Lighting the Way

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Misconceptions about academic research organisations are deep-rooted within the industry, yet they are slowly gaining back their original reputation as thought-leaders who are prepared to push boundaries. It is now time to rethink the definition of their role today

The academic research organisation (ARO) has been around for many years, yet what an ARO actually is and does has evolved over time and has inevitably been shaped by various landmark events, solidifying perceptions which are difficult to alter. For this reason, AROs are often mistaken for teaching hospitals or divisions within a hospital, and seen to be hidden in the shadow of universities or in the guise of pioneering medical researchers.

A look back in history will reveal that some of the most ubiquitous drugs were brought to society by academic researchers. Paracetamol, for example, was tested for the first time on patients by Joseph von Mering in 1887 at the University of Strasbourg. However, since the 19th century, the role of the academic investigator has changed dramatically through the altering landscape of drug development. Historically speaking, drug development took a twisting, winding route, yielding at times tragic yet profoundly formative events (such as the Tuskegee syphilis experiment in 1932, or the Nuremburg trials in 1947). This led to the current regulatory framework for protecting human subjects, prompted

institutionalised ethics review boards, and ultimately contributed to the industrial rise of the contract research organisation (CRO).

AROs were not formally introduced into the mainstream until Goldenburg *et al* revealed the ARO-CRO model, published in *Blood* in 2011 (1). As important as this paper was in defining the roles and responsibilities for key players, including AROs, CROs, pharmaceutical companies and regulators, new developments in the ARO model are already superseding Goldenburg's initial concept.

We are entering a new era of the ARO, one that challenges the current paradigm of clinical development and the numerous offerings of CROs. It will not be long before AROs play a more central role in pharmaceutical clinical development plans.

Here are four perceptions that today's AROs are trying to break:

Table 1: Summary of the differences between AROs and CROs

ARO	CRO
Academic thought-leaders; opinionated, up-to-date, forward-looking	Clinical operations minded; 'plug-n-play' with pharma, project-oriented
Peer-to-peer relationships with sites and investigators; established networks of therapeutic experts with similar clinical research goals	Require feasibility studies within their spheres/geographies of influence
Cross-functional partner	Functional service vendor
Personnel apply and control operational and scientific rigour across sites, investigators, monitors, data managers and so on, using a continuous process improvement philosophy (for example, academic oversight)	Personnel perform operational tasks and escalate issues defined by bureaucratic processes and contractual constraints (such as industrial clinops)
Light overhead; affiliated with universities	Large overhead; maintains offices worldwide
Fixed price model; rewards efficiency	Traditional change order model; rewards inefficiency
Not afraid to challenge the system; proposes new ideas and innovation (most drug development paradigm shifts are driven by AROs)	Business model is influenced primarily by rules and regulations; slow to change (status quo)
Added value: knowledge, influence; methodological rigour	Added value: cost-effective operations; clinical operations rigour

Misperception 1: *"The primary goal for AROs is publication"*

It is easy to see how one may come to this conclusion, given that universities are judged by their publication record in high-impact journals, but the discussion goes much deeper than the act of writing and collecting publications.

The notion that the desire to publish ranks higher than collaborating with pharma and regulators, ensuring sustainability in clinical research or the wellbeing of patients, is misaligned and wrong. For some reason, conducting 'independent' research is automatically assumed to mean not adapting and working with commercial entities, even in the presence of a shared common goal, for the sake of making the next issue of *JAMA* or *The New England Journal of Medicine*.

Nothing can be further than the truth. An average patient outcomes study takes five years to complete, during which time thousands of patients are enrolled and followed until the endpoints of the study can be verified and adjudicated. Proper, systematic collection, cleaning and locking of clinical data, regardless of the outcome of the study, not only satisfies the demands of regulators, but are the hallmarks of good clinical research, which yields important by-products, including publications. The years of careful planning, compliance to guidelines and regulations, and vigilant execution of the clinical protocol should not be taken for granted.

The reason why AROs publish results, whether good or bad, is to ensure that transparency remains the 'holy grail' for its dealings in clinical research. In this way, the outcome of the research conducted can positively influence

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the way medicine is practised; a gold standard of credibility that is valid across all industries and stakeholders for both the lay person and the professional.

Misperception 2: *"AROs are not capable of meeting the rigours of clinical drug development"*

The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) place increasingly high demands on pharmaceutical companies to demonstrate the safety and efficacy of their drug candidates. CROs have answered the call for these rigorous requirements, incorporating them into a business model and industrialising the process of clinical development.

The simplicity of the CRO model has motivated many pharmaceutical companies to view CROs as 'preferred providers' – favourable components to extend their value chain. There are no false pretenses. But what is it that CROs have that AROs do not?

Today's AROs have proven quality management systems; a clear, transparent set of standard operating procedures; and work instructions equivalent to their CRO counterparts. Most AROs are not afraid to claim the right to deploy their clinical database for the purpose of capturing data.

However, the general assumption is that when it comes to clinical operations at the workfloor level, CROs are superior:

Figure 1: Analysis of the average days queries are outstanding – general queries

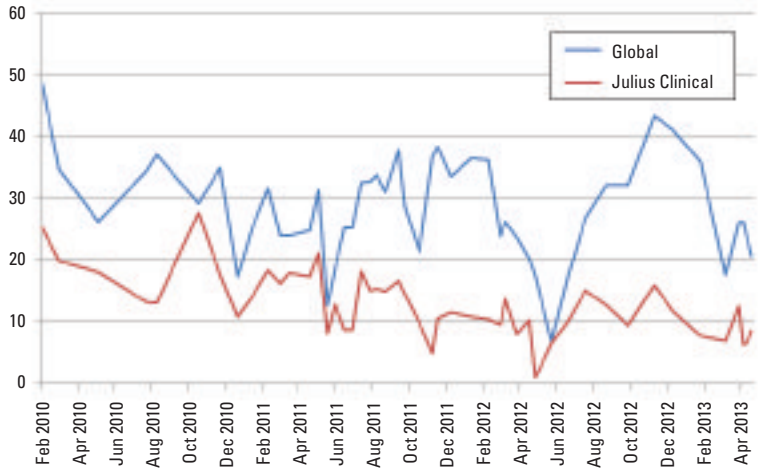
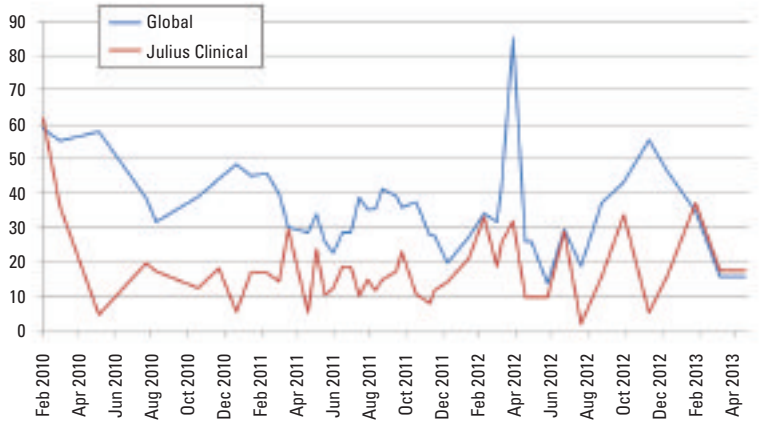


Figure 2: Analysis of the average days queries are outstanding – endpoint queries



a statement which is unfounded. Using a simple analysis of one of the most common monitoring metrics, the average time queries are outstanding – in other words, how quickly monitors follow up with investigators and sites to resolve questions and secure data capture in the clinical database – our ARO outperformed our sponsor and sponsor's partners in the regions we were active (see Figures 1 and 2).

Similarly, resolving endpoint queries – which are critical for determining whether the primary endpoints were met and the overall success of the study – were also handled quickly and efficiently, ahead of the sponsor and their partners. Perhaps a better question to ask now is: what do the AROs have that CROs do not?

Misperception 3: *"ARO investigator networks do not add value"*

Networking is important in every facet of the industry, and only those who have been around long enough can attest to the importance of knowing the right people to address the right research question. But in today's world, there are so many 'social' avenues and individual moments to market oneself that identifying and developing the proper network is even more difficult in the midst of the added noise. Finding the right investigator is like finding a needle in a haystack.

During many conversations with pharmaceutical sponsors, the feedback is that "academic investigator networks are useless – anyone can make their own networks." This is true to some degree, but 'peer-to-peer' relationships, especially within academia, should not be underestimated. Just think: wouldn't you do something quicker and with more purpose for a friend?

Anyone who has ever performed a feasibility study knows how hard it is to motivate investigators to provide information, let alone information that is accurate. This is the reason why feasibilities are often outsourced to companies with enormous databases

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of investigators who employ a ‘shotgun’ approach, sending vast requests and banking on the responses of a few. But what if key opinion leaders performed feasibilities? They would know exactly who to ask and how to persuade their colleagues, if it proved necessary.

In today’s ARO model, academic investigator networks are not limited to serving on executive steering committees and safety data review boards. ARO investigator networks are proactive and enthusiastic to contribute in day-to-day clinical operations.

Misperception 4: *“AROs are difficult to work with”*

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The reality is that AROs need to be forceful in their views to motivate change. To put things into perspective, changes within pharmaceutical companies and CROs take an enormous effort and a lot of time, and changes in the practice of medicine are something far bigger. Without figures that can draw attention to important issues and precipitate decisions that impact the livelihoods of many, imagine how much more vulnerable patients and the healthcare environment would be to the potential neglect of safety.

Once you get past the stereotype, it is clear that AROs work with everyone and are truly ‘spiders in the web’, interfacing between healthcare, academia, pharma, governmental agencies and even CROs. For this reason, AROs are often a manageable size, flexible, agile, opportunistic, engaging, and with a light overhead. Their expertise in clinical operations make for cross-functional teams which are willing and able to work within complex pharma organisations.

An often overlooked advantage of working with AROs is the freedom and space to innovate and try new things. AROs are not afraid to challenge the system. In fact, AROs have kept up with the times by contributing to key innovations such as adaptive clinical trial designs, not only in early phase but also in late phase clinical development.

Conclusion

Although overshadowed by the commercially oriented CRO, the truth of the matter is that AROs have never left the drug development landscape. There are as many (perhaps even more) active AROs today as there were in the pre-CRO era. What is more, AROs are making a huge comeback, challenging CROs head-on for the chance to lead and perform global trials.

New EMA regulations which were passed in July 2013 have done well to address a number of key deficiencies, especially with regard to safety and pharmacovigilance, but they have failed to incorporate expert scientific advisory committees into the early decision-making stages of drug development – an obvious gap which AROs are best suited to fill and also translate into efficient clinical operations.

It will be hard work to demystify the prevailing perceptions of AROs. However, the evidence is accumulating that AROs address the needs of today: scientific and medical relevance; integrity; credibility; agility; operational excellence; and academic networks. AROs are here to stay.

Reference

1. Goldenburg *et al*, Improving academic leadership and oversight in large industry-sponsored clinical trials: the ARO-CRO model, *Blood* 117(7): pp2,089-2,092, 17th February 2011

About the author

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