ROLE OF ACADEMIA IN A GLOBALLY COMPETETIVE DRUG DEVELOPMENT MARKET

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Abstract: 2070-- ROLE OF ACADEMIA IN A GLOBALLY COMPETITIVE DRUG DEVELOPMENT MARKET. D. P. Waller1, P. J. Baneux2 and T. Welsh2, *1University of Illinois at Chicago, Chicago, IL and 2Northwestern University, Chicago, IL.* Sponsor: J. Herman.
Biotechnology companies are increasingly seeking sites within the US and foreign countries to outsource studies supporting drug development. This is driven by high costs for the up to date infrastructure needed to meet government regulations and testing requirements. New directions in drug development related to gene therapy and nanomedicine have created specific needs to move products forward. This support may include accredited vivarium capacity, specialized facilities and state of the art instrumentation. These are expensive and difficult to operate efficiently. Limited use in a company based research program makes it difficult to justify such expenses. Sophisticated systems with high acquisition costs are often found in academic institutions to support their large leading edge research endeavors. Academic institutions leverage several users within their institutions to justify and operate such support systems. Frequently, these support systems are underutilized and require subsidies to operate within the academic environment. Such academic resources can be identified by drug development entities creating an opportunity for the academic community to leverage their assets. However, regulatory compliance rigor, administrative hurdles, timeliness and intellectual property issues associated with private industry working within an academic environment often prevent their use. Contract research organizations can provide an effective pathway to the utilization of such assets, leveraging government research funds spent to provide high tech resources and thereby increasing or keeping research within US institutions. Appropriate oversight and monitoring can establish confidence in a timely and regulatory compliant research project. Preexisting relationships with an academic institution can provide a clear path to the utilization of the academic assets with minimal delay. The leveraging of these expensive assets benefits both the academic institution and the drug industry to provide effective solutions to difficult problems with minimized costs.

Introduction

Escalating drug development costs and the recent economic downturn have created an environment where drug, biotechnology and chemical companies have been searching for more cost effective solutions to product (or device) development. This has led to an increased outsourcing of preclinical and early development costs to contract research organizations. Expanded research capabilities in Asia are beginning to attract customers based solely upon less expensive testing and research opportunities. Most outsourced testing involves the utilization of vivarium facilities which are expensive to build, operate and maintain. New areas of research such as nanopharmacology/toxicology and gene therapies demand also more sophisticated instrumentation and expertise not found in most preclinical contract research organizations. Little effort has been dedicated to developing less costly opportunities for drug and chemical development within the US to compete with the lower cost foreign providers. Substantial funds have been devoted during the last decade to building and staffing vivaria within the US academic community as well as purchasing and operating state of the art instrumentation to support ongoing university research programs. In a recent survey we conducted, all of the laboratories which responded were AAALAC International accredited, indicating a high level of commitment to quality facilities operated with a high standard of animal care, use and concern for their welfare. These facilities must be maintained and made available to the academic research community, but they are often not fully utilized.

Availability of Quality Vivarium Opportunities

We polled both private and public academic research institutions and obtained responses from 23 institutions regarding several questions focused on active vivarium operations.

Animal Housing

All responding vivaria have facilities to maintain and house small animals and rodents. Almost all have significant space dedicated to larger animals. Fewer facilities have dedicated space for non-human primates.

% Space Dedicated	Small Animals/ Rodents	Larger Animals	Non-human primates
Mean(std)	82.0(11.4)	14.0(11.5)	4.5(4.0)
Low-High	65-100	0-29	0-12
# w/dedicated space	22/22	21/22	17/22

In most cases the occupancy for the past 24 months was significant, although few facilities reached the 100 % level. The mean occupancy for the past 24 months and projected forward for 24 months was about the same. However, there was significant capacity not utilized for small animals and larger animals when evaluating how many facilities were operating at 85% or greater capacity. Although the number of facilities with occupancy of greater than 85% for housing non-human primates was greater, half of the institutions were less than 85% utilized.

Past 24 Months	Small Animals/ Rodents (%)	Larger Animals (%)	Non-human primates
Mean (std)	76.5(14.5)	48.1(33.1)	64.6(39.4)
Range	50-100	2-100	1-100
>=85% Occupancy	7	3	8
<85% Occupancy	14	17	9

Next 24 Months	Small Animals/ Rodents (%)	Larger Animals (%)	Non-human primates
Mean (std)	76.5(14.5)	48.1(33.1)	64.6(39.4)
Range	50-100	2-100	1-100
>=85% Occupancy	7	2	8
<85% Occupancy	14	18	9

High occupancy rates are essential to minimize losses to vivarium operations in any setting. However the academic setting usually provides a significant baseline of activities to support most of the facility operation costs. An opportunity to increase occupancy will greatly reduce per unit costs and in some cases provide additional revenue for facilities.

Laboratory Support

Studies frequently require the use of various support laboratories such as hematology, blood biochemistry, microbiology, histology and pathology services. About 50% of the responding facilities have such services available on site with higher numbers providing histology and pathology services. Most were not GLP compliant.

	Hematol	Chem	Micro	Histo	Path
Yes	11	11	12	13	13
No	11	11	10	9	8
GLP Compliant	4	4	3	3	2

Surgical Facilities

Surgical facilities were available in all of the responding facilities averaging more than 1600 sq ft and they were divided into more than one operating suite. No usage data were requested; however the experience of the authors of this poster clearly indicates most such facilities are not fully utilized on a regular basis.

Outside Access to Academic Vivarium Facilities

Many institutions provide opportunities for outside investigators to utilize their facilities. However, the use of such facilities by outside investigators is usually a small part of their total operations (less than 5%). GLPs were implemented in six of the institutions, but most (15) did not. Interestingly, one of the institutions performing GLP studies did not have any outside investigators. The GLP compliant studies for almost all of the institutions were performed by investigators within the academic faculty.

	Allow Outside Investigators	Follow GLP
Yes	14	6
No	8	15

Outside Access to Academic Instrumentation and Expertise

Many academic institutions have sophisticated instruments with faculty and staff dedicated to their operation and maintenance. Although most instruments are dedicated to support focused research programs, some are utilized as shared instruments among several investigators. An example is the University of Illinois at Chicago's Research Resources Center (RRC) which operates a variety of instruments and facilities that are available to faculty on a fixed fee for use basis.

The RRC will allow faculty to operate the instruments, provide direct technical assistance or train outside investigators. Opportunities to utilize these instruments are provided to investigators outside of the institution also on a reasonable fee for service basis which is far less than would be required for purchase and independent operation of sophisticated equipment.

Research Support Areas	Example Instruments
Confocal Microscopy	Zeiss LSM510 and LSM510 META
DNA Services	ABI 3100, 3730 Genetic Analyzer. ABI 7900HT Sequence Detection System..
Electron Microscopy(Types listed only, several available,)	Scanning (SEM & Microprobe), transmission (TEM) and scanning transmission (STEM)
Flow Cytometry	Beckman-Coulter Elite ESP, DakoCytomation MoFlo, Bio-Rad Bio-Plex
Core Genomics	Affymetrix GeneChip System, OmniGrid Accent Array System (Genomic Solutions), dual-laser confocal scanner
Macromolecular Structure	Rigaku R-AXIS-IV++
Mass Spectrometry Examples, several available	ThermoFinnigan LCQ Classic quadrupole, Micromass QTOF-2, ThermoFinnigan TSQ Quantum triple quadrupole, Voyager-DE PRO PS1 (MALDI/TOF)
Nuclear Magnetic Resonance	Bruker AVANCE-500, A Bruker AVANCE-360 MHz
Protein Research	Rainin Symphony multiple peptide synthesizer; ABI 392 and 394 oligo synthesizers; Waters PICO-TAG amino acid analysis system

Assets and Considerations

Academic Institutions

Academic institutions have leading edge scientists with a great deal of expertise. Often this expertise is limited to research in academic settings supported by grants which have few requirements regulating their performance.

Academic institutions have leading edge instrumentation.

Academic institutions often have laboratory space and trained technical assistance available.

Considerations for incorporating Academic Institution assets into a CRO environment

Academic talent has:

- Little training and experience in the competitive conditions in which CRO operate
- Little or no marketing skills in the commercial arena
- Limited training and experience in GLP compliance and drug development regulations
- Lack of sense of urgency in meeting timelines (Animal Care committees, IP legal issues)
- Report writing skills for regulatory filings
- Poor knowledge of US and world regulations governing new drugs, chemicals or devices

Requirements for effectively integrating academic institutions into the CRO environment

Higher administration's willingness to invest in the development of faculty and the operation within a GLP environment.

Academic research rarely meets the standards required for drug and chemical development in the public sector. The commitment of all levels of university administration to GLP compliance is required. They must recognize both the costs and the benefits of developing capacity to work in this competitive environment. Most universities have facilities which are available and staffed by competent employees. However, it will require significant effort to bring the facilities and staff to an adequate level of regulatory compliance. The commitment of the higher administration to support such activities is crucial to initiate and maintain the level of effort required. Identifying and managing such an effort is difficult without expertise in the commercial world of preclinical contract research organizations. Assurances must be provided by administration to any faculty who change career paths or who are hired specifically to perform this type of research that their efforts will be rewarded in a similar manner to the normal research efforts usually supported by government and foundation support for leading edge research.

Intellectual Property

Intellectual property issues often provide a large hurdle for the timely onset of a project within the university. The university setting provides many opportunities for significant IP advancement. However, the university must recognize that most preclinical contract research involves the IP of commercial entities and must provide quick resolution to any IP issues which may prevent timely onset of a project. Universities are also now more protective of their IP rights. It is essential for the university administration to provide a pathway to quick resolution of any potential IP issues

Faculty willing to train and operate within GLP framework

The low level of funding of government research support during the past several years has made it difficult for many faculty to maintain research programs. This has resulted in faculty without adequate research funds and the need to reduce trained staff. Some faculty have expertise closely related to projects often performed at preclinical contract research organizations. However, their experience is limited to grant research projects which have no GLP requirements. The daunting task of instituting GLP practices within their laboratories is often beyond their immediate capabilities. Faculty must be willing to commit significant efforts to develop and use GLP practices within their laboratories as a first step. With appropriate guidance and support, dedicated faculty are quite able to adapt and change their research programs to perform GLP compliant studies.

Academic Partnership with Contract Research Organization

It is advantageous for academic institutions to partner with CRO's s that understand regulatory requirements and can assist the academic institution with the establishment of the documentation and timely reporting needs of industry during product development. A CRO can work with the university to facilitate and establish regulatory compliance prior to utilization of any academic asset. Appropriate interactions of academic institutions and the faculty with a CRO can lead to well performed and documented studies concluded in a timely fashion and meeting regulatory requirements. Establishment of the appropriate cultural environment is one of the most difficult changes for an academic institution. Although most are accredited facilities, many are not aware of the next level they must achieve to perform GLP studies. The assistance of a CRO partner can provide quality assurance and the oversight needed to perform studies that meet regulatory demands.

Advantages To University

Increased desirability of potential employers in the drug and chemical industry for students upon completion of their studies.

Better interface with corporate clients, both for work and for later interactions related to potential for an academic unit's own IP development.

Cost savings to universities by utilization of open space.

Additional funding opportunities for university faculty and staff, particularly from the private sector

Additional support for shared sophisticated instrumentation.

Creation of SOPs if none exist or enhancing quality SOPs to augment the quality of operations and management.

Advantages To CRO

Specialized technical assistance available on an as needed basis.

Projects with small and medium sized companies often require specialized technical assistance to develop products. These companies do not always have an adequate depth of expertise to enter into desired new and expanded areas of research. Similarly, a contract research organization cannot participate in projects which require elements of specialized research expertise not readily available within that organization. Technicians and students are often available for short term projects and could be utilized without requiring the commitment and training costs required for most positions within a commercial research enterprise. This provides access to needed expertise with limited cost, and greatly reduced long term commitments. Most importantly, it expands a contract research organizations' potential to research areas requiring specialized technical skills.

Can Outside Investigators Gain Access To Academic Facilities?

Only one of the responding institutions had a preclinical contract research organization operating within its facility, with four others providing facilities to outside investigators. However an additional eight out of 19 facilities not currently involved with outside investigators would allow such activities.

Conclusions

Academic institutions have significant opportunities to work with a contract research organization to better utilize their facilities and amortize costs of the maintenance and operation of existing, developed research facilities.

Preclinical contract research organizations have an opportunity to expand their operations and the scope of their research opportunities utilizing available academic institutional resources.

Partnering of a CRO with an academic institution can provide cost effective outsourcing solutions to expensive and highly technical research projects which cannot be carried out at small and medium sized pharmaceutical and chemical companies.