

THE REDEVELOPMENT AGENCY OF THE CITY OF SAN JOSE

MEMORANDUM

TO: REDEVELOPMENT AGENCY BOARD	FROM: HARRY S. MAVROGENES EXECUTIVE DIRECTOR
SUBJECT: SEE BELOW	DATE: JULY 10, 2008

INFORMATION

SUBJECT: BIO-MANUFACTURING MARKET AND FACILITY STUDY

Attached is a summary report of the bio-manufacturing market and facility study conducted by PharmaBioSource California, consultants to the Redevelopment Agency.

In January 2008, the Redevelopment Agency Board approved an agreement with PharmaBioSource California to assess the market for a contract biological drug manufacturing plant in San Jose and to recommend the scope and budget for manufacturing facilities that could meet this market demand. PharmaBioSource California was selected as the consultant for this project as the result of a competitive process. The Agency issued a Request for Proposals (RFP), assembled a panel of staff and life sciences experts to evaluate responses to the RFP, and interviewed companies that met the criteria of the RFP and submitted competitive cost proposals. There were five respondents, of which three were interviewed. PharmaBioSource California was unanimously selected by the panel to undertake the study.

Subsequently, PharmaBioSource California interviewed 25 life sciences companies, including 10 companies at the San Jose BioCenter, and prepared profiles of 16 contract manufacturers in addition to other research they conducted for this study. The consultant found that there is a strong demand for a contract biological manufacturing facility in the Bay Area. Furthermore, there are only a few contract manufacturers currently located in the Bay Area, which means that most local biotechnology companies are required to work with manufacturers outside of the region, adding significant time and expense to their product development.

Based on their interviews, PharmaBioSource California believes that demand is strongest for a contract manufacturing facility that would produce drugs for pre-clinical testing, as well as early-stage (Phase I and Phase II) clinical trials; clinical trials are required and regulated by the U.S. Food & Drug Administration as part of the approval process for new drug products. A manufacturing facility focused on early-stage product development would be very helpful to young companies like those at the San Jose BioCenter. It would also be useful to more established companies that are testing new products in their development pipeline.

PharmaBioSource California recommends development of a contract manufacturing facility that meets these needs with approximately 25,000 square feet of space. It is estimated that such a facility would cost up to \$23 million for new construction, or up to \$16 million for the retrofit of an existing building. In addition, the equipment required to outfit the building would cost approximately \$8 million. Because of the costs involved, if the Redevelopment Agency were to pursue an effort to attract a contract manufacturer to San Jose, the Agency would seek funding from the federal and state governments in order to support the development of the facility, and assemble a package of incentives that could include an Agency contribution towards construction and equipment costs. The contract manufacturer would also be expected to contribute to the construction and equipment costs.

Agency staff is currently meeting with contract manufacturing firms to describe the project concept, gauge the companies' interest in establishing a facility in San Jose, and better understand the companies' location requirements. Staff met with six contract manufacturers at the 2008 Biotechnology Industry Organization (BIO) conference in June, and received positive responses and requests for more information from each of these companies. Staff will continue discussions with these and other contract manufacturers.

Please note that the attached report is a summary of several longer, technical reports prepared by PharmaBioSource California for the Agency, which total several hundred pages in length. If you are interested in receiving the full report, please contact Julie Amato, Senior Development Officer, at 795-1845.



HARRY S. MAVROGENES
Executive Director

Encl.

BIOLOGICAL MANUFACTURING FACILITY FEASIBILITY STUDY

PREPARED FOR THE
SAN JOSE REDEVELOPMENT AGENCY
June 2008

Presented by PharmaBioSource California, Inc.

William B. Wiederseim
President & CEO



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Disclaimer

Any opinions, observations or recommendations regarding the opportunity to create a biological manufacturing facility are subject to risks and uncertainties. The San Jose Redevelopment Agency (SJRA) should use its own judgment and interpretation of the information contained in this report.

PharmaBioSource California, Inc. has provided its best efforts to the project consistent with the stated goals of the SJRA; however, PharmaBioSource California, Inc. and its investors, employees, agents and subcontractors cannot guarantee any particular result due to SJRA's ultimate control of the decisions and its staff.

A. Executive Summary

The City of San Jose is committed to making San Jose a competitive location for the Life Sciences Industry. For this reason, the San Jose Redevelopment Agency (SJRA) is seeking to understand how specific investments, such as a proposed Edenvale Technology Park biological manufacturing facility, can help the City achieve this goal. The SJRA asked PharmaBioSource to conduct an analysis of the biological contract manufacturing market, prepare preliminary scopes and budgets for biological contract manufacturing facilities that meet local demand, and recommend models for funding and operating these facilities.

Market Supply and Demand

From our analysis, there are two important drivers supporting the construction of a biological manufacturing facility in Edenvale: 1) the market demand in the Western United States (“Western Region”) for a local biological manufacturing facility focused on clinical manufacturing is high; and 2) there is little competition in the Western Region from current biological Contract Manufacturing Organizations (CMO’s).

All indications are that the current and future need for biological contract manufacturing organizations, particularly in the Western Region, will grow. CMO’s are a relatively new entrant in the biological manufacturing market. Historically, biotechnology companies have been responsible for manufacturing their own products. Today, CMO’s represent a small but rapidly growing portion of the global biological market. In 2008, the CMO market is expected to account for about 5% (\$3.3 billion) of the total biological manufacturing market, and grow at a rate of about 10% to 15% annually. This growth, however, has come with a price: Benchmarking studies show that there is a current worldwide capacity shortage of biological contract manufacturing. In a 2006 survey done by BioProcess Associates, 35% of surveyed CMO’s are experiencing capacity constraints today, and 50% of CMO’s expect capacity to be constrained in 2011.

There are over 600 recombinant biological products in the biotech pipeline, and well over 100 of these are expected to be on the market by 2010. Even though the Western Region has the highest concentration of biotechnology firms in the US (California is home to over 400 firms, representing approximately 20% of the total US market), there are only 16 active biological CMO players in the Western Region; only three of these are in the Bay Area. The lack of CMO production capacity today in the Western Region coupled with the lack of plans for future capacity in the region indicate that this local capacity shortage will continue. As a result, many western companies are forced to use biological CMO’s outside the Western Region, mainly in the Eastern US and Europe.

Interviews with Biotech Companies

PharmaBioSource interviewed 25 Western Regional biotechnology companies for this analysis; ten of the companies interviewed were San Jose BioCenter firms. Our findings indicate that outsourcing is a strong preference for local biotechnology companies. Over 80% of interviewed BioCenter and Western Regional companies indicated a preference for outsourcing their manufacturing needs. Despite this drive to outsource, Western Regional companies are generally dissatisfied with the availability of qualified CMO’s that they can afford. They are also frustrated at not having the choice of a local CMO that can provide the required range of services. Furthermore, as smaller firms, they do not receive the attention of most CMO’s. They are eager to have access to a local CMO that brings a strong track record and manufacturing experience to the Bay Area. Although indifferent to the exact location of a CMO biological manufacturing facility, Western Regional companies believe that a Bay Area alternative to the current CMO offerings would be favorable. San Jose is viewed as an acceptable location for a biological CMO facility.

When asked what an SJRA-supported biological manufacturing facility should offer to the market, interviewed companies stated that the facility should not be a commercial enterprise, but should be positioned to support late-stage pre-clinical through Phase II clinical

manufacturing up to 500 liters. Also, they indicated that the facility should offer both mammalian and microbial expression systems so as to serve the greatest possible client base. Respondents stressed the need for the operation to provide services outside of pure manufacturing to be a viable and desirable manufacturing alternative; these would include process development, scale up, analytical development and support services. There was also a keen desire to have access to “hands on” equipment to conduct process development work. Other important factors include finding the right industry CMO and university partners to encourage the creation of a stable, reliable CMO.

Facility Options

Based on our research, PharmaBioSource identified several facility options that could help the City of San Jose and the SJRA achieve its goal of supporting a local biotechnology cluster while meeting the expressed market needs of Western Regional biotechnology companies as identified in the interview analysis. Leading options were selected for their ability to meet industry needs while providing the SJRA with a range of investment options based on available capital. These options include a Complex and Simple Cell Regulated Facility, a Complex and Simple Cell Non-Regulated Facility, and a Complex and Simple Cell Non-Regulated Micro Facility within the BioCenter.

While there are several options available to the SJRA to address the market demand at a variety of cost points, our research indicates that the construction of the Complex and Simple Cell Regulated Facility would have the greatest impact. This facility would address the largest segment of the Western Regional biotechnology market by offering the ability to produce drug product for human clinical trials in a regulated, cGMP environment using both mammalian cell culture and microbial fermentation manufacturing systems, the two dominant production systems.

Facility Costs and Funding

Each leading facility option has its own unique technology requirements, market focus, size and equipment requirements along with different construction and operating costs. Given this complexity, the cost of constructing a biological manufacturing facility can exceed \$1,200 per square foot, depending on facility size and production technologies.

- Size requirements range from 1,100 square feet to 25,000 square feet.
- Construction costs range from less than \$1 million to \$23 million.
- Equipment costs range from \$2 million to \$8 million.
- Operating costs range from less than \$500,000 to \$8 million.

Federal, state, and local funding should be considered necessary components of an incentive package for a San Jose-supported biological manufacturing facility. Incentives can take the form of building permit fee waivers, equipment investment credits, low cost financing of equipment, pre- and post-employment credits, property tax moratoriums and/or rebates, sales and use tax exemptions, transportation grants, employee training grants and utility rate reductions. Offering a strong incentive package to a CMO partner is important because the higher cost of doing business in California and the lower profit margins of a CMO, as compared to biotechnology companies, make it challenging for a CMO to enter the Bay Area market.

A Life Sciences Cluster in San Jose

Although local business incentives and closer ties to academic institutions would enhance San Jose’s perceived position as a location for biological manufacturing, San Jose has many foundational elements that could make this project successful. A biomanufacturing facility alone, however, will not create a large number of jobs or necessarily encourage companies to headquarter their operations in San Jose. The nature of biological contract manufacturing organizations is such that clinical biological manufacturing facilities of the size and focus

recommended in this study usually have fewer than 50 employees on site. Furthermore, biotechnology companies are used to working with remote CMO partners, sometimes over very great distances.

A biological manufacturing facility could, however, be an important component of San Jose's Life Sciences cluster. A Life Sciences cluster can have a much greater impact on local jobs and the business tax base. Research has shown that Life Sciences clusters have a positive impact on employment and a high ability to attract firms to headquarter in a given location. This is due to the fact that a Life Sciences cluster provides a complete offering to Life Sciences companies including universities, hospital research centers, R&D laboratories, manufacturing, packaging, and storage and distribution facilities.

San Jose is not the only city interested in developing a Life Sciences cluster. As more and more Life Sciences firms have products ready for the clinic and the market, the competition between states and cities for their corporate offices, research and development laboratories, manufacturing facilities and jobs will become more intense. A unique local Life Sciences cluster, such as an applied Life Sciences cluster, can be an effective tool in encouraging firms to consider San Jose. An applied cluster can support the transition of Life Sciences companies from the lab into the clinic, effectively turning "innovation into industry." Creating a biologics CMO could be an important step in developing an applied Life Sciences cluster.

B. Project Concept

Request for Proposal Overview

The City of San Jose is committed to making San Jose a competitive location for the Life Sciences Industry. For this reason, the San Jose Redevelopment Agency (SJRA) is seeking to understand how specific investments, such as a proposed Edenvale Technology Park biological manufacturing facility, can help the City achieve this goal. The Agency asked PharmaBioSource to conduct an analysis of the biological contract manufacturing market, prepare preliminary scopes and budgets for biological contract manufacturing facilities that meet local demand, and recommend models for funding and operating these facilities.

The SJRA asked PharmaBioSource to accomplish a number of tasks, including:

- Describe and profile the SJRA's biological manufacturing concept;
- Evaluate the current competitive landscape of international, national and US Western Regional manufacturing suppliers;
- Perform a comparative analysis of other public / private biomanufacturing facilities;
- Assess the biological manufacturing demand and needs of local and Western Regional biopharmaceutical companies, including those at the BioCenter;
- Describe San Jose's comparative advantage in the Life Science and Biotechnology Industry;
- Identify leading biological manufacturing facility options available to the SJRA and develop conceptual scopes and cost estimates for these leading options; and
- Recommend funding and operating models for each of the leading facility options.

Current Situation and Project Drivers

The City of San Jose is committed to becoming a competitive location for the Life Sciences market. As such, the SJRA is seeking to understand how specific investments, such as a proposed Edenvale Technology Park biological manufacturing facility, can help the City achieve this goal.

The 2001 economic recession encouraged the City of San Jose to diversify its industry base and enhance its presence in industries outside of high technology. Over the past five years, The City of San Jose and the San Jose Redevelopment Agency have implemented a series of strategic initiatives to create a Life Sciences cluster in San Jose. An important first step is the SJRA's investment in the development of the San Jose BioCenter, a laboratory facility and business incubator for small Life Sciences companies located in the Edenvale Technology Park. The City of San Jose wishes to expand its efforts and aggressively compete for a greater share of the Western Regional Life Sciences market. As such, the City and the Redevelopment Agency are interested in investing in new Life Sciences-oriented assets and programs to support this market.

In this project, the feasibility of a biological manufacturing facility in Edenvale was evaluated. The City believes local and Western Regional companies could benefit through access to qualified contract manufacturing facilities to make product for their commercialization needs. The Redevelopment Agency believes that the location of a manufacturing facility in Edenvale to provide these products could help the companies currently located at the BioCenter grow and potentially attract more Life Sciences companies to Edenvale.

Life Sciences Market Segmentation and Drug Development Process

There are five types of Life Sciences companies and each is unique. Biological drugs represent the fastest growing segment of the market and the focus of this project. The biological drug market represents the greatest area of opportunity for an SJRA-supported manufacturing facility.

PharmaBioSource and the Life Sciences Industry in general define the Life Sciences market as broadly segmented into five types of companies.

- Pharmaceutical drug (small molecule) firms;
- Biological drug (large molecule) firms;
- Device / diagnostic firms;
- Nutraceutical firms; and
- Service provider firms.

The research, development, manufacturing and regulatory requirements are unique to each of the five segments above. It is important to note that the San Jose BioCenter's tenants represent all five of these market segments.

Pharmaceutical and biological drug segments represent the largest portion of the Life Sciences Industry. This combined industry generated total worldwide revenues of \$534.8 billion in 2005. Biological drugs were over \$50 billion of that value, and the biological market is the fastest growing segment at 10-15% per year. However, the complexity, cost and skills required for manufacturing biological drug products are much greater than for any other Life Sciences segments. The US is the center of activities and innovation for biological drug manufacturing due to the technological complexity of the manufacturing process and the skilled personnel required to operate them, whereas the manufacturing of pharmaceuticals has largely gone overseas or has strong competition from other countries. This, coupled with the fact that the Bay Area has the greatest concentration of biological drug development companies in the world, supports the fact that the biological drug segment represents the greatest opportunity for an SJRA-supported manufacturing facility.

Taking a biological drug from a lab bench to the market is a time and regulatory-intensive process, requiring up to 15 years and over \$800 million (on average) per drug. There are eight development steps in bringing a biological product to market, which can be broken down into two basic phases. The first phase includes the discovery, research and preliminary testing (lab and animal testing) steps, while the second includes clinical testing (human studies) and commercialization (regulatory review and approval, post-marketing testing, and commercial / manufacturing operations) steps. There are several different types of research and manufacturing facilities that service these two phases, and they are unique to the phase they serve in dimensions such as size, focus, regulatory approval and cost to build and operate.

C. Biological Contract Manufacturing Market Assessment

Overview of Biological Manufacturing

The manufacturing of biological drugs is a multi-step, complex and expensive process. The cost and complexity involved often limits the ability for small, early-stage biotechnology companies to invest in and run their own manufacturing facility. As a result, a growing number of biological contract manufacturing organizations are entering into the market.

The manufacturing of biological products is a multi-step process that can be reduced to three major steps:

- Upstream process: Refers to the process of increasing the population of a desired cell in increasingly larger containers called bioreactors. These cells will in turn produce the protein, which is usually the desired end-state product.
- Downstream process: Once sufficient protein is produced in the upstream process, all ingredients except for the desired protein contained in the bioreactor need to be removed. This is done through a number of chemical and mechanical purification and “filtering” processes until just the desired protein is left in the medium.
- Formulation / fill / finish: Stabilizes and packages the protein (such as in an IV bag or syringe) to allow for storage, transportation and administration to the patient.

The manufacturing of biological products is much more complex and expensive than pharmaceutical manufacturing because it is an organic process. Pharmaceutical manufacturing is a highly refined chemical mixing and packaging process, while biological manufacturing involves using living organisms (cells) to produce the desired material. There are many variables in biological manufacturing, and all variables will affect cell growth. Variables include the type of cell (bacterial or mammalian), culture media, size of bioreactor, and gas mixtures. Given this complexity, the cost of constructing a biological manufacturing facility can exceed \$1,200 per square foot, depending on facility size and production technologies. Construction time is normally two to three years or more.

There are three main aspects that differentiate biological manufacturing facilities: The type of facility; its designation as following current good manufacturing practices (cGMP); and the types and scale of expression systems used in the upstream process of the facility.

- A biological manufacturing facility can be positioned to provide drug product for select or many stages of drug development: Pre-clinical; clinical (Phase I / II / III); or commercially marketed products.
- A facility can be constructed according to cGMP standards or designated as non-cGMP. cGMP standards are required for the production of any biological drug that will be intended for human use, such as in clinical trials or commercial sale. cGMP standards are also required of any facility to be certified by the US Food and Drug Administration (FDA). Non-cGMP standards are used for production of pre-clinical biological drug materials that are not used in humans.
- A facility can utilize a variety of cell-based upstream expression systems, which are the actual cells selected to create the biological protein product. Mammalian cell culture (e.g., Chinese Hamster Ovary (CHO) cells) and microbial fermentation systems (yeast, bacteria such as E. Coli) are the most commonly used expression systems in the industry today. The scale of the upstream production equipment is also important. Capacity of this equipment can range from very small (glass containers less than one Liter) to very large (stainless steel bioreactor tanks as large as 10,000 Liters). Most clinical manufacturing facilities have capacities ranging from 50 Liters to 3,000 Liters.

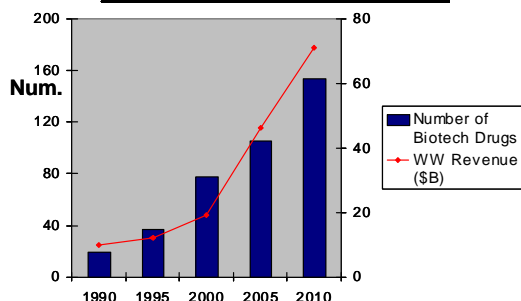
Biotechnology Market Dynamics

The biotechnology pipeline is both rich and diverse, the envy of ‘Big Pharma.’ Recombinant protein-based therapies represent a growing subset of the biological drug market and an important focus for an SJRA-supported biological manufacturing facility.

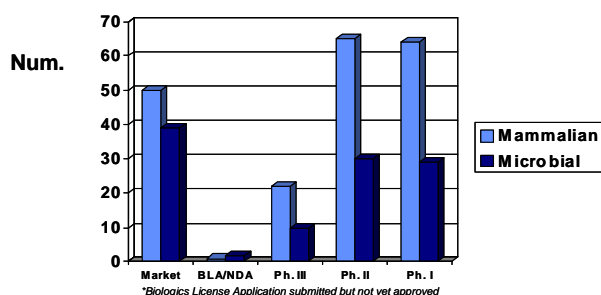
There are a number of types of biological products available and in development today, each at a different stage in its market life cycle. Each of these product types requires unique types of upstream and downstream technologies and, as such, unique manufacturing facilities. Of all types of biological products, recombinant proteins and vaccines represent a growing market with the largest number of products both commercially available and in development today. Our study revealed that the protein biological market is the most attractive market for an SJRA-supported biological manufacturing facility to target:

- The manufacturing technologies for these products are well known and in the process of ongoing optimization.
- There are nearly 600 recombinant biological products in the pipeline and well over 100 are expected to be on the market by 2010.
- Products requiring a mammalian cell expression system dominate the pipeline, but there are a growing number of fermentation (microbial) expression systems in early stage development (Phase I, II).
- Much of the protein biological product pipeline belongs to Western Region biotech companies.

Estimated Number of Biotechnology Drugs in the Market and Revenues



Number of Biotechnology Pipeline Drugs



Overview of the Biological Contract Manufacturing Market

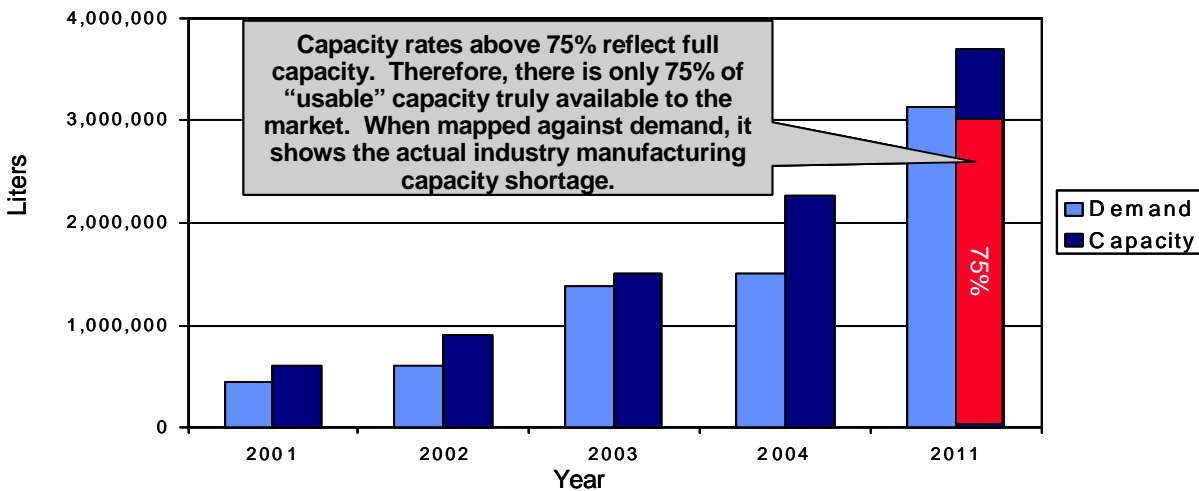
All indications are that the current and future need for biological contract manufacturing organizations, particularly in the Western Region, will grow. Benchmarking studies show that there is a worldwide capacity shortage for biological contract manufacturing. Although the Western US, and specifically California, leads the world in biotechnology companies, it is under-served in CMO manufacturing. Today’s biological contract manufacturing market is highly concentrated among a few, mostly Eastern US and European Union-based firms. Not only is there a lack of production capacity today in the Western Region, there are few planned expansions by Western Region CMO’s, indicating that this local capacity shortage will continue.

There are two types of biological manufacturers: Product Development Companies (PDC’s) and Contract Manufacturing Organizations (CMO’s). PDC’s own the intellectual property of a drug and may also manufacture that drug as well, such as Amgen or Genentech. CMO’s do not own any intellectual property rights of a drug product, but manufacture products for PDC’s. Today, CMO’s represent a small but growing portion of the global biological market. In 2007, the CMO market is expected to account for about 5% (\$3.3 billion) of the total biological market. The CMO market is expected to grow at a rate of about 10% to 15% annually.

Recent surveys indicate that the trend for biotechnology companies to outsource at least some production is growing. This reflects the growing trend toward greater outsourcing of biological drug manufacturing due to the complexities and cost required to manufacture these drug products in-house. These growth trends support the demand for a new Western Region CMO facility such as San Jose is considering.

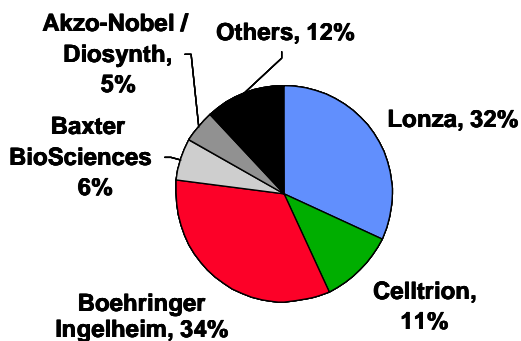
In 2006, global capacity utilization was reported at near full capacity for CMO's (86%); CMO capacity today may not be able to meet predicted market demand for biological drug production, which is expected to increase as the many biological pipeline drugs move through the clinic and into the market. In a 2006 survey done by BioProcess Associates, 35% of surveyed CMO's were experiencing capacity constraints at that time, and 50% of CMO's expected capacity to be constrained in 2011.

Worldwide Demand vs. Capacity, 2001-2011 (Clinical and Commercial Production)

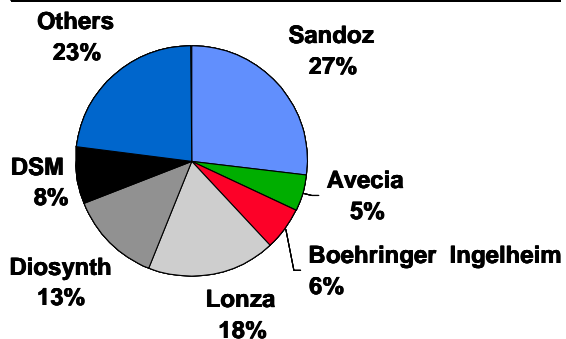


There are over 150 biological CMO's in the world; however, the CMO market is highly concentrated. As of 2006, the top five players (Lonza, Boehringer Ingelheim, Sandoz, Celltrion and Diosynth) accounted for over 70% of the market. The majority of these large CMO's have facilities in the Eastern US and Europe. Only one large CMO, Baxter Biosciences, has a manufacturing facility in the Western US.

2006 Contract Manufacturers Mammalian Capacity Share (~20% of total)



2006 Contract Manufacturers Microbial Fermentation Capacity Share (~15% of total)



Even though the Western Region has the highest concentration of biotechnology firms in the US (California is home to over 400 firms, representing approximately 20% of the total US market), there are only 16 active biological CMO players in the Western Region and only three in the Bay Area. As a result, many western companies are forced to use biological CMO's outside the Western Region.

The combination of global CMO capacity shortages today and those expected in the future, along with the limited number of manufacturing options in the Western Region in general and the Bay Area specifically bode well for a local biological CMO facility.

D. Western Region Biological Contract Manufacturing Demand Analysis

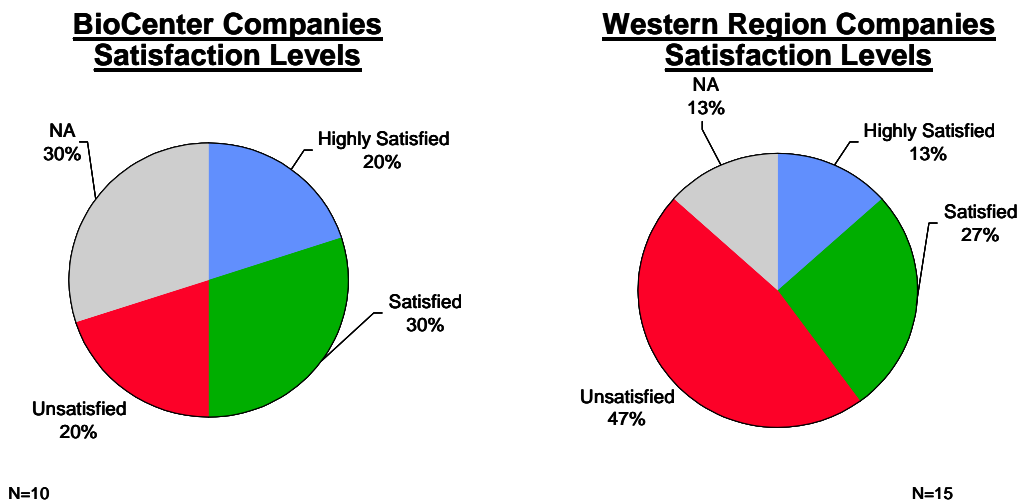
Current Manufacturing Situation and Preferences

PharmaBioSource interviewed 25 Western Regional companies for this analysis; 10 of those interviews were with San Jose BioCenter firms. Our interview findings indicate that outsourcing is a strong preference for local biotechnology companies. Despite this drive to outsource, Western Region companies are generally dissatisfied with the availability of affordable, qualified CMO's. They are also frustrated at not having the choice of a local CMO that can provide the required range of services. They are eager to have access to a local CMO that brings a strong track record and manufacturing experience to the Bay Area.

For this analysis, PharmaBioSource interviewed 10 BioCenter companies. Four of these companies were biological companies. The remaining six interviewed companies included a diverse group representing the nutraceutical, device, pharmaceutical and services segments of the Life Science market.

PharmaBioSource also interviewed 15 Western Region Life Sciences companies. These were selected for their range of disease focus, geographical diversity, and research pipeline of pre-clinical and clinical drugs. The majority of companies interviewed for this project were biological drug companies (n=13) with a select few pharmaceutical firms (n=2); this reflects the preponderance of biological drug firms on the West Coast today.

Nearly 50% of all interviewed BioCenter companies and over 70% of all interviewed Western Region companies currently outsource some aspects of their manufacturing needs, indicating a preference for outsourcing to support their drug development. BioCenter companies are generally satisfied (only 20% were dissatisfied) with their manufacturing options or CMO partners today, but are open to alternatives in the Bay Area. Those few companies not satisfied are concerned about finding a local, qualified, cost-effective partner now and in the future.



Companies outside of the BioCenter are ready for an experienced, local CMO alternative (47% were not satisfied today). Western Region companies expressed significant dissatisfaction with their biological manufacturing options. Many of these companies are frustrated with the availability of qualified affordable CMO's. They are also frustrated at not having a local CMO that can provide the range of services they require, and lament the lack of CMO's that are willing to work with small firms that are characteristic of Western Region biotechnology companies.

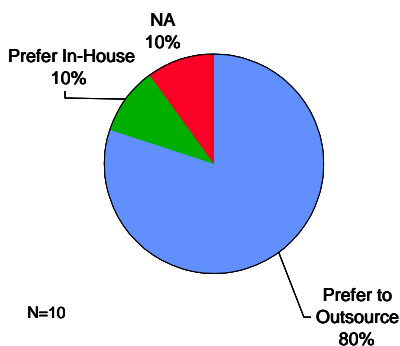
Many BioCenter firms are in a very early stage of drug development and generally have less experience with CMO's. This may be the driver for the higher satisfaction level of these firms. Only three companies at the BioCenter are currently in the market for clinical manufacturing capacity.

However, more than half (53%) of the Western Regional interviewed companies expressed that they were currently in the market for clinical manufacturing capacity. Some Western Region firms, even those with a secured supply, would consider a local provider for additional clinical product manufacturing needs in the future.

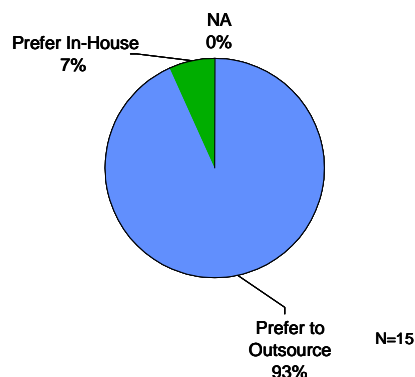
"There are a lot of small companies out West just like us that would be looking for other options for a Western Regional CMO, especially one that could get things done just as fast, for a little less money."

Over 80% of interviewed BioCenter and Western Region companies indicated a preference for continuing to outsource their manufacturing needs.

BioCenter Companies Manufacturing Outsourcing Preference



Western Regional Companies Manufacturing Outsourcing Preference



When asked about how they would select a CMO, Western Region firms indicated that track record was the most important selection criteria for a CMO sourcing partner. Staff expertise was listed as the second most important selection criteria. Cost ranked third.

"Experience is important; we have many unique assays and would need a good partner who knows this area. There is no good such option here in the Bay Area. This is odd because there is such a large customer base here. I don't know why."

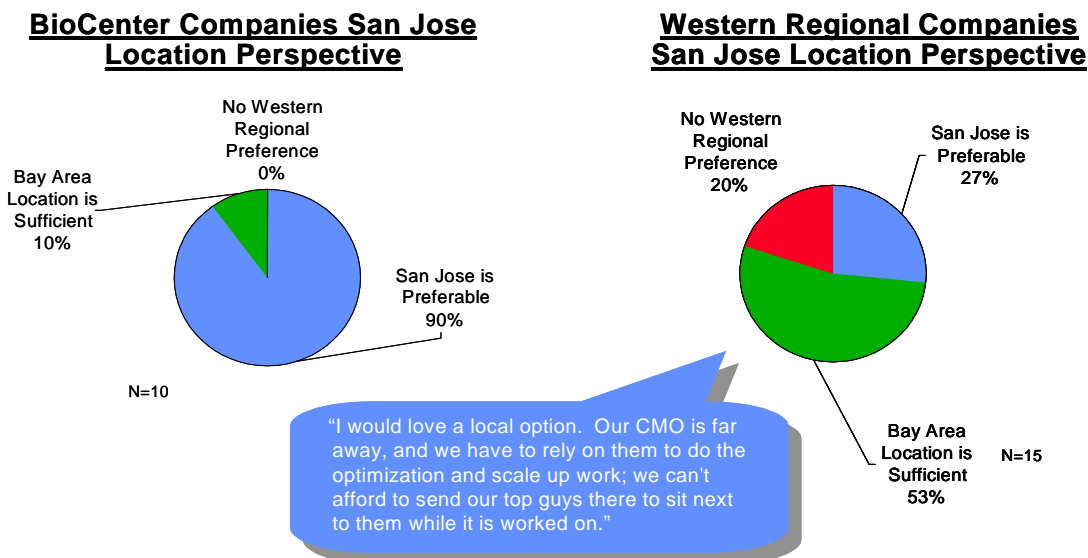
San Jose Location Perceptions for a Biological Manufacturing Facility

Although indifferent to the exact location of a CMO manufacturing facility, Western Regional companies believe a Bay Area alternative to the current CMO offerings would be favorable. San Jose is viewed as an acceptable location for a biological CMO facility.

The vast majority of interviewed companies expressed an overwhelming interest in a local CMO option. BioCenter companies welcomed the idea of a facility that could be close to their current operations in Edenvale, with 90% expressing a San Jose location preference. Western Region companies were very open to a local facility, but only 27% felt the most preferable location would be San Jose. This is likely due to the fact that few company respondents are headquartered in the South Bay.

However, over half (53%) of all respondents indicated that any location in the Bay Area would be positive. In reviewing the demographics of the responses, it is clear that Bay Area firms consider San Jose an acceptable location. A select few consider it preferable, as it is close to

employees who commute from the South Bay. Firms from outside the Bay Area would welcome a California-based option and are open to a Bay Area CMO facility. These firms have no preference as to where in the Bay Area to locate the facility.



"San Jose is fine for us. Even though we're in San Diego, it's still on Pacific Standard Time. A two-hour plane flight is much better than a 6-10 hour one!"

"Yes, there is great talent here, and we need to tap into that talent. I located my company here for the intellectual talent, so why do I have to go outside the Bay Area to find someone to make my product?"

Technology and Service Needs

When asked about what an SJRA-supported biological manufacturing facility should offer to the market, interviewed biological companies stated that the facility should be positioned to support late-stage pre-clinical through Phase II clinical manufacturing. Also, they indicated that the facility should offer both mammalian and microbial expression systems so as to serve the greatest possible client base. Biological company respondents also stressed the need for the operation to provide services outside of pure manufacturing to be a viable and desirable manufacturing alternative; these would include process development, scale up, analytical development and support services. There was also a keen desire to have access to "hands-on" equipment to conduct process development work.

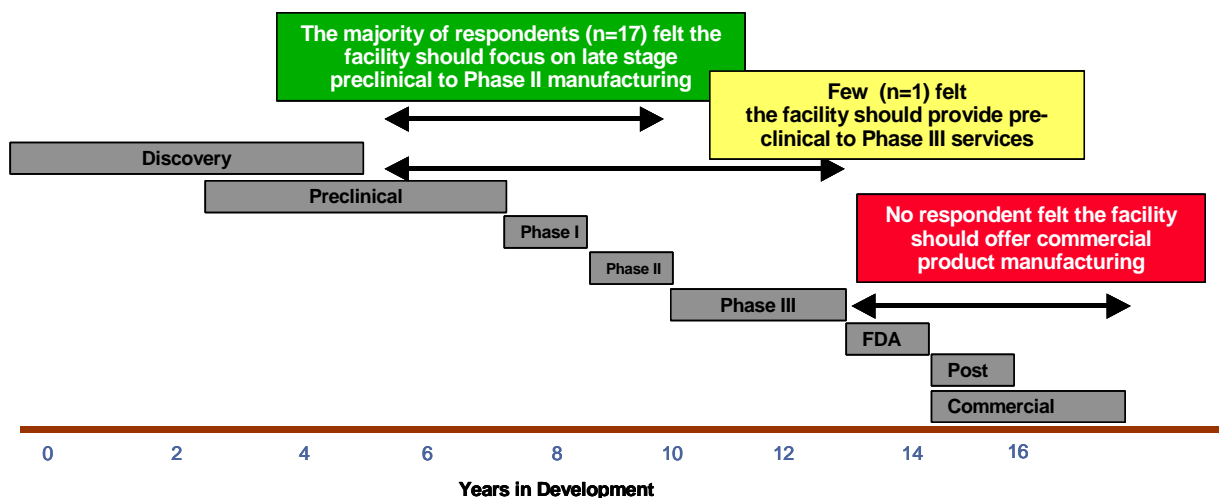
PharmaBioSource also interviewed a select subset of BioCenter and Western Region companies: Those that developed biological drugs. These biotechnology companies were queried on their technology and service requirements for a biological manufacturing facility. These biological companies included four BioCenter and 13 Western Region companies. Discussion points with this group included facility positioning, type and scale, service offerings and operational considerations.

Facility Positioning

The majority of biological company respondents felt that a potential SJRA-supported biological manufacturing facility should be positioned to provide late-stage pre-clinical through Phase II manufacturing. In addition, the majority of respondents felt the facility should be cGMP and focus on late-stage pre-clinical to Phase II manufacturing. Few of the respondents felt the facility should be cGMP and provide a wider range of services (pre-clinical to Phase III services), and no respondent felt the facility should offer commercial product manufacturing.

“This facility should address the needs up to Phase II manufacturing. At that stage, companies are still trying to figure out the manufacturing process, and there are not many available, good options with current CMO’s.”

San Jose Protein-Based Biological Manufacturing Facility Positioning Along The Drug Development Timeline



Facility Type and Scale

Most biological company respondents in our survey believed that a potential SJRA-supported biological manufacturing facility should offer both mammalian and microbial expression systems. These two expression systems represent the bulk (~95%) of the production systems used by biotechnology companies today. Many felt that the dominance of mammalian and microbial expression systems would continue well into the future.

When asked about the scale or size of the facility upstream operations, the most frequently suggested scale was up to 500 Liters for mammalian systems and up to 1,000 Liters for microbial systems.

However, respondents indicate that if costs were to dictate a selection of one expression system, mammalian is the most preferred.

“As a multi-product facility, this has to provide both mammalian and microbial expression systems.”

“I’d specialize in mammalian systems, which is the bulk of the market now and in the future.”

Facility Service Offerings

Interviewed biological companies (n=17) expressed a high degree of interest in working with a local CMO that would provide them with more than just biological drug manufacturing; they want a partner that will work with them in process development and scale up of the manufacturing process. They also want assistance in complying with the rigorous regulatory process necessary to receive FDA approval. Leading service offerings indicated were:

- Process development and scale up: The process by which a product is transitioned from lab-scale research activities in order to deliver a scalable process to the manufacturing environment that can be validated and operated under cGMP controls and that can be commercially viable.

- Analytical development and support: Development of the processes and tests required to analyze or characterize the produced drug material. This includes process, biological, chemical and physical measurements.
- Quality assurance / quality control: The quality systems, processes and tests that are used to control and measure each step of manufacturing to ensure that the product meets all of its specifications and quality attributes, and that all manufacturing was done and documented in compliance with cGMP requirements.
- Development of production records: The development of documentation surrounding the cGMP manufacturing process.

“It’s not just about manufacturing drugs. It’s also about putting in place the processes and systems to support the eventual launch of a drug!”

Facility Operational Considerations

When asked about the most important operational considerations the SJRA should address with this biological manufacturing facility, interviewed biological companies (n=17) were quick to note that the CMO should focus on smaller biotechnology firms. This facility, then, could service start-up biotechnology firms that cannot get the attention of current, established CMO’s.

Several companies noted that the facility should have a diverse client base, including mid-size and small companies from California, the US and other countries in order to maintain a consistent flow of viable clients who could fill the capacity of the facility.

A last suggestion by interviewees was that the facility should comply with national and international regulatory bodies, as the market for clinical biological product continues to be more and more global.

“While there are a lot of small companies struggling to start up clinical manufacturing, most of today’s CMO’s tend to focus only on large companies and ignore the mid-tier or small companies’ needs.”

Key Success Factors

The interview analysis suggests that there is a high demand for an SJRA-supported contract biological manufacturing facility focused on late-stage pre-clinical to Phase II manufacturing needs of biological companies. However, interviewees also suggested several key success factors important for the SJRA to keep in mind as it considers developing a biological contract manufacturing facility. These include finding the right industry CMO and university partners, as well as creating the necessary incentives to encourage investment in the facility and the creation of a stable, reliable CMO.

Respondents suggested three important key success factors for the SJRA to consider in the development of a biological manufacturing facility:

- The right staff and/or partner with the experience to give biological companies confidence that a new SJRA-supported CMO is a reliable manufacturing partner. A known commercial partner would provide instant market credibility and provide clients with a commercial-scale CMO when development required it.
- The SJRA should also address the perceived current biopharmaceutical manufacturing workforce “skill set gap” in the region. This may require partnering with a local or regional university to address this knowledge gap.
- The SJRA should consider incentives to encourage the success of a new biological manufacturing entity.

“I think a partnership with a larger CMO is critical, both for experience and to make sure you have a commercial option as well. Even smaller private CMO’s partner with larger CMO’s today for that. The SJRA would definitely need a strategic partner.”

E. Facility Options and Conceptual Scopes

Biological Manufacturing Facility Options

Using input from the market analysis and interviews, PharmaBioSource identified five facility options that would help the SJRA achieve its goal of supporting a local Life Sciences cluster while meeting the expressed market needs of Western Region biotechnology companies as identified in the interview analysis. Leading options were selected for their ability to meet industry needs while providing the SJRA a range of investment options based on available capital

Facility Option #1 **“Complex Cell Regulated Facility:”** A mammalian cGMP clinical facility that would be positioned to provide pre-clinical through Phase II biological drug manufacturing, this option would be able to serve ~60% of the potential protein biological market.

Facility Option #2 **“Simple Cell Regulated Facility:”** A microbial cGMP clinical facility that would be positioned to provide pre-clinical through Phase II biological drug manufacturing, this option would be able to serve ~30% of the potential protein biological market.

Facility Option #3 **“Complex and Simple Cell Regulated Facility:”** Both a mammalian and microbial cGMP clinical facility positioned to provide pre-clinical through Phase II biological drug manufacturing, this facility would serve the largest portion (~90%) of the protein biological market.

Facility Option #4 **“Complex and Simple Cell Non-Regulated Facility:”** A mammalian and microbial non-cGMP pre-clinical facility serving the needs for pre-clinical manufacturing only, its target client base would be limited to very early-stage biotechnology companies (less than 10% of the protein biological market).

Facility Option #4 [Alternative] **“Complex and Simple Cell Non-Regulated Micro Facility:”** A mammalian and microbial non-cGMP pre-clinical facility located at the BioCenter serving the needs of BioCenter companies only.

After discussions with the SJRA, Options #3, #4 and Option #4 [Alternative] were selected as the leading facility options that warranted further consideration. These options would help the SJRA achieve its Life Sciences Industry goals while providing the SJRA with a range of investment options.

Category	Facility #1 (Mammalian)	Facility #2 (Microbial)	Facility #3 (Combo)	Facility #4 (Pre-clinical)
Market Focus	Addresses 60% of total market	Addresses 30% of total market	Addresses 90% of total market	Addresses only small, start-up biotech companies
cGMP	Yes	Yes	Yes	No
Size	20,000 - 22,000 SF	20,000 - 22,000 SF	22,000 - 25,000 SF	10,000 - 12,000 SF
Construction (Greenfield)	\$20M - \$22M	\$20M - \$22M	\$20M - \$23M	\$7M - \$8M
Construction (Shell)	\$12 - \$15M	\$12 - \$15M	\$13 - \$16M	\$4 - \$5M
Equipment	\$6M	\$5M	\$8M	\$1.7M
Operations	\$7M - \$8M	\$7M - \$8M	\$8M - \$9M	\$2.5M - \$3M
Staff	30 - 35	30 - 35	30 - 40	20 - 25
Revenue	\$8M - \$10M	\$8M - \$10M	\$11M - \$13M	\$3M - \$4M
Partners	Many CMO partner choices	Fewer CMO partner choices	Fewer CMO partner choices	Fewest CMO partner choices

Leading Facility Options Technology and Market Scope

The leading facility options identified are each unique from a scale and positioning perspective. Option #3 would provide regulated clinical manufacturing at a medium-sized scale of 50-500 Liters along with fill / finish capabilities. However, Option #4 and #4 [Alternative] would provide only non-regulated pre-clinical manufacturing at a much smaller scale of up to 50 Liters, with no fill / finish capabilities. These three leading options would provide both mammalian and microbial fermentation capacity, and all would have the necessary supporting laboratory space required to provide process development and scale-up services.

Facility Option #3 “**Complex and Simple Cell Regulated Facility**” Scope:

- Both mammalian and microbial fermentation capacity.
- Bioreactor capacity between 50-500 Liters.
- Flexibility and space for use of disposable technologies.
- cGMP facility to support production of drug product for pre-clinical up to Phase I & II clinical trials.
- Non-cGMP “hands on” development lab with capacity up to 10 Liters.
- Fill / finish suite for production of up to 5,000 vials.
- Stem cell suite.
- Process development lab.
- Analytical development lab.
- QA/QC and release testing labs.
- General support (buffer prep, equipment wash, storage, warehouse).
- Offices for 30-40 staff as well as visitor / client offices and administrative support.

Facility Option #4 “**Complex and Simple Cell Non-Regulated Facility**” Scope:

- Both mammalian and microbial fermentation capacity.
- Bioreactor capacity between 10-50 Liters.
- Flexibility and space for use of disposable technologies.
- Non-cGMP facility to support production of drug product for R&D and pre-clinical studies.
- Non-cGMP “hands on” development lab with capacity up to 10 Liters.
- Stem cell suite.
- Process development lab.
- Analytical development lab.
- General support (buffer prep, equipment wash, storage, warehouse).
- Offices for 20-25 staff as well as visitor / client offices and administrative support.

Facility Option #4 (Alternative) “**Complex and Simple Cell Non-Regulated Micro-Facility**” Scope:

From discussions with the SJRA, it also appears that a smaller version of Facility Option #4 may be desirable to allow the SJRA to enter quickly into the biological manufacturing market while minimizing the cost impact, as it could be incorporated into the current BioCenter facility expansion plans. Such a facility would provide access to “hands on” equipment necessary to produce non-GMP drug product to support pre-clinical studies, conduct experiments for optimizing production yields and downstream purification processes, and develop processes to analyze biotechnology products. The facility would also introduce a laboratory suitable for preliminary stem cell research and expand the tissue culture capacity in the BioCenter. This facility would have:

- Non-GMP upstream process development lab for mammalian cell culture and microbial fermentation with capacity up to 10 Liters.

- Stem cell / tissue culture suite.
- Downstream process and analytical development lab.
- Access to general support (autoclave, equipment wash, storage, warehouse) which already exists within the BioCenter.
- Office space for 1-2 staff.

F. Leading Facility Cost Estimates, Operating and Funding Models

Leading Facility Options Construction, Equipment and Operating Cost Estimates

Each leading facility option has unique technology requirements and market focus, size and equipment requirements and different construction and operating costs. Size requirements range from 1,100 square feet to 25,000 square feet. Construction costs range from less than \$1 million to \$23 million. Equipment costs range from \$2 million to \$8 million. Operating costs range from less than \$500,000 to \$8 million.

Category	Facility #3 (Clinical)	Facility #4 (Pre-clinical)	Facility #4 Alternative (Small Pre-clinical)
Market Focus	cGMP mammalian cell culture and microbial production facility	Non-cGMP mammalian cell culture and microbial production facility	Non-cGMP mammalian cell culture and microbial production lab
Facility Positioning	Late-stage Pre-clinical through Phase II	Pre-clinical only	Pre-clinical only
Size	22,000 - 25,000 SF	10,000 - 12,000 SF	1,100 - 1,300 SF
Staff	30 - 40	20 - 25	1 - 2
Revenue	\$11M - \$13M	\$3M - \$4M	TBD

The cost estimates to construct and equip each of the leading facility options were derived from a number of research sources, including other CMO and industry benchmarks, leading engineering design firm construction benchmarks and vendor equipment pricing.

Facility Option #3 “**Complex and Simple Cell Regulated Facility**” would require approximately 25,000 square feet, up to \$23 million in construction costs, \$8 million in capital equipment costs and up to \$9 million in annual operating costs. It would also provide the greatest yearly revenue of any option: approximately \$11 million to \$13 million per year.

Facility Option #4 “**Complex and Simple Cell non-Regulated Facility**” would require approximately 12,000 square feet, up to \$8 million in construction costs, \$1.7 million in capital equipment costs and nearly \$3 to \$3.5 million in annual operating costs. Annual revenue could be expected to be between \$3 million and \$4 million per year.

Facility Option #4 (Alternative) “**Complex and Simple Cell Non-Regulated Micro-Facility**” would require approximately 1,100 square feet, \$260,000 in construction costs, \$360,000 in capital equipment costs, and close to \$500,000 in operating costs.

Leading Facility Options: Suggested Funding and Operating Models for Leading Facility Options

Each leading facility option identified has its own unique set of technology and service offerings that dictate specific business and legal structures, revenues, and capital and operational needs. All of these categories need to be taken into consideration in the development of a valid operating model for each facility option.

For each facility option available to the SJRA, there are three categories that should be considered to outline the facility operating / funding model:

- Business and legal structure;
- Revenue expectations and capital and operational needs; and
- Funding options.

The research conducted for this study has provided this detail for each leading facility option based on market research, cost estimates, and benchmarks from other similar public/private biological manufacturing programs.

Facility Option #3 “Complex and Simple Cell Regulated Facility”

Business and Legal Structure

For this facility, a developer would retain ownership of the building and land, and would lease the facility to a CMO partner. A CMO partner would own the equipment, employ staff and oversee all manufacturing and regulatory operations. The SJRA would have no direct involvement in the operations of the facility.

Item	Total Cost	SJRA	State	Federal	Developer	CMO	Vendor
Building Size / Acreage Needs	25K SF; 2-4 acres	-	-	-	-	-	-
Construction (including building utilities and permitting)							
Greenfield	\$20M - \$23M	\$13M - \$16M	-	-	\$7M	-	-
Fit-out	\$13M - \$16M	\$6M - \$11M	-	-	\$7M	-	-
Equipment (including upstream, downstream and lab equipment purchase, installation and qualification)	\$8M	-	\$0.5M	\$0.5M	-	\$7M	-
Annual Operating Costs (including labor, utilities, supplies, taxes, other)	\$8M - \$9M	-	-	-	-	\$8M - \$9M	-
Total Land, Construction & Year 1 Costs	\$29M - \$40M	\$6M - \$16M	\$0.5M	\$0.5M	\$7M	\$15M - \$16M	-

Notes: Greenfield costs include land development, facility shell and interior fit-out. Shell costs include only fit-out of “cold shell” space. Capital costs have been adjusted for Bay area and do not include non-utility equipment.

Revenue Expectations

In order to assess the potential tax base, ongoing viability and partnerships for investing in this facility, annual revenues are estimated at \$11 million to \$13 million, with 10% - 20% in profit margins. This facility option has the highest revenue and profit potential. As a result, this option would likely attract interest from the greatest number and types (e.g., large and mid-tier) of CMO partners.

Capital and Operational Needs and Funding Options

Total construction, equipment and first-year operating costs would total \$29 million - \$40 million for Facility Option #3. Because of its high revenue potential, a CMO partner and a developer would likely contribute substantially to these costs. However, the SJRA may need to contribute as much as 20-40% of the construction cost, or \$6 million - \$16 million, to support its construction.

Facility Option #4 “Complex and Simple Cell Non-Regulated Facility”

Item	Total Cost	SJRA	State	Federal	Developer	CMO	Vendor
Building Size / Acreage Needs	12K SF; 2-3 acres	-	-	-	-	-	-
Construction (including building utilities and permitting)							
Greenfield	\$7M - \$8M	\$4M - \$5M	-	-	\$3M	-	-
Fit-out	\$4M - \$5M	\$1M - \$2M	-	-	\$3M	-	-
Equipment (including upstream, downstream and lab equipment purchase, installation and qualification)	\$1.7M	-	\$0.25M	\$0.25M	-	\$1.2M	-
Annual Operating Costs (including labor, utilities, supplies, taxes, other)	\$3M - \$3.5M	-	-	-	-	\$3M - \$3.5M	-
Total Land, Construction & Year 1 Costs	\$8M - \$13M	\$5M - \$7M	\$0.25M	\$0.25M	\$6M	\$4.2M - \$4.7M	-

Note 1: Adding a training aspect to the operation could mean vendor donated and/or university funding for equipment costs.

Note 2: Construction costs for this option are based on non-cGMP construction; there is construction pre-investment costs included (e.g., utilities) to support a future addition of a cGMP section. Greenfield costs include land development, facility shell and interior fit-out. Shell costs include only fit-out of “cold shell” space. Capital costs have been adjusted for Bay area and do not include non-utility equipment.

Business and Legal Structure

For this facility, a developer would retain ownership of the building and the land and would lease the facility to a CMO partner. A CMO partner would own the equipment, employ staff, and oversee all manufacturing and training operations. An academic partner would provide some oversight, specifically if there were a training component provided requiring university staff or student involvement. The SJRA would have no direct involvement in the operations of the facility.

Revenue Expectations

In order to assess the potential tax base, ongoing viability and partnerships for investing in this facility, annual revenues are estimated at \$3 million to \$4 million with 5% - 10% in profit margins. This facility option has a moderate revenue and profit potential. As a result, it is likely that only smaller or mid-tier CMO partners would be interested in partnering with the SJRA.

Capital and Operational Needs and Funding Options

Total construction, equipment and first-year operating costs would total \$8 million - \$13 million for Facility Option #4. While a CMO partner and a developer would likely invest, the SJRA may need to contribute as much as 50-60% of the construction cost, or \$5 million - \$7 million, to support its construction.

Facility Option #4 [Alternative] "Complex and Simple Cell Non-Regulated Micro-Facility"

Business and Legal Structure

For this option, a developer would continue to retain ownership of the building and land, and would continue to lease the facility to the SJRA. The BioCenter operator would maintain oversight of day-to-day operations and manufacturing staff. An academic partner may provide managerial and/or financial oversight, specifically if there were a training component provided requiring university staff / student involvement.

Revenue Expectations

Annual revenues would be based on rental fees for "hands-on" use. This facility option has very small revenue and profit potential. As a result, it is unlikely that a CMO partner would be interested in partnering with the SJRA for this option, as the operation would be too small for their consideration.

Capital and Operational Needs and Funding Options

Total construction and equipment costs would total \$620,000 for Facility Option #4A. As a result of its low revenue potential and lack of CMO partner options, the SJRA should expect to pay for most, if not all, of this cost.

National and International Biological Manufacturing Program Examples

The research conducted for this study revealed several programs to profile based on their similarities to the leading biological manufacturing facility options selected by the SJRA. These programs include Eden Biodesign, Florida Biologix, Maryland Bioprocess Center and the North Carolina State BTEC program. The programs help identify many key success factors for the SJRA to consider including selecting the right CMO partner; appropriately marketing the facility to the local, national and international biotechnology community; and putting in place an exit strategy that preserves the SJRA investment.

There are several biological manufacturing public / private programs in the US and Europe that provide important context for an SJRA-supported facility. Examples of these programs were

selected for additional analysis based on their similarity to the leading biological manufacturing facility options selected by the SJRA. Regulated facility examples include Eden Biodesign, Florida Biologix, and Maryland Bioprocess Center. A strong pre-clinical non-cGMP facility example includes the North Carolina State BTEC program.

PharmaBioSource has identified both key success factors (things these programs have done well) and lessons learned (things these programs could have done better) from each program.

Three biological manufacturing programs (Eden Biodesign, Florida Biologix and Maryland Bioprocess Center) provide important considerations for the SJRA in the development of a potential Regulated facility. These projects were all driven by regional public authorities or state governments.

Three key success factors for these programs were utilizing an RFP-driven process soliciting established CMO partners, working with local and state governments to create strong incentive / funding packages, and aligning the manufacturing facility within a larger biopark / incubator program.

However, there were some things that these programs could have done better. Most failed to fund a marketing and business development budget and struggled to create awareness of the operations in the market. Also, these programs did not develop an exit strategy; in the case of the Maryland Bioprocess Center, the facility was eventually sold and closed by the CMO, resulting in a loss of the State of Maryland's investment in the facility.

The North Carolina State BTEC program can provide several key success factors for SJRA to consider in the development of a potential non-regulated pre-clinical facility:

Two key success factors for the North Carolina State BTEC pre-clinical manufacturing program were that it received equipment and service donations from industry and vendor partners (reducing its initial capital outlay), and that it created a strong link to the university's educational programs, allowing it to tap into a large pool of student and faculty resources. In addition, the program established an excellent partnership with local industry, not only for equipment donations, but also for assistance with the design of the facility and training curriculum.

However, there were some things that the BTEC program could have done better. For example, the facility was not constructed to all the necessary cGMP standards to receive an FDA-approved facility designation. This will prevent the program from providing clinical manufacturing services in the future. Furthermore, the BTEC was designed to meet many of the cGMP requirements necessary in a biological manufacturing facility with the exception of the air supply and exhaust systems. No pre-investment was made to allow for an upgrade of these systems to meet cGMP requirements in the future.

Potential Federal, State and Local Funding Sources and Academic Partners

Federal, state, and local funding should be considered necessary components of an incentive package for a San Jose-supported biological manufacturing facility. In addition to construction funding, the SJRA should strongly consider offering additional incentives. This is important because the higher cost of doing business in California coupled with the lower profit margins of a CMO makes it challenging for a CMO to enter this market. A CMO partner would be eligible for many state and federal funding programs that may not be available to the SJRA.

Local academic program relationships, such as with San Jose State University or San Jose City College, could be important in supporting a biological manufacturing training program such as might be part of a non-regulated facility.

Because of their experience in running complex biological manufacturing facilities and their ability to qualify for a number of federal and state funding programs, a CMO partner is an essential element for successfully creating a biological manufacturing facility. While the SJRA might need to fund some of the initial facility construction costs, the SJRA, in conjunction with the state, should also expect to provide an incentive package to a CMO partner. Based on research into other public / private CMO partnerships, this incentive package could include the following components:

- Building permit fee waivers and reductions / permit assistance;
- Pre- and post-employment tax credits;
- Equipment investment credits;
- Low-cost equipment financing;
- Sales, income and use tax exemptions;
- Property tax abatement;
- Transportation grants for carpooling or use of public transportation; and
- Utility rate reductions.

The amounts of these individual incentives and total package value will depend on the type of facility constructed and a CMO partner's specific requirements.

PharmaBioSource has also identified two categories of funding sources that could be available to support the development of a biological manufacturing facility as well as a larger Life Sciences cluster in San Jose. These are a mix of grants and loan programs as well as industry incentives. Some are available to local governments; most are direct programs for biotechnology companies or CMO partners.

Federal General Funding Programs could include:

- Federal Job Creation and New Market Tax Credits; and
- Federal Economic Development Administration Grants.

Federal Life Sciences-specific programs could include the following National Institutes of Health programs:

- Small Business Innovation Research Program;
- Small Business Technology Transfer Program;
- Research Facilities Improvement Program;
- Advanced Technologies Program; and
- Shared Instrumentation Grants.

California General Funding Programs could include:

- Tax Incentives (AMT / Capital Gains exemption, New Market Tax Credit) for qualified new, small businesses and businesses in designated Community Development Entities, such as those supported by Lenders for Community Development of San Jose;
- Economic Development Areas;
- Foreign Trade Zones;
- Employment Training Panel and Training & Hiring Incentives; and
- Industrial Development Bonds.

California Life Sciences Specific Funding Programs could include:

- R&D Tax Credits, Accelerated Depreciation, Potential Net Operating Loss Carryover
- Technology in Partnership; and
- California Institute for Regenerative Medicine Facility Grants.

Academic program relationships could be critical in supporting a biological manufacturing training program that might be a part of a non-regulated pre-clinical facility, such as Option #4 or #4A. While these academic programs may not offer direct funding dollars for a biomanufacturing facility, it is possible that a relationship with these programs could provide the SJRA with access to funds reserved for academic and/or training programs.

One potential partner for the SJRA could be a California Community College. The California Community Colleges have had a network in place for workforce training and education in biotechnology and biosciences since 1996. All 109 California Community Colleges (CCC's) have the basic math and science education required for employment in the California Biosciences Industry. About 30 of the colleges have current and active skills courses offered for biotechnology; another 20 plan to offer such courses soon, including San Jose City College (SJCC).

SJCC has a division of Applied Science and Technology, and this division often partners with industry to support local workforce training needs. The SJCC works quickly to implement new curricula with industry partners and is also experienced in working with industry to apply for and coordinate grant funding from state and federal sources. The SJCC is highly interested in expanding its applied biology programs and could be a strong partner for the SJRA's biomanufacturing initiative. In addition to the trained technical staff from the SJCC, other professionals will also be key to the success of a biological manufacturing center. San Jose State University may also present a partnership opportunity for needed skills such as biology, microbiology and biopharmaceutical engineering.

G. San Jose Comparative Advantage

San Jose Life Sciences Industry Goals

A goal of the City of San Jose and the SJRA is to develop a local applied Life Sciences cluster. This goal would be supported, in part, by the construction of a biological manufacturing facility that addresses the diverse clinical manufacturing needs of the Western Region biotechnology market.

A goal of the City of San Jose and the SJRA is to develop a local applied Life Sciences cluster. Just as the City of San Jose states its economic development focus to be “turning innovation into industry,” an applied Life Sciences cluster is focused on bringing innovation from the laboratory to the clinic and on to the market.

Unlike a typical research and development Life Sciences cluster, an *applied* Life Sciences cluster would contain a number of unique components to help companies “grow up,” including applied research labs, clinical research services and facilities (such as clinical hospitals), and the manufacturing, packaging and storage assets for the distribution of drug products. A manufacturing facility would be an important component of the infrastructure needed to support clinical and commercial activities of biotechnology companies and develop a successful applied Life Sciences cluster in San Jose.

Life Sciences clusters are growing across the globe. In the US, for example, North Carolina and Boston are recognized as leading Life Sciences clusters. Life Sciences clusters appear to have a strong impact on a given region’s job and business tax base. Many studies have been performed in attempts to quantify the impact of local policymaking in regional economic development programs supporting Life Sciences clusters.

Researchers have found that clusters are perceived as “enclaves of innovation,” giving firms the benefit of certain synergies. The studies show that firms in such clusters have significantly higher survival rates and provide a positive impact to employment gains over time. The parks have high ability to attract firms, especially new ones, to headquarter in a given location.

Not every locale has the capacity to establish, grow, and/or support biotech activity, let alone a biotech cluster. Every successful Life Sciences cluster is unique, and must use its individual strengths to create its mark in the Biotechnology industry. There are several factors that set apart those locations that can support a thriving Life Sciences cluster from those that cannot:

- Universities and research institutions with a Life Sciences focus, such as biotechnology, and a national or global reputation for innovation.
- Incubators, business assistance, and lots of capital to help players grow in every stage of the business cycle.
- A well-educated, abundant pool of scientists and others possessing Life Sciences skill sets and knowledge.
- Direct, generous funding for basic academic research and groundbreaking R&D efforts.
- A supportive infrastructure to enable the successful transfer of innovation from the lab to the patient (from pre-clinical through clinical development and ultimately commercialization).
- Excellent networking and collaborative opportunities within the biotechnology sector and with other allied sectors such as pharmaceutical and chemical industries.
- Access to state-of-the art equipment and facilities for the research, development and manufacture of biotechnology drugs.
- Full and long-term community support in the areas of regulatory issues and taxes, and general support of the Life Sciences Industry.

In addition to these factors, there are several quality of life factors that help lead to the success of any high tech community including:

- Excellent K-12 education system;
- Access to fine dining;
- Arts and entertainment opportunities;
- Good weather; and
- Access to an international airport.

The Bay Area today can certainly be considered a Life Sciences cluster in and of itself due to the sheer number of companies and universities that exist in the region. However, San Jose has a unique opportunity to differentiate itself from the Bay Area through its efforts to develop an applied Life Sciences cluster. However, doing so is not without potential challenges, as there are areas that San Jose must develop in order to become a leading location for an applied Life Sciences cluster. The areas that would need to be more developed include academic partnerships, workforce skills, and industry infrastructure.

An important first step in the creation of an applied Life Sciences cluster would be the addition of a biological manufacturing facility in the Edenvale Technology Park. This facility would contribute to several factors important to the creation of a successful applied Life Sciences cluster in San Jose. Specifically, a biological manufacturing facility would strengthen San Jose's position in its academic relationships, its applied science workforce and its biotechnology infrastructure.

San Jose and Regional Strengths and Challenges

San Jose has many foundational elements to help ensure the success of a biological manufacturing facility. However, local business incentives and closer ties to academic institutions could enhance San Jose's perceived position in making this offering. Nonetheless, San Jose's regional and local industry strengths outweigh its challenges and supports San Jose's expansion into the Biotechnology industry through the construction of a biological manufacturing facility. Despite a few challenges facing the SJRA in creating a biological manufacturing facility, the overall local market need and potential, coupled with San Jose's foundational elements and larger commitment to creating an applied Life Sciences cluster, support its construction.

San Jose, as part of the Bay Area, can capitalize on a number of regional strengths, including:

- As home to the high-technology industry, San Jose and Silicon Valley have an abundance of private venture capital available to many industries, including biotechnology;
- A well-known, large and growing global biotechnology sector;
- There is large innovation in the California biotechnology pipeline. There are over 400 biotechnology companies in California, with a pipeline of nearly 250 biological products. Most are within a 100-mile radius of San Jose. This robust pipeline provides many product opportunities for a pre-clinical through Phase II biological manufacturing facility to target; and.
- There are few Western Regional CMO's servicing local biotechnology companies today.

There are also many San Jose-specific strengths that can be leveraged in support of a biological manufacturing facility, including:

- The City of San Jose and the SJRA are known risk takers with track records of providing incentives for new companies and industries to establish themselves in the city.
- The City of San Jose and the Redevelopment Agency are making the Life Sciences Industry an important economic development focus.

- San Jose is home to the San Jose BioCenter, one of the first Life Sciences incubators of its kind in the Western Region.
- San Jose is a headquarters location for several companies in the Life Sciences and Biotechnology Industries (for example, the 20+ firms located at the BioCenter).
- The hospital network in San Jose is strong and growing: The California Center for Healthcare and Biomedical Technology plans to build a hospital in Edenvale, and Kaiser Permanente's San Jose medical facility is located nearby.
- San Jose State University and San Jose City College provide unique applied science programs that could support an applied research and manufacturing facility.
- The Edenvale Technology Park provides vacant land and available facilities (laboratory, office and shell manufacturing space) for biotechnology firms.
- The Edenvale Technology Park is home to several major Life Sciences companies and service providers, including Stryker, VNUS Medical Technologies and Clinimetrics.
- Edenvale has access to major highways and proximity to international airports. This also provides access to the trained innovation and commercialization talent pool in the Bay Area at large.

There are, however, a few important regional and San Jose-specific challenges that would need to be addressed in order to create a successful biological manufacturing facility:

- The Western Region (including San Jose) has a high cost of living and conducting business relative to other areas in the US. Providing local incentives would help alleviate this cost in San Jose.
- There is a perceived deficit of a skilled biotechnology workforce in San Jose across experience levels, from B.S. lab technologists through Ph.D. researchers. The opportunity exists to develop stronger ties among The City of San Jose, San Jose State University, San Jose City College, and other academic institutions, to develop programs for applied research and development activities in the biological and chemical sciences.

Overall, San Jose's Biotechnology industry strengths outweigh its challenges and support its efforts to create a biological manufacturing facility.

H. Conclusions and Recommendations

The SJRA asked PharmaBioSource to evaluate the feasibility of the development of a biological manufacturing facility in Edenvale. From our analysis, there are two important drivers supporting the construction of a biological manufacturing facility in Edenvale: 1) the Western Region market demand for a local, biological manufacturing facility focused on clinical manufacturing is high; and 2) there is little competition in the Western Region from current biological CMO's.

While there are several options available to the SJRA to address this manufacturing market need at a variety of cost points, our research indicates that the construction of Facility Option #3 "Complex and Simple Cell Regulated Facility," would create the greatest impact. This facility would address the largest segment of the Western Region biotechnology market because it would offer the ability to produce drug product for human clinical trials in a regulated, cGMP environment using both mammalian cell culture and microbial fermentation manufacturing systems.

Given the cost, complexity and risk of constructing and operating a biological CMO facility, a CMO partner is crucial to the success of a biological manufacturing facility. Federal, state, and local funding should be considered necessary components of an incentive package for a potential CMO partner. Incentives can take the form of building permit fee waivers, equipment investment credits, low-cost equipment financing, pre- and post-employment credits, property tax moratoriums and/or rebates, sales and use tax exemptions, transportation grants, employee training grants, and utility rate reductions. Offering a strong incentive package to a CMO partner is important because the higher cost of doing business in California and the lower profit margins of a CMO, as compared to biotechnology companies, make it challenging for a CMO to enter the Bay Area market on its own.

In evaluating the city's comparative advantage in the Biotechnology and Life Science industry, we believe San Jose has many foundational elements that would ensure the success of a biological manufacturing facility. These include the support of City and Redevelopment Agency officials, the current BioCenter initiative and the fact that the Edenvale Technology Park provides vacant land and available facilities (laboratory, office and shell manufacturing space) for biotechnology firms. However, local business incentives and closer ties to academic institutions would enhance San Jose's perceived position in making this offering. Nevertheless, San Jose's regional and local industry strengths outweigh its challenges and supports San Jose's construction of a biological manufacturing facility.

As noted in the analysis, such a biomanufacturing facility alone will not create a large number of jobs or necessarily encourage companies to headquarter their operations in San Jose. The nature of biological contract manufacturing organizations is such that clinical biological manufacturing facilities of the size and focus recommended in this study usually have fewer than 50 employees on site. Furthermore, biotechnology companies are used to working with remote CMO partners, sometimes over very great distances.

A Life Sciences cluster, though, can have a much greater impact on local jobs and business tax base. However, San Jose is not alone in its interest in developing a Life Sciences cluster: Competition between states and cities for the Life Science Industry is intense, and having a local *applied* Life Sciences cluster would differentiate San Jose from other regional Life Sciences clusters and encourage firms to consider San Jose as a place to locate.

Just as the city differentiates its economic development focus as "turning innovation into industry," an applied Life Sciences cluster is focused on bringing innovation from the laboratory to the clinic and the market. It contains a number of unique components to help companies "grow up": Applied research labs, clinical research services and facilities (including clinical hospitals), and the manufacturing, packaging, storage and distribution of drug product. This approach is highly unique and meets a widespread regional need for applied services such as biological manufacturing. A biological manufacturing facility would be a key "first step" in the development of an applied Life Sciences cluster in San Jose.