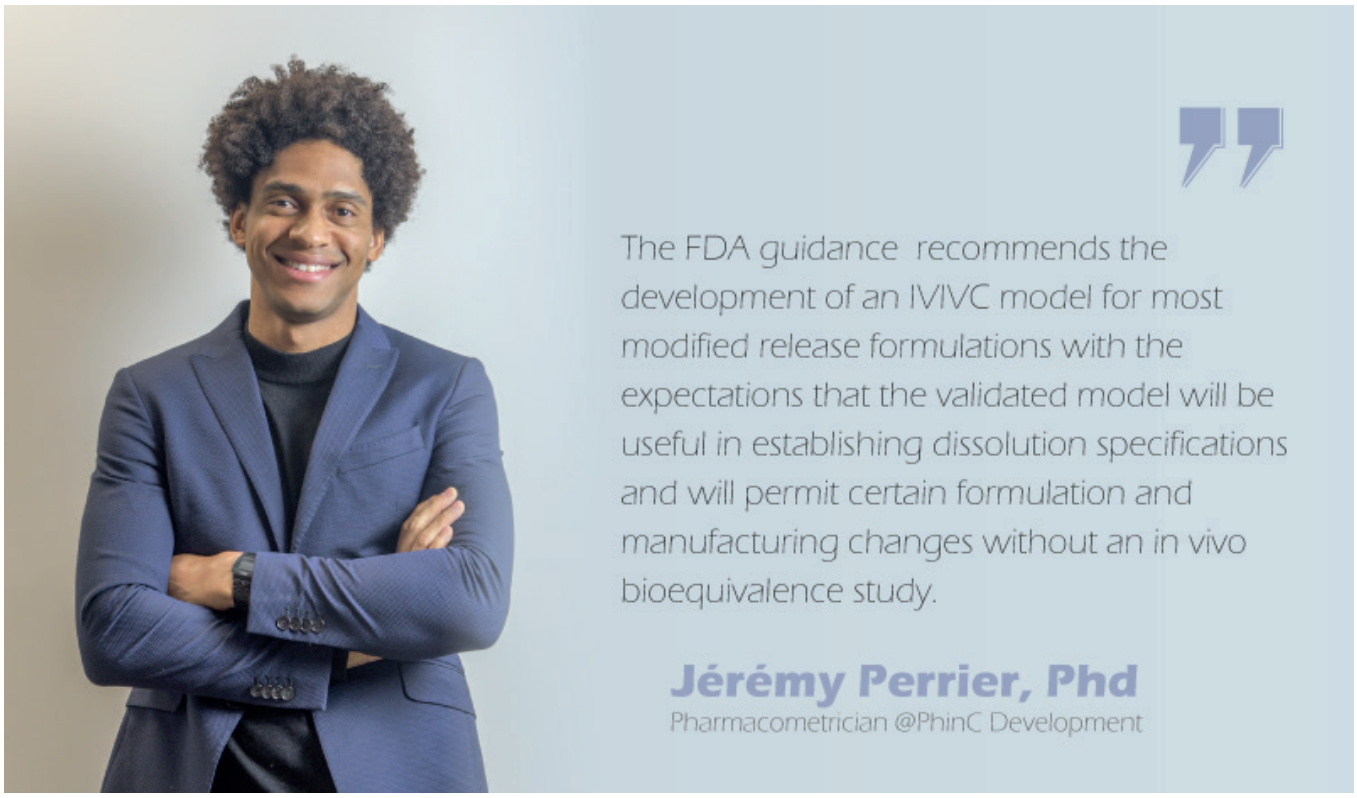
In vitro-In vivo Correlation (IVIVC), a strategic tool in drug development

At PhinC Development, IVIVC is an integral part of the modeling strategy to support each steps of the Drug Development. To present and explain this practice we interviewed Jeremy Perrier, Pharmacometrician at PhinC Development. Jeremy is a major contributor to PBPK practices and new application such as modeling of intra-articular injection.



What is an IVIVC and what are the advantages?

IVIVC is a correlation which allows the prediction of the in vivo outcome of a drug based solely on its in vitro release profile. More precisely it is a predictive mathematical model describing the relationship between an in vitro property of a dosage form and an in vivo response. Generally, the in vitro property is the drug release in a dissolution apparatus and the in vivo response is the corresponding amount that enters the systemic circulation following administration. This relationship is more likely to exist for drugs with high solubility because dissolution will be the limiting factor driving the process of absorption. Once a meaningful IVIVC has been validated the principal advantages are the improvement of the product quality and moreover the possibility to use it as a replacement of in vivo bioequivalence studies.

Why conduct an IVIVC and for what type of applications?

The FDA guidance[1] recommends the development of an IVIVC model for most modified release formulations with the expectations that the validated model will be useful in establishing dissolution specifications and will

[1] FDA Guidance for Industry. Extended Release Oral Dosage Forms: Development, Evaluation, and Application of In Vitro/In Vivo Correlations. Sep 1997

permit certain formulation and manufacturing changes without an in vivo bioequivalence study. The main applications are the optimization of formulation and the application of small changes in the formulation and manufacturing without the need for additional clinical studies. However, IVIVC can be valuable at all stages of the drug development. In the early stages a correlation of the drug in animal models provides an idea about the feasibility of the drug delivery system for a given candidate. Then during the clinical stages and in the post marketing authorization this is where it is most beneficial with the possibility of biowaiver for all the different formulation and manufacturing changes pre- and post-approval.

Can you tell us about your experience as a modeler?

At PhinC Development we support Sponsors throughout their drug development programs. As a pharmacometrician we use the IVIVCPlus module from the GastroPlus® software [author's note: Simulations Plus, Inc Lancaster] for our modeling approaches. It was the first software program to offer "mechanistic deconvolution" which deconvolute or fit the in vivo dissolution versus time along the gut. It is a very powerful tool and the real advantage is that it can be linked to a PBPK and PBBM model which creates the opportunity to widen the potential of IVIVC and biowaivers request especially for orally administered drugs products exhibiting low water solubility.
Our last collaboration was with a Sponsor who wanted to develop an IVIVC for a new gastro resistant modified release formulation. The model developed allowed the definition of dissolution specifications and contributed to guide additional in vitro dissolution testing to eventually establish the IVIVC. It was a very interesting work and it is actually a very good example of the type of accommodated collaboration that PhinC offers with a continuous support throughout the process.

CONTACT

Let's talk about how we can help you in your drug development research.

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