Luminata and Forced Degradation

Accelerate Your Stability Studies by Consolidating Stress Testing Data

Summary

Forced degradation is one of the essential functions of pharmaceutical development, providing insights into the stability of the drug substance and drug product, as well as identifying degradants that may pose a health risk. These studies often require teams spread across multiple sites using large amounts of data. Managing and sharing this data is challenging due to the number of sources and the variety of incompatible data types. Scientists spend more time handling their data and less time performing experiments.

Luminata is software that consolidates all your pharmaceutical development data in one interface. Built on a chemically intelligent platform, this software allows researchers to access and visualize analytical, chemical, and in silico data from across their team.

Pfizer is taking advantage of Luminata in performing forced degradation research. Dr. Hannah Davies, a Principal Scientist at Pfizer, identified that bringing her data together in one interface facilitates rapid decision-making and supports project management.

Luminata enables you to:

- Access in silico degradation data from third-party software in the same application as analytical data
- Create degradation maps from SDFiles
- Simplify data handling and reduce the risk of errors
- Support project management and avoid unnecessary duplication of experiments

Luminata

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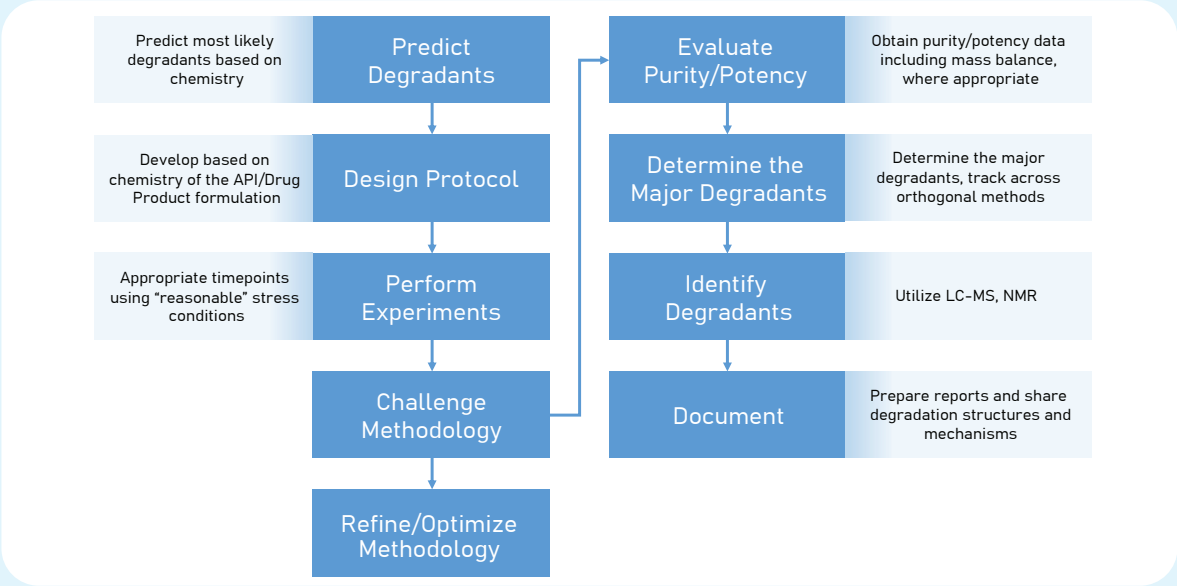
Data Management Challenges in Forced Degradation Studies

Forced degradation studies (also known as stress testing) are critical for determining drug substance and drug product stability. Stress testing "can help identify the likely degradation products, which can in turn help establish the degradation pathways and the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedures used," according to ICH Q1A(R2).[1] This information is then used to assess the safety and efficacy of the medication under a range of storage conditions.



Forced Degradation Process Flow Map[2]

Performing forced degradation studies takes place over many steps. Analytical and chemical data, as well as results derived from simulations, are involved in decision-making at many stages.

Managing this data requires significant effort. Scientists access large amounts of data from disparate computer systems, potentially in multiple organizations, acquired over many years.[3] This leads to several challenges, including:

- Describing complex materials
- Consolidating siloed information
- Coordinating work across a multi-site team

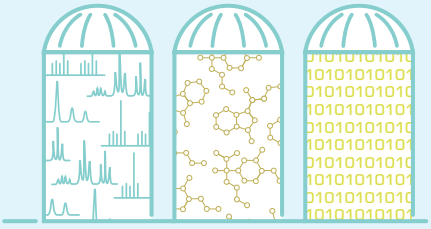
The Complex Material Characterization Problem

Identification of unknown structures is one of the essential functions of the analytical department. While structure elucidation of unknowns still requires effort, methods are consistently becoming more reliable and efficient due to advances in equipment, software, and scientific knowledge.[4]

Analytical method development and analysis become substantially more challenging when describing complex materials. Drug substances or drug products subjected to stress testing will form many degradants, leading to complex mixtures; analytical chemists must both identify the compounds that are present and quantify each degradant so risk can be assessed.

Composite characterization requires bringing together these many streams of data, including NMR, LC, GC, and MS data. This involves considerable effort, which is repeated many times over the course of a project.

Siloed Predicted and Analytical Data



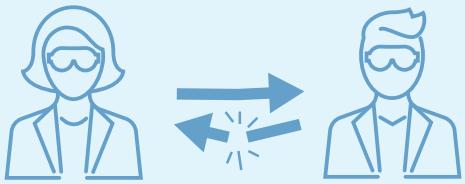
Forecasting the most likely degradants before starting stress testing can accelerate experimental research and identify potential problems early. This is done with in silico predictive tools, such as Lhasa's Zeneth, which can be used to generate degradation maps. Once the experiments are underway, scientists can reference these theoretical pathways to help identify degradants.

Unfortunately, comparing predicted and experimental results can be surprisingly challenging. Multiple pieces of software must first export data which is assembled and analyzed in a separate application, such as Excel, for a scientist to evaluate experimental results. This represents significant lost time and introduces a risk of error.

Collaboration and Coordination Challenge

Collaboration between multiple sites has become the norm in the pharmaceutical industry. Based on our experience with customers, forced degradation is often done, in whole or in part, by expert in-house teams, or contract organizations.

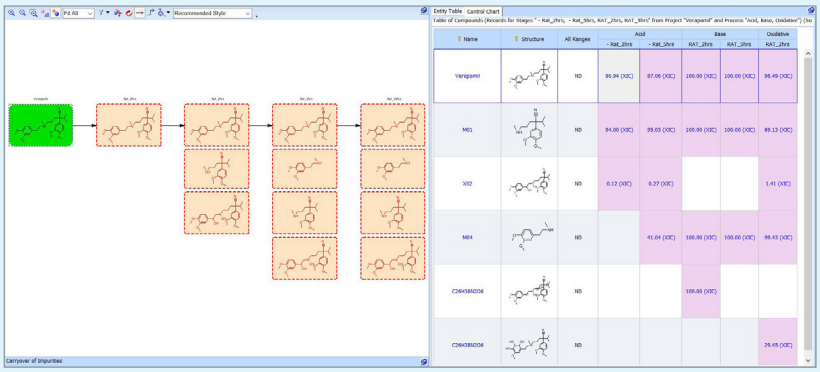
While specialization supports better research, it creates a challenge for project management. By spreading work across multiple sites, experiments may be duplicated unnecessarily due to communication and coordination issues. This leads to wasted time, as well as stress for team leadership.



Better Data and Better Science

These challenges may seem inevitable. Companies accept these inefficiencies and devote considerable effort to implementing cumbersome workarounds. It can feel like sharing, updating, and organizing data has become everyone's full-time job.

Luminata offers a real solution, allowing scientists to consolidate their data in one interface This leads to better, more efficient research. The next section explains Luminata's approach to sharing scientific information, and how it addresses the root causes of pharmaceutical development's data challenge.



Preview of forced degradation in Luminata

References

1 ICH (2003). Q1A(R2) Stability Testing of New Drug Substances and Products.

2 Alsante, K.M., Ando, A., Brown, R., Ensing, J., Hatajik, T.D., Kong, W., Tsuda, Y. (2007). The role of degradant profiling in active pharmaceutical ingredients and drug products. *Adv. Drug Deliv. Rev., 59*, 29–37.

3 DiMartino, J., Baertschi, S.W. (2020) An Update for Pharmaceutical Stress Testing Enabled by Modern Informatics Technologies, ACD/Labs.

4 Elyashberg, M., Argyropoulos, D., (2021) Computer Assisted Structure Elucidation (CASE): Current and future perspectives. *Magn. Reson. Chem. 59*(7), 669-690.

Luminata—A New Approach to Sharing Complex Scientific Knowledge

Forced degradation isn't the only area of pharmaceutical sciences that is facing data management challenges. In fact, a recent survey found that bench scientists spend almost 50% of their time manually extracting and cleaning data.[5] Scientists from across development must bring together analytical, chemical, and process data, as well as in silico predictions to make effective decisions. Each data type uses its own file format and software, which are mostly incompatible.

Many pharmaceutical development teams rely on Excel to resolve these incompatibility issues. Data is exported as spreadsheets, which are then compiled for analysis, project review, and decision making. Excel is a standard business tool, which makes this data accessible.

Unfortunately, this reliance on Excel creates its own problems. This application was not designed to manage chemical data or support the work of pharmaceutical development teams.[6] Some of Excel's limitations include:

No chemical intelligence: chemical structures are at the core of small molecule pharmaceutical development. Spreadsheets don't understand chemistry, making it impossible to search or navigate based on molecular structure.

Dead analytical data: spreadsheets cannot read analytical data. Results are abstracted as peak lists, meaning users cannot reprocess their data. Scientists must regularly spend time searching for experimental data files to verify or interrogate results.

Versioning issues: pharmaceutical development teams are constantly sharing data. With Excel, this means you create many files, which are frequently updated, edited, and resent. Keeping all these versions coordinated requires attention from everyone on the team.

Taken together, Excel has become a significant source of frustration within many companies.

Luminata was built on the following values:

Chemically intelligent platform: Luminata understands chemical structures and reaction schemes. Analytical and chemical data are connected to structures, allowing users to make better decisions. Users can also perform structure-based searches to see where a chemical has shown up in other parts of the same project.

Live analytical data: access complete chromatograms, mass spectra, NMR spectra, and more. Reprocess your data to get a deeper understanding of your results without juggling spreadsheets and multiple file formats.

Collaborative science: share results with your entire development team, no matter if they are down the hall or across the world. Put an end to endless email chains or file-sharing dumping grounds.

FAIR data principles: Luminata adheres to FAIR data principles, meaning it is findable, accessible, interoperable, and reusable.[7] This significantly increases the range of use for your experimental results, including supporting data science initiatives.

But what does this mean in practice? How does consolidating data into one interface improve research and development? One company that has implemented Luminata within their forced degradation research is Pfizer. Their experiences demonstrate how this software supports their pharmaceutical development efforts.

References

5 Pharma IQ, TetraScience, 2022 State of Digital Lab Transformation in Biopharma, https://resources.tetrascience.com/whitepapers/2022-state-of-digital-lab-transformation

6 Moser, A., Waked, A.E., DiMartino, J., (2021) Consolidating and Managing Data for Drug Development within a Pharmaceutical Laboratory: Comparing the Mapping and Reporting Tools from Software Applications. *OPRD, 25*(10), 2177-2187.

7 Wilkinson, M.D. et al (2016) The FAIR Guiding Principles for scientific data management and stewardship. *Scientific Data, 3*(1), 1-9.

Meet the Scientist: Dr. Hannah Davies, Principal Scientist, Pfizer[8]

Like many pharmaceutical companies, Pfizer's development data was spread across multiple platforms.

- Waters Empower to store LC/UV and LC/MS data
- Spectrus DB from ACD/Labs for structure elucidation
- Excel to track batch tables
- Electronic laboratory notebooks (ELNs) to track synthetic route information

... and more

Pfizer decided it needed to consolidate this siloed information. "We required a digital solution for data management so that all that data could be collated in one place," says Dr. Hannah Davies, Principal Scientist at Pfizer. They decided to use Luminata, which allowed them to take data from technique-specific databases and store it in a project-specific database. This data can then be accessed and visualized through different tools.

Implementing Luminata improved research across pharmaceutical development. "The power of Luminata is that all of this data can be visualized, searched, and filtered, all in one place," Davies explained. "This facilitates rapid decision making

> ***"[Luminata] facilitates rapid decision making within CMC, across process development, forced degradation and stress testing, batch genealogy, excipient compatibility, and formulation development."***

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Davies, who leads analytical activities in small molecule development, felt that Luminata greatly simplified project management. "As a project lead, finding a tool that consolidates data into one place for project management—rather than having lots of different Excel spreadsheets with batch tables—just makes life a lot easier."

Luminata has been particularly helpful in forced degradation and stability studies. "As an analytical department, understanding, predicting, [and] monitoring drug degradation is one of the most important deliverables, so it is really important that we can database all that data to build up that understanding," said Davies. She values having access to the stability map, analytical data, impurity amounts, and more, consolidated in a single interface.

While Pfizer has used several software tools to manage their degradation data over the years, they did not offer all the features the company was looking for. In the next section, we describe how Luminata can be used to support forced degradation research.

References

8 Quotes from Dr. Davies are from the "How Pfizer is Using Luminata to Support Pharmaceutical Development," webinar. **Watch the recording**

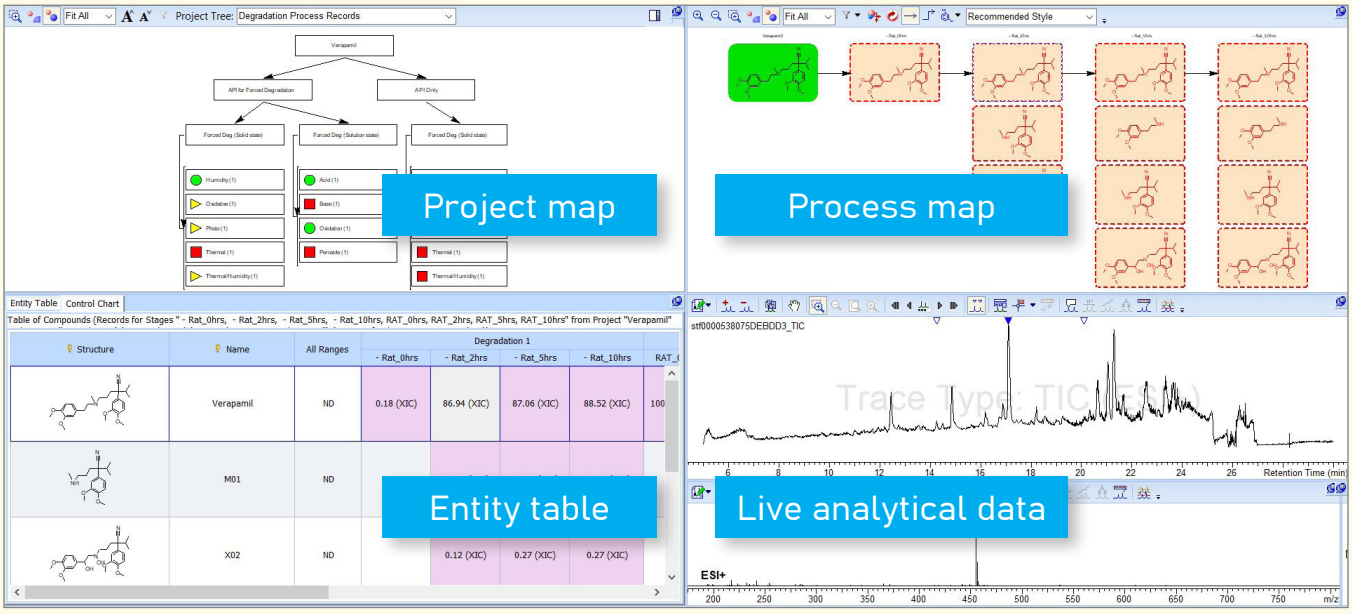
Forced Degradation in Luminata

Luminata helps scientists across pharmaceutical development, but the software includes several features designed to enable forced degradation workflows. These tools allow you to build process maps using SDFiles generated by third-party applications, quickly build experimental study records, and review the status of the entire study for project management purposes.

Building Process Maps from SDFiles

Scientists working in stability research often use software to predict degradation paths, such as Lhasa's Zeneth. While these tools are effective at identifying major degradants, connecting those theoretical results to experimental data is challenging.

Luminata allows you to link the API with all degradants predicted in different conditions. Theoretical degradants generated by third-party applications are represented in degradation pathways. Luminata uses this predicted information to build a process map. Analytical data for each forced degradation study can therefore be stored alongside your predicted results.



Forced degradation view

Integrating the theoretical and experimental data offers several practical benefits. It reduces the need to manage multiple file types, which increases efficiency and lowers the risk of error. It also simplifies the assessment of experimental results, so you can more easily refer to predicted degradation maps to guide analysis. Finally, it allows you to assess the accuracy of their predicted results, which can inform decision-making.

Simplifying Record Handling with the Forced Degradation Wizard

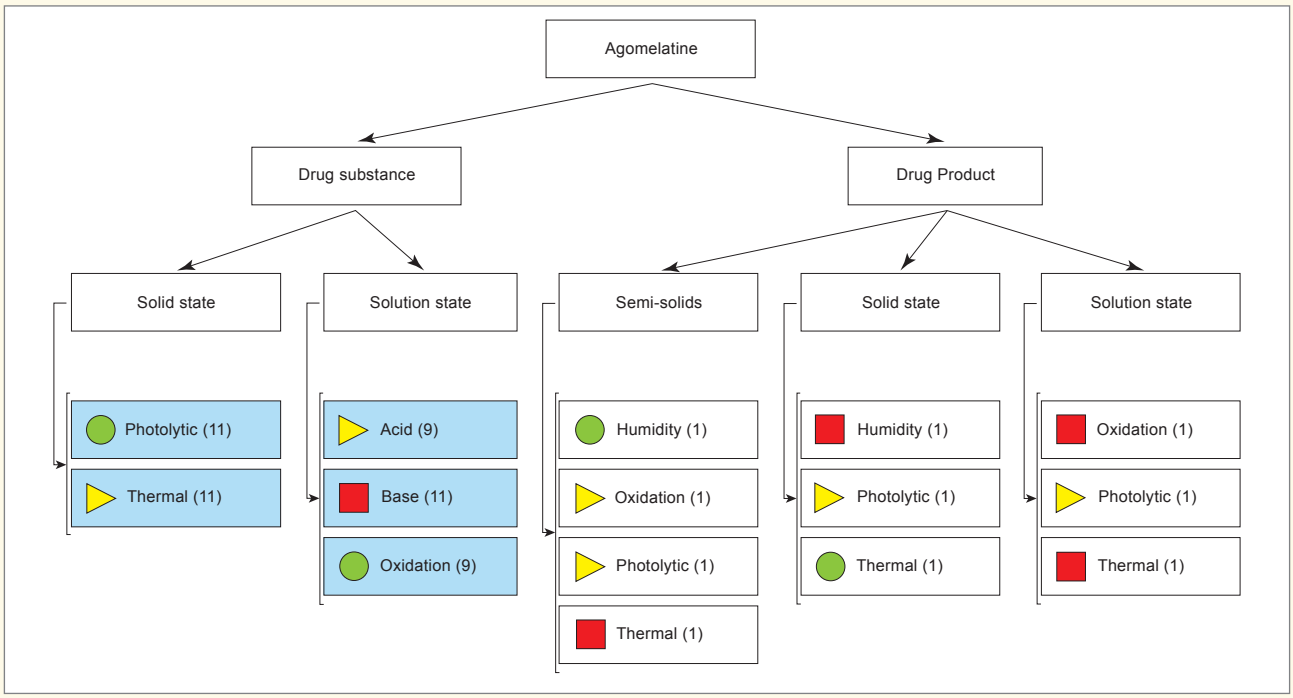
Forced degradation studies typically involve a routine set of experiments. Temperature, pH, and humidity tests are standard elements of any stability testing. Creating and managing individual files for each experiment is repetitive and time-consuming. Development teams may use templated spreadsheets for this purpose, though these often require considerable attention to set up and manage.

To simplify building this set of records, Luminata uses a “Forced Degradation Wizard” to quickly build forced degradation study records. This allows you to select from a list of experiments to run, in addition to custom studies needed for a specific project. The Forced Degradation Wizard simplifies data management, increases consistency, and reduces the risk of error.

Enhanced Project Management Using the Dynamic Project Map

Once all forced degradant records have been created, they can be viewed in the Dynamic Project Map. This allows you to review the status of the forced degradation study. This is particularly helpful for team leaders or management personnel that want to assess project status. It also helps avoids duplicative or forgotten experiments.

Project progress is displayed using a stoplight system, where green represents complete studies, yellow represents studies underway, and red represents studies that have yet to begin. You can access results of completed studies through this dynamic project map.



Dynamic project map in Luminata interface

Next Steps

How Can Luminata Support Your Forced Degradation Research?

Pharmaceutical companies are using Luminata to enhance their development work, with >50% of the world's top 15 biopharma companies using the software. Luminata changes the way scientists access and share data, leading to better, more efficient science. In addition to supporting work across pharmaceutical development, Luminata has specialized tools for use in forced degradation studies, including accessing predicted degradation pathways and dynamic project maps.

Is your organization ready for Luminata? Here are some questions to consider:

1. Do you use in silico tools, such as Lhasa's Zeneth, to predict degradation pathways?
2. Are your theoretical degradant map pathways easily accessible across the organization?
3. Are you storing analytical and chemical data in multiple data silos, that cannot communicate effectively?
4. Does your research team spend significant time preparing degradant reports?
5. Does your stability testing take place at multiple sites, or involve a mix of in-house and contract organizations?
6. If you are working with a CxO, do they provide results as PDF without necessary interpretation?
7. Is time spent performing unnecessary duplicates of degradant studies?
8. Would team leaders or management benefit from more information about the progress of your project?
9. Do you have a methodology to design degradant studies? Is it a challenge to maintain consistency across locations?
10. Do you have the necessary IT infrastructure to deploy an advanced chemical data management solution?

If you answered "yes" to some or all these questions, Luminata may be an effective tool for enhancing your research. To learn more about how Luminata can support research at your company, contact us to talk with one of our representatives.

Contact Us

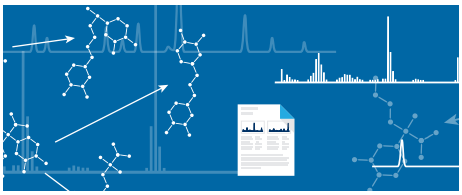
Additional Resources:

Webinar: How Pfizer is Using Luminata to Support Pharmaceutical Development

Dr. Hannah Davies (Principal Scientist, Pfizer) explains how Pfizer is using Luminata to consolidate data and improve project management. Includes an in-depth discussion on Luminata's application to forced degradation workflows.

Watch now

White Paper: An Update for Pharmaceutical Stress Testing Enabled by Modern Informatics Technologies



What is the current state of forced degradation research and data management? Steven Baertschi, Ph.D., (President; Baertschi Consulting) and Joe DiMartino, M.Sc., (Solution Area Manager, ACD/Labs) review the challenges facing the field of stress testing.

Read now

Application Note: Forced Degradation Data Management in Drug Development

How is Luminata used in forced degradation research? Learn more about how this software helps capture structural information, build project maps, and manage experimental data.

Read now

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