# Biotech's rise in externalization of compound management services

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Biotech is a high-risk industry where we have seen an increase of virtual business models. This allows companies to reach proof-of-concept without deploying large sums to cover capital equipment and infrastructure costs. These companies are run by small teams, often one person, who outsource everything needed to support a drug discovery program all the way through to IND filing[1].

Virtual biotechs often quickly find themselves with a rapidly growing collection of compounds across several programs, stored in a manner not suitable for a growing library. The management, tracking, QC and inventory of their collection becomes a serious challenge and highlights the need for personnel, knowledge and/or equipment to become an integral part of the company's in-house design and function. As a result, companies like Evotec have seen an increase in the number of virtual biotechs seeking external support for project management and logistical expertise necessary to manage their growing compound collections which are a crucial part of drug discovery.

At the other end of the biotech spectrum; multi-billion dollar publicly listed biotech companies have also increased externalization of their compound management activities. In contrast to large pharma, that have the capital outlay for equipment and personnel in this space, the large biotechs often need only one or two of the key areas identified above. Evotec has worked with several companies of this size looking for storage of archive samples, and/or to leverage our expertise in building a screening library. There are however several examples of large biotechs that employ Evotec to perform full service "turn-key" compound management. These companies may have grown from the small virtual organization above and simply continued the arrangement that worked well for them in the past, or during a period of growth realized their lack of available space and/or personnel is a potential serious issue needed to be addressed. For the latter, we often see a basic compound management group managed by a medicinal chemist who struggles to keep up with the demands of a growing scientific program.

Regardless of biotech size and focus, there is generally a decisive line that separates these two class of biotechs that centers around informatics support. Virtual companies and small biotech's often have limited to no Laboratory Information Management System (LIMS) software in place. In these cases, they are looking for an external partner to completely manage and drive the compound logistic workflow, reporting

back on a periodic basis. On the other hand, larger companies that have invested in complex LIMS software require the partner to be integrated with their informatics system, with the goal to be as transparent as possible to the suppliers and end-users of the compounds and samples being stored.

Whilst there are plenty of differentiators between companies interested in outsourcing some or all of their compound management needs, the absolute requirements of quality, accuracy, and timeliness remain paramount for all services performed. This is especially evident in the case of project screening workflows that require careful planning between three or more distinct collaborators, and are impacted greatly by increased cycle times. The Key Quality Indicators (KQI's) of compound management are service features or quality attributes, which benchmark the performance of an organization, and are as important as ever[2], shown in Table 1.

| Process | Structural | Analytical | Service |
|---|---|---|---|
| Performance automation | Diversity | Identity | Helpful |
| Storage conditions | Lead-like | Purity | Informed |
| Liquid Handling | Cost | Concentration | Professional |
| Data Management & Tracking | Privileged Structures | Solubility | Timely |

*Table 1. Compound Management KQI's*

Outlining all these key factors on paper is relatively simple. In practice though, a thorough discussion between the biotech and partner is crucial. The following two Evotec case-studies will show the importance of understanding the needs and interaction with collaborators needed for a successful collaboration.

## CASE STUDY 1: VIRTUAL BIOTECH

Evotec began discussions with a venture capital backed virtual biotech with a small physical footprint in a hotbed community. With an eye to growing rapidly, their key requirements were:

- Access to an inventory management database for rapid compound ordering and tracking
- Enable their chemistry teams by providing them with necessary labware to reduce time taken from compound shipment to assay
- Liquid handling capabilities to provide dose response layouts with defined control compounds
- Receive, verify, manipulate & distribute project compounds from chemistry partners to screening scientists locally and around the world
- Store and maintain ongoing collection, including periodic quality control checks

**Inventory management**

Evotec utilizes Titian's Mosaic inventory management system for all clients across its compound management sites. Alongside that system, Evotec has developed an ordering web-portal that allows multiple users in the biotech organization (and collaborators) to order compounds upon request. This allowed the biotech management team to quickly set-up the informatics infrastructure to rapidly initiate chemistry and screening processes. The small number of compounds already in their possession were shipped to the Evotec Branford, CT location to be the precursors to a growing collection.

**Reduce time from shipment to assay**

Evotec provided pre-registered, pre-barcoded glass vials to chemistry partners to use in the fulfilment of custom synthesis work. Not only does this result in a much faster receipt and integration into the process workflows at Evotec, it allows for a check-weigh process to ensure the reported amount of material is being provided, and in conjunction with the inventory database provides a real-time inventory for the project leaders to reference.

**Workflow**
Evotec was able to share established workflows for complex liquid handling, assay plating, and powder management that had previously been established. Capable of weighing 400+ powders per day, plating up to 1536well density with sub-microliter volumes, and shipping globally with preferred couriers, Evotec designed a weekly workflow that met the client's expectations and provided accurate communication and data transfer to the project leaders and compound management liaison.

The initial scale of this case study was one project with ~10 compounds per week. Within six months this biotech had aggressively grown to more than 5 projects totaling 80–100 compounds per week, and an overall compound library size of >1,000 compounds in storage.

## CASE STUDY 2: LARGE BIOTECH

This case study provides insight to the rapid growth of an established biotech that realized their lack of space and know-how to handle the future needs of the company. The key requirements were defined as:

- Integration into an evolving LIMS platform (Dotmatics & Scigillian)
- Creation of a 500,000 compound screening collection over 3 years
- Storage and on-demand cherry picking of screening library and growing project collection
- Receive, verify, manipulate & distribute project compounds from chemistry partners to screening scientists locally, and around the world
- Liquid handling capabilities to meet industry expectations
- Growth from 3 to 10+ unique projects requiring weekly or bi-weekly plating and distribution of 150+ compounds per week
- Fee-for-Service quality control and handling of Merger & Acquisition collections acquired by corporate changes

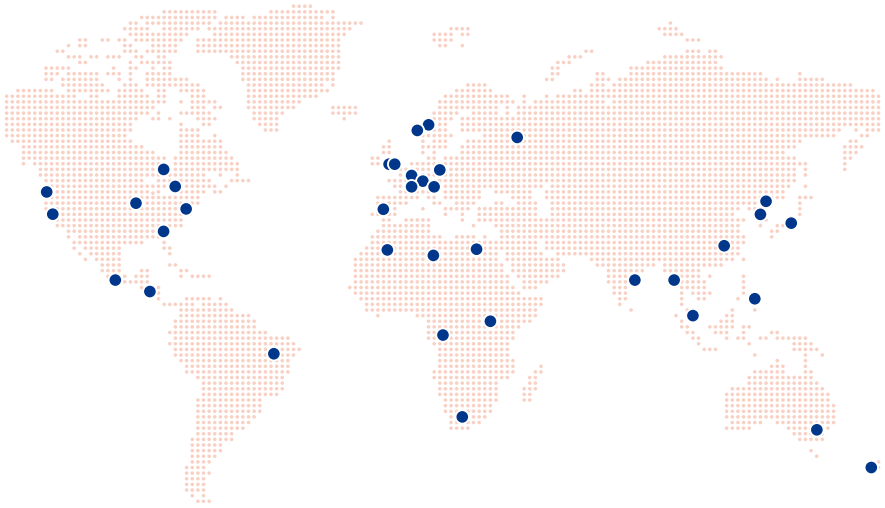
**IT Integration & Database**
Similar to the first case study, Evotec was quickly able to insert this biotech into the Mosaic inventory database structure. However instead of using the web-portal interface, we were able to use our Web Services data exchange to create a direct link to the client's informatics platform. This allowed the scientists and project leaders to continue using the interfaces they were familiar with, as well as ensuring a real-time snapshot of current inventory.

The size, growth-rate and retrieval requirements of the total collection (both screening and project compounds) required an automated storage solution to be in place. Evotec currently utilizes TTP ComPOUND and Brooks Sample Store II to provide these random access, on-demand cherry picking capabilities. Along with semi-automated manual ambient temperature stores, we were able to provide enough storage capacity for powders, DMSO solutions, and plates to meet requirements.

**Screening collection**
A common theme among larger companies is the opportunity for the acquisition of another compound collection into their own, after some form of corporate movement. In this case study, Evotec was asked to perform quality control via LC-MS on 35,000 DMSO samples. This required substantial liquid handling and plate reformatting work, prior to any analytical chemistry. Evotec has extensive experience in performing purity & identity LC-MS, having analyzed more than two million samples for the NIH Small Molecule Repository over the past 15 years. Once complete, the reports were forwarded to the client, who then returned a selected list of compounds to be integrated into their current collection.

**Shipment**
A common requirement of both these biotech companies (as well as most of Evotec clients) is the ability to ship neat and DMSO liquids to collaborators around the world. On behalf of these two examples Evotec ships 30–40 packages per week, either domestically or international. Often these international shipments present unique situations that need specific paperwork, or timing. With the proliferation of chemistry and screening partners in China, Taiwan, and India as well as the traditional European

based organizations, a reliable and timely courier and the correct paperwork is crucial to maintaining assay screening cycle times. Over the past 15 years, Evotec has shipped more than 40 million samples to more than 40 countries worldwide (Figure 1).



## CONCLUSION

Biotechs both large and small have experienced clear benefits from utilizing Evotec compound management services. We provide experienced and knowledgeable compound management personnel and offer access to the state-of-the-art compound handling infrastructure required to meet the challenging timelines of drug discovery today.

## EQUIPMENT AVAILABLE

Evotec's ownership and use of such equipment as TECAN, Hamilton, Agilent and Labcyte for liquid handling, and Brooks and TTP for automated storage means that the services rendered to any client will be as if the biotech company built and purchased a compound management specific laboratory for their own site. However, instead of having an equipment utilization rate of <30% as is normal for such operations, in this case the cost of the equipment and personnel is simply what is necessary to achieve the initiate requirements stated at the beginning of the project.

## BRANFORD, CT SITE

In addition to the capability and capacity stated above Evotec realizes that a flexible facility format is crucial to meet the needs of any future collaborator. To that end, we have recently increased our Branford facility footprint to approximately 23,000 sq.ft. (Figure 2). This will allow for purpose built workspace for large biotech companies

wishing to virtually extend their own facilities, and increase storage and capacity space for those smaller companies requiring the full breadth of compound management services.

## SUMMARY

Evotec is uniquely qualified in delivering your Compound and Library management needs through over a decade of being the world's leading Compound Management operation. Our compound management experience, primarily from the large pharma and government sector, reinforces that Evotec understands our client's needs and deadlines. Each client has a dedicated Project Manager who provides a single point of contact to ensure an open line of communication is always maintained. Our knowledge, experience, capability and capacity provides a unique compound and sample management offering.

**Evotec Key Capabilities for Sample Management**

| | |
|---|---|
| Compound identification, selection and procurement | Building and/or purchasing compound collections on behalf of our clients |
| Compound quality control | Identity and purity |
| Compound Storage | Fully automated storage systems for liquid & solids with high-throughput cherry picking capabilities |
| Compound dispensation & reformatting | Comprehensive liquid handling technologies incl. acoustic dispensing and automated weighing capabilities (liquid & solid) |
| Cell banking and biological sample management | |
| Compound shipment | >40 million samples delivered across 18 different countries |
| Data & quality management | Manage, record and report all manipulations of client samples |
| In-sourcing and consulting services | Scientific staffing specifically designed to give client "non-permanent" work force within their operation from one year to multiyear partnerships |

*1. https://bioprocessintl.com/manufacturing/manufacturing-contract-services/virtual-pharmaceutical-company-new-pathway-market*
*2. The Challenges of Quality Compound Management in Today's Pharma Industry, Holland-Crimmin, S. 2011. https://www.pharmoutsourcing.com/Featured-Articles/37766-The-Challenges-of-Quality-Compound-Management-in-Today-s-Pharma-Industry*