Compound management outsourcing: how to build the trust?

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SVP, Global Compound Management Head
Evotec AG

SLAS conference, March 2017, Olivier Casamitjana
Agenda

Evotec Overview

Outsourcing: Challenges and opportunities

My personal strategic analysis (2012-2015)

Outsourcing: Case study

Conclusions
Adding value to our partners’ research

Innovative and flexible solutions from target ID to pre-clinical candidate

The people
Outstanding scientists (~1,000)
Experienced project management

A wide therapeutic area expertise
Pain, oncology, metabolics, CNS, immunology, inflammation, infection, cardiovascular …

Integrated drug discovery
State-of-the-art capabilities
Best-in-class technology platforms

Flexible deal structures
Integrated collaborations and stand-alone services

A world-class drug discovery expertise and platform to accelerate and maximise our partners’ success
Our global offering in partnerships

Evotec’s global footprint – >1,200 employees, >1,000 scientists in EU & US

Branford, Watertown, Kalamazoo, Princeton and San Francisco, USA
~110 employees
- Compound ID, selection and acquisition
- Compound QC, storage and distribution
- Cell & protein production
- ADME-Tox, DMPK

Abingdon, Manchester, Macclesfield and Alderley Park, UK
~400 employees
- Medicinal chemistry
- ADME-Tox, DMPK
- Structural biology
- In vitro & in vivo anti-infective platform/screening

Toulouse, France
~300 employees
- Compound management
- Hit identification
- In vitro & in vivo oncology
- Medicinal chemistry
- ADME & PK
- Early drug formulation and Solid form screening
- Cell, protein & antibody production

Hamburg (HQ), Göttingen and Munich, Germany
~430 employees
- Hit identification
- In vitro & in vivo biology
- Chemical proteomics & Biomarker discovery and validation
- Cell & protein production
- Antibody discovery
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Compound Management role

What’s the added value of CM?

In a context of the increase of the diversity of Drug Discovery project, the Compound Management play a crucial role in:

- Hosting and delivering a large number of compounds and sample patrimony
- Managing the interaction with different partners for a customer (reception, registration, transformation and shipment)
- Managing the compound collection dynamically
- Managing the associated data
- Proposing innovation
- Contributing to create a link between key players
- Contributing to optimize the cycle time in projects
## What is the situation of compound management in the top 20 Pharmas? Global survey result (2012)

<table>
<thead>
<tr>
<th>Company</th>
<th>CM activity: Internal or Outsourced</th>
<th>CM organisation</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>Internal &amp; outsourced (Sigma)</td>
<td>2 US teams: 1 internal (liquid) &amp; 1 outsourced (central powder store)</td>
<td>Had reason to outsource have a fix price, cost saving (after up-front payment for initial transfer), have more flexibility of the resource. Biggest issue: insurance cost and responsibility. New opportunity offered to Sigma to sell a selection of ops from Pfizer (with or IP issue).</td>
</tr>
<tr>
<td>Novartis</td>
<td>Internal</td>
<td>One site house the corporate powder collection in automated storage systems, two HTS-sites house the complete collection as tubes for cherry picking and in plates for primary screening + 6 satellites with local manual powder and solution stock</td>
<td>All inventories are visible at a global level with sample tracking and ordering tool. Why internal? Flexibility! We need to build flexible processes and adapt our processes to the changing needs of our drug discovery projects. We have evaluated outsourcing the storage of the powder collection. Costs were slightly higher (10 to 50%), turnaround times would have been extended by a couple of days, process flexibility would have greatly suffered and a long-term redundancy would have been generated. A commitment for 10 years would have been required to make it financially viable. This would have only been possible if we would have greatly reduced our service.</td>
</tr>
<tr>
<td>Takeda</td>
<td>Internal</td>
<td>1 central (US, Fr, Ge) + 2 satellites (US: Fr)</td>
<td>Strategic asset</td>
</tr>
<tr>
<td>Merck</td>
<td>Internal</td>
<td>Internal centralized global repositories for solution and solid + 4 satellites teams</td>
<td>For management of program-specific lead identification and lead optimization compounds with limited short-term local solution storage. Outlining the plan: use of Space to increase the capacity temporarily (eg: massive reformulation)</td>
</tr>
<tr>
<td>Roche</td>
<td>Internal (outsourced (Evotec))</td>
<td>3 sites have a CM team (powder and small liquid store): HTS supporting liquid store are global. CM outsourced due to a site closure in the US (plan for future)</td>
<td>Outsourced CM: initial set-up costs (high) but yearly maintenance costs (lower). High price per compound, increase of turnaround time.</td>
</tr>
<tr>
<td>AstaZeneca</td>
<td>Internal</td>
<td>1 major CM (powder and liquid archive) + 2 satellites</td>
<td>CM is part of the core business (strategic asset)</td>
</tr>
<tr>
<td>Johnson &amp; Johnson [J&amp;J]</td>
<td>Outsourced (Sigma)</td>
<td>1 internal (Belgium) + 1 satellite (US)</td>
<td>No benefit for GSK to outsource. A lot of question about the process - e.g. data integrity</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Internal (outsourced)</td>
<td>1 repository - liquid sample &amp; solid sample + 3 satellites teams</td>
<td>No back up for solids. Duplicate of collection and liquid main drivers to keep internal: extremely flexible (have to change frequently) to fit with the business needs. High value of the discovery (strategic asset). Very cost effective (internal indications): the overhead cost is extremely competitive mainly because infrastructure. IT and robotic system are in place</td>
</tr>
<tr>
<td>Abbott</td>
<td>Internal</td>
<td>1 repository (Us) and 3 smaller stores for powder and liquid</td>
<td>No benefit to GSK to outsource. A lot of question about the process - e.g. data integrity</td>
</tr>
<tr>
<td>Bristol Myers Squibb [BMS]</td>
<td>Internal</td>
<td>100%: Global repository, 1 global opt collection</td>
<td>No benefit to GSK to outsource. A lot of question about the process - e.g. data integrity</td>
</tr>
<tr>
<td>Amgen</td>
<td>Internal</td>
<td>1 central CM (powder + liquid) + satellites on multiple site</td>
<td>Reason to keep it in-house: in place, automated storage. Work on a plan to outsource the solid store. Main reason: need to re-invest on a new store (several millions) even if the cost is higher and less flexible (outsourced).</td>
</tr>
<tr>
<td>Bayer</td>
<td>Internal</td>
<td>2 central stores (1 powder / 1 solid) + 1 local team</td>
<td>Consider as a &quot;mirror&quot; of the company</td>
</tr>
<tr>
<td>Takeda</td>
<td>Internal</td>
<td>1 central CM (powder + liquid) + satellites on multiple site</td>
<td>Outsourcing: exceptional case (eg: reformulation) to increase the capacity</td>
</tr>
<tr>
<td>Boehringer Ingelheim</td>
<td>Internal</td>
<td>2 CM (powder and liquid): local and global support</td>
<td>100%: Internal: fast delivery, flexible, cost-effective, high quality. Global network if outsourced: additional cost (eg: IS adaptation)</td>
</tr>
<tr>
<td>NeoNovo</td>
<td>Pharlin</td>
<td>2 CM (powder and liquid): local and global support</td>
<td>100%: Internal: fast delivery, flexible, cost-effective, high quality. Global network if outsourced: additional cost (eg: IS adaptation)</td>
</tr>
<tr>
<td>Chem manger</td>
<td>Ete</td>
<td>2 CM (powder and liquid): local and global support</td>
<td>100%: Internal: fast delivery, flexible, cost-effective, high quality. Global network if outsourced: additional cost (eg: IS adaptation)</td>
</tr>
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</table>

- All of the 14 companies have central stores with a unique governance team
- None of the 14 companies have fully outsourced the compound management (strategic asset)
- 11 companies have compound management fully internal (~80%)
- 3 companies have a mixed model (20%)
What is the situation of compound management in the top 20 Pharmas? Global survey result (2017)

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<td>Pfizer</td>
<td>1 central (US, Fr, Ge) + 2 satellites (central powder store)</td>
<td>6 satellites with local manual powder and solution stock</td>
<td>Reason to outsource have a fix price, cost saving (after up-front payment for initial transfer), have more flexibility of the resource. The biggest issue: insurance cost and responsibility. All inventories are viable in a global research wide sample browsing and ordering tool.</td>
</tr>
<tr>
<td>Navarths</td>
<td>Internal</td>
<td>4 satellites</td>
<td>1 outsourced (central powder and liquid)</td>
</tr>
<tr>
<td>Shire</td>
<td>Internal</td>
<td>4 satellites</td>
<td>1 outsourced (central powder and liquid)</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Internal</td>
<td>1 central (US, Fr, Ge) + 2 satellites (US, Fr)</td>
<td>Outsourcing: no, risk of decrease of quality and increase of turnaround time</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>Outsourced</td>
<td>5 satellites</td>
<td>2 satellites (US, Fr)</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Internal</td>
<td>3 satellites</td>
<td>1 central (US, Fr, Ge) + 2 satellites</td>
</tr>
<tr>
<td>Abbott</td>
<td>Internal</td>
<td>1 central (US, Fr, Ge) + 2 satellites</td>
<td>Reason to keep it in place, automated stores, no back-up for solids, duplicate of collection and liquid.</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>Internal</td>
<td>1 central (US, Fr, Ge) + 2 satellites</td>
<td>Concept = option to be charged if used (e.g. QC, solidification).</td>
</tr>
<tr>
<td>Amgen</td>
<td>Internal</td>
<td>3 satellites</td>
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<td>Bayer</td>
<td>Internal</td>
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<tr>
<td>Taiho</td>
<td>Internal</td>
<td>2 satellites</td>
<td>1 central (US, Fr, Ge) + 2 satellites</td>
</tr>
</tbody>
</table>

- All of the 14 companies have central stores with a unique governance team.
- There is now at least one example of fully outsourced compound management.
- 6 companies have compound management fully internal (~40%)
- 8 companies have a mixed model (~60%)
Do you currently outsource your Compound management function?

Trend in 2015

**In or Out?**

DO YOU CURRENTLY OUTSOURCE YOUR COMPOUND MANAGEMENT FUNCTION?

- **43% YES**
- **57% NO**
Challenges for a pharma company

Internal challenges

- Capex investment high
  - Automated store (initial investment, renewal)
  - LIMS (Mosaic)
  - Stand alone equipment (Liquid Handler, weighing station)
- Control the operational cost (maintenance, consumables)
- Unique expertise (critical mass)
- Maintain a high level of quality (process, compound, environment) from storage to compound deliveries (compound integrity)
- Capacity to adapt the process to several formats
- Keep a rapid turnaround time with several partners (internal and external)
- Manage the increase of the diversity of collaborations
- Avoid the silos and understand the “client” needs/constraints (HTS, DMPK, etc.)

Top management challenge the running cost and the investment (ROI) and the business continuity
Challenges for a CRO

How to demonstrate the added value?

- Understand the client needs and adapt the team and the environment to the need (flexibility)
- Dynamic allocation of resource (FTE management)
- Set-up phase and business continuity
- Quality of the process
- Turnaround time
- Shipment (dangerous goods regulation)
- Confidentiality

- Some internal challenges
  - Innovation
  - ROI
  - Investment

How to build the trust?
Challenges in Sample Management
Opportunities in working with a CRO

How to create a win/win project?

- Increase the professionalism in this domain (ex: manage legacy inventory)
- Access or increase capacity (automated store)
- Avoid or share massive investment (new or renewal)
- Improve the process (turnaround time)
- Outsource an activity non strategic
- Share innovation (IT, automated store & new technologies)
- Share a compound collection
- Propose different business models (archive, in-sourcing, FTE, fee for service)
- For the CRO
  - Investment: Possibility to use 100% of the equipment (automated stores), ROI
  - Critical mass (expertise)
  - Flexibility to cope with different customer demands can provide more efficient solutions
What are the top requirements for a successful compound management system?

Requirements for success

- Ability to maintain the business continuity
  - Compound accessibility (ordering, delivery time)
  - Availability and integrity of inventory data (confidentiality management)
- Ability to maintain a dynamic collection
- Flexibility of the staff
- Ability to build a mid-/long-term partnership
  - Transparency of process used and issues
  - Good communication

How to select your partner?
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## SWOT Analysis – Global CL (2010)

### Strengths

- In some areas behind competitors (e.g. nanodispensing, biorepository)
- Limited incorporation of novel chemical structures in SA compound deck
- Risk of disconnection between BSUs/TSUs and SCPs
- Focus on biologics will lead to a decrease in small molecule research
- Limited resources in FF and VA after headcount reduction
- Limited budget for investments in state of the art technologies
- Outsourcing of CL operations

### Weaknesses

- Global logistic network
  - alignment of processes
  - close communication between CL sites
- Close working relationship with TSUs and SCPs in managing and distributing cpds
- Easy accessibility of all SA cpds in CL through global ordering system
- IDG process allows local supply of test samples within 24h
- High capacity/throughput automated stores in FF and TL
- Flexibility in adaptation and set up of new workflows according to customer needs
- Installation of new logistics software at all sites
- Further improvement of customer support
  - shorter delivery timelines
  - additional support of research projects
- Support of external collaborations
- Biosample management

### Opportunities

### Threats

- Outsourcing of CL operations
3 options studied for a future compound management

Define a strategic recommendation

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<table>
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<tbody>
<tr>
<td>1</td>
<td>Build one internal compound management team serving both, internal and external partners (to lower running cost)</td>
</tr>
<tr>
<td>2</td>
<td>Externalized facility serving internal and external partners</td>
</tr>
<tr>
<td>3</td>
<td>Move the compound management activity to other location and close facility</td>
</tr>
</tbody>
</table>
Strategic analysis

Main conclusions

- In the past, Compound management was considered as a strategic asset
  - Key items: experts and expertise, global compound flow, automated store, specific LIMS
  - Cost driven, no possibility to use internally all the capacity

- Outsourcing solution selected
  - CRO is a solution to reduce the operational cost
  - CRO solution to share the collection
  - CRO solution to access to innovation

- Recommendation was to set-up a long and strategic partnership in Drug Discovery with a CRO
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Case Study – Client “Y”

European Pharma

Project Overview (multi year agreement)
- Outsourcing of 100% of compound management activity
- Integrated Informatics solution leveraging Titian Mosaic and Evotec web service
- Sources: <10 suppliers
- Set-up phase (compound repatriation)
- Compound storage: long-term storage
  - Neat compound (>300 k)
  - Collection plates (>200 k)
  - Individual solution (>400 k)
- Pre-programs support: delivery on demand
  - Internal and external delivery (global support): weighing, cherry-picking and collection plates
  - QC on demand
- Collection management (>100 k compounds)
  - Collection assembly
  - Yearly update
- Model: FFS and FTE rate including some flexibility
  - Technology centric, industry defined best-practices, Flexible workflow and deliverables, scalable capacity
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Conclusions
Conclusions

The trend is confirmed ...

- Collaboration between partners will probably increase due to the diversity of drug discovery projects
- The outsourcing strategy of Compound management (partial or total) is predominantly used and will continue to increase
- The compound inventory needs to be managed in a highly flexible and professional way
- Compound management technologies are key to ensure the compound integrity, the data management, the confidentiality and a good turnaround time
- Build a partnership with a CRO is based on trust and allows to share operational cost and investment
- The selection of the appropriate CRO is crucial to maintain the business continuity
- For a CRO, the essential question to demonstrate its capacity to answer the partner’s need and to build the trust?
- For a pharma company is How to select a strategic partner?
Your contact:

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SVP, Global Compound Management Head

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Compound management overview
Evotec Toulouse
Toulouse Compound Management
A center of excellence

State-of-the-art facility and a an experienced team

A state-of-the-art facility
Compound flow, temperature and humidity controlled, fire detection and extinguishing system, access control

Capacity
- Neat storage and delivery
  - RTS 3.1 m capacity (60% of free capacity)
  - Vertical stores 0.5 m capacity (30% of free capacity ~20/30ml)
- Single solution, custom plates/combi plates: storage, preparation and delivery
  - RTS capacity: 2.1 m 2D microtubes (40% of free capacity)
- Collection management and delivery
  - RTS capacity: 100 k plates (30% of free capacity)
- Process controlled and qualified shipment according to dangerous goods regulation

LIMS
- Dedicated to manage, record and track activities

Qualified business processes
- To support programs all along the R&D value chain
- BCP and precertification audit ISO 22301

A group of 34 experts with recognized know-how
10 years experience in automation, compound/sample management and project management

Track record
- Drug Discovery projects support
- 168 projects supported / ~3 k orders fulfilled
- 40 k + 236 k (ARP) compounds delivered
- 4.5 m compounds in collection
- 3.3 k new compounds registered
- 1,267 packages shipped
- 97.3% shipment within timelines
- External collaboration support
- Project management for external collaborations
- Shipment up to 50 different partners (~785 k compounds delivered)
Qualified processes to support CM activities
Supporting programs all along the R&D value chain

- **Target**
  - Target validation
    - Collection plates (validation library)
  - Collection plates / Assay Ready Plates for 1ary screen
  - Plates for virtual screening (cherry picking)
  - Combination plates

- **Screen**
  - Screening to Hit
    - Collection plates / Assay Ready Plates for 1ary screen
  - Plates for virtual screening (cherry picking)

- **Hit**
  - Hit to lead
    - Custom plates for confirmation and QC (Cherry picking)
    - Dose response plates
    - Individual solutions
    - Powder deliveries

- **Lead**
  - Lead to Candidate
    - Individual solutions / custom plates
    - Dose response plates
    - Powder deliveries
    - Powder deliveries (Building Blocks)

- **Candidate**
  - Development
    - Powder deliveries (candidate compound)

- **Patrimony hosting**
  - Powder/solid, individual solutions, collection plates
A secure and dedicated facility of 4,500m²

B21 building

A state-of-the-art building (2010) designed for sample management

- Compound flow flexible and optimized
- Dedicated area for laboratory, storage, logistics and offices
  - 1,000m²: laboratories; 1,000m² logistics and storage zone; 1,000m² administrative zone and corridors; 1,500m² technical and utilities zones
- HVAC, humidity and temperature controlled (laboratories, robot enclosures)
- Controlled access
- Video monitoring
- Fire detection and extinguishing system; leak detection
- Centralized alarm monitoring
A customized LIMS to support and track activity

Mosaic

Sustained by an oracle database

- On-line or off-line connection with robots
- Connected with the storage systems
- Container tracking and audit trail of activities
- Linked to a global ordering (option) or Evotec web service
# Talented and experienced scientific leaders

## Toulouse compound management

<table>
<thead>
<tr>
<th>Olivier Casamitjana</th>
<th>Véronique Leblanc</th>
<th>Evelyne Gros</th>
<th>Eric Thibault</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVP, Global head of compound management</td>
<td>Group Leader Compound Management</td>
<td>Group Leader Compound Management</td>
<td>Team Leader Compound Management</td>
</tr>
<tr>
<td>Biochemistry Engineer, MBA</td>
<td>PhD in Human genetics</td>
<td>Post graduate diploma in biological sciences</td>
<td>Bachelor diploma in biological sciences</td>
</tr>
<tr>
<td>&gt;18 years experience in pharmaceutical industry</td>
<td>&gt;16 years experience in pharma and Biotech companies</td>
<td>&gt;30 years experience in pharmaceutical industry</td>
<td>&gt;30 years of experience in pharmaceutical industry</td>
</tr>
<tr>
<td>14 years experience in compound and sample management and automation for several companies (Pfizer, Fournier Abbott, Sanofi)</td>
<td>8 years experience in Compound and sample management lab head</td>
<td>10 years experience in Compound and sample management</td>
<td>2 years experience in Compound and sample management lab head</td>
</tr>
<tr>
<td></td>
<td>Project leader management of collaborations</td>
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