

PHARMACEUTICAL OUTSOURCING

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Attenuon, LLC (2000-2007)

Idun Pharmaceuticals, Inc. (1994-2000)

La Jolla Pharmaceuticals, Inc. (1993-1994)

Eli Lilly and Co. (1984-1993)

PHARMACEUTICAL OUTSOURCING

1. What is “Outsourcing”?
2. R&D Historical Perspective and Current Trends
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What is “Outsourcing”?

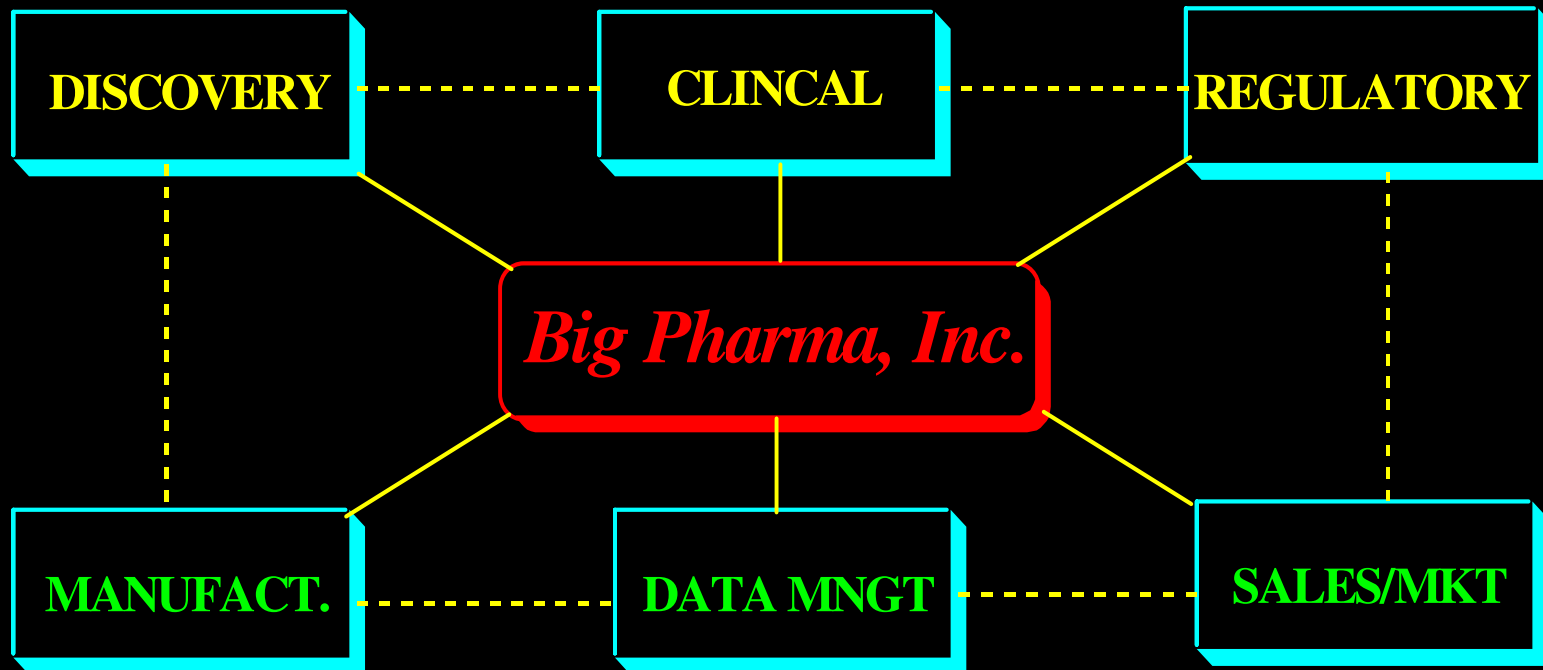
- Contracting with an independent firm to accomplish a defined task required for the discovery and development of a new drug
- “renting” expertise rather than “buying” it
- Contract Research/Manufacturing CRO’s and CMO’s (CO’s), now exist to handle activities from early research and pre-clinical development to clinical development and post-NDA approval activities

R&D Historical Perspective

Traditional Pharmaceutical Model:

- “Fully Integrated Pharmaceutical Company” (FIPCo)
- In-house research, development, manufacturing, clinical, regulatory affairs, data management, sales and marketing, etc.
- Advantage: CONTROL....ultimately all have the same boss
- Popular model for biotech start-up’s during the 80’s
- example: La Jolla Pharmaceutical Co. (founded 1989) built cGMP manufacturing in 1993...first product still not approved

R&D Historical Perspective



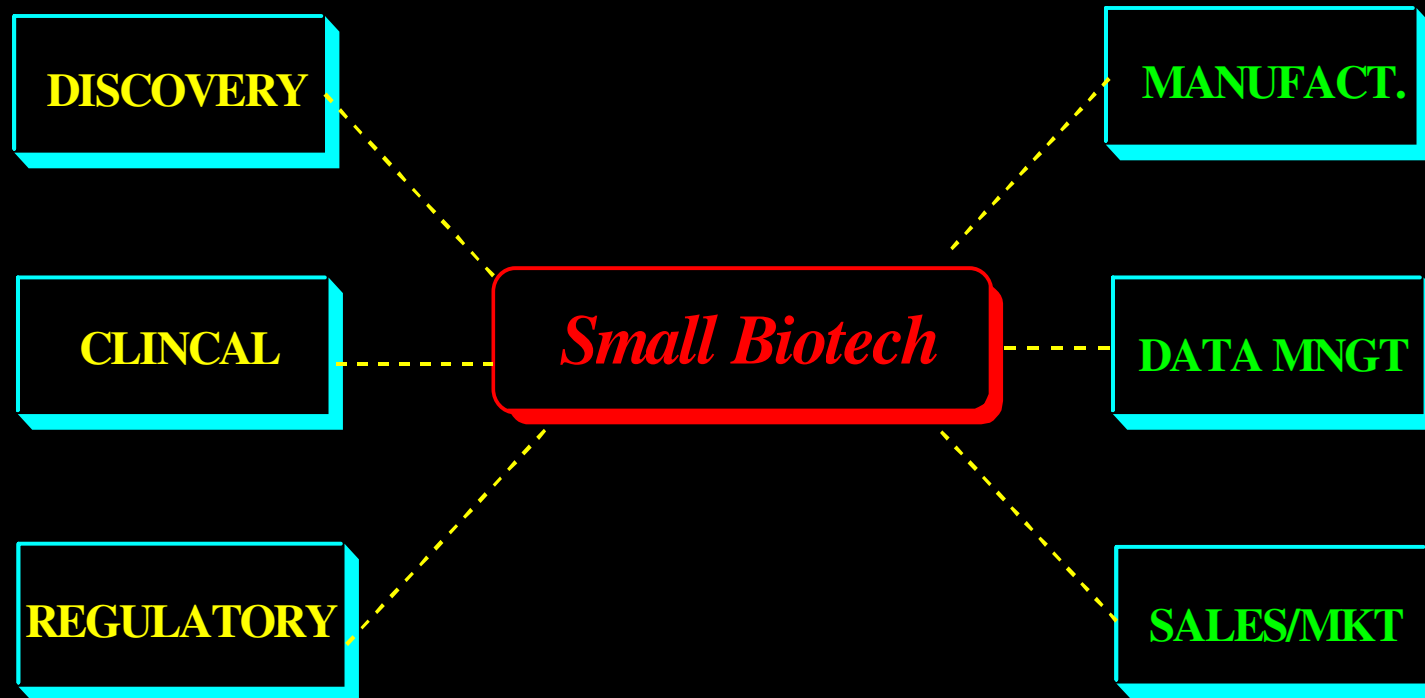
ADVANTAGES: Continuity; Communication; Control

R&D Historical Perspective

New Biotech Model:

- Virtual company: small (3-10) staff with no laboratory
- Outsource all R&D activities
- “Semi Virtual”: have small staff with wet laboratory capabilities
- Advantage of Semi-Virtual
 - no substitute for “hands-on” experience with new drug candidates
 - can focus on other business needs such as developing proprietary position (defensive)
 - preliminary experiences can be translated to CO and accelerate development

R&D Historical Perspective



CHALLENGES: Continuity; Communication; Control

Current Trends

- A recent survey* of 37 leading pharma and biotech companies indicated that 70% of their studies had at least some component outsourced
- Those surveyed all anticipated increased use of COs for the foreseeable future
- Sponsors are looking for a single CO to handle a broader scope of activities (*wanting*: continuity, communication and control)
- The FIPCo model is *history*

* Cambell Alliance, Pharmaceutical Executive, June 2004 (www.pharmexec.com)

Why Outsource?

- Convert fixed costs to variable costs
- Rent expertise as needed
- Reduce overhead/infrastructure costs
- *BECAUSE INVESTORS SAY SO*

Selecting a CO

- I. Shopping
- II. Conduct Due Diligence (DD)
- III. Sign Agreements/Contracts

Selecting a CO

Shopping

- Find COs on line (Google “pharmaceutical outsourcing”)
- INTERPHEX is the largest trade show for COs (WHY do potential customers have to pay???)
- Sorting through the junk: dealing with cold calls...once you begin shopping, you will be deluged with calls....learn to screen quickly (eg: API synthesis at Attenuon requiring use of H₂S gas)

Selecting a CO

Due Diligence (DD)

- Initial screening: capacity; timing; past related experience; CO structure; communication methods
- Obtaining references: references supplied by CO are for CYA purposes only....personal references are best
- Second level screening: site visit; regulatory audit (with consultant); organization chart; employee makeup and number; number of projects undertaken
- Obtain competitive bids

Selecting a CO

Important issues to consider when selecting a CO:

- Location-can the sponsor access the facility readily?
- Cost-(sometimes) you get what you pay for
- Size-can be too large or too small (management issues)
- Manufacturing capabilities-commercial vs clinical scale
- Employee retention-high turnover is red flag and bad for sponsor
- Expertise, years of experience of senior staff
- What experience has the CO had with your type of project?

Selecting a CO

Important issues to consider when selecting a CO:

- How proactive is the CO? Do they only act upon request of sponsor?
- Is the CO at capacity or under capacity?
- What quality systems are in place?
- What documentation systems are in place?
- What experience has the CO had with vendor switching (examine transfer in/transfer out procedures)?
- What experience has the CO had with your type of company?

Selecting a CO

Important issues to consider when selecting a CO:

- Has the CO been inspected by the FDA? by the California FDA?
- Has the CO received any 483's (FDA documentation of non-compliance with cGMP)? How have they been handled?
- Financial viability of CO

Selecting a CO

Contracts/Agreements

- Need Confidential Disclosure Agreement (CDA) or Non-Disclosure Agreement (NDA) in place before discussing project with CO
- Be sure that financial terms are clearly described with an upper limit specified
- Ownership of inventions and co-operation with sponsor in patent filing should be specified

Selecting a CO

Contracts/Agreements

- A quality agreement should be included (not standard)
- A Master Services Agreement (MSA) is often useful if more than one project is anticipated
- Where reasonable, define milestones and tie some payments to these
- Deliverables should be explicitly spelled out in the contract (final reports, etc.)

Managing a CO

A recent survey* indicated that:

- 50% of outsourced studies go over budget
- nearly 50% said they needed to improve their CO management skills significantly
- less than 30% had standard CO management tools and processes in place
- 55% established “preferred vendor” relationships with select COs. Although this aided in the contracting process, no discernable difference in performance (as defined by achieving results within timeline and budget) was realized between studies conducted by preferred vendors and others.

* Cambell Alliance, Pharmaceutical Executive, June 2004 (www.pharmexec.com)

Managing a CO

- The sponsor's employee who is managing the CO needs to have a certain amount of expertise in the area being managed
- Consultants can be utilized where necessary to augment the sponsor's skill set
- The sponsor must be the gatekeeper, making sure that costs and timelines are being controlled (in spite of contract)
- Close and regular communication with the CO is essential
- Ideally, weekly meeting should be held in person or by telecon

Managing a CO

- Reports from CO should be standardized as much as is reasonable
- Sponsor must make sure that reports are delivered in a timely fashion
- Sponsor often must be the source of innovation or problem-solving ideas
- Sponsor should never assume that the CO, being the expert in a certain area, has any common sense
- Sponsor representative must communicate with sponsor's development team with regards to CO activities

Managing a CO

- Sponsor must act as QA overseeing the CO (sponsor is ultimately responsible party to FDA)
- Sponsor should initiate and conduct frequent audits (bring regulatory consultant if necessary)
- Sponsor's representative must coordinate with other internal disciplines at all times (eg; communicate with clinical regarding drug supply needs)
- Sponsor's representative should attempt to identify back-up COs to avoid delays in case of unexpected problems
- Sponsor's representative should never assume that anything will proceed as planned or promised

Real World Examples

The following stories are all true. The names have been changed to protect the guilty. In all cases, I have been personally involved in the incident described and provide first-hand accounts for your education and, in some cases, your amusement. For obvious reasons, I will not disclose the identities of the COs involved in the negative depictions.

Real World Examples

- Wing-and-a-Prayer (WaaP) Pharmaceuticals, Inc. is Founded. The company in-licenses a compound from academia shown preclinically to be effective in eradicating the “urge to shop” (trade name: ‘*nospend*’)
- Dosage form: powder which is dissolved in white wine for administration

Real World Examples

Case Study #1: Who's Watching the Meter?

- ❖ Analytical All-Stars (AAS) was hired to develop analytical method for ID and quantitation of a degradant of *nospend*
- ❖ AAS scientist project leader was PhD analytical chemist
- ❖ WaaP chemist was also PhD chemist
- ❖ WaaP chemist and AAS chemist designed elaborate experiments to solve the problem
- ❖ Original contract was for \$30K
- ❖ The project was not completed yet the charges added up to \$150K
- ❖ Bill not paid and AAS relationship with WaaP ended on a very bad note

Real World Examples

Case Study #2: Let's Build a Lab in Our Garage

- ❖ We Make-Em, Inc. (WME) was evaluated as a potential API manufacturer for *nospend*
- ❖ WME was recommended to WaaP by *nospend* inventor
- ❖ WME president assured WaaP that he has made kilo quantities of *nospend* before and was ready for FDA inspection of his cGMP manufacturing facility
- ❖ Site visit by WaaP reps found a warehouse with roll-up (garage) door and a printout from the FDA website on cGMP regulations
- ❖ After a brief visit, WaaP reps took WME president to lunch and suggested he re-think his business plan

Real World Examples

Case Study #3: We Can Tell You, But Then We'll Have to Kill You

- ❖ Big Chemical Company (BCC) was evaluated as a supplier of *nospend* API...they had supplied academic inventor with cGMP material for his clinical trials
- ❖ BCC was reluctant to share any information regarding manufacturing with WaaP representatives
- ❖ BCC sales reps were aggressive in attempting to engage WaaP (very irritating)

Real World Examples

Case Study #3: We Can Tell You, But Then We'll Have to Kill You

- ❖ WaaP representatives attempted to audit BCC but could not obtain much information or inspect many documents even with a CDA in place (how to confirm compliance?)
- ❖ WaaP representatives were told to “not worry”
- ❖ WaaP declined to engage BCC

Real World Examples

Case Study #4: Size Doesn't Matter

- ❖ Mom and Pop Pharmaceuticals, Inc (MAP) was evaluated as a supplier of *nospend* API
- ❖ MAP had been around for many years but was still rather small (~50 employees)
- ❖ MAP was located in the same state as WaaP
- ❖ MAP was producing a commercial product
- ❖ MAP was not put off by the need to use a highly toxic gas in the synthesis of *nospend*
- ❖ MAP was very forthcoming during audit by WaaP
- ❖ WaaP has worked with MAP since and has been very pleased with the results

Real World Examples

Case Study #5: Know When to Walk Away, Know When to RUN

- ❖ Wanna-Be Pharma, Inc. (WBP) was engaged to develop the DP for *nospend*
- ❖ WBP was also engaged to develop the DP for a second WaaP clinical compound...the two projects were managed by different WaaP representative
- ❖ WBP was located in the same city as WaaP and passed all DD with no concerns
- ❖ WBP had good reviews from WaaP consultants

Real World Examples

Case Study #5: Know When to Walk Away, Know When to RUN

- ❖ Within the first month of working with WBP, the *nospend* WaaP representative noticed a lack of adherence to deadlines, a lack of follow-through on the part of WBP, and too much of an effort to be “big” pharma (lots of meetings with arrogant, pontificating PhD’s but no follow-up action)
- ❖ After 2 months, the WaaP representative for *nospend* terminated the relationship with WBP but the other project remained

Real World Examples

Case Study #5: Know When to Walk Away, Know When to RUN

- ❖ Ultimately, the second project was removed from WBP but the poor performance of WBP haunted the project as well as the CO that took over the work for years to come
- ❖ WBP followed the mantra to “fail fast”
- ❖ WaaP *nospend* representative was able to recognize this early due to close monitoring of WBP

Real World Examples

Case Study #6: A Start-Up Without a Cause

- ❖ Following the WBP fiasco, We're a Phront Pharma (WP²) was hired to develop the DP for *nospend*
- ❖ WP² was very new and small CO, located in the same city as WaaP
- ❖ WP² principal scientists were impressive
- ❖ WP² management was questionable
- ❖ WaaP decided that the scientific ability would trump any managerial deficiencies

Real World Examples

Case Study #6: A Start-Up Without a Cause

- ❖ WP² was so new that it was not possible to audit their quality systems or to obtain references
- ❖ WP² developed a strange formulation and DP with a complex manufacturing process
- ❖ WP² manufactured two lots of *nospend* DP for WaaP clinical trials but soon after the company imploded due to poor management
- ❖ WP² was very short on funds and WaaP learned that employees were not getting paid

Real World Examples

Case Study #6: A Start-Up Without a Cause

- ❖ WaaP needed to transfer manufacturing to a new CO as well as stability samples, etc.
- ❖ WaaP found it difficult to identify a CO willing to take on the convoluted manufacturing process
- ❖ Ongoing clinical trials required that *nospend* supplies be available
- ❖ Most WP² employees relocated making it difficult to obtain assistance

Real World Examples

Case Study #7: Why is Everyone Smiling?

- ❖ Drugs-R-Us (DRU) was selected by WaaP as the CO to take over *nospend* DP manufacturing
- ❖ DRU was new, small CO located in the same city as WaaP
- ❖ DRU had excellent management and a young but seemingly talented and enthusiastic (naïve?) scientific team
- ❖ DRU successfully transferred the complex WAP² manufacturing process and successfully produced several lots of *nospend* DP

Real World Examples

Case Study #7: Why is Everyone Smiling?

- ❖ DRU worked with WaaP to develop a new, straightforward manufacturing process
- ❖ DRU had a very low turnover rate (0% for 2-3 years)
- ❖ WaaP met weekly with DRU team and found them to be responsive and timely
- ❖ DRU management and good science provide a winning combination for a CO
- ❖ DRU's challenge will be to manage growth as they are sought out by others for CO services