

ACD/LABS [ADVANCED CHEMISTRY DEVELOPMENT, INC.]

Forced Degradation Data Management in Drug Development

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Introduction

Forced degradation studies are critical for first developing stability indicating methods and then characterizing degradants. A stability indicating method is a chromatographic method used to validate analytical procedures. It measures the active pharmaceutical ingredient (API) in a drug substance or drug product. Once these methods are developed, they are applied to measuring the byproducts formed during stress testing.

Stability indicating method development and degradant characterization are aided by understanding the process scheme and efficient inter-department communication. Teams are often spread across multiple locations and use different electronic systems to capture information, which impedes coordination. As a result, teams resort to unspecialized programs such as Microsoft Excel or PowerPoint to share data.

While easily accessible, these applications are not built to handle complex scientific data. They lack chemical intelligence, cannot process analytical data and are not suitable for collaborative workflows.

This application note will discuss how Luminata[®], a CMC decision support tool, captures structural degradant-related data. It will explore how Luminata's forced degradation tools simplify data management, improve collaboration, and accelerate research.

Capturing Structural Information

One of the steps of planning stress test conditions is to first use *in silico* software to predict the degradant pathways. Once you obtain these degradants, they are either stored as an SDF file or Word document within a file sharing system, such as SharePoint. The degradant structures and meta data are then disconnected from the actual observed molecules. This becomes another instance within drug development, where structural and analytical data are not easily accessible for project teams. Within Luminata, we can link the API with all degradants predicted in differing conditions.

Luminata represents the theoretical degradants generated by a third-party application in the degradation pathway. This was described in a previous whitepaper.¹ Entities identified and characterized during forced degradation experiments can be added to the process scheme along with the predicted degradants. The reaction scheme can be filtered to show only the degradant pathway.

Luminata includes common degradation studies recommended by ICH guidelines (acid, base, peroxide, heat, and UV). These are made available in the software to facilitate data input and visualization (Figure 1).

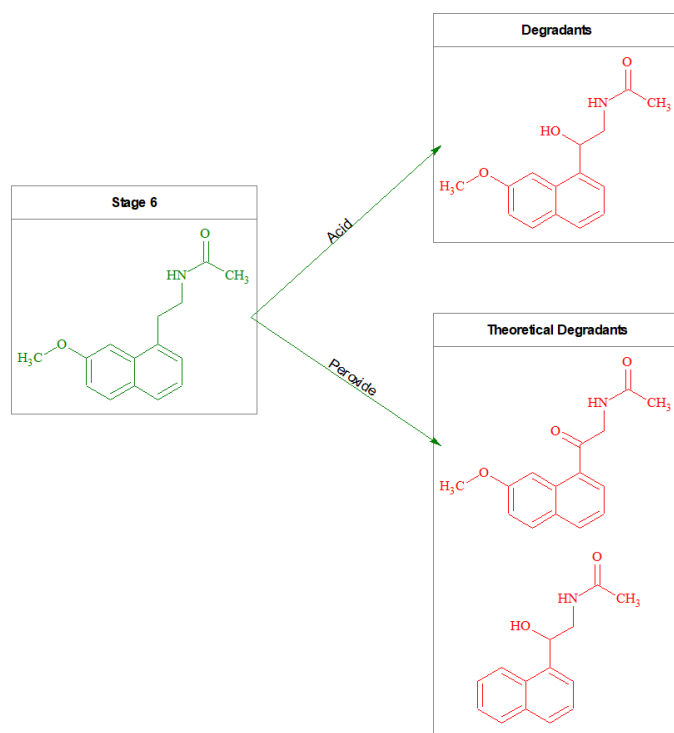


Figure 1. Observed and predicted degradants within the filtered process map.

This capability allows users to store all structural and meta data predicted using third-party software, such as a Lhasa Zeneth. Luminata also stores this predicted information alongside relevant analytical data for each forced degradation study. Previously, this would be segregated across multiple programs, creating challenges when researchers attempted to compare experimental and predicted results.

Forced Degradation Wizard

For any stress testing studies that are done for a project, there will be a set of experiments that must be completed. Previously, Luminata users could create process maps manually, but this can be repetitive in the case of forced degradation.

The forced degradant wizard within the Navigation panel allows users to select a pre-defined list of experiments to run (Figure 2). Users can also create custom studies that are needed for a specific project.

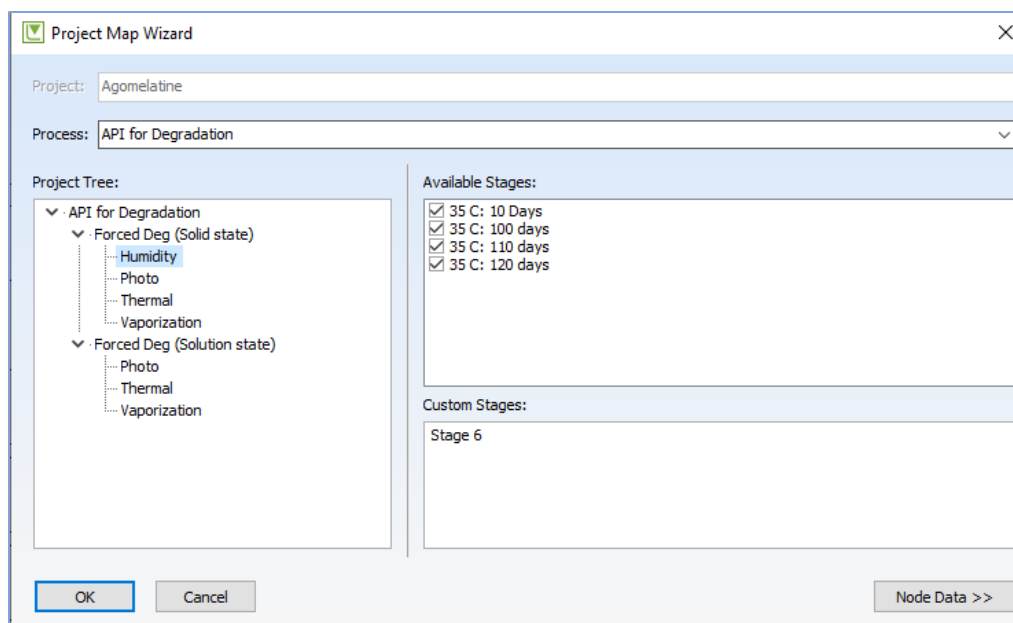


Figure 2. Forced degradation wizard to capture structural information. Note: this wizard has four sub-levels but these levels can be customized as well.

Dynamic Project Map

Once all forced degradant records have been created, the user can view the progress of the forced degradation solution state and solid-state landscape using the Dynamic Project Map (Figure 3).

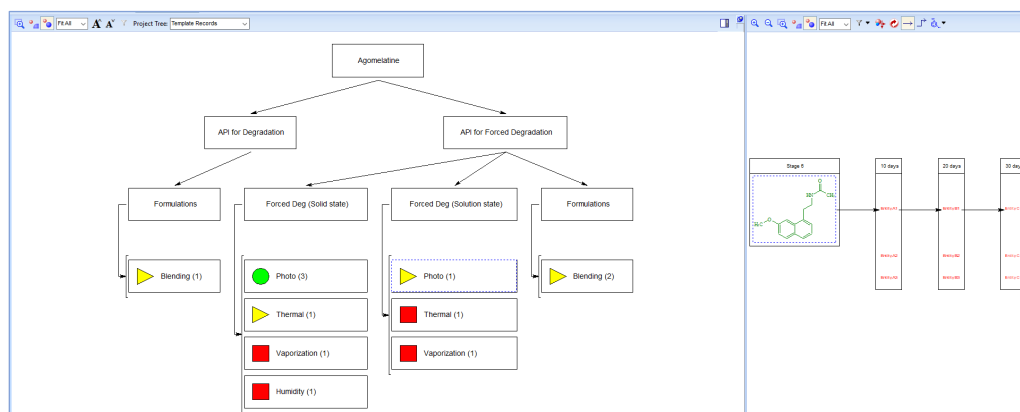


Figure 3. API degradation products landscape.

Users can view all activities in process and product development in the API degradation map. Progress is displayed using a stoplight system. Clicking on a forced degradant study will display the record of interest and project progress. Metadata, such as ELN numbers and registration numbers, can also be added at any sub-level.

Conclusion

API route development generates large quantities of data. Scientists have designed processes that allow them to understand and document API forced degradation. This knowledge is typically disconnected from all other sources and is often distributed across multiple systems found in separate locations. Developing stability indicating methods and managing forced degradation data in this way is time consuming, error-prone, and cumbersome.

Luminata enables a read across for the forced degradation products within a given project. Luminata also improves forced degradation studies by allowing users to:

- Collaboratively develop stability indicating methods
- Build forced degradation records with the forced degradation wizard
- Track task completion using the dynamic project map

References

- 1 <https://www.acdlabs.com/download/whitepaper/whitepaper-stress-testing.pdf>