Enhancing Impurity Control with Data Management

Executive Summary

Standards for pharmaceutical quality are constantly rising. Regulators expect pharmaceutical development teams to demonstrate in-depth knowledge of their chemical processes. Unfortunately, scientists must devote significant time and resources to handling their data, which interferes with effective decision-making.

Luminata® software consolidates all your pharmaceutical development data in one interface. It is built on a chemically intelligent platform, allowing researchers to access and visualize analytical, chemical, and in silico data from across their team.

Novartis is a pharmaceutical company implementing Luminata to manage their impurities data. Dr. Dorina Kotoni explained how Luminata is enabling Novartis to share data more effectively between formulation, analytical, and chemistry departments.

Luminata enables you to:

- Easily calculate impurity carryover, as well as the fate and purge of impurities
- Visualize experimental results to support better decision making
- Avoid errors and save time with built-in reporting tools.

Luminata

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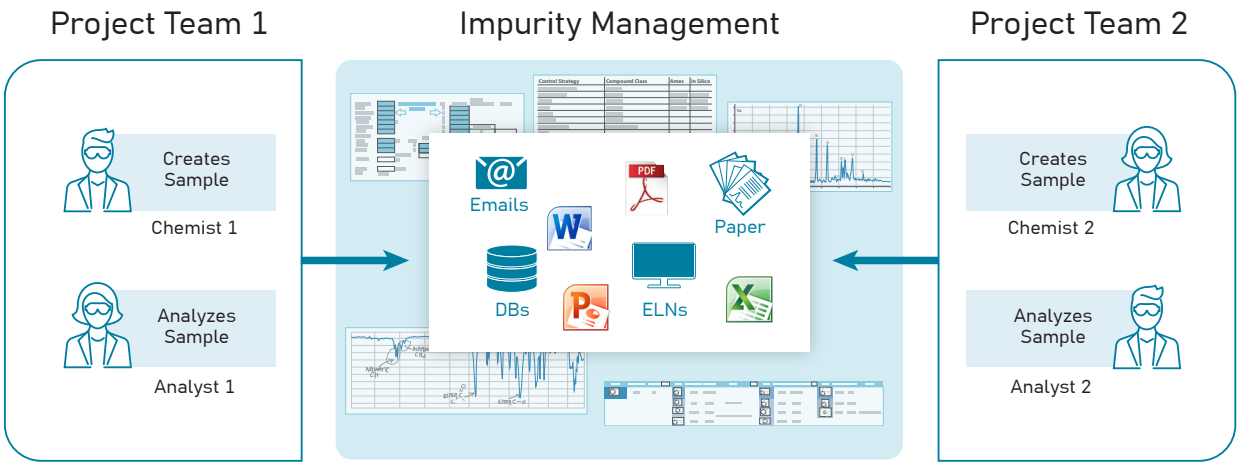
Data Management Challenges in Impurity Control

Patients expect medications to be high quality, effective, safe, and free of toxic impurities. While this has always been true, regulators have been elevating their standards in recent years to ensure the quality of medications on the market. Pharmaceutical development teams are therefore expected to demonstrate a detailed understanding of their chemical processes.

Many companies have implemented "quality by design" (QbD) principles to support this goal. This is the practice of intentionally developing chemical routes to avoid the production of impurities and reduce the chance they make their way into the final product.[1] While QbD ultimately leads to higher-quality pharmaceuticals, it also requires an in-depth knowledge of the entire route when developing impurity control strategies.

One critical obstacle to improving the quality of pharmaceuticals through practices such as QbD is access to data. Chemists often find it challenging to develop a holistic view of pharmaceutical development because chemical, analytical, and process data is spread across a patchwork of incompatible systems. This leads to problems when identifying impurities, developing control strategies, and compiling regulatory documentation.



Pharmaceutical development data is scattered across a variety of systems and data silos.

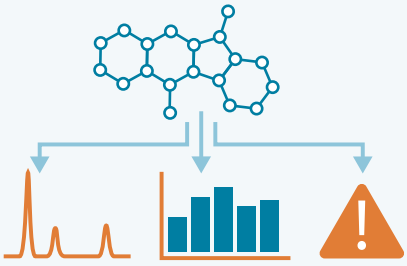
“What’s that Peak?” – Managing Structure Elucidation Data

Impurities that occur beyond a certain threshold must be identified and characterized during pharmaceutical development to ensure that drugs are safe and effective. Verifying the identity of an unknown peak often requires assembling many types of data from both early and late development, which may not be readily accessible. Handling these files can be time-consuming, error-prone, and frustrating.

Many companies rely on Excel to consolidate these disparate streams of data together. This general-purpose software is used widely in pharmaceutical development due to its accessibility and long history of use. Structures and experimental results are aggregated in these Excel files to track the identity of all the impurities within a project.

Unfortunately, Excel is not designed for pharmaceutical development. It lacks chemical intelligence, making searching based on molecular structure impossible. Excel also struggles with versioning issues, making coordinating multi-site research activities challenging. Overall, Excel is not sufficient for managing the data of pharmaceutical development teams.[2]

Barriers to Effective Decision-Making



Identifying impurities is just the first hurdle scientists must overcome. Next, they must classify each identified impurity, develop accurate analytical techniques, and then find control strategies that adhere to the applicable limits. Experts across pharmaceutical development must collaborate and share data to complete this demanding work.

This challenge is particularly acute with DNA-reactive impurities such as nitrosamines, as evidenced in the recent drug recalls issued by the FDA.[3] The ICH Q7 guidelines recommend that the intake of mutagenic impurities not exceed 1.5 µg/day.[4] This strict standard can be even lower for compounds with known toxicological properties.

Accessing all the information necessary to complete this work is difficult. Toxicological, analytical, and process data require separate software tools due to compatibility issues. This acts as an obstacle to effective collaboration and decision making.

Time-Consuming Document Compilation

The ultimate hurdle for impurity data is during regulatory approval. Each result needs to stand up to the scrutiny of regulatory officials, including details about the experimental and analytical methods used. Typically, this information resides in electronic laboratory notebooks (ELNs) but accessing this data through a centralized reference is impossible.

In practice, those assembling results to prepare regulatory documentation often must compile data manually. This process is both stressful and tedious. Scientists must input thousands of entries into tables that must be double- and triple-checked. This process is a massive time investment, taking weeks or months.

Better Data and Better Science

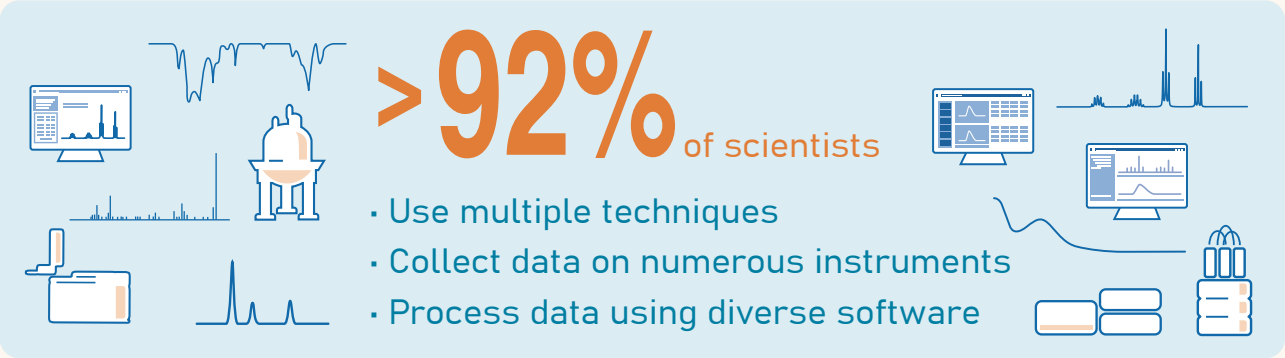
Many organizations accept these inefficiencies as inevitable, implementing cumbersome workarounds without addressing the problem of data management. It can feel like sharing, updating, and organizing data has become everyone's full-time job.

Luminata offers a solution to these challenges. Scientists can consolidate their data in one interface, accessing all the experimental and chemical information across development. This leads to better, more efficient research. The following section explains Luminata's approach to sharing scientific knowledge and how it addresses the root causes of pharmaceutical development's data challenge.

Share Complex Scientific Knowledge with Luminata

Impurity control isn't the only area of pharmaceutical sciences 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]

Why has data management become so time-intensive? A 2022 survey of chemical researchers by ACD/Labs found that over 92% of respondents collect data on numerous instruments, use multiple techniques, and rely on diverse software for processing analytical data. Managing these multiple data sources is a real challenge—68% of respondents said using or sharing data was hard.[6]



The survey also found that the most popular tool for storing analytical data was Microsoft programs, such as Excel.[6] As described above, Excel is not designed to support complex research teams and lacks key features such as chemical intelligence or live analytical data. While many companies attempt to overcome Excel's challenges with a combination of plug-ins and workarounds, spreadsheets are not designed to keep up with pharmaceutical development research.

Luminata was created to upgrade how research teams access chemical and process data. These many streams of information are all available in a single interface. Luminata was built on the following principles:

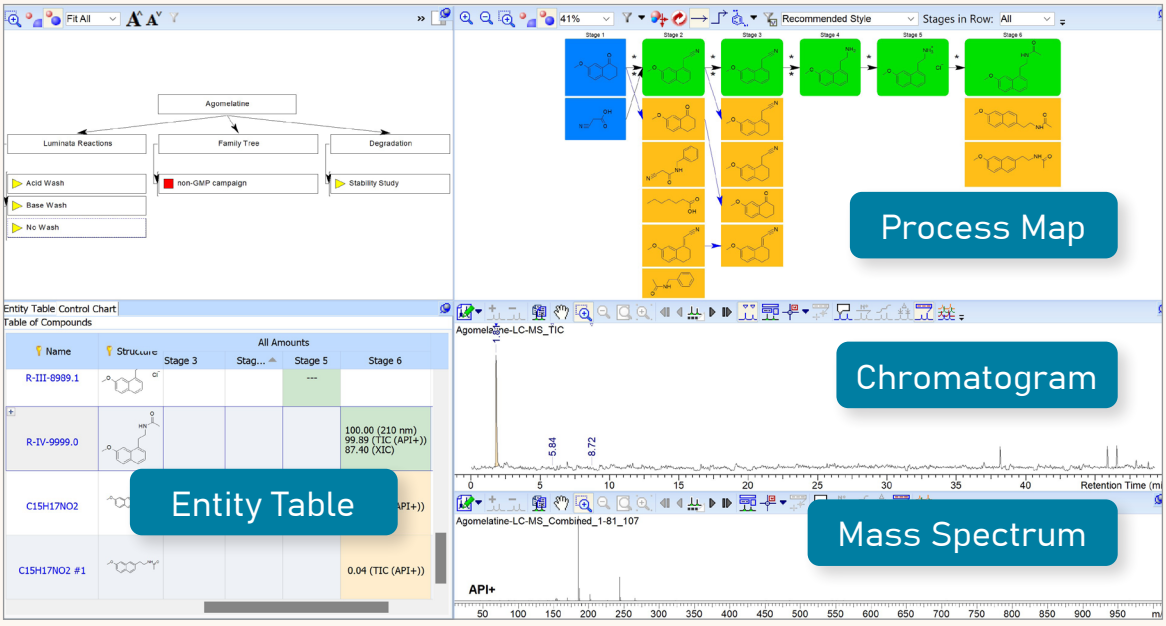
Chemically intelligent platform: Luminata understands chemical structures and reaction schemes. Analytical and chemical data are connected to structures, allowing users to make better decisions. Users can also perform structure-based searches to see if a chemical has been identified previously.

Live analytical data: access all your chromatograms, mass spectra, NMR spectra, and more in a single interface. Reprocess your data to better understand 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 stored data is findable, 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 impurity control? One company that has implemented this tool is Novartis. Their experiences demonstrate how Luminata supports pharmaceutical development efforts.



Luminata allows users to access impurity data and information, include process maps, chromatograms, entity tables and more.

Meet the Scientist:

Dr. Dorina Kotoni[8], Associate Director, Novartis

Novartis has its own CSI, though it might not be the CSI you are thinking of. Instead of solving crimes, the Chemical Structure Investigation group is dedicated to solving structures. “We are responsible for structure elucidation and impurity investigation for the entire new chemical entities division,” explains Dr. Dorina Kotoni, Associate Director and Chemical Structure Investigation Group Lead. This includes both compounds under development, as well as medications that are already commercialized.

In practice, the CSI group carries out analytical chemistry experiments, such as:

- Isolating impurities for Ames testing or creating reference standards
- Identifying process impurities
- Performing forced degradation studies

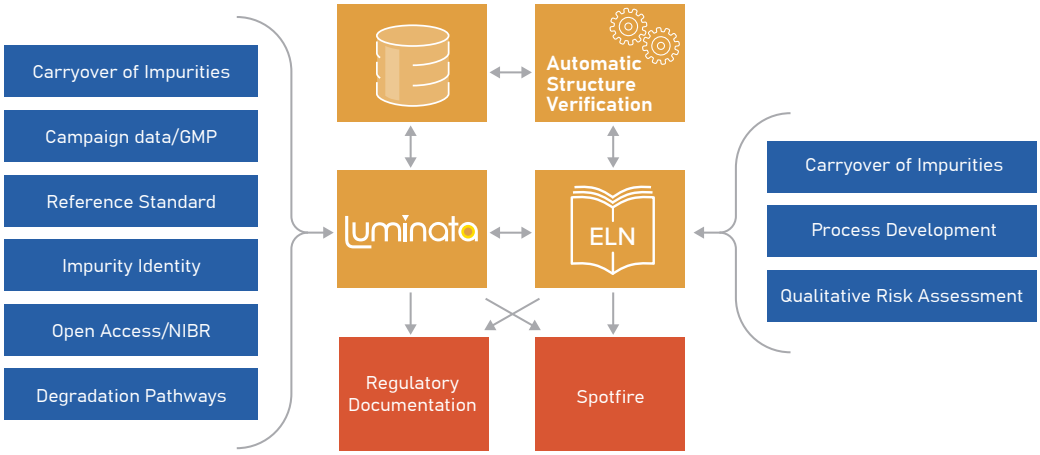
Overall, the team performs approximately 400 structure elucidations and 700 verifications per year. They use an automated structure verification system to keep up with their demanding schedule, which uses a machine learning approach to process analytical results and verify chemical structures. An expert scientist then reviews these structures before entering them into the impurities database.

In addition to running experiments and reviewing analytical results, the CSI group is responsible for managing impurity elucidation data across projects over time. Drug development often takes place over many years, meaning it is sometimes challenging to find results from early development when preparing regulatory documents due to data silos or employee turnover. Centralizing impurity data reduces the chance of data being lost.

This work involves a massive amount of data, which creates a data management challenge. The CSI requires information from pharmaceutical development to carry

out their work and must send results to other teams to perform downstream functions such as assembling regulatory documentation. Managing these many streams of data can become impractical and time-consuming.

Kotoni's team decided to use Luminata to gather their data in a single interface. The flow of this data is summarized in the diagram. This software simplified data access for the CSI team and made impurity information available to others in the organization. Luminata also includes contextual information that is essential for solving chemical structures. "We are able to capture, at the same time, the reference information, information about a specific patch, and what is most important, how it connects to the different synthetic steps it was observed," said Kotoni.



Management of impurity data within Novartis CSI. Blue indicates sources of data, yellow indicates systems for managing analytical data, and red indicates system outputs. By adding data to central repositories, it simplifies information retrieval and centralizes access.

Kotoni explains that one of the advantages of Luminata is the ability to share impurity data across teams. "For us, the most important part is how we will be able to share this data between the formulation, analytical, and chemistry departments," she explained. "We feel this is where we can really make a difference with the tool."

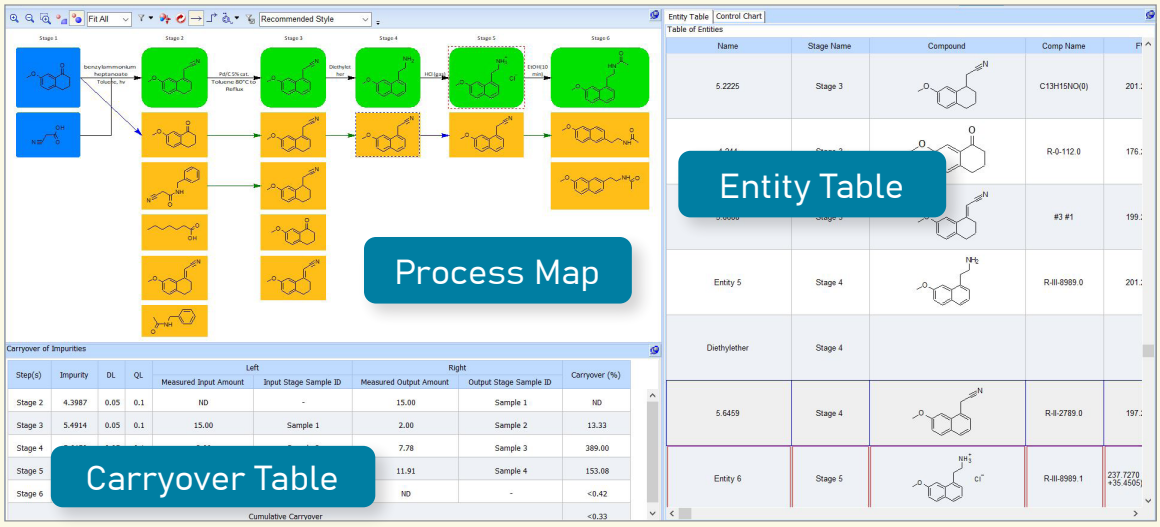
Effectively Controlling Impurities with Luminata

Luminata consolidates chemical, process, and analytical data from across pharmaceutical development, allowing all your team members to share information effectively. In addition, the software includes several features that are helpful for impurity control. This includes performing calculations, visualizing experimental results, and generating reports to prepare regulatory filings.

Fast Carryover Calculations for Fate and Purge Testing

Luminata is built around process maps. Chemical reaction schemes are laid out, including every intermediate and impurity produced throughout the reaction. Users can directly access analytical data such as chromatograms and mass spectra from the process map to assess performance.

Once experimental data is in the software, you can use Luminata to automatically calculate carryover at each reaction stage or over the entire route. This edit helps assess at which stage each impurity is removed and what factors influence the product quality.



Luminata's Carryover Table allows users to review impurity removal.

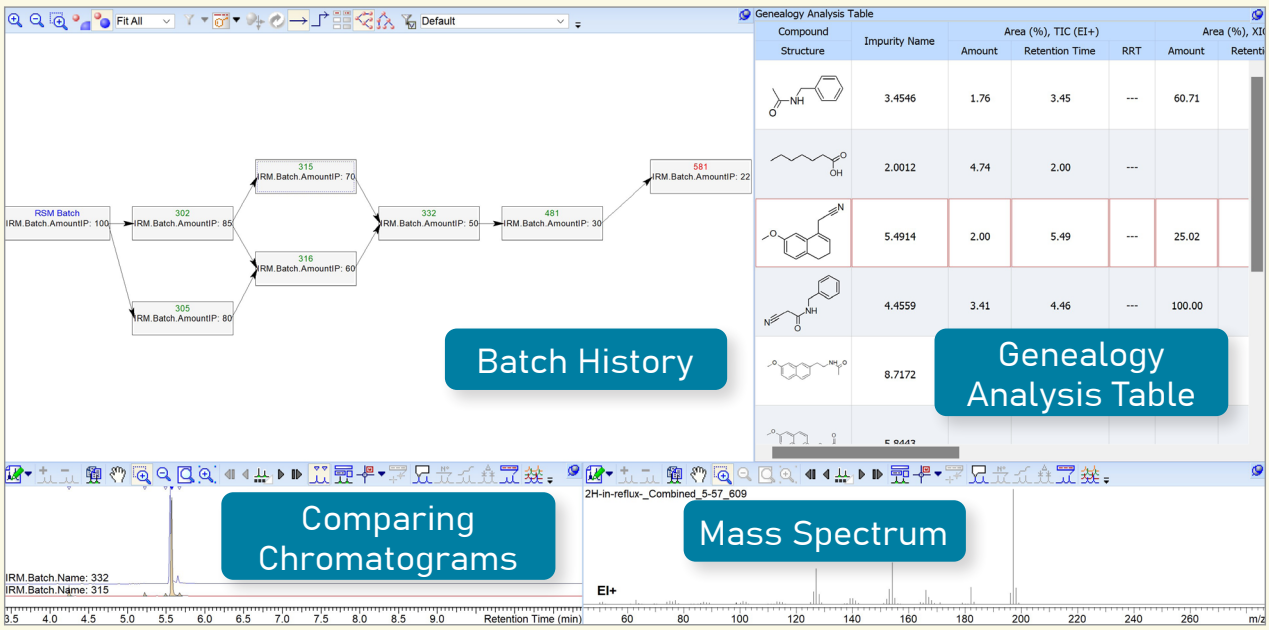
These tools can also be applied to "spike and purge" studies, where batches are intentionally spiked with chemical impurities at different stages of the route. You can use this data to determine purge factors, which are used to justify impurity control strategies.[9]

Visualizations for Effective Decision Making

Effective impurity control is ultimately about decision-making. Scientists use information about their reaction routes to avoid risks and increase efficiency. Luminata's data visualization tools allow you to understand your experimental results quickly.

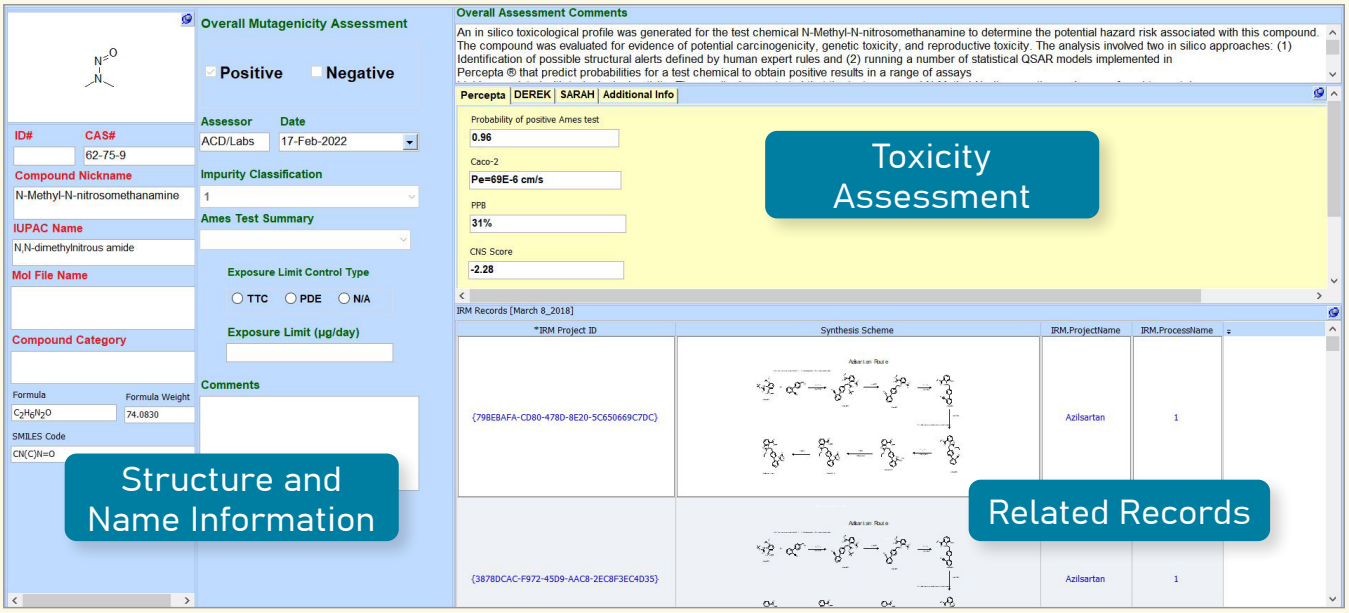
These visualization tools can be used for batch-to-batch comparison. Imagine you have switched suppliers for a critical reagent such as a catalyst—you need to verify that your product quality is consistent. Without Luminata, you would need to go through the time-consuming process of assembling data to assess your experiment. Luminata's batch-to-batch view allows you to quickly compare results in a table or stacked chromatograms.

Some users prefer to see their data using business intelligence software such as TIBCO Spotfire. You can display web pages in Luminata so that you can use a third-party data visualization without having to leave the software.



Batch-to-batch comparisons in Luminata allow users to identify quality issues.

You can also access any predicted or experimental toxicity information through the "tox assessment view." This has many applications, such as identifying genotoxic or mutagenic impurities, which require special attention during drug development. Review analytical reference data is also accessible, ensuring compound identification is accurate.



The Tox Assessment View offers in-depth information about an individual chemical, including the list of records where it is found.

Avoid Errors and Save Time with Reporting Tools

Ultimately, data is not meant to be left inside analytics software—results must be available for regulatory documents. Luminata offers many options for exporting your experimental data into reports, including carryover and control strategy reports. It also includes audit trails, which allow you to track where each data point came from without needing to track down the scientist who ran each experiment. This saves time when you prepare submissions to regulatory bodies such as the FDA and EMA.

Next Steps

How Can Luminata Support Your Impurity Control Research?

>50% of the world's top 15 biopharma companies are using Luminata to enhance their development work. Luminata changes the way scientists access and share data, leading to better, more efficient product development. This includes several tools that have been developed to support impurity control research.

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

1. Is it ever necessary to review the analytical data to confirm the abstracted data or make comparisons?
2. Do you have difficulty finding all the associated project documents?
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 fate and purge reports?
5. Does your impurity management research take place at multiple sites, or involve contract organizations?
6. If you are working with a CxO, do they provide results as PDF without necessary interpretation?
7. Do you have a consistent methodology of adding information into a summary Excel spreadsheet?
8. Would team leaders or management benefit from more information about the progress of your project?
9. Is it difficult to create control strategy reports?
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

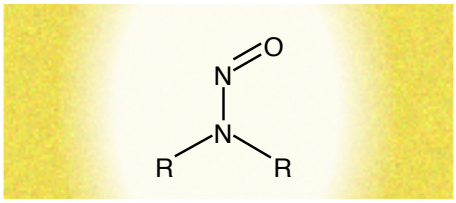
Additional Resources:

Case Study: Results from Bridging Data Management Gaps

Read now

See how a process development team at a top biopharmaceutical company streamlined chemical and process data management and lowered their dependence on unreliable Excel spreadsheets with the help of Luminata.

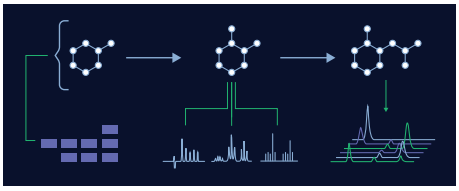
Webinar: Using CMC Decision Support to Enhance Nitrosamine Control



Watch now

N-nitrosamines are a growing challenge in pharmaceutical development. This class of mutagenic impurity has been responsible for multiple rounds of recalls that have hit several major pharmaceutical companies. Learn how Luminata can help avoid issues with these mutagenic contaminants.

Application Note: Applying QbD in Process and Impurity Control Strategy Development



Read now

Pharmaceutical development groups need support from their informatics infrastructure to implement quality-by-design (QbD). Luminata helps researchers leverage QbD, visualizing all their analytical data in a single environment.

ACD/Labs

www.acdlabs.com/luminata

Toronto, Canada | Bracknell, UK | Strasbourg, France
Frankfurt, Germany | Shanghai, China

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