

Window on the Workplace 2003

A Training Needs Assessment
for the Biomanufacturing Workforce
March 2003



**North Carolina Biotechnology Center
Education and Training Program**

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Acknowledgements



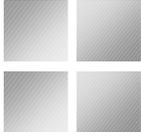
This study was funded by the Golden LEAF Foundation.

The North Carolina Biosciences Organization also provided support for this study.

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Executive Summary

The biopharmaceutical industry is poised for major expansion globally as many new biotechnology-based products enter the FDA approval pipeline. Since the existing worldwide capacity to manufacture such drugs is now saturated, biopharmaceutical companies will need to increase capacity drastically by building new manufacturing facilities over the next several years. North Carolina can gain great economic benefits by attracting as much of this new manufacturing capacity as possible.

North Carolina is home to a growing number of biotechnology research and development companies, biomanufacturing companies, and many other pharmaceutical manufacturing companies. The biomanufacturing sector has grown by an average of 10% per year over the last several years and we project it will continue to grow at that rate. Jobs in pharmaceutical manufacturing, including biopharmaceutical manufacturing, are among the highest paid manufacturing jobs in the state. The average annual wage is \$68,210. Pharmaceutical and biomanufacturing companies now employ about 20,000 workers in North Carolina.

A key constraint on this industry's growth is the availability of skilled workers. All companies now have difficulty finding qualified employees. There is a critical need for new training programs to provide a qualified workforce for company expansions and for new manufacturing enterprises locating in North Carolina. This is especially true now in light of heated global competition to share in the economic growth possible in biomanufacturing.

Workers need a basic foundation in chemistry, biology, mathematics, engineering, and engineering technology. They also need knowledge and skill sets specific to biomanufacturing and pharmaceutical manufacturing that are not typically taught in colleges as a part of traditional academic programs.

Employees with high school diplomas, certificates, or AAS degrees make up 67% of the total workforce in biomanufacturing and pharmaceutical manufacturing. BS graduates make up 27%, and those with graduate degrees comprise 6%. Thus, the task of training this workforce will fall to both community colleges and universities. (While many jobs require only a high school diploma, graduates are almost never hired directly out of high school for this industry.)

Employers place a premium on prior experience in the pharmaceutical industry, and new graduates are at a distinct disadvantage in competing for jobs at any level with applicants with prior experience. Since the number of such experienced job applicants is limited in our market, it is essential to find ways to prepare graduates better.

The value of prior industry experience lies chiefly in the fact that pharmaceutical manufacturing is a highly regulated enterprise. FDA-mandated Good Manufacturing Practice (GMP) guidelines govern every aspect of the process, and it takes time for new employees to absorb the mind-set that is required for compliance. Average on-the-job training time for new hires with prior experience in the industry is half that required for new hires without this experience. Also because of these regulations, it is difficult for companies to allow new employees hands-on practice without very close supervision. This limits co-op or internship opportunities for students.

Industry respondents to our survey noted several characteristics they think are critical for programs established to train the biomanufacturing and/or pharmaceutical workforce:

- Operation in a GMP-like manner
- Provision of hands-on experience with production equipment, at least at pilot scale, as well as laboratory equipment
- Training in aseptic manufacturing processes and clean-room work
- Instruction by faculty with prior experience in the industry
- Close oversight of curricula and programs by industry

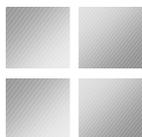


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Introduction

Biotechnology, in its broadest sense, is the use of living organisms to solve problems or make useful products. From this point of view, biotechnology is as old as the first domestications of crop plants or fermentations to make wine or beer. In the latter half of the twentieth century we made rapid progress in understanding how cells work at the molecular level and how genetic information impacts the characteristics of organisms. Thus, modern biotechnology is a body of knowledge and methods that enable us to harness cells and their molecules for useful purposes.

Each living cell is like a tiny chemical plant with the capacity to make thousands of different molecules. *Bioprocessing* is the culture of cells to make desired products, as well as the purification of biomolecules from cells or the use of such molecules in other kinds of manufacturing. We also term this collection of technologies *biomanufacturing*.

Biomanufacturers have for decades grown microorganisms (bacteria and fungi) in large quantities — up to thousands of gallons at a time — to make a variety of commodity products. Examples made in North Carolina include:

- Amino acids for nutritional products
- Citric acid, a common food additive
- Enzymes for use in brewing, baking, textile manufacturing, and laundry detergents

The newest biomanufacturing technology employs mammalian cell culture to produce proteins (usually human proteins) that have therapeutic value. These new kinds of drugs are called *biopharmaceuticals*. This area of the biomanufacturing industry is poised for explosive growth over the next several years and is a primary focus of this report.

Biotechnology and Industrial Development

Based on the development in the mid 1970s of recombinant DNA technology and research in other areas of biology, the enterprises we call *biotechnology companies* began to spring up. They might be called “bioentrepreneurial” companies and are typically tracked together as the “biotechnology industry.” The Center maintains a directory of these companies in North Carolina. This group includes many small companies engaged in research and development, larger established agricultural and pharmaceutical companies that employ the methods of biotechnology in their research, and a group of biomanufacturers that use biotechnology in manufacturing, as described above.

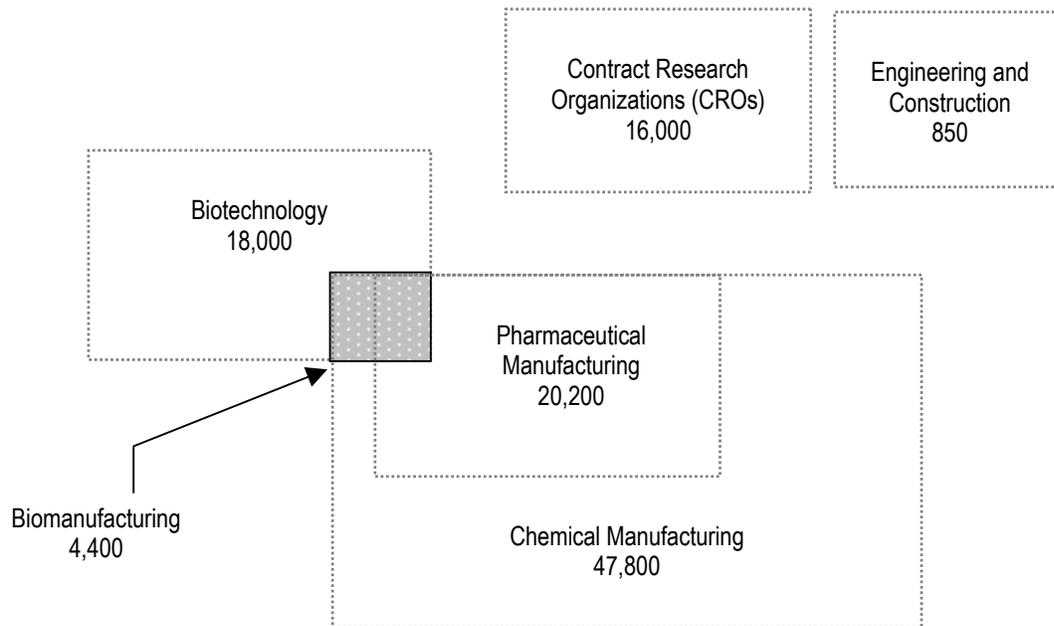
As the biotechnology research and development firms mature and move into manufacturing and sale of their products, they also become defined not only by the technologies they employ but also by the types of products they make and the markets in which they do business. They become, for example, agricultural or pharmaceutical or chemical companies. It's important to remember that the methods of biotechnology have the potential to impact a variety of established industries — both in research and manufacturing.

Biotechnology will play an increasing role in research and manufacturing in the chemical, agricultural, pharmaceutical, and environmental industries.

Biomanufacturing and Related Industry Groups

See Figure 1. Of the 18,000 employees who now work in North Carolina's biotechnology community, 4,400 work in biomanufacturing. When we last surveyed the biomanufacturing group in late 1995, there were 2,160 employees in 16 companies. Since then, overall employment has doubled — representing an annual average growth rate over 7 years of 10%. This growth has been due both to expansion of existing companies and the startup of new sites.

Figure 1. Biomanufacturing and Related Industry Groups



This small group of biomanufacturing companies is considered part of the much larger chemical manufacturing group in the classification system used by the North Carolina Department of Labor.

Companies classified as chemical manufacturers make a wide variety of products — from rubber and paint to food additives to pharmaceuticals. These companies employed 47,800 workers as of the second quarter of 2002. Despite the diversity of products that companies in the large chemical manufacturing group make, these companies share some similar technologies, their employees need knowledge of science and engineering, and their employees have skills that may be transferable to other companies.

From a high in 1998 of 50,700, employment in the chemical manufacturing group as a whole declined to 47,800 by the end of 2001, possibly due to growing global competition in the commodity product sector of the chemical industry (more than half the North Carolina chemical manufacturers are in this sector).

The pharmaceutical manufacturing sector of this group employed 20,200 of these workers. These companies include the entire spectrum of pharmaceutical manufacturing, making drugs, reagents, and medical devices, diagnostic kits and supplies. Over 75% of the employees of biomanufacturing companies work in biopharmaceutical manufacturing, and thus form a small but significant part of the pharmaceutical manufacturing sector. Many of the biotechnology research and development companies included as “Biotechnology” in Figure 1 focus on clinical applications of new developments in genetics and cell biology. They potentially identify new drugs that might find their way into the pharmaceutical manufacturing pipeline.

Two other groups of companies are tracked in the Center’s company directory. The CROs are contract research organizations that provide a variety of services to all types of pharmaceutical companies — both those that use conventional manufacturing technologies and those that use biotechnology in manufacturing. The services they provide include analytical laboratory work, product development studies, management of clinical trials of new drugs, and the analysis of data from such trials. The engineering and construction firms listed in the Center directory specialize in the design, engineering, commissioning, and construction of new pharmaceutical and biopharmaceutical manufacturing facilities. Both these groups that serve the pharmaceutical industry as a whole have expanded their presence in North Carolina significantly in recent years.

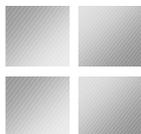
Though the pharmaceutical manufacturing companies employ only about 3% of the state's total manufacturing workforce, they have posted significant job growth recently and their workers are among the most highly paid manufacturing employees in the state. The table below illustrates this.

Table 1. Manufacturing in North Carolina

	All Manufacturing	Chemical Manufacturing	Pharmaceutical Manufacturing
Job growth 2001-2002	-9.6%	-0.2%	+8.5%
Average Annual Wage 2 nd Qtr. 2002	\$37,097	\$56,902	\$68,210

Data from North Carolina Department of Labor; second quarter 2001 to second quarter 2002.

Although biomanufacturing at present constitutes a small fraction of overall pharmaceutical manufacturing, it is poised to grow dramatically in the next several years, both in the number of biopharmaceutical products made and the number of jobs created.



Biopharmaceutical Research, Development, and Commercialization

Throughout the 1970s and early 1980s, biotechnology companies were engaged primarily in basic research and development activities. When they discovered biological molecules that looked promising under lab conditions, they began the lengthy process of shepherding these potential therapeutics through regulatory tests to establish safety and efficacy. This process is generally the same for all new drugs, whether they are biopharmaceuticals or not. See the table below.

Table 2. Drug Discovery and Development Process

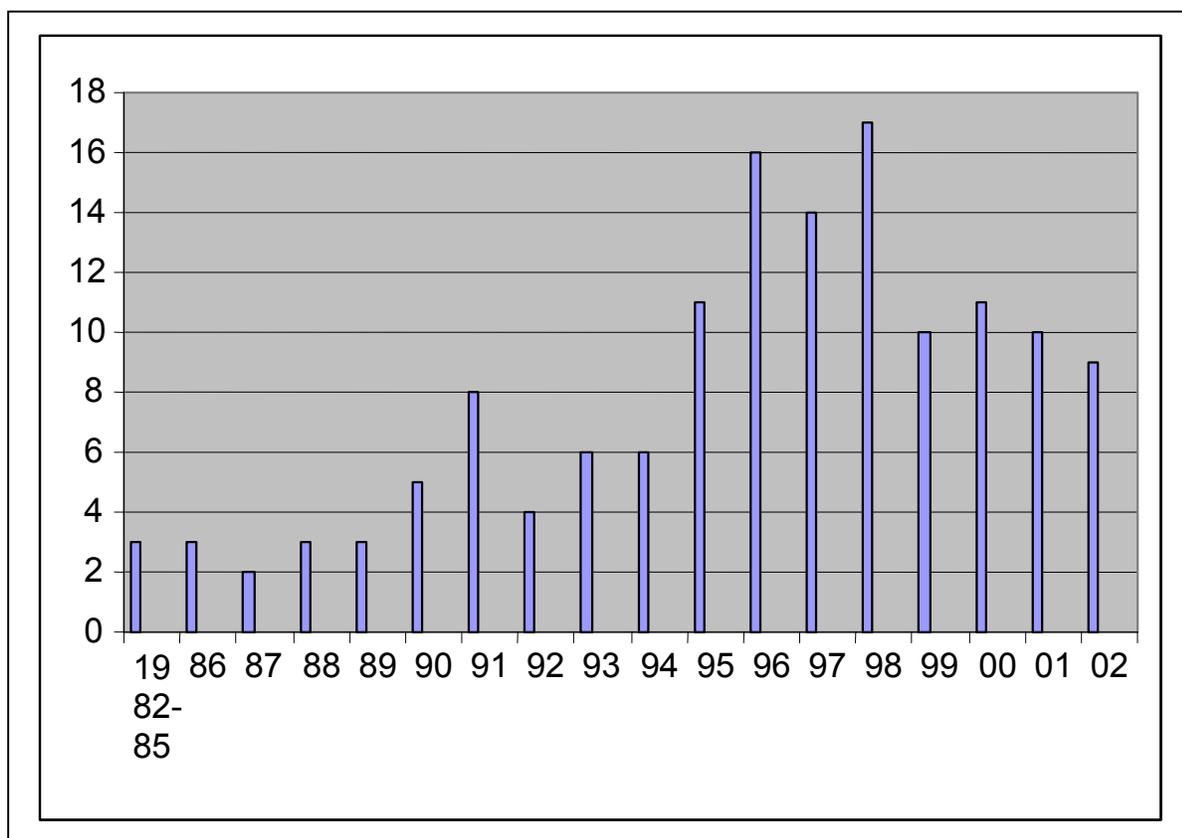
Year	Stage/Phase	Probability of advancing to next stage
0	Discovery of a promising compound Patent clock begins ticking	
1–4	Pre-clinical testing Lab and animal tests	1/1,000 (.1%) of the promising compounds results in an Investigational New Drug (IND) submission
	Investigational New Drug (IND) application submitted to FDA	85% to Phase I clinical trials
4–6	Phase I clinical trials Assess safety and metabolism 30–50 volunteers	80% to Phase II clinical trials
6–8	Phase II clinical trials Assess efficacy and safety 100–300 volunteers	28% to Phase III clinical trials
8–12	Phase III clinical trials Assess efficacy and safety 1,000–5,000 volunteers	65% to New Drug Application (NDA) submission
12–14	New Drug Application 100,000 pages of data reviewed by FDA	90% of the NDAs are approved by FDA
14	Drug reaches market Post-market evaluation	
17	Patent expires	

Sources: Association of Clinical Research Professionals / Pharmaceutical Research and Manufacturers of America

Once the U.S. Food and Drug Administration (FDA) approved their therapeutics for commercial use, the biotechnology companies began to build the unique manufacturing facilities required for biopharmaceutical production and started large-scale manufacture. A parallel evolution was occurring in well-established pharmaceutical companies. They began incorporating biotechnology into their research and development activities in the 1970s and received their first regulatory approvals for the commercial manufacture and sale of biopharmaceuticals in the early 1980s.

From 1982 to 1992, the FDA approved 31 biopharmaceuticals and companies commenced manufacturing. In 1992, the U.S. Congress passed the Prescription Drug User Fee Act, which provided funds to hire additional FDA staff to review New Drug Applications. Consequently, in the following decade (1992-2002) the number of approvals rose to 110, an increase of more than 200%. (See Figure 2.)

Figure 2. FDA Approvals of Biopharmaceuticals



*Number of FDA approvals for applications of biopharmaceuticals to treat specific indications.
Source: Pharmaceutical Research and Manufacturers of America (PhRMA), October 2002*

Limited Biomanufacturing Capacity

The accelerated rate of biopharmaceutical product approval quickly saturated worldwide biomanufacturing capacity. Because the time required for facility design, construction and validation is 3 to 5 years, companies must commit to these capital-intensive projects years before the FDA approves the biopharmaceuticals they hope to market. While large, well established pharmaceutical companies with guaranteed revenue streams from commercialized drugs may be willing and able to risk the \$300 million to \$500 million necessary for biomanufacturing facility construction, equipment procurement and licensing, the smaller biotechnology companies receiving their first commercial approval have little revenue to commit to such a project and are not in position to gamble on an FDA approval. As a result, production shortfalls have occurred for some new therapeutics. Unable to meet the needs of patients wanting their products, smaller companies have lost millions of dollars in biopharmaceutical sales revenues. Many have turned to contract manufacturing organizations (CMOs) to manufacture their products until FDA approval is assured and they build their own manufacturing facilities. North Carolina is home to one such biopharmaceutical contract manufacturing company — Diosynth.

The shortage of biomanufacturing capacity will only worsen in the coming years as the rate of product approvals increases further. Biotechnology investment analysts expect the number of FDA product approvals granted during the next 5 to 6 years to equal those approved in the last 10 years. According to the FDA and the Pharmaceutical Research and Manufacturers of America, more than 370 biopharmaceuticals were in various stages of the U.S. regulatory approval process in October 2002. More than 1,000 biopharmaceuticals are in the worldwide biopharmaceutical pipeline.

In 2001-02, estimates of current worldwide biomanufacturing capacity (for mammalian cell culture alone) ranged from 400,000 to 450,000 liters, all of which was being utilized. According to Biogen executives, worldwide mammalian cell culture capacity is increasing by 100,000 liters per year, resulting in a worldwide capacity of approximately 750,000 liters by 2005. Others calculate a worldwide capacity of 1 million liters by 2006. In either case, all who have looked at the problem of biomanufacturing capacity predict a serious shortfall by 2006 — possibly by nearly a million liters. And this estimate does not factor in products in the approval pipelines outside the U.S.

The economic impact of limited manufacturing capacity is major. Many of the biopharmaceuticals produced by different companies to treat the same disease have similar modes of action. Therefore, companies unable to meet customer demand or start manufacturing run the risk of losing their market to a competitor that does have manufacturing capability. In addition, as can be seen from the previous table, the lengthy regulatory approval process greatly diminishes the length of time a company has exclusive patent rights to a certain biopharmaceutical. Any delay in manufacturing initiation significantly shortens the effective life of the patent and reduces profits. Moreover, many biopharmaceuticals now in the approval pipeline represent the first means of treating previously intractable diseases — thus the manufacturing shortfall has human costs, too.

Trends Affecting Biotechnology Workforce Development

This continuing evolution of biotechnology from primarily a basic research enterprise to large-scale manufacturing has important implications for the profile of the workforce that will use the tools and techniques of biotechnology. First, the total number of employees increases as a biotechnology company moves from research and development to commercial-scale manufacturing. Second, while research requires more PhDs, manufacturing is heavily weighted towards workers with AAS degrees or high school diplomas. Third, as the methods of biotechnology are applied increasingly in other industry groups — chemical manufacturing, agriculture, and environmental industries — the number of workers needing appropriate knowledge and skills can be expected to increase.

Employment in pharmaceutical manufacturing, especially in biopharmaceutical manufacturing, will continue to grow. To support this growth in North Carolina, we need to prepare a capable workforce with specialized skills and knowledge.



Scientific and Technical Job Growth

So far this report has encompassed all employees in various industry groups. Its focus from this point forward will be exclusively on biomanufacturing and pharmaceutical manufacturing, and on scientific and technical employees working in these two sectors.

We consider “scientific and technical employees” to be those who require a background in science, or training in the many technologies that are used in these kinds of manufacturing. The spectrum of knowledge and skill required is broad. (See the section *Knowledge and Skills*.) It encompasses biology and chemistry, specialty fields within those disciplines, engineering, statistics, process instrumentation and control, and an array of other technologies specific to pharmaceutical manufacturing and biomanufacturing. Another — and perhaps most significant — area of knowledge is the body of practices required to implement the FDA regulations that govern every aspect of pharmaceutical manufacturing. These are called Good Manufacturing Practices.

We estimate that 85% of the employees in biomanufacturing firms require elements of this kind of background; about 65% of employees in the broader pharmaceutical manufacturing group are scientific and technical.

The Survey Population for this Report

Because of demonstrated job growth in the biomanufacturing and pharmaceutical manufacturing sectors, anticipated future growth, and the close alliance of the skill and knowledge base for biopharmaceutical and general pharmaceutical manufacturing, we surveyed all biomanufacturing sites in North Carolina and a selected group of pharmaceutical manufacturers. Following is a map of the company sites and a table describing the survey group.

Figure 3. Map of Survey Group Sites

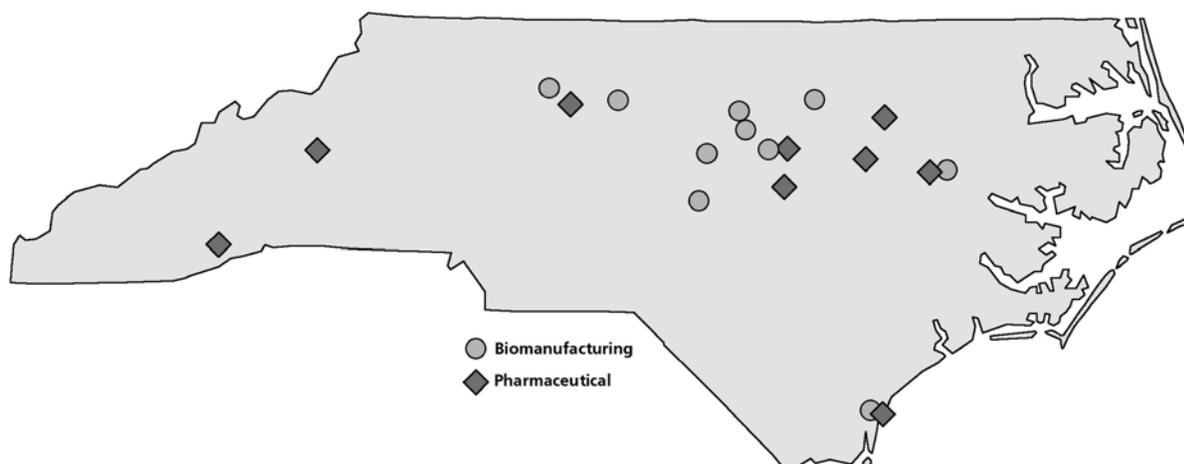


Table 3. Survey Group

Company Type	Number of Companies	Total Employees
Biomanufacturing: Commodity Producers	4	734
Biomanufacturing: Biopharmaceutical Producers	7	3,484
Biomanufacturing: Research & Development Cos.	9	170
Pharmaceutical: Chemical Synthesis	2	35
Pharmaceutical: Formulation and Sterile Filling	4	5,999
Pharmaceutical: Solid Dosage Formulation	3	1,723
Pharmaceutical: Contract Analytical Services	2	1,090
Pharmaceutical: Other	1	178
Total	32	13,413

DSM Pharmaceuticals in Greenville is included in this table as a formulation and sterile filling operation; however it also has chemical synthesis and solid-dosage formulation capability. It is a contract pharmaceutical manufacturing facility providing a full range of services. Its sterile filling operation involves work with biopharmaceuticals. Novo Nordisk Pharmaceuticals does final formulation and filling of recombinant insulin, a biopharmaceutical. The contract analytical services companies serve the biopharmaceutical industry as well as providing services to companies that synthesize more traditional types of drugs. Operations such as these can be expected to increase as the manufacture of biopharmaceuticals increases in the years to come.

The biomanufacturing R&D companies included in the survey group were chosen because they are investigating new methods of production, or are manufacturing at pilot scale. Their employees can be expected to need skills and knowledge in process development similar to their counterparts in large biomanufacturing companies.

The pharmaceutical companies included in the survey group were chosen because their employees share a significant skill and knowledge overlap with those in biopharmaceutical manufacturing; therefore, their training needs can be expected to be similar. The chemical synthesis group is under-represented.

A description of how this survey was conducted is in Appendix D.

Job Growth in the Survey Group

The companies in the survey group created 777 new scientific and technical jobs in 2002. This was a 6.1% increase in the overall job base. Almost all the new jobs created in the biomanufacturing group were in biopharmaceutical companies.

Table 4. Scientific and Technical Jobs Created in 2002: Survey Group

Company Type	Jobs Created	% Growth in total employment
Biomanufacturing	293	+7.2
Pharmaceutical	484	+5.7
Total	777	+6.1

The survey group companies predicted their job creation over the next 3 years as shown in the table below. Again, all the projected growth among biomanufacturers is in the biopharmaceutical companies.

Table 5. Projected New Scientific and Technical Jobs, 2003-2005: Survey Group

Company Group	2003	2004	2005
Biomanufacturing	561 (+12.8%)	275 (+5.6%)	332 (+6.4%)
Other pharmaceutical	391 (+4.3%)	209 (+2.2%)	241 (+2.5%)
Total	952 (+7.1%)	484 (+3.4%)	573 (+3.9%)

(Percentages are based on total employment.)

Overall, on the basis of past performance and projected new job creation over the next 3 years, the biopharmaceutical group is ahead of the remainder of the pharmaceutical sector. Since construction of new facilities for biopharmaceutical manufacturing is an urgent concern for the industry in the next several years, we can expect job growth in the biopharmaceutical sector to continue to outpace that in other areas of pharmaceutical manufacturing.

Predicting Future Growth in the Industry as a Whole

This is always difficult because in any given year or group of years market forces can change hiring patterns drastically in different industry sectors. We can only extrapolate from the data that seem most reliable.

Biomanufacturing

The 10% average annual growth we have observed in this well-identified and closely-tracked group of companies can be taken as a reasonable predictor of future growth. Based on the current total employment in this company group of nearly 4,400, this would lead to roughly 440 to 530 jobs created per year over the next 3 years. Of these, about 370 to 450 would be scientific and technical workers. This is in reasonable agreement with the average of 389 new scientific and technical jobs per year that biomanufacturing companies in the survey group estimated they would create in the next 3 years. As noted before, we can expect most of this growth to take place in the biopharmaceutical companies.

Other Pharmaceutical Manufacturing

Since the Center has not tracked these companies in prior years, we rely on N.C. Department of Labor statistics showing an increase in overall employment of 8% from 2001 to 2002. This figure presumably includes both expansion of existing facilities and startup of new ones. The pharmaceutical companies in our survey group had job growth of only about 6% over the last year, and they predict an average of only 3% growth over the next 3 years.

The total employment in this group is approximately 20,200. About 4,000 of these jobs are in biopharmaceutical manufacturing, which we accounted for above. Subtracting these leaves the remaining pharmaceutical job base of about 16,200. At a growth rate of 3 to 8%, this leads to about 490 to 1,300 new jobs per year, gradually increasing as the job base increases. Based on our survey data, we could expect that about 65% of these jobs would be scientific or technical. Therefore, we could expect that about 325 to 845 new scientific and technical jobs per year would be created.

Annual Job Openings

Job openings occur when new jobs are added, and when existing positions become vacant (turnover). While new jobs are important from an economic development perspective, all job openings are important from an educational perspective since each job opening for an entry-level position is an opportunity for a graduate to enter the industry.

Two factors from survey data are important in predicting the annual number of job openings accessible to new graduates:

1. Human resource managers estimated average annual turnover to be 10%. This figure is consistent with what we have observed in prior surveys of the biomanufacturing group.
2. 35% of predicted new jobs created in the survey group will be *entry level*. We define an entry-level position as one for which people with appropriate education but no prior pharmaceutical industry experience could be acceptable applicants. An entry-level position by this definition could require a PhD or an AAS degree.

How Many Job Openings per Year?

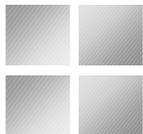
The table below summarizes our best guesses, averaged over the next 3 years. In this table, the biomanufacturing sector includes all biopharmaceutical producers and commodity producers that use biomanufacturing technology. The pharmaceutical sector includes all pharmaceutical companies that are not biomanufacturers.

Table 6. Estimated Job Openings per Year: Pharmaceutical Industry

	Biomanufacturing	Pharmaceutical
New job creation	490	500-1,400
Turnover	490	1,720-1,890
Total	980	2,220-3,290
Scientific/Technical	830	1,440-2,140
Overall total scientific/technical job openings		2,270-2,970
Entry-level job openings		790-1,040

We did not survey companies about their plans beyond 2005. We have reviewed the prospects for recruiting new biopharmaceutical companies to North Carolina, considering those prospects known about now, as well as some additional prospects we can expect in the first two quarters of 2003. If all these companies located in North Carolina, they could generate 500 to 1500 new jobs per year from 2007 to 2012 as they ramp up employment after constructing or outfitting new facilities. However, we cannot reasonably expect to land every one of these prospects. We estimate more conservatively that about a third of the prospects could be successfully attracted to our state. Therefore, we could reasonably expect about 300 to 350 new jobs per year during this period due to new biopharmaceutical company locations.

Employment in the biomanufacturing industry in North Carolina has grown at an annual average of 10% over the last several years. Continuing growth in biomanufacturing and pharmaceutical manufacturing as a whole can be expected, possibly generating around 1,000 to 2,000 new scientific and technical jobs a year.



How Pharmaceuticals Are Made

The following table outlines how a new drug moves through the pipeline and into the manufacturing process for both the pharmaceutical and the biopharmaceutical industry. At this summary level, there are many similarities in the overall process. As noted previously, it can take up to 14 years to get from an idea in the laboratory to the drug store shelf.

As the process moves from laboratory to manufacturing plant, the size of the workforce grows. At early stages, more people with graduate degrees in science are required; when manufacturing begins, more people with only a high school diploma or community college education are required.

Figure 4. Changes in Size and Type of Workforce

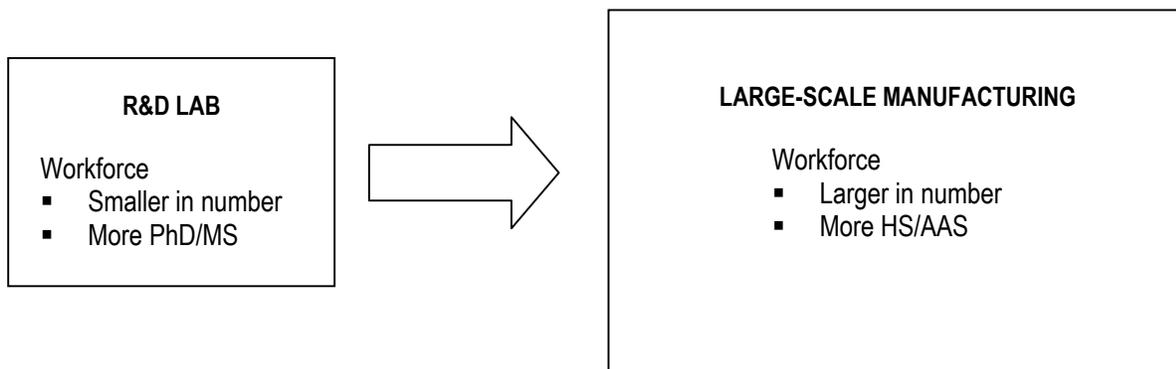


Table 7. How a New Drug Gets to Market	
Research and Development	The development of a new drug is a lengthy process. Drug development begins in the laboratory, where scientists look for compounds that alleviate or prevent disease. This has traditionally involved much trial and error, but the drug-discovery process is now enhanced by the research tools of biotechnology, which can make the process more targeted and informed by increased understanding of life processes. Many biotechnology companies in North Carolina carry out this kind of drug-discovery research.
Pilot-Scale Manufacturing	A promising drug candidate is then manufactured at <i>pilot scale</i> . For biopharmaceuticals produced by cells grown in culture, this means growing cells in a volume of about 10-200 liters. (Lab scale culture is usually only 1-5 liters.) For a traditional pharmaceutical product, this might involve a small-scale chemical synthesis process. At this stage, scientists and engineers are beginning to work out details of what the manufacturing process will be like, and making enough of the drug for initial studies and to use in clinical trials. Some contract manufacturers in North Carolina can do this pilot-scale manufacturing for their pharmaceutical and biopharmaceutical company clients who might not have their own facilities.
Clinical Trials and New Drug Application Process	Described previously in this report, this is the process of testing a new drug candidate in volunteer subjects and applying to the U.S. FDA for approval. North Carolina is home to several contract research organizations that manage clinical trials.
Scale-up to Commercial Production	Even while clinical trials are still under way, scientists and engineers may begin to work out how to scale the manufacturing process up to the eventual desired production volume that will be needed when (they hope) the drug goes to market. Manufacturing processes sometimes have to be quite different than in the laboratory, and scaling-up requires experienced judgment in process or bioprocess development as well as knowledge of scientific and engineering principles.
Large-scale Manufacturing	Now the new drug is ready to go to market and will need to be manufactured in quantity. This is the stage at which the great majority of employees of pharmaceutical and biomanufacturing companies work. The pages that follow focus on this stage in more detail.

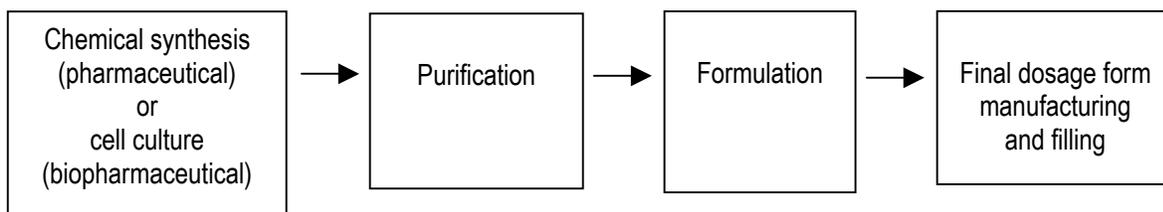
Large-scale Manufacturing

Figure 5. Pharmaceutical Manufacturing Process

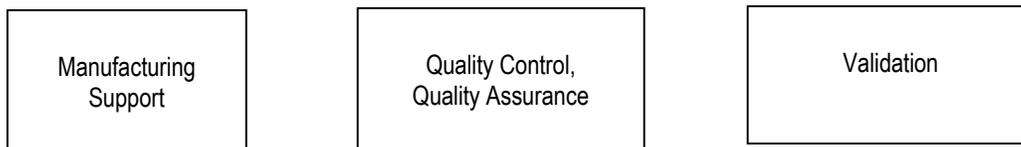
Research and Development



Production



Support Functions



Manufacturing Functions

A large corporation may have many manufacturing facilities in different locations; each dedicated to a particular product or set of products, and in some cases to only a part of the manufacturing process. However, each product requires the major functions described in Figure 5, whether all the work is completed at one site or multiple sites.

Functions in a pharmaceutical or biomanufacturing facility typically fit within the following major divisions. In this section, we describe the work in each of these divisions and indicate some typical job titles and educational background needed for the work. While formal departmental organization may differ from one company to another, these divisions capture most of the manufacturing-related functions. We organized survey data by these divisions.

Research and Development

Research and development within a manufacturing context does not refer to the drug discovery type of research and development previously discussed. Rather, it refers to research and development as it pertains to the manufacturing processes and product. This could range from developing new assays to test the stability and activity of the product in various stages of manufacturing, to researching a new type of manufacturing technology. This type of work is generally referred to as process development, and it is applied research at the interface between basic research and production. Most employees in this kind of work are engineers and scientists, many with advanced degrees.

Production

Production is the heart of manufacturing. There are many different steps involved in pharmaceutical and biopharmaceutical manufacturing. The processes involved, particularly for the biopharmaceutical industry, are often complex and lengthy operations.

Synthesis

The first step involves preparing the materials required for creation of the products. This involves mixing and measuring chemicals and reagents for both pharmaceutical manufacturing and biomanufacturing. In the latter case these ingredients frequently need to be sterilized to avoid introducing contamination. Then the product itself is created, either by chemical synthesis for traditional pharmaceuticals or through cell culture for biomanufacturing.

Purification

After the desired product (called the active pharmaceutical ingredient) is synthesized, it has to be purified. That means separating it from the chemicals left over from a chemical synthesis reaction or from living cells and cellular nutrients and byproducts. (Some biomanufacturers purify products from natural sources instead of growing cells in pure culture.)

The end result of production is called *bulk product*. The bulk product may be sold as is, processed further at the same plant, or shipped to another plant for further processing.

Formulation

Several other operations are required to get the bulk pharmaceutical into the final dosage form in which it will be retailed. Dosage forms can be solid (e.g., tablets or capsules), liquid, gels or creams, or aerosols. Biopharmaceuticals are almost always sold as sterile liquids or sterile dry powders.

Formulation involves chemical mixing operations to blend the active pharmaceutical ingredient with other agents required in the final dosage form, such as granulating agents, fillers, or buffers.

Final Dosage Form Manufacturing

The formulated preparation is put into its final form, for example tablets or sterile solutions, and then dispensed into containers. The containers are labeled and packaged. These kinds of operations typically require the least skilled labor, except for filling of sterile solutions, which requires specially trained technicians.

Most production employees work directly with the manufacturing process. They monitor and operate the manufacturing equipment, prepare media and chemicals for the various stages of production, and transfer materials from one operational unit to the next. These workers are usually called process operators (or alternatively manufacturing associates or process technicians). Process engineers make sure the processes are running efficiently, optimize them, and bring new processes to make new products on line.

Manufacturing Support

A variety of other functions support manufacturing. In this division we have included maintenance of the plant and all its utility systems. Utilities include electrical systems, water-purification systems, and heating, ventilation, and air conditioning (HVAC), for example. Employees in manufacturing-support groups also maintain the complex equipment (pumps, valves, piping, and the specialized manufacturing equipment). Process control technicians and engineers design, program, and maintain the extensive automated instrumentation and control systems that run the processes.

Another area of manufacturing support is waste management. Employees in this group include technicians with specialized backgrounds in industrial trades, environmental technicians who have some of the same skills as process technicians, and mechanical and electrical engineers.

Quality Control (QC) and Quality Assurance (QA)

The standards are high in pharmaceutical manufacturing because the stakes are high. Poor quality products can harm or even kill consumers. Companies generally ensure quality through their quality control, quality assurance, and validation divisions. While all employees must conform to the guidelines (Good Manufacturing Practices or GMP) established by the U.S. FDA, the QC, QA, and validation groups have the specific responsibility for making sure that all aspects of a manufacturing process conform to the regulations.

Quality control employees sample and assay both the raw materials and the product during every phase of its manufacture. Quality assurance involves setting up and checking the systems of standard operating procedures and documentation that ensure product quality. Much broader than quality control, quality assurance focuses on the overall system of manufacturing.

Quality control laboratory technicians usually require college degrees (AAS or BS) in either chemistry or microbiology. More senior positions can require an MS or PhD degree. Entry-level QC technician positions are a common entry point into the industry for BS graduates. Quality assurance staff generally must have extensive prior experience in the pharmaceutical industry.

Validation

Validation proves that a standard operating procedure will consistently produce product to described specifications when carried out exactly, with specified equipment. The operation of every part of a plant has to be validated: manufacturing equipment, utilities, and even the computer data-processing systems used to record and document all aspects of production. If the manufacturing process is to be changed, or a new product or process introduced, all steps and parts of the new process have to be validated. Validation scientists and engineers generally need extensive experience in the industry. They must be thoroughly familiar with the FDA regulations and how they are implemented. Thus, there are typically few entry-level positions (i.e., those not requiring prior work experience) in these groups.

Other Divisions

Scientific and technical staff within a pharmaceutical or biomanufacturing operation may also work in other divisions. Examples of these other divisions are listed below.

Regulatory affairs

Keeping up with regulatory issues that could affect the company (this is outer-directed, as opposed to the inner-directed activities of QA/validation).

Information Technology

Setting up, managing and maintaining electronic documentation systems.

Technical Support

Providing expert insights to production staff regarding details of the product or process; troubleshooting problems with the process and/or work on introducing new process.

The pharmaceutical and biomanufacturing industries also need scientific and technical employees in the post-manufacturing stages (such as trained sales staff, etc.). However, these divisions are not covered within the scope of this survey.

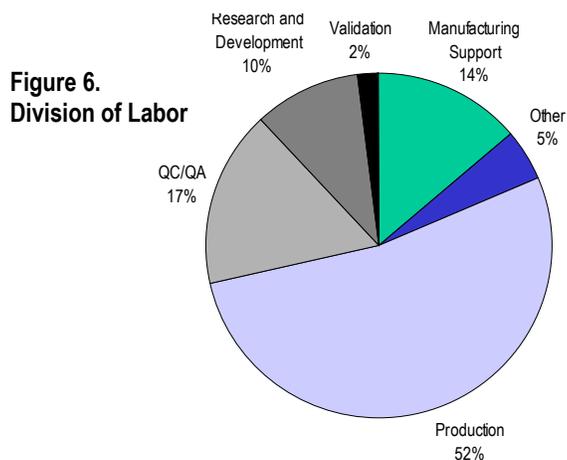
Typical job descriptions for the industry are in Appendix A.



Profile of the Biomanufacturing Workforce

Division of Labor

The overall division of labor in the biomanufacturing and pharmaceutical facilities surveyed is shown in the figure. Company divisions are as described in the previous section. The largest number of workers is in production.



Educational Profiles

The educational needs of each segment of the workforce differ, as previously indicated. The figures that follow depict the current educational makeup of each group.

Figure 7. Profile of the Workforce

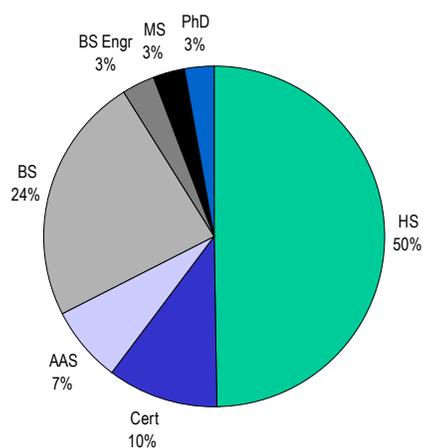
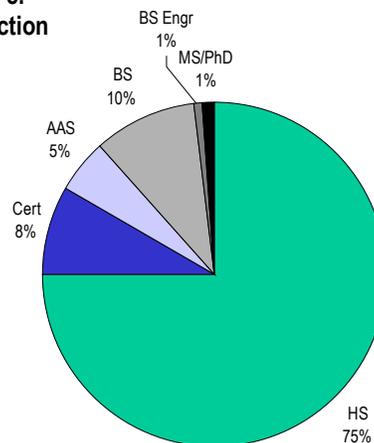


Figure 8. Production



Educational Profiles continued

Figure 9. QC/QA

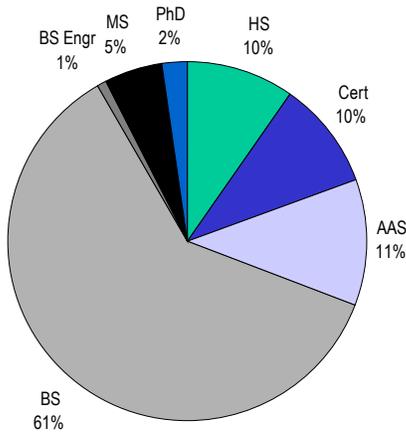


Figure 10. Manufacturing Support

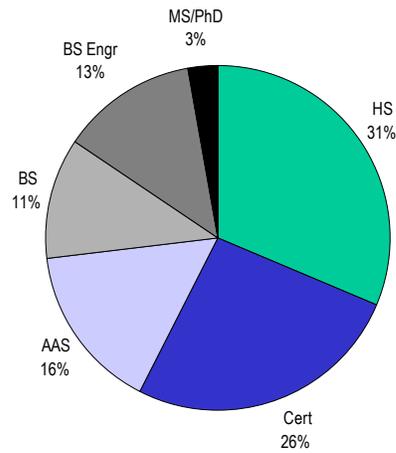


Figure 11. Research and Development

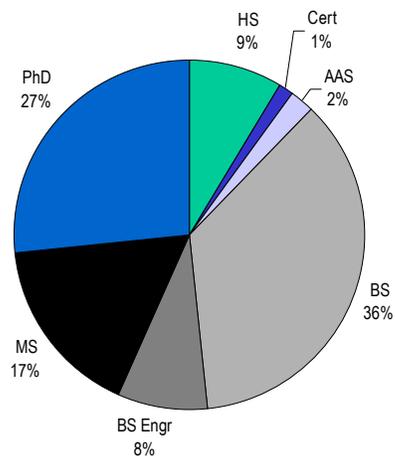
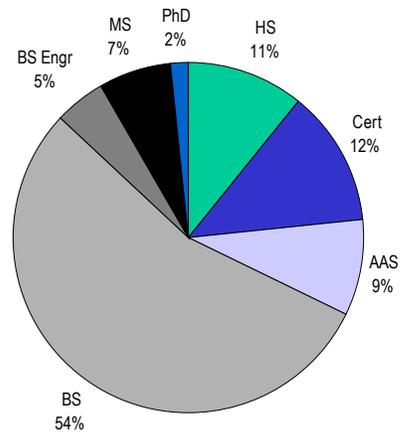


Figure 12. Validation



About 50% of all employees work in production divisions. Employees with HS diplomas, certificates, or AAS degrees make up 67% of the total workforce. BS graduates make up 27%, and those with graduate degrees comprise 6%.



Recruitment and Hiring Practices

In the discussion that follows, and elsewhere in this report, the term “entry-level position” is used. We define such a position as one for which companies are willing to hire someone with appropriate education, but no prior work experience in the *pharmaceutical* industry.

Virtually all of the companies we interviewed have difficulty finding qualified applicants for such entry-level positions. Many applicants lack the necessary combination of education, basic employability skills, and prior work experience in other industries that could provide some transferable skills. Job applicants for higher-level positions that specifically require prior pharmaceutical industry experience are in short supply in North Carolina, and companies are routinely hiring each other’s employees.

Pharmaceutical Industry Experience

Companies value prior experience in the industry for all types of jobs. Many respondents said experience in the industry supersedes educational achievement as a qualification for most positions in their company. This is chiefly because the pharmaceutical industry is highly regulated by the FDA. As we will discuss in more detail later in this report, the Good Manufacturing Practices (GMP) mandated by the FDA pervade every aspect of manufacturing. Implementing these practices requires behaviors learned only after living them day by day in a GMP environment. Training times for new hires are half as long, on average, if they have prior pharmaceutical industry experience. Most of this difference is due to GMP experience, not specific technical experience.

Common Deficiencies in Applicants

There is almost unanimous concern about the poor literacy and math skills of high school graduates. Many companies are concerned about this not only in job applicants but also in their incumbent workforce. Virtually no one hires graduates for technical positions straight out of high school. This is not only because they may lack basic skills, but also because they lack maturity. For positions that may nominally require only a high school education, employers typically look for something more: a year of college or a certificate, or *BioWork*, and/or military experience or other work experience.

Oral and written communication skills as well as math, computer, and problem-solving skills are especially lacking in high school, and in two-year and four-year degree applicants. While many students are computer-literate, they often lack proficiency with basic office software.

Survey respondents typically see Bachelor of Science graduates as lacking proficiency in basic lab skills, and most seem to have insufficient hands-on experience with analytical instrumentation. Thus, they require significant training time to be able to operate independently in industrial laboratories.

Across the board, graduates at all levels are:

- Unaware of how the pharmaceutical industry works, so they do not understand how what they do on the job can affect other aspects of the manufacturing process;
- Unaware of the constraints required in working in a regulated environment;
- Often lacking in problem-solving skills;
- Often unrealistic in their expectations concerning pay or job demands;
- Lacking in interpersonal/team skills and project-management skills.

All of these issues decrease the employability of new graduates and increase their training time on the job if they are hired. In contrast, virtually all companies mentioned seek out military personnel because of their work ethic, team orientation, and discipline. Many also have relevant general industrial skills.

Other Recruitment Constraints

Shift work is a major issue, because almost all the plants operate 24 hours a day, 7 days a week. All companies noted that shift work is undesirable to many applicants. This is a problem that is most relevant to the process technician population, though some employees in other divisions may also have to work shifts. Applicants with prior work experience in other kinds of manufacturing that require shift work have an advantage.

Location (i.e., commuting time) is another issue. Some companies noted that most employees — especially below the BS degree level — are typically recruited from within a 30-mile radius. Companies prefer to recruit locally because this enhances stability of employees. However, companies also recruit nationally, especially for higher-level positions requiring prior industry experience or advanced degrees.

Lack of awareness of careers in pharmaceutical manufacturing or biomanufacturing may prevent many students from considering and seeking adequate preparation for these jobs.

Hiring Process Technicians

Process technicians are the largest group of employees in the manufacturing industry. However, because of the shift work issue and because of the education and experience requirements, few applicants are deemed suitable.

Discussions with company representatives indicate that an ideal candidate for this position might have an AAS degree from a program such as the Wake Technical Community College Pharmaceutical Manufacturing program plus a co-op or internship in the pharmaceutical industry. High school graduates who have military experience or 2 to 3 years of manufacturing experience that entails some transferable skills (e.g., mechanical, chemical mixing, food production), and who have completed the *BioWork* course, also could be good candidates.

The majority of the companies prefer not to hire persons with BS degrees for process technician positions, since they often become dissatisfied with what they may view as menial or routine tasks, have work and pay expectations that exceed reality for process technicians, and do not stay long in the job. However, at companies that employ the most advanced new technology in manufacturing, or that have a multiplicity of products, or a frequent need to manufacture new products, BS graduates may sometimes be hired as process technicians. This work experience provides them with a production background that is valuable when they are transferred into more research-oriented positions in the company.

There is a general desire to increase the proportion of the process technician population that has an AAS degree. Some companies that have been in North Carolina for many years originally hired only high school graduates to establish their workforce. With new demands on technicians in today's workplace, these companies often seek to increase the overall educational level of their process technician group. In other cases, some newer companies that originally started with a large proportion of BS graduates among their technicians seek to decrease that proportion and hire more AAS-degreed technicians.

Hiring for QC/QA/Validation Positions

Entry-level positions (typically laboratory technicians) are filled in three ways:

1. From within: some companies promote process technicians into these positions. The advantage is that they already are familiar with the company's GMP procedures and operations. Moreover, many process technicians are required to perform some in-process lab assays and so are already familiar with the lab techniques.
2. From AAS degree programs.
3. From BS degree programs.

Some companies prefer applicants with AAS degrees, while others prefer BS degrees. Some respondents note that employees with AAS degrees can't be promoted beyond a certain level without obtaining a BS degree.

Applicants with experience in GMP environment are ideal. Nonetheless, a number of companies will hire new graduates for entry-level QC lab tech positions. Higher-level positions in QC and most positions in QA and validation require prior pharmaceutical industry experience.

Hiring for Positions in Manufacturing Support/Engineering

In these areas, there are several types of positions differing in specific skill requirements and level of education, but in general, all personnel in these areas need an understanding of GMP and the manufacturing technologies characteristic of pharmaceutical operations. Following are some typical hiring profiles for employees in this category.

Maintenance Technicians/Mechanics Facilities Operation and Maintenance Technicians and Mechanics: Are generally high school or AAS graduates, or hold certificates in various types of industrial technology. They are usually hired as already competent in their various trades (e.g., HVAC or electrical work).

- Computer System Technicians: Often do not have degrees, many are former military personnel. They acquire skills — often informally — beyond their formal education.
- Instrumentation and Calibration Technicians: Experienced people are hard to find for entry-level jobs. Most candidates lack instrumentation experience, knowledge of measurement principles and how electrical systems work. In general, these kinds of technicians are trained in-house, either by experienced staff or using commercially available programs.

Engineers

The greatest training deficiencies in new engineering graduates that survey respondents noted were lack of experience or knowledge of GMP and other pharmaceutical topics such as sanitary engineering design, process control technology, bioprocessing equipment design, and facility design. Companies prefer to hire graduates who have co-op experience in the industry. For senior engineers, virtually all companies recruit nationally. Work experience is required, preferably in the pharmaceutical industry.

Recruiting from Education/Training Programs

Community colleges

Of the companies that commented on recruiting from specific community colleges, about half recruit from Wake Technical Community College's Pharmaceutical Manufacturing Technology Program and some also recruit from relevant AAS programs at other colleges. A third of the respondents recruit from the *BioWork* program at various colleges. Some companies, in collaboration with their local colleges, have in-house *BioWork* training programs to train new hires and/or incumbent employees. Several companies reported recruiting from certificate programs, typically in industrial technology areas.

Four-year degree programs

Of the companies that commented on recruiting employees from four-year college and university programs, two thirds recruit from North Carolina State University, half recruit from UNC-Chapel Hill, and about a quarter recruit from NC A&T, Duke, and Campbell University. Several other institutions were also mentioned.

Conclusion

Interview comments indicate that while many educational programs provide at least part of the requisite background for new employees in pharmaceutical or biopharmaceutical manufacturing, none provide the complete package. This, together with the other observations noted above, make it apparent that there is a strong need to establish comprehensive, targeted training programs to support future growth in the biomanufacturing and pharmaceutical industries in North Carolina.

It is difficult to find qualified applicants for pharmaceutical manufacturing and biomanufacturing positions. New graduates generally lack knowledge about the industry as well as basic skills; and are at a disadvantage in competing with applicants who have prior experience in the industry.



Knowledge and Skills

In the pages that follow, we will describe the array of knowledge and skill that employees in biomanufacturing and pharmaceutical manufacturing need. Some of this knowledge base is commonly taught in colleges and universities. Commercial training providers that serve the industry teach other parts of the knowledge base. Those topics that are not covered in either way are difficult to access outside the industry. One of the challenges in preparing the workforce will be to bring materials from all these sources together to develop training programs at all the different educational levels as appropriate.

The list that follows is a generally complete description of all the fields and topics that are the foundation for work in the manufacturing side of the pharmaceutical industry. Later in this section, we will discuss subsets of this list that are required in specific manufacturing divisions.

Knowledge and Skill Base for Biomanufacturing and Pharmaceutical Manufacturing

General Knowledge Base

Biology	
<ul style="list-style-type: none"> General biology Microbiology Virology Immunology Cell biology Biochemistry 	<ul style="list-style-type: none"> Protein chemistry Molecular genetics Environmental science Occupational health Toxicology
Chemistry	
<ul style="list-style-type: none"> General chemistry Inorganic chemistry Organic chemistry 	<ul style="list-style-type: none"> Analytical chemistry Physical chemistry Pharmaceutical chemistry
Mathematics	
<ul style="list-style-type: none"> Basic lab math Calculus Statistics 	<ul style="list-style-type: none"> Mathematical modeling Trending analysis

Computer Science	
Word processing Spreadsheets Database use/management	Programming Networking/network management
Engineering Curricula	
Mechanical Electrical Chemical	Biochemical Biomedical Materials science
Business Courses/Workshops	
Business/technical writing and Communication Business economics Organizational psychology	Teamwork principles/practices Supervisory skills Project management

Industrial Knowledge and Skills

Regulatory Compliance	
GMP principles and procedures GLP principles and procedures GCP principles and procedures QA principles and procedures SOP writing Validation methodology Validation study design	Industrial safety practices Laboratory safety practices Safety audits OSHA regulations Environmental regulations — waste disposal Environmental health and safety
Maintenance and Engineering	
Facility design Facility commissioning and qualification Electrical systems Mechanical systems HVAC	Pipefitting Power distribution Instrumentation Utility systems Process equipment maintenance
Instrumentation and Process Control	
Measurement of process variables Instrumentation calibration Process control system operation	Process control system tuning Process control system design/ programming Metrology

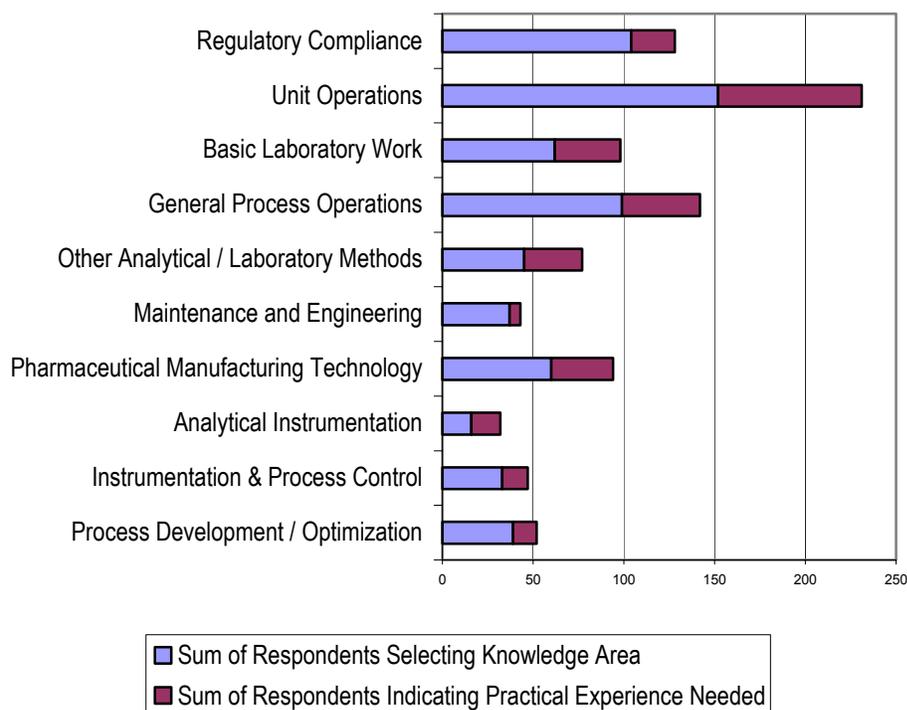
General Process Operation	
<ul style="list-style-type: none"> P&IDs Equipment commissioning, qualification Common pumps, piping, valves, tanks Solids handling equipment CIP & SIP systems Clean-out-of-place and sterilize-out-of-place operations 	<ul style="list-style-type: none"> Heat exchangers, evaporators, condensers Chemical materials handling, transport, storage Biological materials handling, transport, storage Simple mixing and dosing operations General equipment inspection, monitoring
Unit Operations	
<ul style="list-style-type: none"> Batch chemical reaction operations Continuous chemical reaction operations Distillation/stripping Growth media prep for mammalian cells Growth media prep for microbial cells Bioreactor operation for mammalian cell cultures Bioreactor operation microbial cell cultures Bioreactor operation for other types of cultures Cell disruption Centrifugation Depth filtration 	<ul style="list-style-type: none"> Membrane filtration (micro/ultra/nano/RO) Diafiltration Chromatography — affinity Chromatography — ion-exchange Chromatography — hydrophobic-interaction Chromatography — size-exclusion Liquid-liquid extraction Precipitation Crystallization Lyophilization Granulation Pasteurization/flow-through sterilization Immobilized enzyme technology
Pharmaceutical Manufacturing Technology	
<ul style="list-style-type: none"> Solid dose forms preparation Aerosol formulation Injectables formulation Filling Sterile filling 	<ul style="list-style-type: none"> Other aseptic operations Work in cleanrooms Working in laminar flow hoods Isolation technology
Process Development/Optimization	
<ul style="list-style-type: none"> Process design Equipment selection/sizing/design Scale-up principles Raw materials selection/specifications 	<ul style="list-style-type: none"> Material and energy balances Mass transfer modeling/calculations CAD

Basic Laboratory Work	
Glassware selection/use/cleaning Making solutions/dilutions Measuring pH/titration Basic equipment calibration Colorimetric assays — manual Colorimetric assays — automated Microscopy — basic	Microscopy — phase contrast Microbiological culture methods Mammalian cell culture methods Viral culture methods Sampling technique Sample labeling/handling/storage
Analytical Instrumentation	
UV/visible spectrophotometry Fluorescence spectroscopy Infrared spectroscopy NMR spectrometry Mass spectrometry	Atomic absorption spectroscopy Gas chromatography HPLC Refractometry Polarimetry
Other Analytical/Laboratory Methods	
Dry weight determinations Dissolution assays Flame tests Environmental monitoring methods Water quality monitoring Microbial identification methods Toxicology assays Laboratory animal care RIA/ELISA assays	Other immunoassay methods Enzyme assays PCR Electrophoresis Capillary electrophoresis Chromatography, standard FPLC TLC Viral growth/purification/assays

Knowledge and Skills Required for Different Manufacturing Divisions

Technical managers were asked to indicate training needs for their current employees. The bar graphs that follow summarize the number of technical managers responding in each division that selected a topic from the industrial knowledge and skills portions of the list above. The graphs depict these topics grouped in broad categories. The managers were asked to prioritize their selections, and those that received higher priority were given extra weight in scoring the responses. Below each graph is a list of the most often selected specific topics in each category.

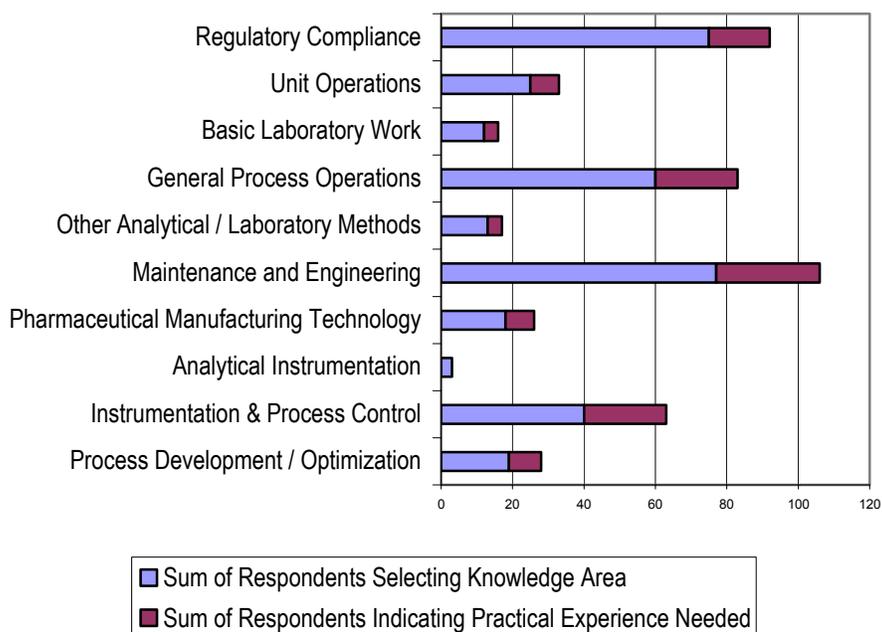
Figure 13. Production Division



Production: Priority Topics

1. Unit Operations
 - a. Membrane filtration and diafiltration
 - b. Chromatography methods
 - c. Growth media preparation
 - d. Bioreactor operation
2. Regulatory Compliance
 - a. GMP principles and procedures
 - b. SOP writing
 - c. Validation methodology
 - d. Industrial safety practices
 - e. Safety audits
3. General Process Operations
 - a. CIP & SIP systems
 - b. Chemical material handling, transport, storage
 - c. General equipment inspection and monitoring
 - d. Common pumps, piping, valves, and tanks
 - e. Clean-out-of-place and sterilize-out-of-place operations
4. Basic Laboratory Work
 - a. Measuring pH/titration
 - b. Making solutions/dilutions
 - c. Sampling technique
 - d. Microscopy – basic
 - e. Basic equipment calibration
5. Pharmaceutical Manufacturing Technology
 - a. Work in cleanrooms
 - b. Other aseptic operations
 - c. Filling/sterile filling
 - d. Working in laminar flow hoods

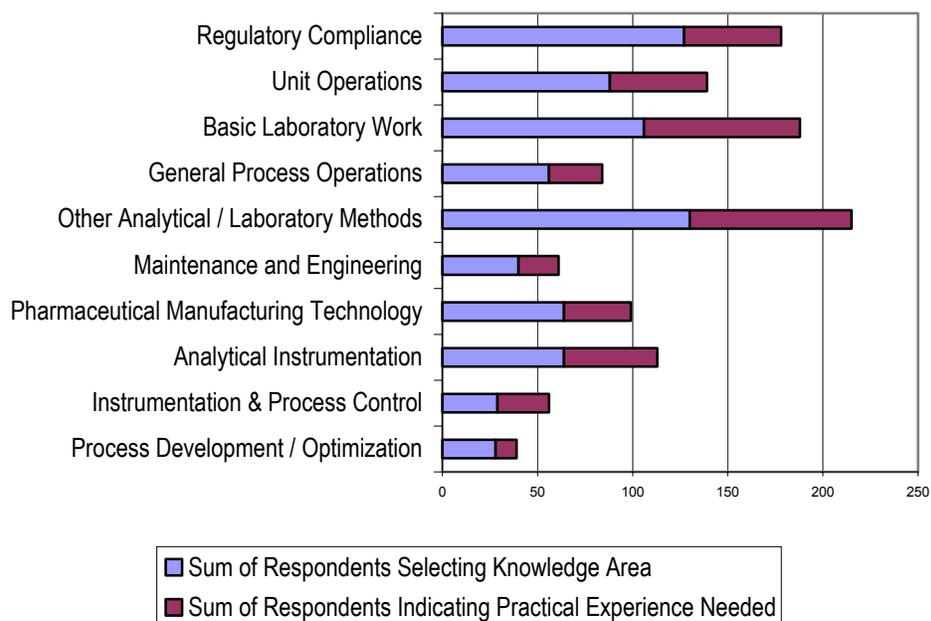
Figure 14. Manufacturing Support Division



Manufacturing Support: Priority Topics

1. Maintenance and Engineering
 - a. Instrumentation
 - b. Utility systems
 - c. Mechanical systems
 - d. Electrical systems
 - e. HVAC
2. Regulatory Compliance
 - a. GMP principles and procedures
 - b. Environmental regulations – waste disposal
 - c. Environmental health and safety
 - d. OSHA regulations
 - e. Industrial safety practices
3. General Process Operations
 - a. P&IDs
 - b. Common pumps, piping, valves, and tanks
 - c. Equipment commissioning and qualification
 - d. Heat exchangers, evaporators and condensers
 - e. General equipment inspection and monitoring
4. Instrumentation & Process Control
 - a. Process control system operation
 - b. Process control system tuning
 - c. Instrumentation calibration
 - d. Process control system design/programming
 - e. Measurement of process variables
5. Unit Operations
 - a. Centrifugation
 - b. Membrane filtration
 - c. Distillation/stripping
 - d. Depth filtration
 - e. Precipitation

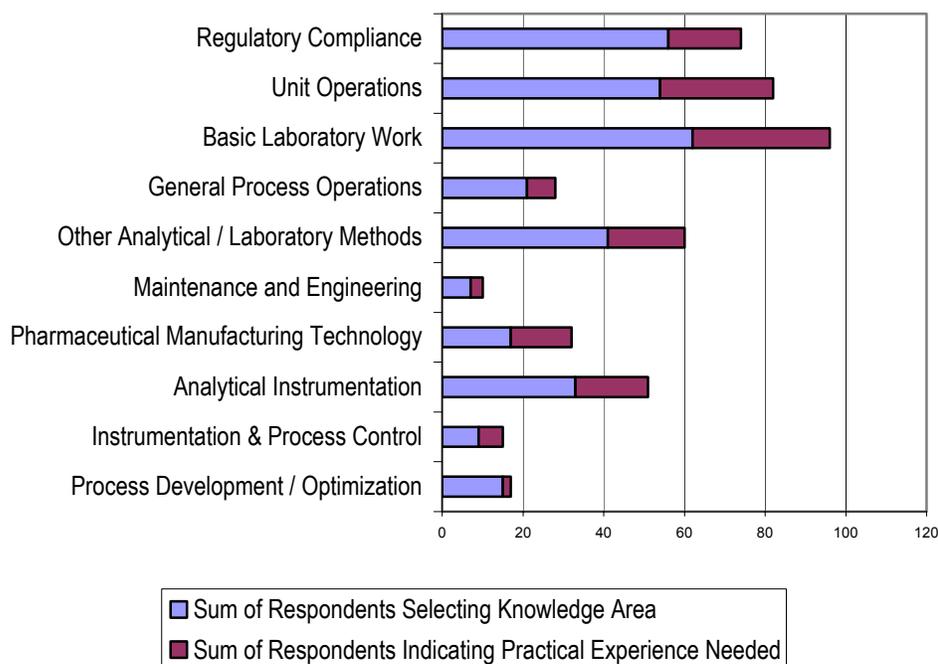
Figure 15. QC/QA Division



QC/QA: Priority Topics

1. Analytical / Laboratory Methods
 - a. Water quality monitoring
 - b. Microbial identification methods
 - c. Environmental monitoring methods
 - d. RIA/ELISA assays
 - e. Chromatography
2. Regulatory Compliance
 - a. GMP principles and procedures
 - b. Validation methodology
 - c. QA principles and procedures
 - d. Validation study design
 - e. SOP writing
3. Basic Laboratory Work
 - a. Sampling technique
 - b. Microbiological culture methods
 - c. Colorimetric assays – automated
 - d. Sample labeling/handling/storage
 - e. Basic equipment calibration
4. Pharmaceutical Manufacturing Technology
 - a. Working in laminar flow hoods
 - b. Work in clean rooms
 - c. Sterile filling
 - d. Other aseptic operations

Figure 16. Research and Development Division



Research and Development: Priority Topics

1. Basic Laboratory Work
 - a. Basic equipment calibration
 - b. Colorimetric assays – manual
 - c. Making solutions/dilutions
 - d. Measuring pH/titration
 - e. Sampling technique
2. Regulatory Compliance
 - a. SOP writing
 - b. Laboratory safety practices
 - c. Validation methodology
 - d. QA principles and procedures
3. Unit Operations
 - a. Centrifugation
 - b. Chromatography—all types
4. Analytical / Laboratory Methods
 - a. RIA/ELISA assays
 - b. Enzyme assays
 - c. Chromatography, standard
 - d. Electrophoresis
5. Analytical Instrumentation
 - a. HPLC
 - b. UV/visible spectrophotometry
 - c. Fluorescence spectroscopy
 - d. Infrared spectroscopy

More detailed profiles for specific types of entry-level jobs are in Appendix B.



Training Needs

Given the constraints on finding qualified applicants as described in a previous section, it appears essential that North Carolina grow a group of new workers to support expansions projected for the biomanufacturing and pharmaceutical industry. New employee candidates must be sufficiently well-qualified to compete with job candidates who have prior experience in these industries. Without net growth in the state's pool of qualified candidates, companies will probably continue to hire employees from each other.

This is emphasized by the responses of site managers of companies in the survey group to the following questions:

“Identify the three strategies you regard as most important for maintaining a capable workforce now.”

“Identify the three strategies you regard as most important to build your workforce to prepare for future change in your operations.”

In both cases, the top three answers chosen by 75% or more of the respondents were:

- Hire people with biomanufacturing experience from within the state.
- Work with educational institutions to improve training/recruitment.
- Continuously train employees on site.

Making New Workers Competitive

What will it take to make new graduates competitive job applicants? Survey respondents agreed that the value they place on prior experience in their industries comes mainly from simply being there—that is, being exposed on a daily basis to a GMP-regulated environment, learning about the overall process of manufacturing and about the demands of employment in the industry.

On average, it takes over 9 months to train new entry-level employees—and only half that if they have prior pharmaceutical industry experience. The majority of site managers estimated that college students should spend 6 months to a year in a GMP-like training environment as part of their educational program.

These observations imply that certificate programs or other short programs like *BioWork* need to operate in a GMP-like manner throughout the semester or year of their duration.

Major Fundamentals

Across all divisions, job functions, and educational levels of workers, survey respondents in interviews time and again spoke of three fundamental factors that successful employees need:

1. Understanding GMP and learning to live it.
2. Understanding the big picture of a manufacturing enterprise and how workers' actions affect the entire process.
3. Understanding effective approaches to problem-solving.

All involve acquiring certain mindsets and/or habits as well as learning technical specifics. All involve learning how to think in certain patterns, and thus are not learned overnight or in one week. Ideally, they should be exercised throughout all teaching.

The importance of these fundamentals and their specific grounding in the manufacturing environment makes it essential that instructors in specialized training programs have industrial background, and survey respondents universally recommended this.

Training Needs for New Entry-level Job Candidates

Following are recommendations that survey interviewees had for training employees of different types.

Process Technicians

The content of the *BioWork* course is a good foundation. It needs to have more hands-on work with both laboratory and process equipment. Many companies emphasized the importance of having appropriate equipment and facilities to implement this at community colleges, both for *BioWork* and AAS degree program training. Training in clean room work is important. (Nearly 9,500 employees work in North Carolina facilities that carry out aseptic manufacturing processes.) This type of training — like GMP training — requires time to inculcate appropriate behaviors.

Quality Control Technicians

New BS graduates need more practical lab work in their degree programs to develop basic skills. They need at least a general introduction to manufacturing technology, and a thorough understanding of quality assurance and validation principles.

Facility Maintenance Technicians/Mechanics

These workers also need clean room training in facilities that do aseptic manufacturing. They need an acquaintance with utilities and equipment specific to pharmaceutical and/or biomanufacturing and the opportunity to get hands-on experience with such equipment.

Instrumentation/Calibration Technicians

These technicians often need courses in metrology, and GAMP or Good Automated Manufacturing Practice in addition to general GMP training.

Engineers

Whether they work as process or facilities engineers, they need to understand principles of validation, facility design, and the design and operation of process control systems and instrumentation. Process engineers need to know how to manage change control and new projects, as well as have an understanding of biomanufacturing unit operations and process scale-up principles. Ideally, engineering students should spend considerable time with hands-on work in a pilot-scale manufacturing environment.

Training Needs for Incumbent Employees

Company respondents indicated that their needs for training incumbent employees are just as important as their needs for better-qualified new hires.

Process Technicians

Many respondents expressed a need for experienced process technicians to learn the basic science behind the processes they have learned to operate—at least mechanically—on the job. This kind of background can be provided in a laboratory or classroom environment.

Mid- to Senior-Level Scientists and Engineers

These employees need short courses in a broad spectrum of topics ranging from new manufacturing technologies to the implementation of various aspects of Good Manufacturing Practices. Most respondents would like to see nationally recognized providers of such training for the pharmaceutical and biomanufacturing industries brought to North Carolina on a frequent basis. Having workshops from these providers locally would save time and travel costs.

Companies were also interested in the idea of a forum for seeing new equipment and technologies in operation (particularly in areas such as separation technologies, mammalian cell culture technologies, robotics, and other areas where the technology is rapidly evolving).

Availability of Training

It is often hard for manufacturing operations to send more than a few employees, especially process technicians, away for training at one time—except during shutdown operations. Respondents also noted that it can be difficult for employees to be away from home for long periods. There was interest in having training available near plant sites; and with flexible scheduling. Some respondents suggested having a mobile training lab with process equipment on board; and/or mobile instructors that could visit manufacturing facilities or local colleges.

Asked about their preferred means of training delivery, technical managers overwhelmingly indicated hands-on or classroom instruction; only 10% of responses were for on-line instruction.

Training Topics

The survey yielded a wealth of additional data about specific technical topics, areas of specialization, and training ideas from respondents; as well as other information. The Center will make this detailed information available to educators interested in planning specialized training programs, courses, or centers.

In preparing a workforce for biomanufacturing and pharmaceutical manufacturing, the choice of *what* is taught will be important; but *how* it is taught can be even more important.



Appendix A. Job Descriptions: Examples

Production Positions

HS Diploma or Two-year Degree Positions

Process Technician. Responsible for the commercial-scale manufacture of the active pharmaceutical ingredient; sets controls, operates and maintains production and separation equipment; weighs, measures and checks raw materials; feeds raw materials into manufacturing equipment; monitors the production and separation equipment and process; ensures that manufactured batches contain the proper ingredients and quantities; maintains records and clean production areas to comply with regulatory requirements, good manufacturing practices, and standard operating procedures; and may also assist with in-process testing to make sure batches meet product specifications.

Manufacturing Prep Process Technician. Responsible for washing, drying and sterilizing glassware; maintains glass-washing facilities and performs routine maintenance on glass-washing equipment; weighs, measures and checks raw materials used in the manufacturing process; prepares media, reagents and buffers; maintains records and cleans the glass-washing and preparation areas to comply with regulatory requirements, good manufacturing practices, and standard operating procedures.

Formulation/Fill Technician. Responsible for preparing the finished product from the purified active pharmaceutical ingredient; operates and maintains equipment such as sterile filling machines; weighs, measures and checks to ensure the manufactured batches contain the proper ingredients and quantities; maintains records and cleans production areas to comply with regulatory requirements, good manufacturing practices, and standard operating procedures.

Packaging Technician. Uses manual and/or automated packaging systems to label, inspect and package the finished product; enters data and imprints computer-generated labels; maintains records and maintains the packaging area to comply with regulatory requirements, good manufacturing practices and standard operating procedures; and may perform initial checks of completed documents for completeness and accuracy.

BS Engineering Positions

Production or Process Engineer in Manufacturing. Designs, develops and implements manufacturing methods and equipment and maintains the day-to-day operation of a manufacturing process, including taking corrective action when required; works directly with operators to ensure that a particular product is manufactured, formulated and packaged according to specifications; works on implementing methods for manufacturing new products; reviews current methods for cost effectiveness and makes recommendations for process improvements for existing product lines; prepares reports, feasibility studies and cost analyses of processes; and maintains records and reporting systems for the coordination of manufacturing operations.

Process Engineer in Process Development. Responsible for the design, scale-up and validation of new processes from laboratory through pilot plant to large-scale manufacturing; participates in the design and start up of new manufacturing facilities, instruments and equipment; optimizes existing processes by developing and recommending new process formulas and technologies to achieve cost effectiveness and product quality.

QC/QA Positions

Two-year Degree Positions

Quality Control Assistant. Conducts routine and non-routine analysis of raw materials, in-process samples and finished formulations according to Standard Operating Procedures (SOPs); calibrates and maintains chemistry and microbiology lab equipment; compiles and analyzes data for documentation of test procedures and reports abnormalities.

Quality Assurance Assistant. Responsible for coordinating all activities related to providing the required documentation and implementing related documentation systems; coordinates the review and revision of procedures, specifications and forms; assists in compiling regulatory filing documents and maintaining computerized files to support all documentation systems.

BS Degree Positions

Quality Control Associate. Writes, revises and updates SOPs, quality control lab protocols and procedures; may perform special projects on analytical and instrument problem-solving; reviews data obtained by QC Assistant for compliance to specifications, GMP and regulatory requirements and reports abnormalities.

Process Quality Inspector. Performs a wide variety of inspections, checks, tests and sampling procedures for the manufacturing process; performs in-process inspection and documents results; monitors critical equipment and instrumentation; writes and updates inspection procedures and checklists as necessary

QA Auditor. Performs audits of production and quality control, ensuring compliance to in-house specification, standards, and regulatory requirements; ensures all documentation manuals are accurate, current and consistent with good manufacturing practices and regulatory requirements.

Quality Assurance Associate. Writes and edits Standard Operating Procedures, laboratory procedures, manuals and other documents; integrates various sources of information into a uniform style and language for regulatory compliance; assists in documentation for instructional, descriptive, reference and/or informational purposes.

Quality Control Engineer. Develops, revises and maintains standards for converting raw materials into products; designs and implements methods and procedures for inspecting, testing and evaluating the precision and accuracy of the manufacturing process; monitors the manufacture of a product to ensure that it conforms to in-house specifications, good manufacturing practices and regulatory requirements; prepares SOPs for testing procedures.

Validation Specialist. At the entry level, responsible for executing test validation procedures/protocols to demonstrate facility, equipment and process consistency and GMP compliance to ensure a product is manufactured in accordance with appropriate regulatory requirements and in-house standards; compiles and analyzes validation data; prepares reports and makes recommendations for changes and improvements; maintains appropriate validation documents.

Manufacturing Support

HS Diploma or Two-year Degree Positions

Instrumentation/Calibration Technician. Responsible for performing maintenance, testing, troubleshooting, calibration, and repair on a variety of circuits, components, analytical equipment, and instrumentation; calibrates instrumentation; performs validation studies; analyzes results and may develop test specification and electrical schematics; maintains logs, required documentation and spare parts inventories and may prepare technical reports with recommendations for solutions to technical problems.

Manufacturing Support Technician. Solves production problems caused by machinery in a specific process; determines why a particular machine is not performing as designed; maintains computer systems, electrical systems, heating and air conditioning systems, and other plant utilities.

Environmental Technician. Performs routine environmental monitoring tests; compiles and analyzes data; documents test procedures and results and reports abnormalities; carries out waste-treatment operations; assists in compiling regulatory filing documents.

BS Degree Positions

Maintenance Engineer. Manages the design, planning construction and maintenance of buildings and other facilities; plans, schedules and inspects all work on building, including preventive maintenance, repairs to air handlers, steam boilers, air conditioning, pumps and pipes, compressors and refrigeration.

Process Control Engineer. Designs and installs instrumentation and computer programs for automated monitoring and control of certain processes; establishes operating equipment specifications and improves manufacturing techniques; works closely with process-control technicians and equipment operators to get feedback on the operations of each process and determine how to avoid shut-downs.

Environmental Engineer. Develops techniques to reduce and recover usable materials from waste created during manufacture of a product; designs waste storage and treatment facilities, as well as pollution-control strategies for plant operations; may be responsible for monitoring all systems in a facility for compliance with government environmental regulations and preparing required documents.

Research and Development

Two-year or BS Degree Positions

Research Associate. Seeks out new and more efficient ways of using and producing existing products; explores new products or special variations of existing products and determines their usefulness and applicability; may work with marketing to ensure that a product will meet the needs of customers and with patent attorneys to determine if a new product or process is patentable.

Research Assistant. Performs laboratory experiments and tests according to GLP, under the direction of the Research Associate; makes detailed observations, analyzes data and interprets results; maintains laboratory equipment and keeps records according to regulatory requirements.

Other

Regulatory Affairs Specialist. Coordinates and prepares document packages for submission to regulatory agencies, internal audits and inspections; compiles all materials required for submissions, license renewals and annual registrations.

Customer Support Specialist. Responsible for ensuring delivery of the product in accordance with customer requirements and manufacturing capabilities; may serve as a contact for customers on technical issues; and responds to customer product inquiries.



Appendix B. Entry-level Job Profiles

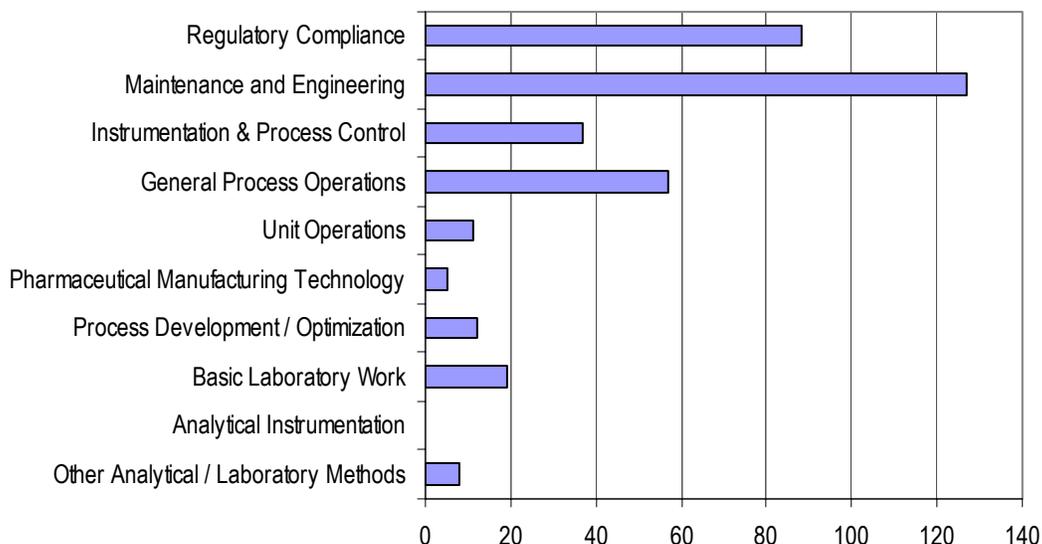
This section presents profiles of some of the most common entry-level positions. Bar graphs summarize supervisors' selections of industrial topics in which training is most desirable in preparing candidates for these positions. Respondents were asked to prioritize their choices and priority choices were given extra weight in scoring the responses.

Manufacturing Support Technician

Starting Salary Range: \$27,500-\$38,500

Education Level: AAS-BS

The manufacturing support technician is a key entry-level position in biomanufacturing. An employee in this position solves production problems caused by machinery in a specific process; determines why a particular machine is not performing as designed; and maintains computer systems, electrical systems, heating and air conditioning systems, and other plant utilities. Eleven surveys outlined qualifications for this job.

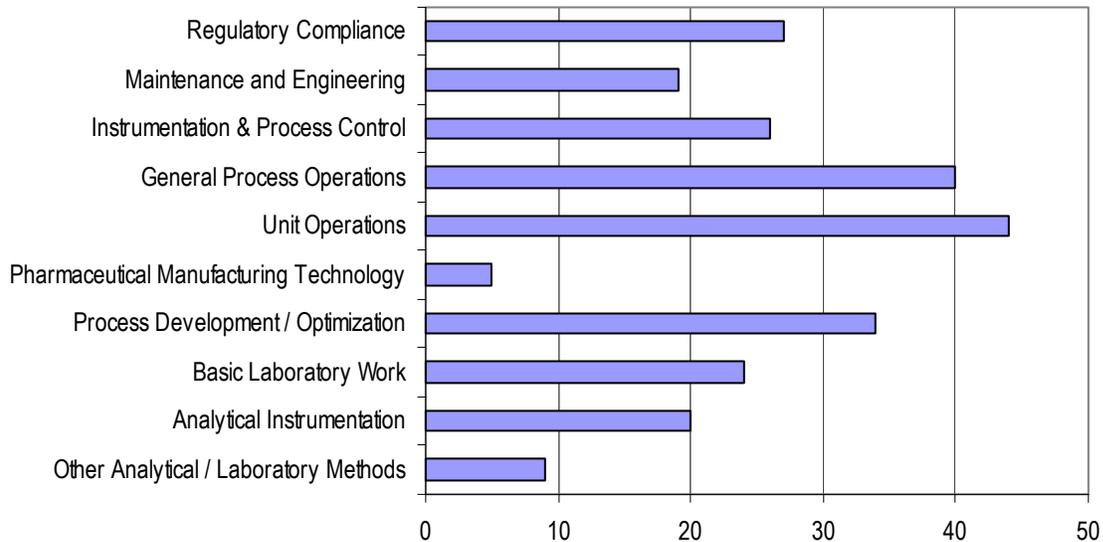


Data for the following job titles are included in this category: Manufacturing Support Technician – Engineering Technician, Maintenance Mechanic, Maintenance Tech, Calibration Specialist I, Electronics & Instrumentation Tech I, Instrumentation Technician, Mechanic, and Mechanical Maintenance Tech I.

Process Engineer

Education Level: BS

The process engineer is responsible for the design, scale up, and validation of new processes from laboratory through pilot plant to large-scale manufacturing; participates in the design and start up of new manufacturing facilities, instruments, and equipment; and optimizes existing processes by developing and recommending new process procedures and technologies to achieve cost effectiveness and product quality.



Data for Chemical Engineer also are included in this category.

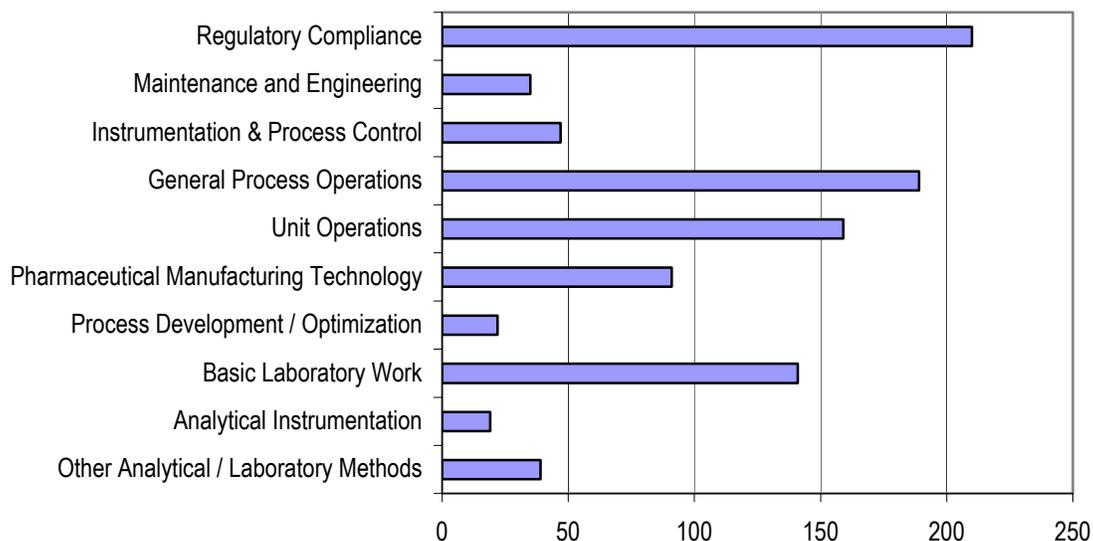
Median starting salary range for all entry-level engineering positions (including positions in facility maintenance, project management, production, and R&D) was \$46,000-\$50,000.

Process Technician

Starting Salary Range: \$22,250-\$30,000

Education Level: High School-AAS

The process technician has a variety of production responsibilities from manufacturing preparation to formulation and filling. The tasks may include setting up controls of production equipment; operating and maintaining equipment; washing, drying and sterilizing glassware; checking, weighing and measuring pharmaceutical ingredients, and packaging finished products. Twenty-seven surveys outlined requirements for this entry-level position.



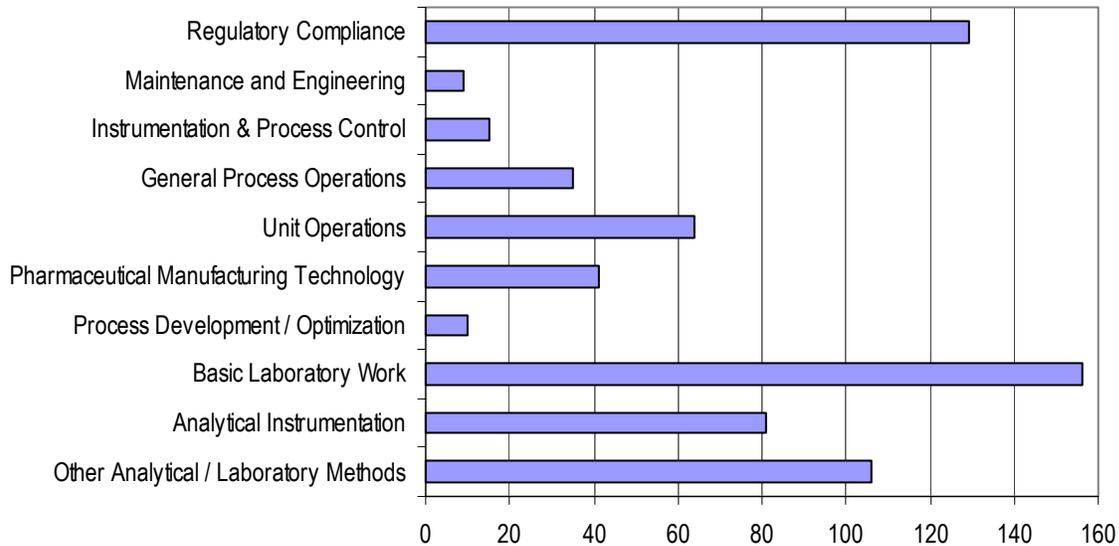
Data for the following job titles are included in this category: Fill Tech I, Formulation Tech I, Formulation Technician, Component Preparation Technician, Enviro/Facility Cleaning, Manufacturing Associate, Packaging Technician I, Chemical Operator, Chemical Technician, Entry-Level Production Operator, Packaging/Manufacturing Operator, Pharmaceutical Operator, Pharmaceutical Processor, Plasma Fractionation Operator, Production Associate, Production Technician, and Vialing Technician.

Quality Assurance Assistant/Associate

Starting Salary Range: \$26,000-\$35,000

Education Required: AAS-BS

An employee in this position coordinates all activities related to providing the required documentation and for implementing related documentation systems; coordinates the review and revision of procedures, specifications and forms; assists in compiling regulatory filing documents; and maintains computerized files to support all documentation systems.



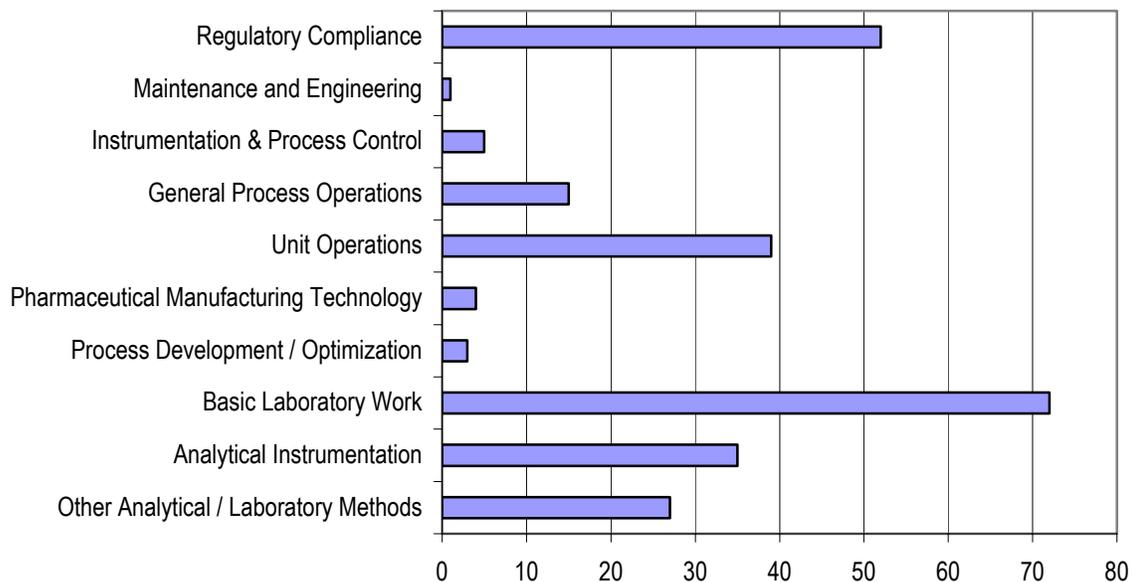
Data for the following job titles are included in this category: Laboratory Analyst, Review Specialist I, Assistant Quality Control Analyst, Chemical Technician, Chemist, Chemistry Technician, Laboratory Technician, Microbiology Technician, and Quality Control Technician.

Research Assistant/Associate

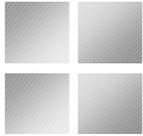
Starting Salary Range: \$26,000-\$50,000

Education Required: BS-PhD

Research assistants and associates perform laboratory experiments and tests according to GLP, seek out new and more efficient ways of using and producing existing products, make detailed observations, analyze data and interpret results, maintain laboratory equipment, and keep records according to regulatory requirements.



Data for the following job titles are included in this category: Laboratory Assistant, Raw Materials Tech, Chemist I, Microbiologist I, and Scientist I.



Appendix C. Bibliography

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Appendix D. Study Description

Data collected about North Carolina biomanufacturing workforce needs were from several sources during October 2002-February 2003:

- Comprehensive surveys of biomanufacturing and selected pharmaceutical companies
- Site visits to North Carolina biomanufacturing and selected pharmaceutical companies
- Meetings with industry representatives and consultants to the biomanufacturing industry

In 1995, Center staff conducted a detailed survey of biomanufacturers and their workforce training needs, published as *Window on the Workplace*. Further in-depth interviews with companies led us to the conclusion that process technicians were the most strategic workforce resource that needed development. In response to this need, the Center's Education and Training program, in collaboration with the community colleges, developed and published the *BioWork* course. In this process, we convened several meetings of industry experts and consulted numerous other sources of information about the industry.

The conclusions in this report, while based principally on the present survey, are informed also by all our prior research.

Site visits were made to nine biomanufacturing companies and to four pharmaceutical-related companies. Those interviewed during visits included human resource managers, site managers, plant managers, engineers, technical and production managers, researchers, quality control/quality assurance directors and validation specialists.