IQ Predictive Dissolution Models for Real-time Release Testing: Development and Implementation Workshop

11-12 November 2021

References, Publications, and Presentations of Interest

Standards and guidelines:

USP <711> Dissolution: https://www.usp.org/sites/default/files/usp/document/harmonization/gen-method/stage_6_monograph_25_feb_2011.pdf

USP <1039> Chemometrics:
https://online.uspnf.com/uspnf/current-document/1_GUID-9E862365-D262-4D50-8CA9-CFF0D4577262_2_en-US?source=emailLink

ICH guidance: Q8(R2) Pharmaceutical Development, Q9 Quality Risk Management, and Q10:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q9-quality-risk-management
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q9-quality-risk-management
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q10-pharmaceutical-quality-system

ICH Quality IWG Points to consider for ICH Q8/Q9/Q10 guidelines
https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use/q9/q10-guidelines_en.pdf
Q8, Q9, and Q10 Questions and Answers(R4)
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q8-q9-and-q10-questions-and-answers
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q8-q9-q10-questions-and-answers-appendix-qas-training-sessions-q8-q9-q10-points-consider

ICH draft guidance Q13: Continuous manufacturing of drug substances and drug products
https://www.ich.org/page/quality-guidelines#13-1

FDA draft guidance: The Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls Guidance for Industry (Draft, Sep 2020) https://www.fda.gov/media/142500/download
FDA guidance: Development and Submission of Near Infrared Analytical Procedures
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-submission-near-infrared-analytical-procedures

EMA guideline: Use of near infrared spectroscopy (NIRS) by the pharmaceutical industry and the data requirements for new submissions and variations
https://www.ema.europa.eu/en/use-near-infrared-spectroscopy-nirs-pharmaceutical-industry-data-requirements-new-submissions#document-history---revision-2-section

Predictive dissolution modeling and dissolution RTRT:
J. Siepmann, F. Siepmann. "Mathematical modeling of drug dissolution," *International Journal of Pharmaceutics*, **453**(1) 2013, p. 12-24. https://doi.org/10.1016/j.ijpharm.2013.04.044

Nikolay Zaborenko, Zhenqi Shi, Claudia C Corredor, Brandye M Smith-Goettler, Limin Zhang, Andre Hermans, Colleen M Neu, Md Anik Alam, Michael J Cohen, Xujin Lu, Leah Xiong, Brian M Zacour. "First-Principles and Empirical Approaches to Predicting In Vitro Dissolution for Pharmaceutical Formulation and Process Development and for Product Release Testing." *AAPS J*. 2019;21(3):32. Published 2019 Feb 21. doi:10.1208/s12248-019-0297-y
Nikolay Zaborenko. "IQ Analytical LG Dissolution Working Group Webinar Series: Predictive Dissolution Modeling - When and How?" 2019 June 7. Webinar recording.
https://register.gotowebinar.com/recording/2632594075073280771
Review paper with numerous references therein on specific dissolution modeling topics and webinar based on same paper.

Daniel Markl, Martin Warman, Melanie Dumarey, Eva-Lotta Bergman, Staffan Folestad, Zhenqi Shi, Leo Francis Manley, Daniel J Goodwin, J Axel Zeitler. "Review of real-time release testing of pharmaceutical tablets: State-of-the art, challenges and future perspective." Int J Pharm. 2020; 582:119353. doi:10.1016/j.ijpharm.2020.119353
Review paper with numerous references therein on specific RTRT topics.

Nagy, B. (2021). *Mathematical modeling for the quality assurance of continuous pharmaceutical manufacturing processes* [Doctoral dissertation, Budapest University of Technology and Economics]. Proquest Dissertations and Theses Global.
https://repozitorium.omikk.bme.hu/bitstream/handle/10890/15752/ertekezes.pdf?sequence=2
https://repozitorium.omikk.bme.hu/bitstream/handle/10890/15752/tezis_eng.pdf?sequence=5&isAllowed=y
Thesis and thesis summary on a range of pharmaceutical RTRT.

Costa P, Sousa Lobo JM. "Modeling and comparison of dissolution profiles." *Eur J Pharm Sci.* **13**(2), 2001, pp. 123-33. https://doi.org/10.1016/s0928-0987(01)00095-1

Singhvi, Gautam & Shah, Abhishek & Yadav, Nilesh & Saha, Ranendra. "Prediction of in vivo plasma concentration-time profile from in vitro release data of designed formulations of milnacipran using numerical convolution method," *Drug development and industrial pharmacy.* **41**, 2013. http://dx.doi.org/10.3109/03639045.2013.850706

Disintegration mechanisms:
Markl, D., Zeitler, J.A. "A Review of Disintegration Mechanisms and Measurement Techniques," *Pharm Res* **34**, 2017, 890–917. https://doi.org/10.1007/s11095-017-2129-z

In vitro dissolution method development and bioequivalence
Xie F, Ji S, Cheng Z. "In vitro dissolution similarity factor (f2) and in vivo bioequivalence criteria, how and when do they match? Using a BCS class II drug as a simulation example." *Eur J Pharm Sci.* **66,** 2015; pp. 163-72. https://doi.org/10.1016/j.ejps.2014.10.002

S. Suarez, P. Marroum and M. Hughes. "Biopharmaceutics considerations in drug product design and in vitro drug product performance." Applied biopharmaceutics and pharmacokinetics, 7th Ed., Chapter 15, Pp 415-476.
https://accesspharmacy.mhmedical.com/content.aspx?bookid=1592&sectionid=100673007

Dajun D. Sun, Hong Wen, Lynne S. Taylor. "Non-Sink Dissolution Conditions for Predicting Product Quality and In Vivo Performance of Supersaturating Drug Delivery Systems." *Journal of Pharmaceutical Sciences*, **105**(9) 2016, Pages 2477-2488. https://doi.org/10.1016/j.xphs.2016.03.024

FY 2020 Generic Drug Regulatory Science Initiatives Public Workshop, May 2020, FDA. https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/fy-2020-generic-drug-regulatory-science-initiatives-public-workshop-05042020-05042020 (with recordings).

Jieon Lee,Yuqing Gong, Sid Bhoopathy, Charles E. DiLiberti, Andrew C. Hooker, Amin Rostami-Hodjegan, Stephan Schmidt, Sandra Suarez-Sharp, Viera Lukacova, Lanyan Fang, Liang Zhao. "Public Workshop Summary Report on Fiscal Year 2021 Generic Drug Regulatory Science Initiatives: Data Analysis and Model-Based Bioequivalence." *Clin Pharm & Therapeutics*, **110**(5) 2021, p. 1190-1194. https://doi.org/10.1002/cpt.2120

Numerical methods and chemometrics:
Emanuele Tomba, Pierantonio Facco, Fabrizio Bezzo, Massimiliano Barolo. "Latent variable modeling to assist the implementation of Quality-by-Design paradigms in pharmaceutical development and manufacturing: A review." *International Journal of Pharmaceutics*, **457**(1) 2013, p. 283-297. https://doi.org/10.1016/j.ijpharm.2013.08.074

Handbook of Chemometrics and Qualimetrics: Part A, Edited by D.L. Massart, B.G.M. Vandeginste, L.M.C. Buydens, S. De Jong, P.J. Lewi, J. Smeyers-Verbeke. Volume 20, Part A, Elsevier (1998). https://www.sciencedirect.com/bookseries/data-handling-in-science-and-technology/vol/20/part/PA
Handbook of Chemometrics and Qualimetrics: Part B, Edited by B.G.M. Vandeginste, D.L. Massart, L.M.C. Buydens, S. De Jong, P.J. Lewi, J. Smeyers-Verbeke. Volume 20, Part 2,

Elsevier (1998). https://www.sciencedirect.com/bookseries/data-handling-in-science-and-technology/vol/20/part/P2

Nagy B, Petra D, Galata DL, Démuth B, Borbás E, Marosi G, Nagy ZK, Farkas A. "Application of artificial neural networks for Process Analytical Technology-based dissolution testing." *Int J Pharm*. **567,** 2019**.** p. 118464. https://doi.org/10.1016/j.ijpharm.2019.118464

Ibrić, S., Djuriš, J., Parojčić, J., & Djurić, Z. "Artificial neural networks in evaluation and optimization of modified release solid dosage forms." *Pharmaceutics*, **4**(4), 2012, p. 531–550. https://doi.org/10.3390/pharmaceutics4040531

Johan Trygg and Svante Wold. "O2-PLS, a two-block (X–Y) latent variable regression (LVR) method with an integral OSC filter." *Journal of Chemometrics*, **17**, 2003, p. 53-64. https://doi.org/10.1002/cem.775

Rinnan, Åsmund & Berg, Frans & Engelsen, Søren. "Review of the Most Common pre-Processing Techniques for Near-Infrared Spectra." *Trends in Analytical Chemistry*. **28**. 2009, p. 1201-1222. http://dx.doi.org/10.1016/j.trac.2009.07.007

Quality by design and model lifecycle:

Kourti T, Lepore J, Liesum L, Nasr M, Chatterjee S, Moore CMV, Korakianiti E. "Scientific and regulatory considerations for implementing mathematical models in the quality by design (QbD) framework." *Pharmaceutical Engineering* **34**(6) 2014, p. 1-21. https://ispe.org/sites/default/files/pe/online-exclusives/14ND-online_Kourti.pdf

Gregory Doddridge, Steven Doherty, Nina Cauchon, Tony Wang, Jerome King, Vivien Le-bras, Jack Bowers, Shailen Singh, Busolo Wabuyele, Karen Xu, Christopher Cowan, Mark Czeterko, Alessandra Starling, Zhenqi Shi, Orna Wisniak, Clarice Hutchens, Victor Saucedo, Christian Airiau, Zheng Huang, Andrew Fiordalis, Mark Henson, Ting-Kuo Huang, Isabelle Lequeux. "Industry proposal: Regulatory submission and lifecycle management strategy of models used in the manufacture of pharmaceutical and biological products." BioPhorum, January 2021. https://www.biophorum.com/download/industry-proposal-regulatory-submission-and-lifecycle-management-strategy-of-models-used-in-the-manufacture-of-pharmaceutical-and-biological-products/

Industrial case studies and examples:

Melanie Dumarey, Daniel J Goodwin, Chris Davison. "Multivariate modelling to study the effect of the manufacturing process on the complete tablet dissolution profile." Int J Pharm. 015;486(1-2):112-120. doi:10.1016/j.ijpharm.2015.03.040

Jenny M. Vargas, Sarah Nielsen, Vanessa Cárdenas, Anthony Gonzalez, Efrain Y. Aymat, Elvin Almodovar, Gustavo Classe, Yleana Colón, Eric Sanchez, Rodolfo J. Romañach,
"Process analytical technology in continuous manufacturing of a commercial pharmaceutical product," *International Journal of Pharmaceutics*, **538(**1–2), p 167-178, 2018. https://doi.org/10.1016/j.ijpharm.2018.01.003

Kesisoglou, Filippos & Hermans, Andre & Neu, Colleen & Yee, Ka & Palcza, John & Miller, Jessica. "Development of In Vitro - In Vivo Correlation for Amorphous Solid Dispersion Immediate-Release Suvorexant Tablets and Application to Clinically Relevant Dissolution Specifications and In-Process Controls." *Journal of pharmaceutical sciences.* **104**(9) 2015. http://dx.doi.org/10.1002/jps.24362

Li H, Prichard J, Swinney KA. "Dissolution modeling for real time release testing (RTRT)." M-CERSI, Baltimore, MD 2016.
https://www.pharmacyumarylandedu/media/SOP/wwwpharmacyumarylandedu/centers/cersievents/dissolution/day1_hanlin-li.pdf.

Academic dissolution prediction and RTRT presentations/publications:

Guolin Shi, Longfei Lin, Yuling Liu, Gongsen Chen, Yuting Luo, Yanqiu Wu and Hui Li. "Pharmaceutical application of multivariate modelling techniques: a review on the manufacturing of tablets." *RSC Adv.*, 2021, **11**, 8323-8345. https://doi.org/10.1039/D0RA08030F
Review paper with numerous references therein on modeling of pharmaceutical processes.

Pallavi Pawar, Yifan Wang, Golshid Keyvan, Gerardo Callegari, Alberto Cuitino, Fernando Muzzio. "Enabling real time release testing by NIR prediction of dissolution of tablets made by continuous direct compression (CDC)." *International Journal of Pharmaceutics* **512**(1) 2016, p 96-107. https://doi.org/10.1016/j.ijpharm.2016.08.033

Hernandez, Eduardo & Pawar, Pallavi & Keyvan, Golshid & Wang, Yifan & Velez, Natasha & Callegari, Gerardo & Cuitiño, Alberto & Michniak-Kohn, Bozena & Muzzio, Fernando & Romañach, Rodolfo. "Prediction of dissolution profiles by non-destructive near infrared spectroscopy in tablets subjected to different levels of strain." *Journal of Pharmaceutical and Biomedical Analysis*. **117**, 2016. 568-576. http://dx.doi.org/10.1016/j.jpba.2015.10.012

G. Drazer, P. Pawar, Y. Wang, G. Keyvan, G. Callegari, A. Cuitino and F. Muzzio. "Enabling Real Time Release testing (RTRt) with NIR-based prediction of dissolution for Tablets made by Continuous Direct Compression (CDC)." M-CERSI, Baltimore, MD 2017
https://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumarylandedu/centers/cersievents/dissolution/day1_german-drazer.pdf

Yuxiang Zhao, Wenlong Li, Zhenqi Shi, James K. Drennen, Carl A. Anderson, "Prediction of Dissolution Profiles From Process Parameters, Formulation, and Spectroscopic Measurements. Journal of Pharmaceutical Sciences," **108**(6) 2019, p. 2119-2127.
https://doi.org/10.1016/j.xphs.2019.01.023

Natalie Maclean, Erin Walsh, Mithushan Soundaranathan, Ibrahim Khadra, James Mann, Helen Williams, Daniel Markl. "Exploring the performance-controlling tablet disintegration mechanisms for direct compression formulations," *International Journal of Pharmaceutics* **599,** 2021, p 120221.
https://doi.org/10.1016/j.ijpharm.2021.120221

Galata, D.L.; Farkas, A.; Könyves, Z.; Mészáros, L.A.; Szabó, E.; Csontos, I.; Pálos, A.; Marosi, G.; Nagy, Z.K.; Nagy, B. "Fast, Spectroscopy-Based Prediction of In Vitro Dissolution Profile of Extended Release Tablets Using Artificial Neural Networks." *Pharmaceutics* **2019**, *11*, 400. https://doi.org/10.3390/pharmaceutics11080400

M-CERSI Workshops and proceedings on dissolution and modeling

Workshops in collaboration between FDA's Center for Drug Evaluation and Research (CDER) and the University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), in Baltimore, MD

"Current State and Future Expectations of Translational Modeling Strategies to Support Drug Product Development, Manufacturing Changes and Controls", September 2019. https://cersi.umd.edu/current-state-and-future-expectations-translational-modeling-strategies-support-drug-product

Xavier J.H. Pepin, Neil Parrott, Jennifer Dressman, Poonam Delvadia, Amitava Mitra, Xinyuan Zhang, Andrew Babiskin, Vidula Kolhatkar, Sandra Suarez-Sharp. "Current State and Future Expectations of Translational Modeling Strategies to Support Drug Product Development, Manufacturing Changes and Controls: A Workshop Summary Report." *Journal of Pharmaceutical Sciences,* **110**(2) 2021, p 555-566. https://doi.org/10.1016/j.xphs.2020.04.021

Pepin XJH, Dressman J, Parrott N, Delvadia P, Mitra A, Zhang X, Babiskin A, Kolhatkar V, Seo P, Taylor LS, Sjögren E, Butler JM, Kostewicz E, Tannergren C, Koziolek M, Kesisoglou F, Dallmann A, Zhao Y, Suarez-Sharp S. "In Vitro Biopredictive Methods: A Workshop Summary Report." *J Pharm Sci*. 2021 Feb;**110**(2):567-583. https://doi.org/10.1016/j.xphs.2020.09.021

Parrott N, Suarez-Sharp S, Kesisoglou F, Pathak SM, Good D, Wagner C, Dallmann A, Mullin J, Patel N, Riedmaier AE, Mitra A, Raines K, Butler J, Kakhi M, Li M, Zhao Y, Tsakalozou E, Flanagan T, Dressman J, Pepin X. "Best Practices in the Development and Validation of Physiologically Based Biopharmaceutics Modeling. A Workshop Summary Report." *J Pharm Sci*. 2021 Feb;**110**(2):584-593. https://doi.org/10.1016/j.xphs.2020.09.058

Mitra A, Suarez-Sharp S, Pepin XJH, Flanagan T, Zhao Y, Kotzagiorgis E, Parrott N, Sharan S, Tistaert C, Heimbach T, Zolnik B, Sjögren E, Wu F, Anand O, Kakar S, Li M, Veerasingham S, Kijima S, Lima Santos GM, Ning B, Raines K, Rullo G, Mandula H, Delvadia P, Dressman J, Dickinson PA, Babiskin A. "Applications of Physiologically Based Biopharmaceutics Modeling (PBBM) to Support Drug Product Quality: A Workshop Summary Report." *J Pharm Sci.* 2021 Feb;**110**(2):594-609. https://doi.org/10.1016/j.xphs.2020.10.059

"Dissolution and Translational Modeling Strategies Enabling Patient-Centric Product Development", May 2017. https://www.pharmacy.umaryland.edu/centers/cersievents/dissolution-and-translational-modeling-strategies/agenda/

Abend, A., Heimbach, T., Cohen, M. et al. "Dissolution and Translational Modeling Strategies Enabling Patient-Centric Drug Product Development: the M-CERSI Workshop Summary Report." *AAPS J* **20**, 60 (2018). https://doi.org/10.1208/s12248-018-0213-x

"In Vitro Dissolution Profiles Similarity Assessment in Support of Drug Product Quality: What, How, and When", May 2019 (With webinar recordings) https://www.pharmacy.umaryland.edu/centers/cersievents/dissolution-similarity/agenda/

Suarez-Sharp S, Abend A, Hoffelder T, Leblond D, Delvadia P, Kovacs E, Diaz DA. “In Vitro Dissolution Profiles Similarity Assessment in Support of Drug Product Quality: What, How, When-Workshop Summary Report.” AAPS J. 2020 May 19;**22**(4):74. https://doi.org/10.1208/s12248-020-00458-9