

# Library logistics: managing comprehensive compound collections

Compound management may seem straightforward but in reality, as the number of new compounds increases dramatically year-on-year, the management of large collections has become increasingly challenging. As high-throughput technologies have become the norm, Bayer HealthCare, a global healthcare company, has seen its HTS library increase to more than 3.2 million compounds stored in solution at its Berlin research facility. To address the demand of multiple user groups, each having different requirements and needing access to the huge compound and data collection, a large investment has been made to set-up a comprehensive compound management unit in Berlin – the Compound Logistics Lab. This specialised unit has improved the efficiency and capacity of compound management in an R&D environment, processing up to 500 distinct compound requests each month. Served by an underlying sample management software platform, Bayer HealthCare's Compound Logistics Lab standardises compound tracking, ordering and reformatting for streamlining workflows across a large part of the company's drug discovery process.

**T**he pharmaceutical and biopharmaceutical industries have witnessed a dramatic increase in the number of small molecule compounds and biologicals handled during the drug discovery process. With significant advancements in parallel synthesis techniques and rapid expansion in areas of genomics and proteomics, it is unsurprising that thousands of new compounds are generated each year, designed to interact with particular drug targets. While these novel agents may hold significant potential as future therapeutics, handling the increasing number of different

compounds and managing the ever-expanding collection is critical. At the very minimum, each new compound must go through numerous steps to ensure that it is accurately and appropriately quantified, labelled and stored, ideally alongside any associated existing compound data. These steps are necessary for any form of repository management which, at a basic level, comprises all of the daily logistical operations involved in sample ordering, processing, storage and tracking.

Many pharmaceutical organisations work across multiple sites and so inter-site communication and

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**Figure 1**  
Automated compound store  
at Bayer HealthCare's Berlin  
facility



access to shared screening data and compound profiling information is important for effective collaboration. The demand therefore is for a more comprehensive and high capacity sample management set-up, although achieving this can be difficult. Juggling large R&D libraries and a plethora of discrete user groups that all require access to these libraries can pose management and inventory tracking problems.

### **The approach at Bayer HealthCare**

For many smaller compound stores, sample management can be performed using in-house software that is tailored to suit specific workflow requirements. However, even for moderately-sized compound collections this task is becoming increasingly difficult as internal resources have limited capacity and expertise to maintain the software systems which quickly become outdated. For large pharma and biopharma organisations, compound management has to be propor-

tionally more sophisticated, to cope effectively with bigger stores, varying sample types, larger amounts of associated data, multiple access points and high daily throughput.

Bayer HealthCare, a subgroup of Bayer AG, is one of the world's leading, innovative companies in the healthcare and medical products industry. With a strong emphasis on R&D, Bayer HealthCare has one of the largest compound libraries worldwide. To address the growing needs for efficient compound storage and management, all main activities concerning compound logistics at Bayer HealthCare's Berlin facility were consolidated into a single function – the Compound Logistics Lab (CLL). At the Berlin facility, the CLL acts as the sole interface between the compound suppliers and all of the various users (Figure 2). This dedicated logistics lab manages high compound throughput on a daily basis and plays an essential role in streamlining the drug discovery process from HTS through to lead optimisation (Figure 3).

## Building the test compound library

Acting as the central point for compound management, the CLL is responsible for the ordering, tracking, storage and distribution of all test compounds.

While a significant proportion of test compounds are generated in-house by the Project Labs and Automated Medicinal Chemistry groups, Bayer HealthCare also utilises external libraries as a screening source. These externally-sourced compounds must be managed and integrated into the existing library, so for efficiency and consistent library navigation, Bayer HealthCare proactively provides external suppliers with specific vials, each with a unique barcode. This approach ensures that all stock compounds can be instantly recognised by the CLL's software and therefore handled and automatically processed in the same way as internally-synthesised compounds.

On receipt of an external compound, the CLL registers the new compound and its accompanying data in the central database, while the container-related data is uploaded into the CLL software. This container-specific information is linked to the main, central database to allow users to access additional information if required, for example structure related data.

Supporting the efficiency of the drug discovery process, comprehensive test compound data collections are important, providing R&D groups with detailed compound information and broad experimental results. Access to this wealth of compound-associated data enables scientists to develop more efficient screening strategies during the different stages of drug discovery, including determination of the most appropriate assays. Ultimately, this translates to precious time and cost savings. However, as libraries become larger and more complex, compound tracking, storage and data management must be effectively streamlined.

## An open-access system

The involvement of the CLL spans from HTS to late stage lead optimisation (Figure 3), where it is responsible for the co-ordination of compound management across numerous drug discovery projects. In 2012, the CLL in Berlin supported more than 100 distinct research projects. Each research project focuses on identifying and optimising lead candidates based on the results of up to 35 different compound tests. With these multiple drug discovery projects on the go, each at a slightly different stage of the process, the CLL often has to process up to 500 highly variable compound requests every month for hit validation, lead finding and lead optimisation.

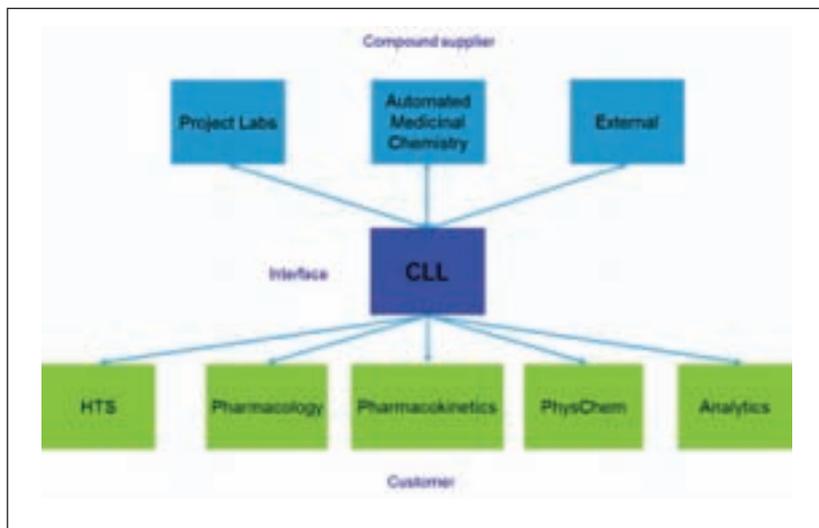


Figure 2: The Bayer HealthCare Compound Logistics Lab interface

As well as many different projects running in parallel, there are also numerous scientists within these research groups that require direct interaction with the CLL – to access compound information and submit order requests. Currently the CLL responds to 320 active (compound requestors and recipients) and 280 passive users (recipients of compounds only). The CLL set-up has to be highly accessible and flexible in order to support the various inputs from all research groups.

The first of the user groups supported by the CLL are the HTS laboratories, which rapidly conduct assays for the initial identification of active compounds. During this HTS phase the CLL has to cope with the sheer number of different compounds that are requested and run through screening assays and then evaluated as potential lead candidates. As such, there is the need for high throughput and rapid processing of these types of requests.

Following the HTS, the identified hits require validation, a process which brings in other CLL customers from pharmacology, physiochemical, pharmacokinetics and analytics groups (Figure 2). In some cases, the CLL also performs and co-ordinates test compound shipments to external contractors where more unique or specialised assays

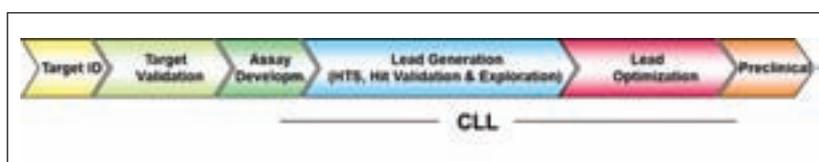


Figure 3: The involvement of the CLL in the drug discovery process

**Table 1:** The CLL's underlying software coordinates the workflow process

WORKFLOW STEP	DETAIL
Compound ordering	<ul style="list-style-type: none"><li>● Requests based on templates</li><li>● Validated by software</li></ul>
Compound processing	<ul style="list-style-type: none"><li>● Picking and placing of labware items</li><li>● Weighing of solids</li><li>● Preparation of customised plates according to client needs</li><li>● Online integration of automated equipment within CLL for these steps</li></ul>
Compound despatch	<ul style="list-style-type: none"><li>● User informed by e-notification when compound/plate is ready for collection</li></ul>

and analysis are required. To ensure traceability and association with the resulting experimental data, the CLL has to track the compound, its format and despatch. Throughout the lead generation and optimisation process, compounds are assessed for their potency, safety and pharmacokinetic properties to ensure that only the most promising candidate is selected for late stage optimisation and progression into toxicological and clinical studies.

Supporting the drug discovery process, the CLL manages various reformatting operations. While high throughput screening stages mainly pose challenges associated with the handling of a large number of requested compounds, the lead candidate optimisation requires directing numerous formatting processes in order to provide approximately 6,000 samples a month. This involves managing requests on a much more customised level and involves formatting the compound to suit user-group specific assays, for example selection of specific container types and plate layouts, as well as the use of different solvents and compound concentrations. With these request variables, the CLL can see the number of test compound formats increase significantly – from four standard formats used in the HTS phase, to around 60 different formats by the time a compound enters the lead optimisation process. Having software that can manage these formatting operations efficiently is fundamental to the CLL's success.

### Sample distribution

Alongside test compound tracking and processing, the CLL is also responsible for the distribution of compounds and biological material to external laboratories involved in preclinical investigations. This process includes the logistics and administra-

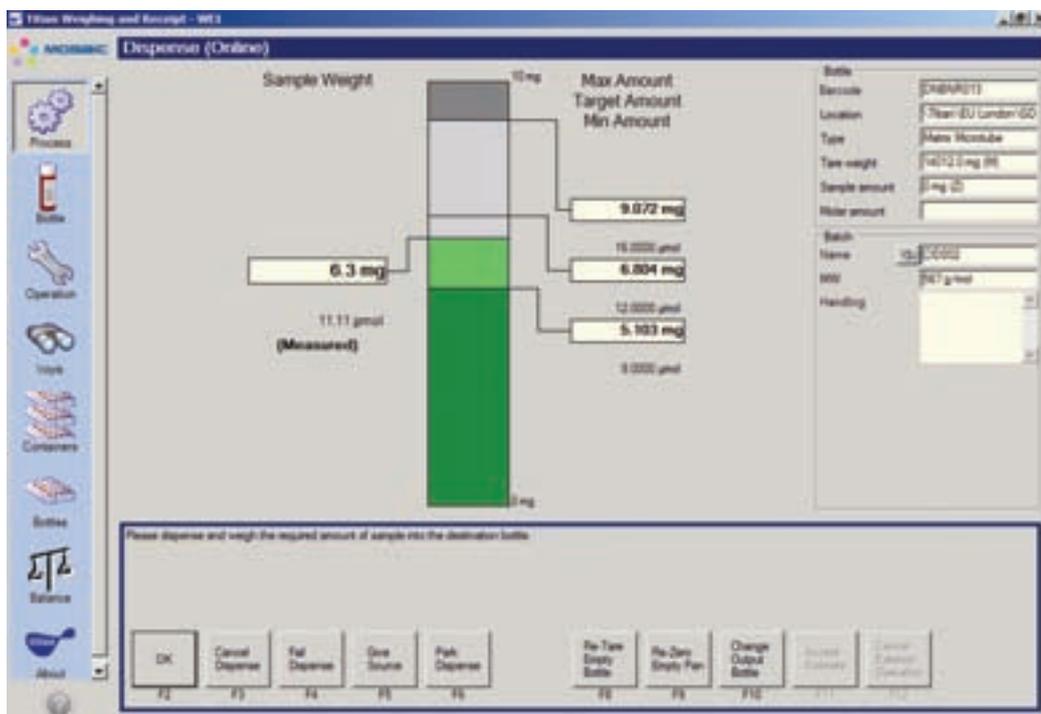
tion associated with the shipment of samples. The CLL in Berlin co-ordinates the despatch and compiles all necessary documentation for the shipment of such samples.

### The software solution

To manage all the different phases of the drug discovery process, the Compound Logistics Lab requires a comprehensive software set-up. Initially, on establishment of the CLL, Bayer HealthCare was running two software platforms at its facility in Berlin for the management of test compounds – a commercial software for HTS support, and an internally developed software for the management of compounds undergoing lead optimisation. However, the drawback of this approach quickly became apparent and several difficulties arose from juggling two distinct software systems. Notably, the Hit-to-Lead process that sat between the initial HTS and the lead optimisation phase proved problematic, as users were required to work with two separate systems. Using different platforms bears the risk of inconsistencies with data recording and makes it more difficult and labour-intensive for users to submit their requests. In addition to this, working with two operational software systems had an impact on resources, requiring a considerable investment of time and maintenance work with a subsequent impact on costs.

Ultimately the CLL required a platform that could manage the entire drug discovery process, including all ordering, tracking and formatting workflows, from HTS through to lead optimisation. So, to support the CLL's different workflow demands, Bayer HealthCare introduced Titian Software's Mosaic sample management software. This underpins all inventory management, ordering operations and workflow processes of test compounds at Bayer HealthCare's Berlin R&D facility, streamlining and supporting the high number of requests handled monthly by the CLL.

With the installation of a single software platform, the CLL has been able to integrate workflows more effectively and efficiently. All user groups now work with the same software interface, enabling them to access the same information and process all requests and workflows in the same way. This is extremely important in an R&D environment for consistent data recording and the subsequent establishment of comprehensive and accurate compound libraries – particularly in organisations such as Bayer HealthCare where this material is shared and accessed by multiple users.



**Figure 4:** Mosaic's intuitive interface – sample weighing during dispense

## Automated ordering templates

At the Berlin facility, newly synthesised compounds can be easily requested in Mosaic using order templates with pre-set outputs. By simply entering the barcode of the labware item or the unique compound identifier, CLL users can submit order requests based on the predefined templates. This enables groups to place orders for frequently used assays with minimal hassle, as the order templates require minimal alteration or user input. The implementation of this efficient ordering process via the CLL saves researchers valuable bench-time.

## A step-by-step workflow

With a dedicated underlying software system, the CLL and its users are guided through entire workflow processes with complete assurance and simplicity (Table 1).

Following the request submission via existing order templates, requests are validated by the CLL's software platform to ensure that sufficient amounts are available and, if compounds need to be processed from different labware types, requests will be automatically divided into multiple part-orders. Technicians within the Compound Logistics Lab are then guided through compound handling and reformatting stages, and automated instruments are integrated with the software at stages such as pipetting for high precision and reproducibility.

At the end of the workflow, a last-step inspection is conducted visually by CLL technicians before an e-notification is sent to the compound recipient. At this point the user simply needs to collect their requested and reformatted compound from the CLL, ready for instant use.

## The CLL advantage

Despite managing libraries of 3.2 million compounds and processing around 500 new requests every month, the CLL in Berlin only employs six staff. Its ability to cope at high flexibility and high throughput with minimal manpower demonstrates the efficiency of the CLL as a compound management solution, attaining consistent high standards and enabling streamlined workflows in a cost-effective manner.

Not only does the establishment of the CLL make 'business-sense' in terms of its operational and staffing costs, but it brings a significant level of accountability and traceability to the compound management process. The CLL was specifically developed for compound management and logistics, and as such, its roles and responsibilities are clearly defined and recognised. Its centralised set-up ensures that the highly valuable test compounds are being tracked, managed and stored in a consistent manner, and in a way that allows highly efficient work of its users.

**Figure 5**  
The Compound Logistics Lab  
for high throughput compound  
processing



### Keeping up with the throughput

The technology progression is very rapid. With continuous advancements in technology, not only is our knowledge of science advancing, but so too are the approaches we use for furthering this knowledge. The drug discovery process is a prime example of this, and has been revolutionised with the progression of parallel synthesis techniques and high throughput screening strategies. However, coping with ever-growing compound collections is imperative.

Bayer HealthCare at its facility in Berlin has established a laboratory – the CLL – to cope with the logistics associated with high volume, shared-access compound collections. Spanning a comprehensive stretch of the drug discovery process, the CLL deals with test compound ordering and tracking, as well as supporting compound reformatting, to enable identification and optimisation of compounds with promising biological and therapeutic function. With multiple users and a need for standardisation, a dependable software system has proven to be essential for the management of test compounds at the facility in Berlin, enabling drug research at the required high throughput and flexibility. **DDW**

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