Arxspan - Innovative Compound-Registration Workflow Using a Web-Based, Cloud-Hosted Electronic Lab Notebook

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Sunovion Pharmaceuticals Inc. is a fully externalized drug-discovery organization with CRO partners located around the globe. Arxspan LLC's electronic lab notebook (ELN) product was implemented at Sunovion and has streamlined Sunovion's research operations, providing a unique solution to the challenging task of managing and documenting outsourced activities taking place across multiple geographically remote sites.

The implementation has created additional opportunities for efficiency gains at Sunovion, in large part due to its flexible design and centralized placement in outsourcing workflows. One such opportunity for improving productivity was identified within Sunovion's internal compound-registration process. The compound-registration system originally in place at Sunovion relied on a custom-designed in-house application built using Java® Server Pages and Accerlys' Accord chemistry cartridge Java® API. This API allowed the in-house application to seamlessly integrate with Sunovion's internal therapeutic database (utilizing the underlying Accord Oracle schema).

The original registration system was accessed through a web-based interface that allowed users to input new chemical structures, attach any necessary accompanying data, and then submit the compounds for registration in Sunovion's database. The application served its original core purpose of capturing and storying Sunovion's proprietary chemical research data; however, it was approaching the end of its useful lifespan and had become increasingly unreliable requiring significant development efforts.

Moreover, the entire process needed to be fast, accurate and adhere to strict security requirements. The design also needed to be sufficiently flexible to allow for potential future adaptations.

"Accelrys' Accord chemistry cartridge is a thoroughly vetted, highly stable product that has been a work horse for discovery organizations to manage chemical information. But as the technological landscape evolves, Sunovion's needs may change. Hence we anticipate the eventual need to consider alternative database solutions."

The initial conception for the ELN-integrated registration system was designed in collaboration with Arxspan. It was decided to build the initial version using the Accord chemistry cartridge on top of our existing Accord Oracle schema. Arxspan developed a secure web-service protocol to link Accord, with an emphasis on a modular design that would allow the web-service to be integrated with other database products without affecting the end-user experience. This anticipates the possibility of moving to alternative database technology and ensures that the transition could occur with minimal disruption.

"The design phase occurred over roughly 8-10 hours during the span of two weeks. It then took approximately 6-8 months to thoroughly test and optimize to establish the final protocols. As with any highly novel project, there were a few unanticipated challenges and unique roadblocks that developed along the way. Additionally, the requested deliverables evolved as we adapted feedback on the new system from users during testing.Due to the consistently clear communication between Sunovion and Arxspan, all hurdles were successfully navigated in a timely manner to arrive at a product that met or exceeded our expectations."

The end result was a highly adaptive service that replaced Sunovion's entire registration workflow from concept declaration to secure and accurate CRO compound registration. The integrated design (Figure 1) uses the cloud-hosted ELN, but maintains the integrity of proprietary information behind Sunovion's corporate firewall.

"A significant aspect in the design of the ELN-housed registration system is its unique ability to allow CRO scientists to register new chemical compounds without risking the integrity of Sunovion's proprietary database."

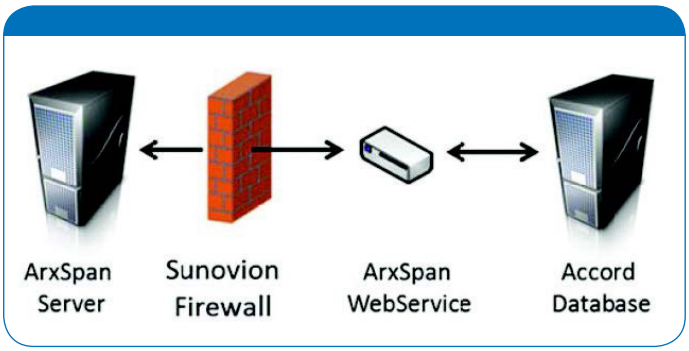

Figure 1: Sunovion integration of Arxspan and compound registration

A full description of the new registration workflow can be broken down into a number of interactive and automated steps, which are described in detail:

Step 1–Requesting Compounds:

The new workflow for the ELN-based registration procedure begins when a Sunovion scientist, or principle investigator (PI), conceptualizes a list of compounds, which becomes the table of contents (TOC) of a notebook. The TOC is easily generated by uploading a file containing the compound structural information (e.g. a ChemDraw CDX file). The ELN performs several procedural checks after the user uploads a new chemical file, including a structure search across the entire ELN performed automatically for each new molecule. This search alerts the PI to any potential duplicate structures present in the ELN database (Figure 2).

"A unique feature of the compound upload process is that a chemist can upload a single Chem-Draw® file to the ELN and have a duplicate check performed for every compound in the file."

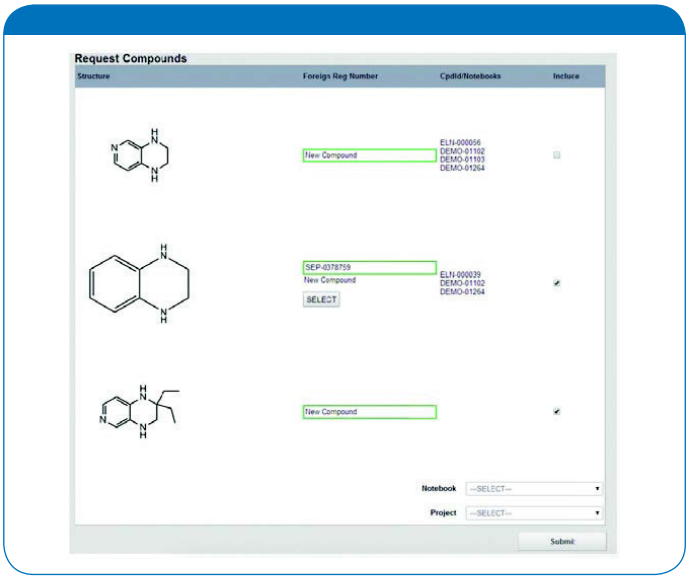

Figure 2: Duplicate checking process. Entry A–compound has previously been requested (ELN-ID), but not synthesized. Each instance in which a compound has been requested is logged (e.g. notebook DEMO-01102). Upon registration the compound will receive a new SEP-ID. Entry B–structure has been requested (ELN-ID) and synthesized (SEP-ID). Upon registration this compound will receive a new lot (batch) number. Entry C–compound is new. There is no record of this compound in Arxspan or the corporate database. The PI can choose to incorporate some or all of the requested compounds into the TOC of a newly created notebook using the results from the duplicate checking process.

Step 2–Table of Contents:

The TOC (Figure 3) of a new notebook serves multiple purposes: 1) it constitutes a work order request that is sent to a CRO; 2) it establishes an audit trail that preserve the origination of each chemical structure in the notebook; 3) it serves as a quality-control check during the registration of a chemical structure; and 4) it provides a simple interface to monitor progress for each compound as it progresses through the workflow of an external CRO scientist.

Every compound requested for synthesis gets assigned a unique ELN identification number (ELN-ID), which allows each compound to be individually tracked. The ELN-ID is used to refer to any particular compound during communications between the CRO and the PI until the compound has been synthesized.the PI until the compound has been synthesized.

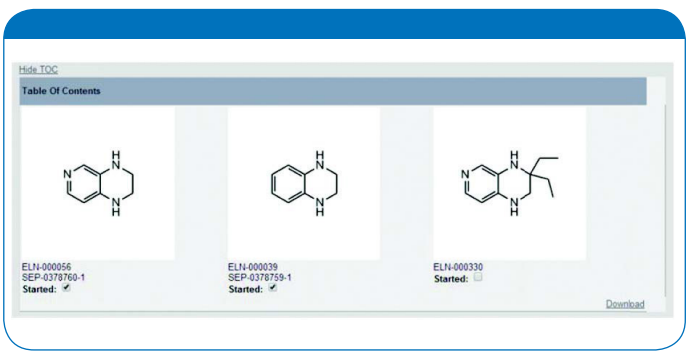

Figure 3: The TOC of a new notebook

Step 3–CRO Registration:

Upon successful synthesis, a CRO scientist initiates the Sunovion registration procedure by clicking on a link labeled "Register" under the compound product tab (Figure 4). The ELN then performs another series of quality control checks and internal audits to eliminate common mistakes. For example, a compound can only be registered if the structure drawn by the CRO matches exactly a structure from the corresponding TOC. IF the compound does not exactly match the structure in the TOC, the registration will be halted and the CRO scientist will receive a structural alter error message (Figure 5). This quality-control check is essential to ensure that only correct structural information is loaded into Sunovion's database. Furthermore, it ensures that only compounds designed by the PI can be registered, which helps maintain clear audit trails for compound design.

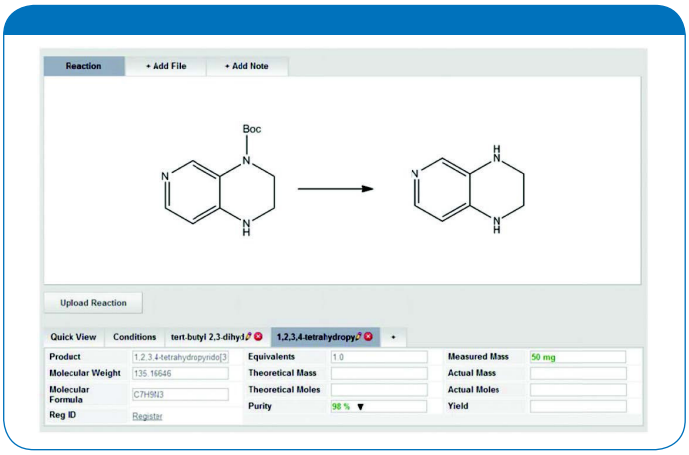

Figure 4: Initiation of the registration process by the CRO

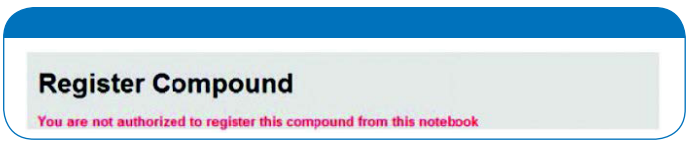

Figure 5: Structural alert error message.

Once the structural information has been determined to be correct, compound registration proceeds (Figure 6). The ELN contacts the Arxspan web service to perform a standard battery of corporate database quality-control checks. Compounds that successfully pass these checks receive a new, unique identification number. Compounds that have no record in the corporate database will receive a new SEP-ID; compounds that have an existing record will receive a new lot (batch) number.

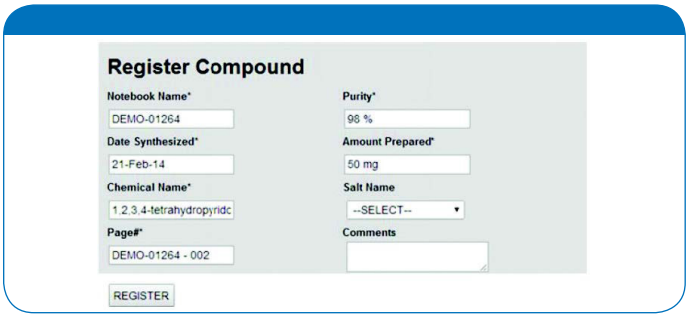

Figure 6: The web-service integrated registration screen, which is configured to push only requested information into the Accord database.

Step 4–Record Keeping:

The web service returns the SEP-ID to the ELN (Figures 7 and 8) such that a compound is assigned both an ELN-ID and SEP-iD. Upon successful registration, the CRO scientist closes and signs the experiment, and the TOC is updated to show the status change. The SEP-ID and ELN-ID, now fully embedded in the ELN, provide Sunovion scientists and CRO scientists with an easy search handle if follow-up on the compound is warranted.

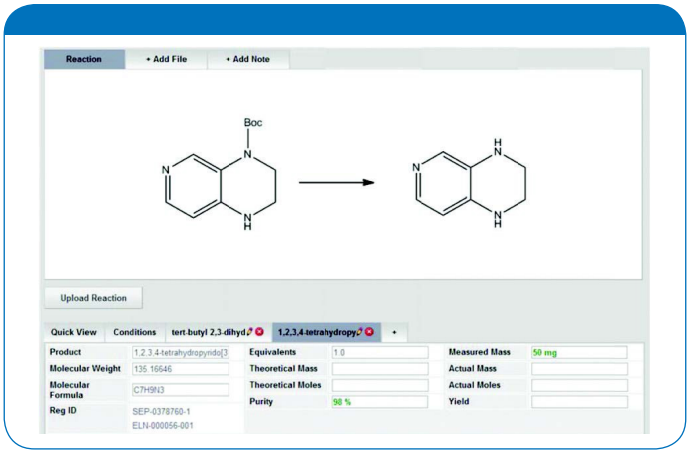

Figure 7: The SEP-ID is captured on the experiment page for easy reference.

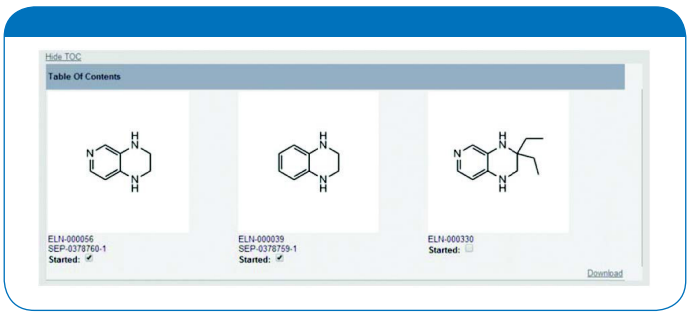

Figure 8: The SEP-ID is captured in the TOC to serve as quick status update.

This innovative registration process has greatly facilitated Sunovion's discovery-research program, and thus saved time and money while maintain the high level of accuracy and quality assurance needed for proprietary database management.

"With the new process fully implemented, the initial design and request process takes five minutes versus an hour with the old process. It has integrated seamlessly into our existing workflow and has enabled our CRO colleagues to register compounds directly into our system. In line with Sunovion's fully externalized discovery model, allowing our CRO colleagues to register compounds also provided the unanticipated benefit of facilitating global compound distribution. This cut timelines and accelerated Sunovion's drug-discovery process."

Key Points:

- Innovative and forward thinking design
- Steam-lined workflow
- Full integration with synthesis workflow
- Easy and rapid process
- Provides error and duplicate checking
- Allows QC oversight by primary investigators
- New web service uses existing systems
- Web service can easily be redirected to different back end storage

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