ACD/LABS [ADVANCED CHEMISTRY DEVELOPMENT, INC.]

# Accelerated Stability Assessment with Luminata®

Joe DiMartino

## Challenges in Accelerated Stability Assessment

APS studies are an efficient, cost-effective alternative to experimental methods for determining shelf life of APIs and drug products, especially in the early stages of drug development. In particular, the Accelerated Stability Assessment Program (ASAP) is an established method for accurate prediction of long-term stability of small molecule drugs.

While ASAP calculations—based on a humidity-modified Arrhenius equations—are clear in theory, there are several practical obstacles to completing these assessments, including:

- Processing the analytical data to determine the degradant levels for each set of conditions
- Calculating the reaction rate variables based on the analytical results
- Visualizing results and cross-referencing predicted degradation levels with toxicological information

These obstacles are artificially exacerbated by the fact that many of the tools used to perform accelerated stability analysis do not integrate with analytical and chemical software. Researchers must manually transcribe data and manage files, which is inefficient and tedious. Luminata® includes features that address each of these challenges.

## Streamlined Analytical Data Processing

Processing chromatograms to determine the level of each degradant is time-consuming and error prone. Using Luminata, scientists can connect chromatography data from their degradation experiments to the stages of a process map. Luminata then calculates the level of each degradant for each set of conditions.

It is worth noting that users do not need fully elucidated structures to complete this assessment, as shown in Figure 1. Degradation rates can be calculated without structural information. Researchers often use relative retention time (RRT) values during stability research, especially in the early stages of a project. As work progresses, structures can be populated.

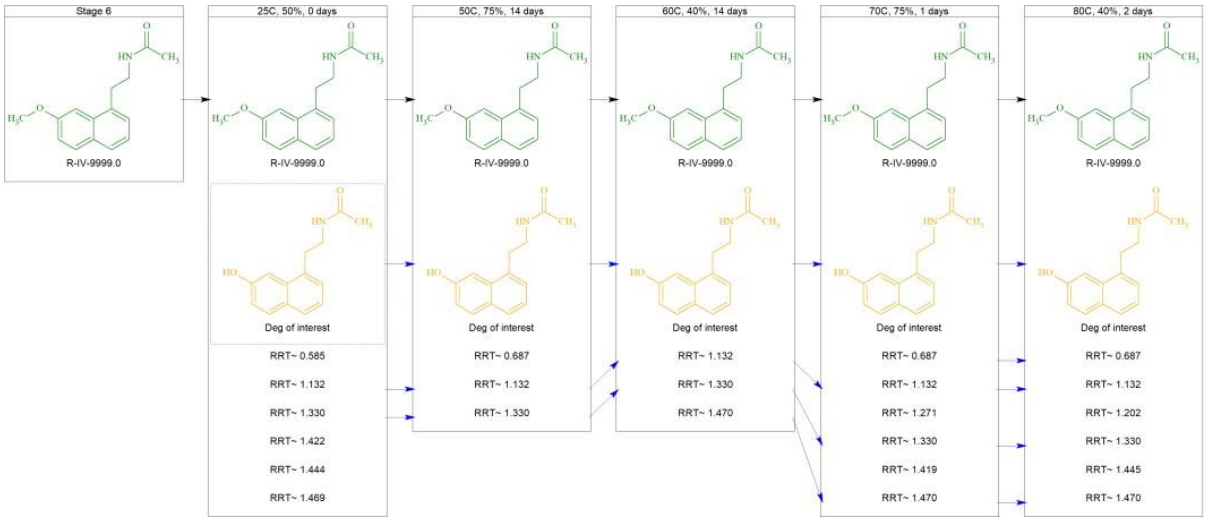


*Figure 1. Example degradation map for Agomelatine. RRT values are used for unknown structures; these can be added as development progresses. Structures are not required to perform predicted stability calculations.*

## Simplified Stability Calculations

As stability data is added to Luminata, users can include temperature, relative humidity, and time points for each experiment. This information is used to calculate the modified Arrhenius equation parameters A, $E_a$, and B, necessary for accelerated stability prediction.

Luminata also includes $R^2$ and $Q^2$ values, which quantitatively assess how well the experimental data fits the model. These are useful checks to ensure the results are consistent and will help users identify data input or experimental errors.

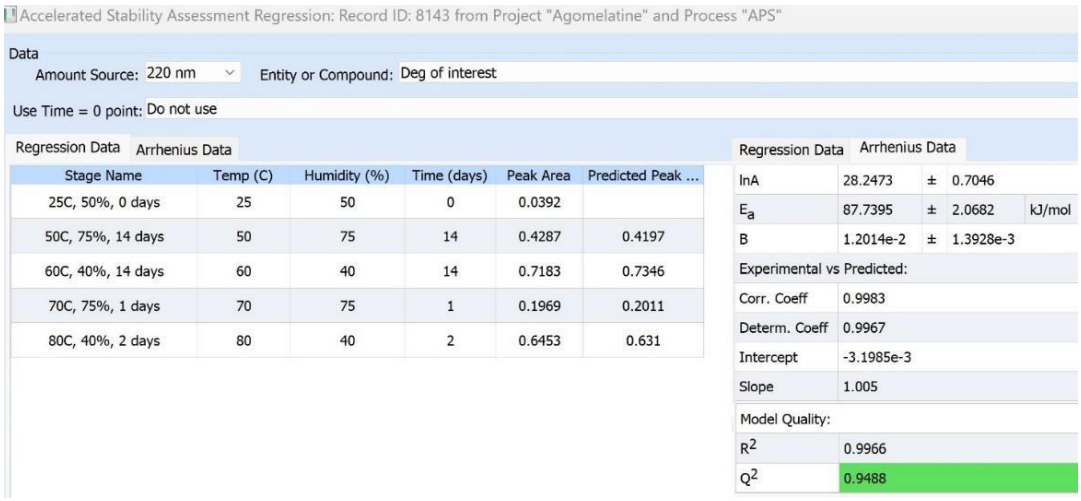


*Figure 2. Arrhenius variables are automatically calculated from experimental data in Luminata—this includes $R^2$ and $Q^2$ values to assess model fit.*

## Modeling and Visualization

Once these steps are completed, users can model and predict the stability of the drug substance or product being analyzed. Luminata offers visualization tools to help users interpret and communicate the results of their accelerated stability analysis, allowing scientists to:

- → Compare the rates at which different degradants are formed
- → Forecast degradant profile at a specified stability study time point
- → Create a PDF report that summarizes the results of the accelerated stability assessment

By performing their chromatographic analysis, stability calculations, and predictive modeling in one place, users will save considerable time. This also limits the need to carry out complete experimental stability tests, which are resource intensive.

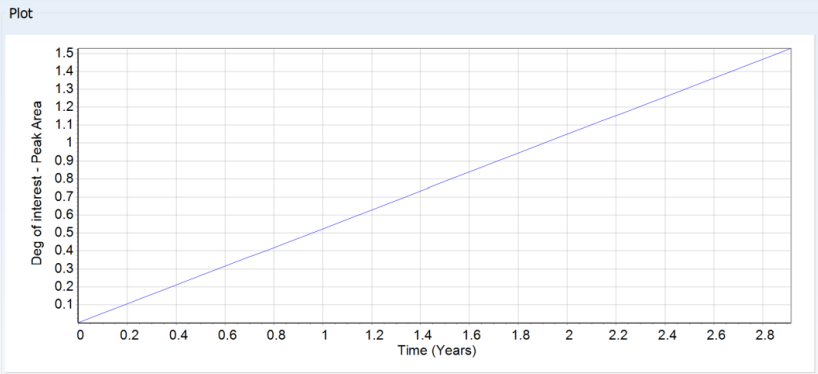


*Figure 3. Predicted levels of degradant formation over a three-year time span.*

## Stability Study Decision Support with Luminata

As development continues, RRT values used in the original degradant map can be replaced with structures. Luminata offers a rich set of structure elucidation tools to help with this process. These structures can then be linked to physiochemical properties, reference data, toxicity predictions, and more.

Luminata offers many other features designed to streamline stability research. This includes importing predicted stability maps from third-party software (e.g., Lhasa Zeneth), forced degradation study templating tools, and a dynamic project map for managing research teams. Users have a complete dashboard to assess stability for all stages of pharmaceutical development, leading to better productivity and better medicines.

Learn more about Luminata's tools for stability studies.