

What to consider when choosing your CRO?

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ABSTRACT

The pharmaceutical and biotech industries are experiencing a lot of changes these days, and they often face tough decisions to be made. Many of these decisions are directly related to the steep decline in research and development (R&D) efficiencies that is being observed for decades. It is all clear that changes are inevitable and desired, and several models are already outlined and in practice, including portfolio management, R&D cost cuts, open innovation and crowdsourcing. In addition to these, outsourcing has become one of the most viable solutions in externalizing the R&D activities of life sciences companies. However, in the growing and constantly changing landscape of service providers you have to ask yourself the question: How can I be sure that I have picked the right provider that not only fits right into the structure of the company at the time being, but can also be considered for a longer period? Here we are trying to cover all the important aspects that you need to consider when in the process of choosing a service provider as well as what we think the characteristics are of an “outstanding” one.

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BACKGROUND / PROBLEM STATEMENT

Current trends throughout the pharma & biotech industries strongly emphasize the need for collaborative partnerships, as opposed to operating as “lone wolves” that was often practiced in the past. The main cause behind these trends is the decreasing number of new medicines launched with regards to the exorbitant money that the companies spend on R&D.^{1,2} This painful observation raises a lot of daily discussions in top managements throughout the pharma world. From the operational point of view the most important questions to answer include to shorten development times and to contain costs associated with the product development life-cycle of marketable drugs. How to accelerate the evolution of new drugs and how to minimize the expenditure from the discovery process through the market entry of new therapeutics?

Many of the companies concerned with the above are looking for solutions to maximize their R&D opportunities outside of their task forces and apply the term externalization.³ Outsourcing R&D activities to experts who are highly specialized in the different steps of the overly complex drug discovery processes is a currently well-accepted way of freeing up cash, personnel, time and facilities. However, the offerings from such service providers vary a lot, and sometimes it is really difficult to oversee them. Some organizations are capable of doing more than just a few steps and can cover a wider spectrum of drug discovery, from synthetic chemistry through running biological assays to conducting regulatory steps and clinical trials. While others, for example, keep their focus only on conducting custom design and synthesis of small molecules or building blocks.

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According to a recent article the global outsourcing market (pre-clinical) is already featuring a staggering amount of \$14 billion (2014), and there is an ongoing and expected growth to top \$25 billion by 2018.⁴ Although the exact number of CROs is hard to guess (in the 1000s), we all agree that it is very much of a dynamically changing landscape. Acquisitions and mergers are making it colorful, new organizations are getting founded, while less successful ones are going out of

business every day. Attempts have been made previously to rank top CROs based on their revenue⁵, but many of these have organizations not providing clinical developments eliminated, hence they lack of providing the full picture. Not to mention that deciding purely on revenue is a false concept in itself, because smaller organizations (with less income) are usually capable of faster reaction times and more innovative thinking as they face less resistance during decision making. Therefore, it is still a question, causing a lot of headaches to the responsible managers, to find the best fitting partner that could thrive R&D while minimizing IP and security risks. In the following sections, we attempt to outline the key characteristics that need to be considered when choosing your service provider.

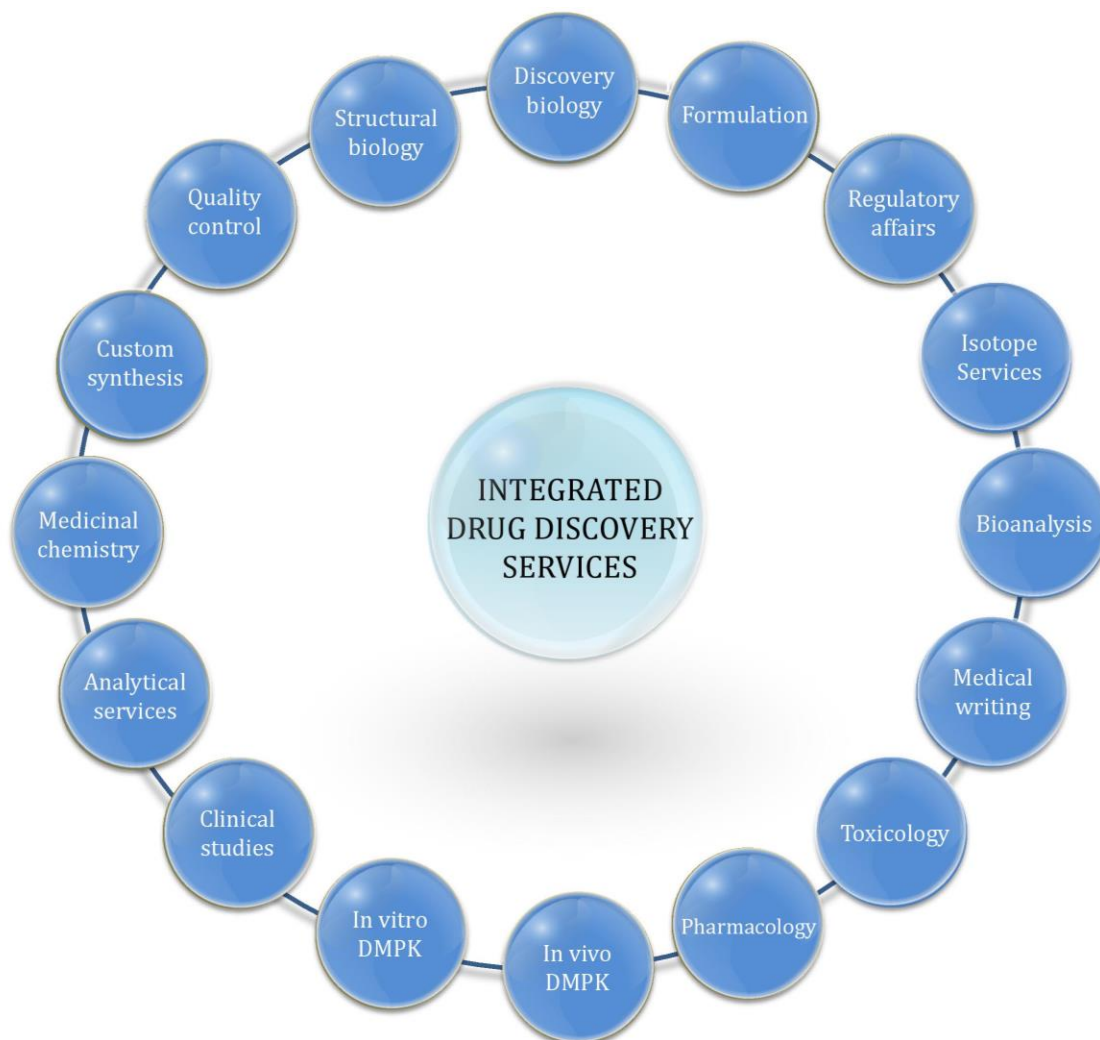


Figure 1. Services offered by CROs

SOLUTIONS

Applying agile principles in work

Usually, pharma companies are still operating via using the “Waterfall” development approach, meaning that a number of steps that need to be sequentially completed by the collaborating partners are well-ahead identified by the project managers.⁶ These steps are then transmitted to the CROs, whose task is to complete the steps in time and on budget, step by step. However, often the missing evolutionary development and adaptive planning caused by the lack of communication brings false deliveries on the table, and the projects need to be reviewed and revised again and again causing money out the window. Instead, using “Agile” methodologies⁷ (e.g. Scrum) not only would allow, but encourage rapid and flexible responses in order to follow the changes of directions for the best possible outcome. How to achieve this? The key is to plan with smaller steps (sprints, how they call in the software business) and be open to conduct frequent communications with your counterpart(s). Careful with the expectations though! In order to make this system work both sides should apply the same methodology. It does not work if only the CRO is working in dynamic sprints,

while the pharma company thinks that everything is clearly stated and being static. Also, it has to be stated here that Scrum is only a tool, a framework, not the solution. In software development, the applied sprints involve parts, such as the planning, daily standups, development, reviews and retrospectives, which can be directly adopted or modified at wish. The purpose of having these parts in place is to provide a framework for continuous learning and development in case the scope of the project is about to change. From the above mentioned, it is better to choose a service provider with some experience in agile product development and a proven track record of applying scrum methodologies, and You will realize the value of this kind of collaboration almost right away.

To me, getting into partnership with a chemistry service provider is not much different than choosing a life partner, a wife or a husband. And just like in any long-term partnership, here the aim is to find a trusted, reliable, and responsive partner that we can openly and regularly conduct discussions with about how to make our journey more enjoyable and effective together. It requires constant work, and not just at the beginning. In this sense, it is also very similar to agile software development where flexibility and stability is balanced and products are iteratively developed. In fact, it leads us to one of my main points, and that is to emphasize the utilization of agile principles in order to best align CROs with and around the mothership organization.

Versatility vs. focus

Let's spend some more time on the required experiences. Another important factor to consider in this bucket is the versatility of the CRO. Although, having an all-around service provider offering integrated end-to-end solutions is definitely advantageous from the communication and integrability points of view, organizations should still be careful about not getting locked in with just one provider. Therefore, it is recommended to mix and match this with the best of breed strategy. It brings back the old Swiss Army knives vs. life size tools problem. However, just like in the latter case, one does not necessarily rule out the other one. I have a Swiss knife in my bag with me all the time, while single-purpose tools at home. The purpose of the former is to be able to act quickly whenever and wherever needed, while that of the others is to maximize the effort on creating something unique within a given period of time.



One shoe does not fit all, so utilizing a hybrid strategy is actually suggested to gain the best of both worlds. This could in practice mean having one larger CRO with many services offered from synthetic chemistry through *in vivo* pharmacology studies to running biological assays, while many other smaller ones offering only custom syntheses specific to single problems.

Technology access and know-how

Further onto technology. Having a collaborating organization with access to state-of-the-art instrumentation, highly developed infrastructure as well as a great deal of field expertise can further roll the ball. CROs these days need to be highly resourceful. They need to make the same or very similar compounds faster, smarter and, last but not least, cheaper than the competition, otherwise they can very quickly shut the door. Technology is the key here!



It can mean better synthetic techniques, robotics, scaling instrumentation, more precise analytics, scientific IT support, cheminformatics and bioinformatics tools and toolkits in place, nearly anything that speeds up existing processes significantly or makes an impossible possible.

Some CROs are forced to overcome the lack of accessible technology with manpower, but in my opinion that clearly leads to a dead end, especially, when the scope of a project is quickly changing. Although, we cannot skip human intuition from the equation. It is absolutely needed to solve complex problems that machines are unable to do, not to mention the vast amount of knowledge that is in the head of an experienced organic chemist. This latter information is priceless and can be routinely placed in work when designing reaction steps for novel compounds. Therefore, the best to find and apply a delicate balance between utilizing machines and human minds.



Staying with technology, it is also true that they might as well mean threat to part the CRO industry. Thinking about robotic process automation (RPA), which can be applied in smart pharma to optimize operation and reclaim certain functions previously outsourced to clinical research organizations in the hope of reducing cost and achieving a nicer looking ROI.⁸

Providing flexibility

Being able to offer flexible business models to accommodate the pharma company's own is almost a commodity these days. Large companies are usually slower, have their own processes in place and might be a little more reluctant to change, therefore, it is common sense for a service provider to highlight many possible business models and have the pharma company choose the one that suits the best. Selling data, complex problem solving services, chemical compounds, working on full time employee rate (FTE), charging fixed fee, offering a spectrum of exclusivity models are all examples for the types of operation that the future customer may find useful and relevant, perhaps even looking for in a fruitful collaboration.

Distance matters

Geographic location of the CRO, more precisely the distance between the collaborating organizations matters a lot. Why? First of all, time difference can really mess up your day. It is especially true if a meeting with the attendance of all the partners from all around needs to be organized. Secondly, shipping products overseas might contribute a lot to the cost as opposed to staying within a continent. Last, but not least, distance often does not just mean miles, but language barriers

and cultural differences as well, all of which can have strong influence on the common understanding of a running project. It's worth mentioning here a largely different yet very successful adaptation of the traditional outsourcing model, and that is *insourcing*.⁹ Insourcing means that a company hires a CRO (or a group of trained experts) to provide its services in-house using its full or partial resources, but under the close look and control of the sponsoring organization. It is easy to see that this model is truly maximizing the real-time scientific information exchange, and therefore can be considered as a very effective way of setting up strategic partnerships. However, the values of the CROs that a sponsor should look for is largely overlapping with the one coming from the more traditional approach, therefore, differentiating these models is out of the scope of this paper.

Competitive cost

Finally, cost of the service needs to be considered as well. In many cases, it is partly determined by the portfolio, in other words the versatility (see above) offered by the service company in question. If the company stands on multiple legs the FTE rate might be smaller. One minor setback related to a specific business type does not have that much influence on the total revenue as opposed to a company which is focusing on just a handful of clients and / or businesses. Of course, size matters here as well. On the one hand, larger CROs need to operate on larger added cost, but on the other hand, they are the ones usually keeping more sticks in the fire.

X-factor

So, the above are fairly easy to measure, and you would expect to have it all in a first class candidate. However, there are things that can neither be measured nor expected, only hoped for. These are not required characteristics, but more like ones in software development they call "nice to have features". I simply just call it the "X-factor". This cap contains values of being customer centric, but even beyond what is expected. Taking the extra mile, being available on short notice calls, having a good sense of humor, always being constructive and open to offer alternative solutions goes a long way, and in a tight competition this is what makes a provider to stand out from the crowd. Imagine if a provider has to say no to a business proposal due to lack of technology (or similar), however, suggests another CRO, a competitor to do the job. This shows that not only the competition is known by the provider, but it is able to come up with constructive suggestions always putting customer values in front. Who would not go back to the same provider with another proposal in the future?



EXAMPLE CASE

Our company, ComInnex Inc.¹⁰ operates on 3 main pillars, which is outlined in the followings:

- One of the main values of the company is the highly dedicated and very much customer centric chemistry team that has an extensive knowledge in synthetic organic chemistry. A big portion of the staff owns PhD in relevant fields, and many of the employees have long time experience with medicinal chemistry often learned at different pharmaceutical companies.
- Much of the chemistry ComInnex Inc. is doing would not be accessible if it was not for its sister company, Thalesnano¹¹ having a strong focus on the instrumentation part of life sciences R&D. Through this synergistic collaboration ComInnex Inc. is able to propose technology enabled unique compounds and compound libraries to our highly valued customers.
- Our Research and Production facilities are supported by first in class cheminformatics and IT tools / toolkits, helping us to make sure the customer always receives the highest quality value and return on investment.

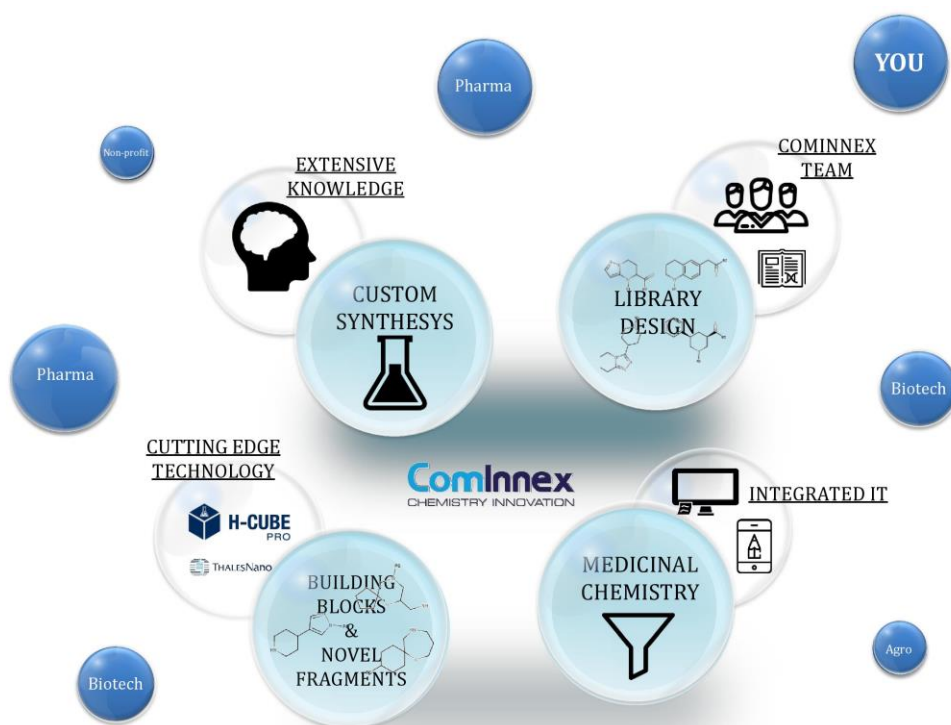


Figure 2. ComInnex's value chain

Let us get back for a minute to point #2, which I find the most important advantage we gain over the competition in our size. One of the positive outcomes of this synergistic collaboration (accessibility to state-of-the-art synthetic methods) between ComInnex and ThalesNano is materialized in the technology enabled diversity libraries ComInnex offers to its highly valued partners. What it means in reality is that our synthetic chemists are well set using flow chemistry principles in running reactions more effectively (e.g. boost selectivity and conversion) and more safely, reactions, that otherwise would cause difficulties to proceed with. As a result, a fine assortment of lead-like compounds, free of undesired and toxic functionalities and featuring novelty and high-quality, are created on a daily basis. These compounds and compound libraries make the center of discussions that our sales team are to conduct with prospecting clients. So, what's in it for the technology provider? You may ask. In return to their service, we, considered as an end-user of ThalesNano's flow reactors, constantly feedback invaluable information that is quickly and efficiently transformed back into product development. Therefore, it is a win-win situation for all parties, and looking for a win-win in all cases greatly determines success and distinguishes well-working businesses from the ones that are barely surviving.



Figure 3. ComInnex's information feed loop

Although our company is a relatively small one, therefore we do not have the luxury of having a wide and in-depth portfolio, yet in a world where there are an abundance of CRO companies, we are able to offer truly unique and technology enabled services in medicinal chemistry and compound libraries with dedication and flexible business models.

CONCLUSION

I can only admit realizing the above is pretty ambitious and can be quite challenging to find all in a single CRO, but the details and the priorities of the above-mentioned characteristics largely vary depending on the needs of the company looking for a partnering organization. Nevertheless, these are some key considerations that apply to essentially all alliances. By ensuring a contract research organization (CRO) meets these criteria above (most of it anyway) before entering into a partnership, pharma and biotech companies can increase the likelihood of an external partner to live up to their expectations.

To conclude, to me these are the most relevant selling points featuring service providers that need to be looked for, together with the values they represent to a partnering organization:

SELLING POINTS	VALUES	POINTS (1-10)
AGILITY	be able to react quickly and accurately	
VERSATILITY	provide end to end solutions vs. focus on specialties	
TECHNOLOGY ACCESS	creativity, speed, data & information	
KNOW-HOW	smartness	
FLEXIBILITY	customer centric	
LOCATION	shorten development time	
COST	quality of service	
X-FACTOR	uniqueness	
		total score:

Furthermore, as oppose to scoring CROs purely based on their revenue I propose to set up a matrix that contains these selling points in a way that they are weighted on a 1 – 10 scale based on their importance to the partnering organization or for a particular project. And then create the sum, and if the scoring results in a tie for several different CROs there is still the X-factor to take into account.

ADDITIONAL RESOURCES

- ¹ Kola I. *et al. Nat. Rev. Drug Discov.* (2004) 3 711
- ² <http://info.evaluategroup.com/rs/607-YGS-364/images/wp15.pdf>
- ³ <http://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/new-frontiers-in-pharma-r-and-38d-investment>;
<http://www.prnewswire.com/news-releases/rd-trends-2012---pharmaceutical-companies-use-externalization--collaboration-to-drive-growth-152247565.html>
- ⁴ Schuhmacher A. *et al. J Transl Med* (2016) 14 105
- ⁵ <http://www.clinicalleader.com/doc/an-overview-of-top-clinical-cros-0001>
- ⁶ http://www.contractpharma.com/issues/2014-10-01/view_features/agile-drug-development-lessons-from-the-software-industry
- ⁷ Larman, C. (2004). *Agile and Iterative Development: A Manager's Guide*. Addison-Wesley. p. 27.
- ⁸ <http://www.pharmafile.com/news/503664/outsourcing-and-robots-how-smart-pharmas-are-optimising-rd-operations>
- ⁹ <http://www.biopharminternational.com/case-insourcing>
- ¹⁰ www.cominnex.com
- ¹¹ www.thalesnano.com

Pictures: <http://www.flaticon.com/>

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