Why Pharmaceutical Companies Look to Lighthouse to Generate Electronic Reports for CMC-related Submissions

Structured Data for Better Drug Stability Reporting

INTRODUCTION

Cognition® SaaS solutions support the creation of process-driven templates to guide users toward compliant development and documentation practices in the highly regulated life sciences industry. By taking a structured data approach to compliance, the solutions enable medical device and pharmaceutical product development teams to create an environment that guides users through required tasks in a systematic and consistent manner. This ensures a common approach is used for product development, design control, reporting, and submission documentation.

Underlying all Cognition software applications is the Cognition Cockpit Framework which provides the engine to create structured data items, configurable workflow, comprehensive audit logs, document review/approval/release, and compliant electronic records and signatures. Cognition's approach to structured data and content management ensures high data integrity, a strong chain of evidence, and improved credibility with health authorities.

Cognition offers three industry solutions: Compass®, Cockpit® Enterprise, and Lighthouse™. These solutions are built on a two-level technology stack starting with the Knowledge Center Core Platform. It goes beyond just storing data and excels at modeling the relationships between data, which translates into enhanced traceability and data integrity. Built on the Knowledge Center Core Platform's environment, the Cockpit Framework is the engine that powers intelligent product development and reporting. Together, they provide the foundation for Compass, Cockpit Enterprise, and Lighthouse. This paper focuses on the Lighthouse Application Suite and the Drug Stability (DS) Reporting Application.

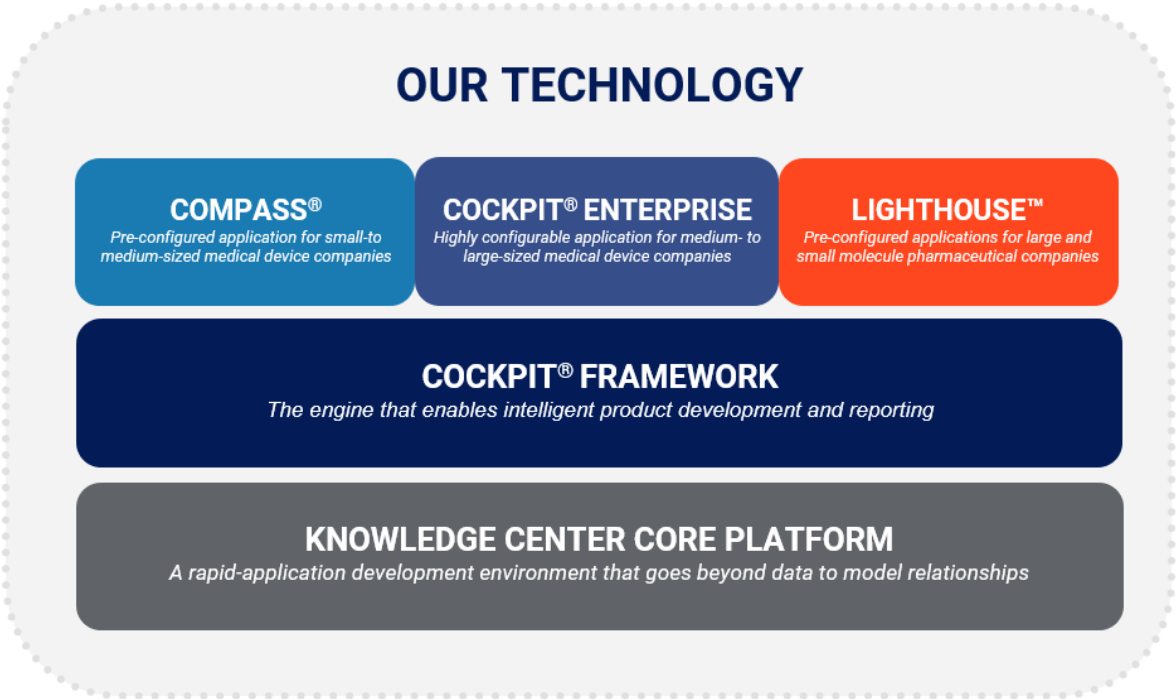


Figure 1: Our Solutions for A Structured Data Approach to Compliance

THE NEED FOR STRUCTURED DATA AND CONTENT IN CMC

Today, the majority of CMC Module 3 reports are created manually, entailing repetitive work and an excess of time and human resources spent verifying data and piecing together disparate pieces for submission deliverables. With the massive amounts of interrelated data in drug and biologics development, managing data manually is prone to human error which creates errors that are difficult to unravel and fix. Scientists today spend much too much time inefficiently verifying data and fixing errors.

There has been recent recognition in the global pharmaceutical industry that CMC-related data and content must be structured to not only bring quality and efficiency to the process, but to ultimately enable a standard way to manage data across global regulatory frameworks. The goal is to get therapies to patients in need faster. The Lighthouse Application Suite supports that goal.

LIGHTHOUSE APPLICATION SUITE

Cognition's Lighthouse suite of applications supports improved quality, speed, and efficiency of both R&D and manufacturing-related report deliverables in pharmaceutical CMC processes, primarily for Module 3 of the Common Technical Document (CTD). Lighthouse is used to create structured data and content for both internal reports and formal Dossier reports through seamless integration with source data systems and corporate document management and quality systems. Lighthouse applications help users automate the generation of large, complex data tables and report documents while providing workflow, audit, history, and electronic signature capabilities, ensuring data integrity and protecting the chain of evidence for reporting activities.

Figure 2 shows the overall structure of Cognition software including the Lighthouse Application Suite. This document focuses on the Lighthouse Drug Stability (DS) Reporting Application.

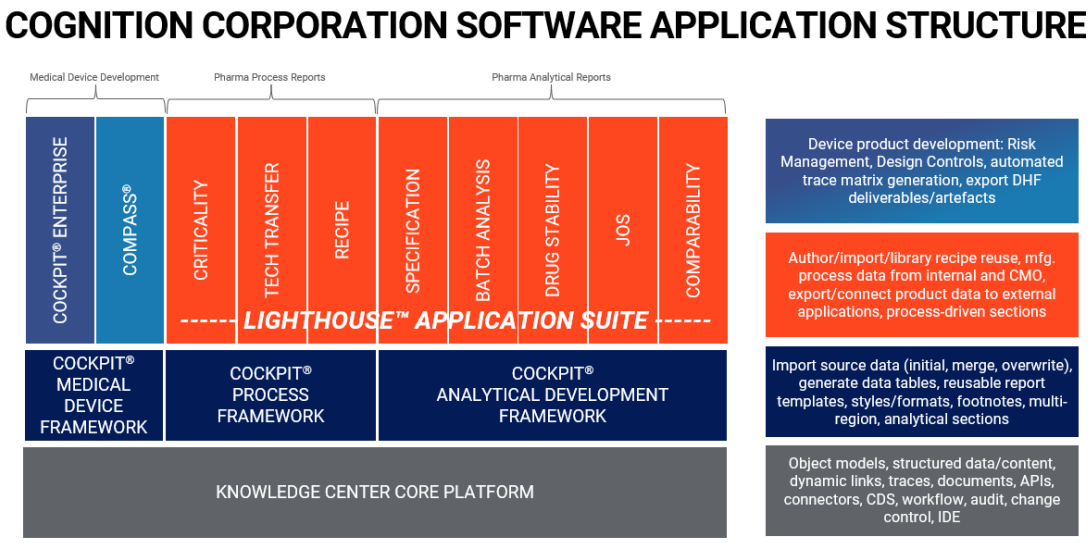


Figure 2: Cognition Corporation Software Structure

WHY LIGHTHOUSE?

IMPROVE DATA INTEGRITY

The software provides a consistent, traceable, enforceable chain of evidence as well as comprehensive audit logs from project level down to individual item level. Global, unique data item ID management ensures data integrity. Interaction with the software is tracked and controlled through workflow, roles, and privileges. Data imports include definable rules for detecting variations from expected values. Cognition can also assist customers with risk-based validation and software assurance following GAMP 5.

REDUCE ERRORS

Automated import rules from LIMS or other source data systems maintain accurate transcription. Precise commands allow for error-free aggregation of data. Report errors are reduced with parameter settings for typographical adjustment on import, parameter merging, naming conventions, numerical thresholds, etc. Templates ensure users follow prescribed processes and instructions to completion for all tasks, reports, and document deliverables.

IMPROVE REPORT QUALITY

Lighthouse supports contextualized, data-driven decision making in analytical reporting, process reporting, and risk management. Reports and documents are generated through predefined, reusable templates. It provides automatic data table generation with unlimited numbers of data items and levels/connections between items.

REDUCE TIME-TO-MARKET

Users have instant access to all data within and across projects (with appropriate roles and privilege controls). Cycle times are optimized for Dossier development and submission. Reuse of data, templates, and narrative content across projects eliminates the time required for tedious, manual searching and updating of disparate documents and tools.

“I like to tell the story that it took us maybe 5 or 6, 2-hour meetings to assess [drug name] with our previous process. With Lighthouse we are able to complete our work with two meetings in one week. “
-Pharmaceutical Company

INCREASE COMPLIANCE

Business and compliance processes, with embedded job aids and work instructions, can be enforced throughout all reusable templates. Corporate procedures or standard operating procedures can be linked to or embedded in Lighthouse. Templated and controlled report formats can be created for repeatable, reliable results. Lighthouse supports Part 11 for Electronic Records and Signatures.

REDUCE RESOURCE COSTS

Connections to source data systems like LIMS are automated, eliminating the use of Word and Excel, and eliminating the visual examination of tens of thousands of data points to significantly reduce time and resources. Data verification time is reduced due to the automation of data table creation with built-in rules and controls for report generation. Reusable templates minimize configuration time and costs. Role-based access and actions guide users to quickly complete required actions, approvals, etc. Elimination of manual verification of large data tables reduces resource needs for tedious verification and error-correction.

REDUCE IT BURDEN

Lighthouse is provided as a SaaS/cloud environment; it can also be hosted by the customer. Lighthouse is browser-based with no client computer installation. The software provides secure and reliable connections for real-time, global access. Preconfigured templates enable teams to implement quickly with the ability to configure templates as needed for specific project and team needs. Lighthouse provides off-the-shelf templates for easier management of pharmaceutical data.

PREPARE FOR THE FUTURE

Reports, and all structured data items, are dynamic objects with traceability, history, and access control. Reports can export to XML, PDF, JSON, and other formats for true structured data and content delivery. There is complete chain of evidence and data integrity for submissions and audits. Source data can be imported from external systems to generate formal reports and documentation. Reusable templates can be updated at any time to reflect the changing regulatory environment.

LIGHTHOUSE DRUG STABILITY (DS) REPORTING APPLICATION

Cognition's Lighthouse suite includes the Drug Stability (DS) Reporting Application. Lighthouse DS supports the creation and maintenance of dynamic stability reports that grow over time as initial and future testing data are added. Stability reports are used to support initial filings as well as annual product updates and reviews. Lighthouse DS uses Cognition's unique approach to creating structured data and content, reusable report templates, and comprehensive workflow controls to increase confidence in report accuracy and to increase credibility with health authorities. Reports from Lighthouse DS are used to populate various internal reports and Module 3 Dossier sections such as 3.2.S.7.3 and 3.2.P.8.3.

Figure 3 shows a general schematic of the Lighthouse DS application structure. In this figure, the light blue boxes represent structured items and containers of items. The lines between boxes represent links or relationships between structured elements. All Cognition software uses the

concept of structured data items as the initial infrastructure from which to generate complex relationships, data tables, and reports.

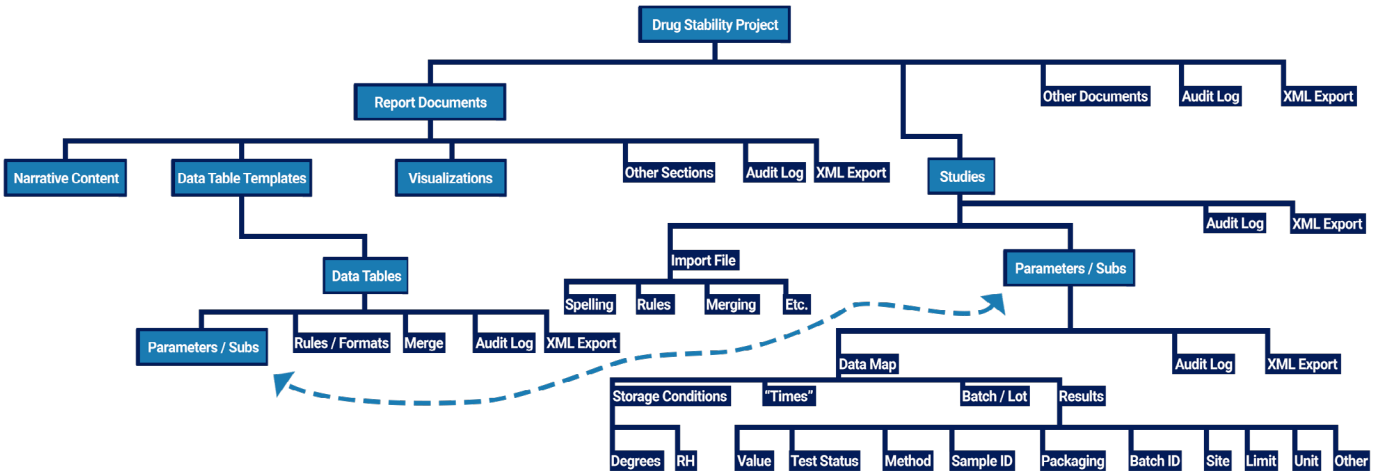


Figure 3: : Drug Stability Reporting Application Schematic

"Without Cognition's support, the eReporting system that Product Quality Management has built using Lighthouse would not be making such a 'real' impact on our critical business processes."
-Pharmaceutical Company

LIGHTHOUSE DS KEY FEATURES

Cognition software's use of structured data, content, links, documents, and reusable data table and report templates helps companies reduce the time and resources required to complete critical reporting activities for both internal consumption and health authority submissions. Automated creation of data-heavy tables eliminates errors resulting from manual table generation. The below list highlights key features of the Lighthouse Drug Stability Reporting Application as reported by our customers.

1. QUALITY-ENFORCED, SOURCE-AGNOSTIC DATA IMPORTS

The Lighthouse DS application uses source-agnostic data import to create individual, structured data items to render Studies, Parameters, Storage Conditions, Time Points, test results, data tables, documents, and overall reporting projects. The application supports three import types. Initial imports take all data from source systems into Lighthouse and generate unique structured data items. Later imports into the same project provide the user a choice between overwriting data or merging data. Merging imports new timepoint data and fills in data gaps and does not overwrite any existing data. Overwrite imports all data and replaces any existing data with new values. Figure 4 provides an overview of the three import methods.

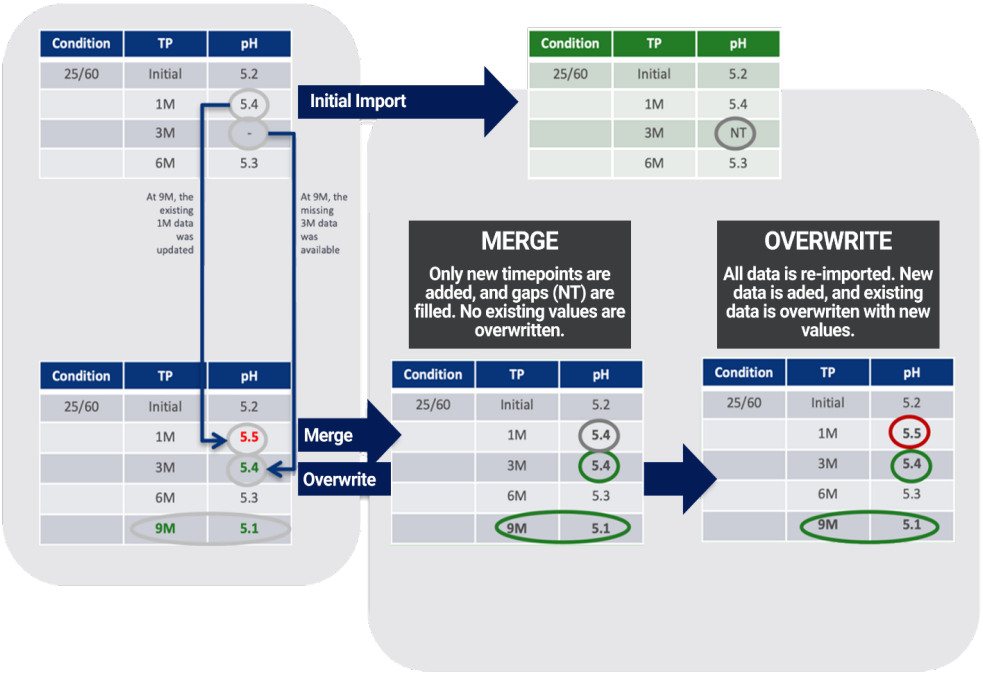


Figure 4: Drug Stability Reporting—Three Import Methods

2. STRUCTURED PARAMETERS

Lighthouse DS Parameters are fundamental data items as they represent the actual testing information for stability studies. Parameters may decompose into sub parameters as required. Parameters and sub parameters use Lighthouse data mapping to combine information about storage conditions, time/pull points, and test results. Parameters retain comprehensive, "life-long" audit logs of all activity. Figure 5 shows a Parameter, sub parameters, and mapped relationships. Parameters can be used in multiple stability reports over any period of time.

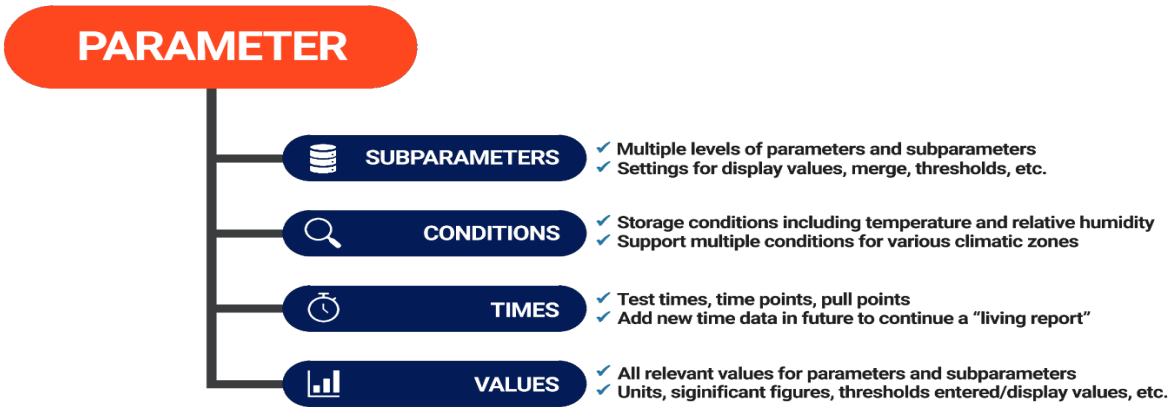
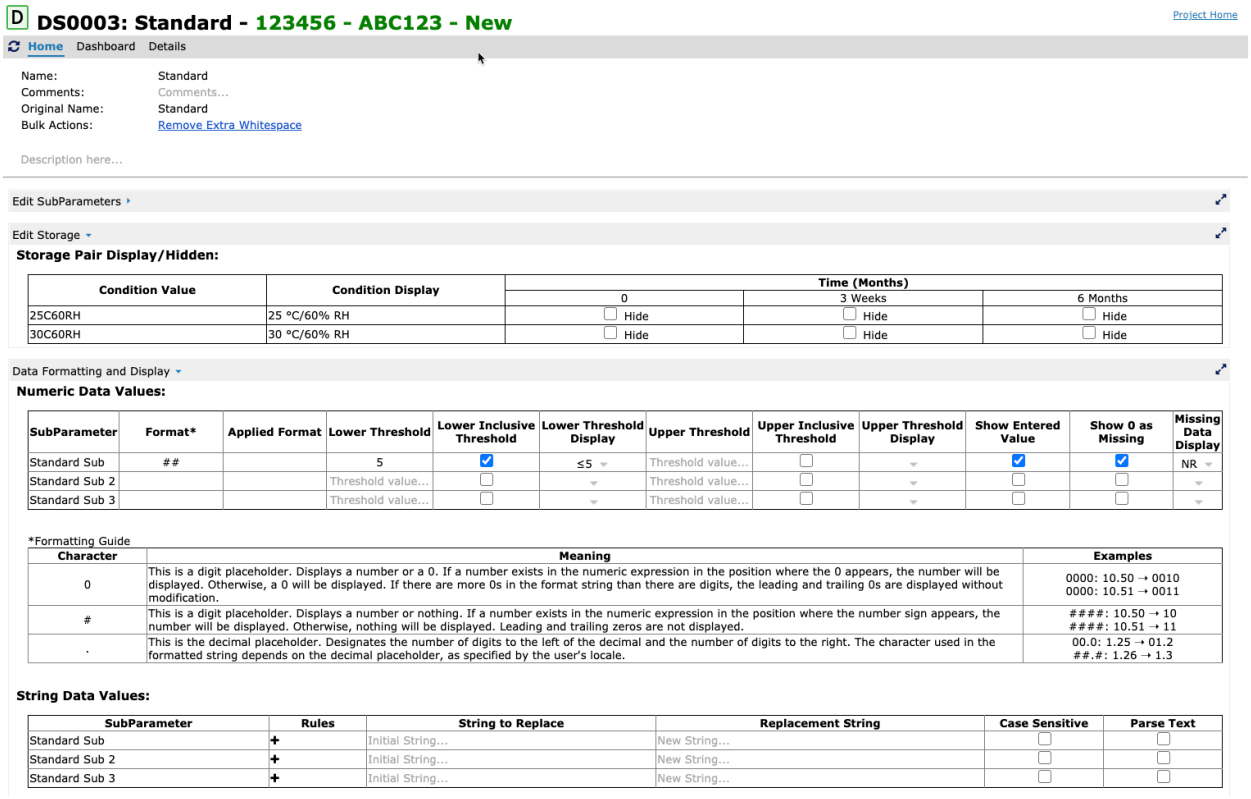


Figure 5: Drug Stability Reporting Application Parameters

Every parameter is a unique, structured data item in Lighthouse. Parameters have "home pages" where authorized users can make decisions about how parameters are displayed and rendered within data tables. Settings include numerical thresholds, significant figures, entered versus

displayed values, time points displayed, parameter ordering, etc. Settings on parameters drive how the parameters appear in data tables. ***Lighthouse never alters any actual source data values.*** Figure 6 shows a portion of a Parameter home page.



DS0003: Standard - 123456 - ABC123 - New

Project Home

Home Dashboard Details

Name: Standard
Comments: Comments...
Original Name: Standard
Bulk Actions: Remove Extra Whitespace

Description here...

Edit SubParameters

Edit Storage

Storage Pair Display/Hidden:

Condition Value	Condition Display	Time (Months)		
		0	3 Weeks	6 Months
25C60RH	25 °C/60% RH	Hide	Hide	Hide
30C60RH	30 °C/60% RH	Hide	Hide	Hide

Data Formatting and Display

Numeric Data Values:

SubParameter	Format*	Applied Format	Lower Threshold	Lower Inclusive Threshold	Lower Threshold Display	Upper Threshold	Upper Inclusive Threshold	Upper Threshold Display	Show Entered Value	Show 0 as Missing	Missing Data Display
Standard Sub	##		5	☑	≤5	Threshold value...	☐		☑	☑	NR
Standard Sub 2			Threshold value...	☐		Threshold value...	☐		☐	☐	
Standard Sub 3			Threshold value...	☐		Threshold value...	☐		☐	☐	

*Formatting Guide

Character	Meaning	Examples
0	This is a digit placeholder. Displays a number or a 0. If a number exists in the numeric expression in the position where the 0 appears, the number will be displayed. Otherwise, a 0 will be displayed. If there are more 0s in the format string than there are digits, the leading and trailing 0s are displayed without modification.	0000: 10.50 → 0010 0000: 10.51 → 0011
#	This is a digit placeholder. Displays a number or nothing. If a number exists in the numeric expression in the position where the number sign appears, the number will be displayed. Otherwise, nothing will be displayed. Leading and trailing zeros are not displayed.	####: 10.50 → 10 ####: 10.51 → 11
.	This is the decimal placeholder. Designates the number of digits to the left of the decimal and the number of digits to the right. The character used in the formatted string depends on the decimal placeholder, as specified by the user's locale.	00.0: 1.25 → 01.2 ##.#: 1.26 → 1.3

String Data Values:

SubParameter	Rules	String to Replace	Replacement String	Case Sensitive	Parse Text
Standard Sub	+	Initial String...	New String...	☐	☐
Standard Sub 2	+	Initial String...	New String...	☐	☐
Standard Sub 3	+	Initial String...	New String...	☐	☐

Figure 6: Portion of Home Page of a Drug Stability Report Parameter

3. REUSABLE STUDY DATA AND REPORT TEMPLATES

Lighthouse DS supports an unlimited number of reusable data table, report, and project templates. Figure 7 shows part of the off-the-shelf Drug Stability project template. This template includes report documents for both Large Molecule and Small Molecule products as well as Shelf Life for Large Molecule. It also contains all of the imported studies with associated parameters and results.

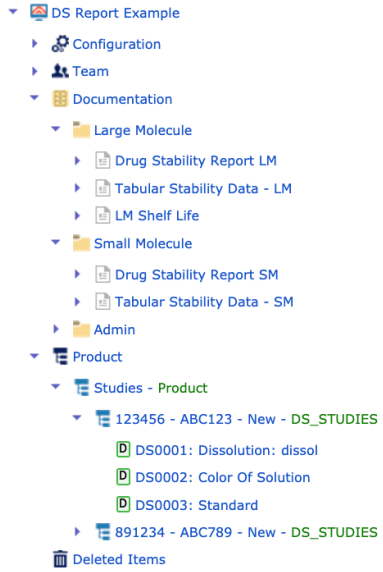


Figure 7: Portion of Table of Contents of Typical Drug Stability Report Project

Drilling down further, users can create and maintain multiple report templates to satisfy requirements for internal reporting needs and health authority submissions. Figure 8 shows the off-the-shelf Drug Stability report template for Small Molecule. Section 8 of the template contains the data tables. The image shows only one section for a data table: section 8.1. Users can create many more data tables and sections as needed for different reports. Other sections of the report are completed through a combination of auto-insertion (from Studies and Data Tables) and direct authoring by the user.

Figure 8: Table of Contents of Small Molecule Stability Report

4. AUTOMATED GENERATION OF DATA TABLES

Data tables are at the core of the Lighthouse DS application. Tables are carefully structured, automatically generated, reusable parts of report templates. Figure 9 shows an example of how a Small Molecule report may render rows and columns and how it combines storage conditions into one table. A Large Molecule report would break out the storage conditions into separate tables. Lighthouse DS supports the definition of how tables are structured so users do not manually build

tables. Instead, users choose a set of parameters which Lighthouse DS uses to automatically generate the appropriate data table.

Table 1: Study 123456 - Batch ABC123 - (bottle) - Standard

Storage Condition	Storage Time (Months)	Standard Sub	Standard Sub 2	Standard (Units...) Standard Sub 3		
				Standard SubSub	Standard SubSub 2	Standard SubSub 3
25 °C/60% RH[a]	0	less than -3 [b]	0	greater than or equal to 2 is cool	The value is >5	NT
	3 Weeks	≤5	≥3	word	≥5	NT
	6	another word with some 4 number in it	29.45	0	5.1	NT
30 °C/60% RH	0	greater than 5, less than -3 !	0	greater than or equal to 2 is cool	The value is >5	NT
	3 Weeks	≤5	≥3	word	≥5	≥6
	6	≤5	≥3[a]	word	NT[b]	5.5

[a] My footnote
[b] Yet one more Footnote
Enable Footnotes Editing

Additional Notes
Add NT Note Add NR Note

Figure 9: Portion of Data Table for Small Molecule Report

Figure 10 shows an example of a data table displaying red exclamation points to notify the user of multiple values found for a parameter. To the lower right in the figure is the Lighthouse Multiple Values Editor where the user determines the appropriate value to use. The application captures and tracks all decisions made by the user as they work to create all tables.

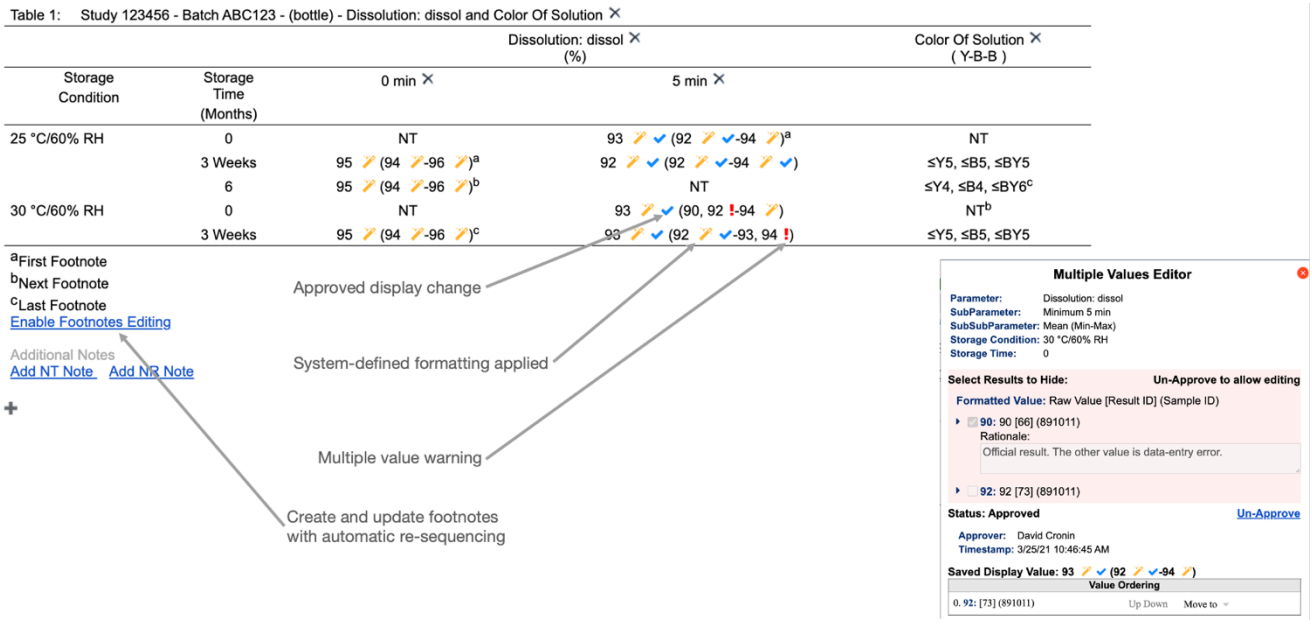


Figure 10: Portion of Data Table UI Controls

The software also supports creating and maintaining footnotes. While footnotes may not at first seem to be a complex matter, some tables require many, which may change or be updated

over time. As users add, edit, and remove footnotes, the software automatically updates them as needed and re-sequences footnote numbers and letters to ensure all footnotes are correctly ordered and identified.

"I just wanted to pass along some feedback. The team completed their report in Lighthouse including the criticality table during a one hour teleconference. This is a significant improvement over the old manual format which often took weeks of back and forth between the functions."
-Pharmaceutical Company

5. ADAPTIVE TO BUSINESS PROCESSES AND JOB AIDS

Lighthouse DS supports the definition and enforcement of prescribed business processes to generate structured data tables and documents for internal consumption and external submission. Source-agnostic data imports can apply import rules on incoming data. Users cannot alter actual source data values. Comprehensive workflow and roles ensure a clear chain of evidence with electronic signatures. Customer-definable, reusable data table and report templates can be created and altered only by administrative actions with audited controls. Figure 11 shows the process flow of Lighthouse DS beginning with source data and ending with completed drug stability reports.

Figure 11: Electronic Report Generation Process

THE BOTTOM LINE

Managing data and reporting on CMC processes is hard, and without a structured data approach it is nearly impossible to do accurately and efficiently. The cost of doing it wrong is an unnecessary financial burden on pharmaceutical companies and has the potential to delay time to market.

A current Cognition customer using the Lighthouse Drug Stability Reporting Application reports a 55%-65% reduction in burden for analytical CMC report creation. This customer is available for reference.

Using Cognition's Lighthouse DS application provides significant reduction in the burden of creating structured reports, allowing scientists to spend more time doing science and less time creating, verifying, and correcting errors in report documentation.

ABOUT COGNITION

For more than 20 years, Cognition Corporation has designed its product development solutions specifically for the life sciences industry including medical device, pharmaceutical, laboratory equipment, and combination products. Cognition software uses a unique technology of generating structured data items, dynamic links between items, reusable templates, and structured documents and reports to support the generation of both internal technical reports and submission deliverables to global health authorities.

FOR MORE INFORMATION

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