doi:10.1017/S143192762100163X
Microsc. Microanal. 27 (Suppl 1), 2021

Cloud-based image management solutions for digital transformation of drug product development

Shawn Zhang[1] and Joshua Lomeo[2]

[1]DigiM Solution LLC, Winchester, Massachusetts, United States, [2]DigiM Solution LLC, United States

Microscopy and microanalysis are at the foundation of optimizing drug formulations, process parameters, and release performance. From the particle size of active ingredients to microporosity, these factors are critical towards understanding release mechanisms and engineering an effective drug product. High-resolution 3D imaging, including X-ray microscopy (XRM) and focused ion beam scanning electron microscopy (FIB-SEM), are powerful techniques to visualize these microstructures.

Quantitative analytics from images have been demonstrated to save significant time and resources in drug development, and lead the charge in its digital transformation.[1-2] However, the complexities in managing image data, analysis workflow, and computing resource requirements have created a barrier to widespread adoption and sharing. For example, capturing both structural arrangement and uniformity of features often requires a correlative imaging approach at multiple resolutions. The build up of data from multiple imaging modalities and resolutions requires significant storage. Derived data from segmented and processed images adds on to the load. For analyzing images, workflow management is key to producing timely and consistent quantitative results. Typical analysis software also requires dedicated computing hardware, restricting visualization and analysis of the data to one local workstation. Lack of data accessibility, storage and computing limitations, and workflow management are significant pain points in microstructure imaging analytics of drug products.

A cloud-based platform such as DigiM I2S can mitigate the challenges associated with managing and analyzing large image data.[3] The software combines management database with artificial intelligence analysis and image-based simulation modules designed for pharmaceutical microstructures. I2S utilizes machine and deep learning segmentation for complex phase mixtures (e.g. amorphous solid dispersions) and discrete features (e.g. thin coatings). Critical quality attributes including particle size, porosity, and phase connectivity can be directly quantified. Imaged-based simulation modules, including release prediction, allow a mechanistic understanding of drug release from image data. For data management, an accessible browser-based interface allows complete workflow management. Analyses can be launched and visualized within the platform, requiring no upfront computing hardware. All images and derived data can be tracked following FDA 21 CFR Part 11 Compliance.

Through the cloud-based computing system, image data can be constructed into a digital sample of the real drug products or intermediates. This serves as a database of digital twins, allowing for continuous reuse and future enhanced analysis. The sensitivity of quality attributes to drug formulation parameters (such as drug loading, polymer choice, and particle morphology) and under various processing conditions (such as process temperature and compaction force) can be thoroughly studied.[4-5] Numerical drug

formulations can be constructed from the real image data, evaluating factors such as optimal drug loading and porosity.[6] The numerical model allows a pharmaceutical scientist to rapidly traverse multi-variable parameter space, and narrow down formulation parameters and optimal processing conditions.

The I2S platform has been utilized and validated for a variety of dosage forms and challenge areas. Applications for formulation design, performance assessment, process development, and Q3 microstructure bioequivalence will be reviewed. Through an unprecedented understanding of microstructures, digital transformation through software tools such as DigiM I2S brings a new paradigm for optimizing drug design and for shortening drug formulation and process development cycles via reduced testing, reusable data, and advanced mechanistic understandings.

References

1. Zhang, S., and Byrne, G. (2020). Characterization of transport mechanisms for controlled release polymer membranes using focused ion beam scanning electron microscopy image-based modelling. With Merck.
2. Goldman, J., Chen, X., Rowe, J. , Zhang, S., Lin, S., Zhou, L. (2020). Non-Invasive, Quantitative Characterization of Lyophilized Drug Product Using Three-Dimensional X-Ray Microscopy Analytics. *Drug Development & Delivery.* January/February 2020. Pg. 32-40.
3. Byrnes, A. P., Jankovic, J., Neilly, J., & Zhang, S. (2019). Management, Analysis, and Simulation of Micrographs with Cloud Computing. *Microscopy Today*, 27(2), 26-33.
4. Xi, H., Zhu, A., Klinzing, G.R., Zhou, L., Zhang, S., Gmitter, A.J., Ploeger, K., Sundararajan, P., Mahjour, M., Xi, W. (2020). Characterization of Spray Dried Particles Through Microstructural Imaging. *Journal of Pharmaceutical Sciences.* August 2020. With Merck.
5. Yost, E., Chalus, P., Zhang, S., Peter, S., & Narang, A. S. (2019). Quantitative X-Ray Microcomputed Tomography Assessment of Internal Tablet Defects. *Journal of Pharmaceutical Sciences*, 108(5), 1818-1830. With Genentech, Lonza, and Roche.
6. Wu, D., Zhou, L., Zhang, S. (2020). Characterization of Controlled Release Microspheres Using FIB-SEM and Image-Based Release Prediction. *AAPS PharmSciTech*. July 2020. With Bausch Health.

https://doi.org/10.1017/S143192762100163X Published online by Cambridge University Press