The AAPS Journal (2023) 25:104
https://doi.org/10.1208/s12248-023-00871-w

EDITORIAL

Perspectives on clinical drug development of Long-Acting Injectables

# The AAPS Journal Theme Issue: "Perspectives on Clinical Drug Development of Long-Acting Injectables"

**Huybrecht T'jollyn[1] · Oliver Ackaert[1]**

Received: 23 October 2023 / Accepted: 25 October 2023 / Published online: 14 November 2023


The development of long-acting injectable (LAI) drugs has gained increased interest during the last decades because of their favorable properties towards compliance, safety, and efficacy by maintaining stable drug concentrations throughout an extended period following a single intramuscular (IM) or subcutaneous (SC) injection. Historically, several LAIs have been successfully marketed, mainly as lifecycle product extensions of oral formulations (1). More recently, several therapeutics are also being developed for LAI use only with limited or no information available from oral administration to be leveraged (2). There is therefore a need for more quantitative understanding of (i) the physicochemical properties, (ii) the influence of the formulations, and (iii) the observed preclinical and clinical pharmacokinetics for successful LAI drug development, i.e., from compound selection up to dose-regimen optimization. This theme issue aims to provide a perspective on the role of and emerging opportunities for quantitative methods in the trajectory of long-acting injectable drug development in three comprehensive and complementary review articles. As most LAI of the latest generation are aqueous-based suspensions for IM administration (3), that focus is maintained in the current theme, although many principles discussed can be applied to other LAI formulation platforms.

The review by Holm and colleagues summarizes some of the central talks of the workshop on "Patient-Centric Design of Long-Acting Injectable Drug Products," organized by The American Association of Pharmaceutical Scientists (AAPS). During this workshop, various topics of LAI development from formulation and manufacturability challenges/opportunities, selection of adequate *in vitro*/*in vivo* models, to computational modeling were presented (3).

In another article, Siemons and co-authors focus their review on the role of modeling and simulation in LAI drug development. The authors identify the current scientific and practical challenges that exist in LAI drug development and discuss their perspectives on how quantitative methods can provide valuable input in various stages of LAI drug development. This review is illustrated by various examples of LAI development of small molecules formulated as aqueous crystalline suspensions (4).

Finally, Nguyen and colleagues extensively discuss the influence of drug substance and formulation properties, administration site properties, and host response towards drug particles on the *in vivo* performance of aqueous suspensions. To advance LAI development, it is imperative to understand the interplay of important factors driving the release of the drug from the LAI formulation and subsequently the pharmacokinetics, using quantitative methods such as physiologically-based pharmacokinetic (PBPK) modeling (5).

These review articles bundled in the current theme issue highlight the (need for) use of quantitative methods, from mechanistic PBPK modeling to more empirical population pharmacokinetic and pharmacokinetic-pharmacodynamic (PKPD) models. In silico modeling can provide benefit at various stages of drug development, at the time of compound or platform screening, during the transition from preclinical into clinical, and further at late clinical development through population PKPD modeling for optimal dose-regimen selection and covariate assessment. Although progress has been made in the field, further applications of quantitative modeling are required to optimize and accelerate drug development of LAIs.

Communicated by Huybrecht T'jollyn and Oliver Ackaert.

✉ Oliver Ackaert
oackaert@its.jnj.com

[1] Janssen Research and Development, Turnhoutseweg 30, B-2340 Beerse, Belgium

## References


1. Bauer A, Berben P, Chakravarthi SS, Chattorraj S, Garg A, Gourdon B, et al. Current state and opportunities with long-acting injectables: industry perspectives from the innovation and quality consortium "long-acting injectables" working group. Pharm Res. 2023;40(7):1601–31. https://doi.org/10.1007/s11095-022-03391-y.
2. Bassand C, Villois A, Gianola L, Laue G, Ramazani F, Riebesehl B, et al. Smart design of patient-centric long-acting products: from preclinical to marketed pipeline trends and opportunities. Expert Opin Drug Deliv. 2022;19(10):1265–83. https://doi.org/10.1080/17425247.2022.2106213.
3. Holm R, Lee RW, Glassco J, et al. Long-acting injectable aqueous suspensions—summary from an AAPS Workshop. AAPS J. 2023;25:49.
4. Siemons M, Schroyen B, Darville N, et al. Role of modeling and simulation in preclinical and clinical long-acting injectable drug development. AAPS J. 2023;25:99.
5. Nguyen VTT, Darville N, Vermeulen A. Pharmacokinetics of long-acting aqueous nano-/microsuspensions after intramuscular administration in different animal species and humans—a review. AAPS J. 2023;25(1):4.