

Mapping Your Future

CAREERS IN BIOMANUFACTURING



AN EDUCATIONAL MODULE FOR GRADES 6-12

NCABRR
North Carolina Association for
BIOMEDICAL RESEARCH

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CAREERS IN BIOMANUFACTURING

**An Educational Module for Grades 6-12
2nd Edition**

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Introduction

This educational module introduces middle and high school students to one of the exciting growth areas in the job marketplace: the bioprocessing industry. As more and more companies employ the tools of biotechnology to create marketable products, they seek workers in all areas of the biomanufacturing process.

From the line operator to the process engineer, opportunities are available for workers at all educational levels. These jobs generally offer higher pay than those in other North Carolina manufacturing industries.

The module is divided into five units. Unit I and Unit II introduce current applications of biotechnology and provide details about the lengthy and highly regulated process of bringing a drug to market. Because many of

the biomanufacturing jobs involve the production of biopharmaceuticals, this unit will help the student understand why employee attributes such as attention to detail are so important. Unit III describes the various jobs in a bioprocessing facility along with the education required for them. Unit IV focuses on career success skills and an overall activity simulating a biomanufacturing company. Unit V provides resources for the first four units.

Your students who want to explore options in biomanufacturing after high school have several pathways they can follow, depending on whether they want to obtain a two- or four-year degree. It is important to emphasize to students that pharmaceutical and biomanufacturing companies rarely hire anyone

straight out of high school. Employers typically look for at least some additional college work, prior employment or military experience.

North Carolina community colleges have been developing innovative biomanufacturing training programs in parallel with the growth of this industry sector. Many community colleges in North Carolina offer certificates and associate degrees in biotechnology, bioprocessing and related programs, such as industrial pharmaceutical technology. Community colleges also offer the BioWork program, which brings together the basics of manufacturing technology and the fundamentals of science — two essentials for competent, entry-level technicians in biotechnology, pharmaceutical and chemical manufacturing.

The 140-hour introductory course is intended for high school graduates, traditional manufacturing workers who have lost jobs or anyone interested in a new line of work. BioWork prepares students for the statewide Process Technician Certification examination, established by the industry. For more information about community college programs related to biotechnology, see www.ncbionetwork.org.

The North Carolina Community College BioNetwork is part of NCBioImpact, a collaboration among industry, the North Carolina Community College System, the University of North Carolina system and the North Carolina Biotechnology Center. NCBioImpact is developing new education and training programs for the biomanufacturing industry. Links to all its member institutions are available at the NCBioImpact website, www.ncbioimpact.org. In addition, check out the North Carolina Biosciences Organization (NCBIO), at ncbioscience.net. NCBIO is North Carolina's state-level affiliate of the national Biotechnology Industry Organization and the trade association for the North Carolina bioscience industry. NCBIO has more than 160 members.

Several four-year colleges and universities statewide have biotechnology-related courses included in most biological science degree programs, and a number offer specialized degrees related to biotechnology. At a variety of UNC system schools, for instance, students can earn a minor, a certificate or a specialization in biotechnology, and several institutions offer or are planning to offer a biotechnology major. In addition, specialized degree programs and facilities

have been established at North Carolina State University and North Carolina Central University. At N.C. State, the Biomanufacturing Training and Education Center (BTEC) simulates a large bioprocessing facility (www.btec.ncsu.edu). At NCCU, the Biomanufacturing Research Institute & Technology Enterprise (BRITE) Center for Excellence provides research laboratories for undergraduates and outstanding scholars conducting research in several areas critical to biotechnology and biomanufacturing (www.nccu.edu/brite).

Students who desire a career in biotechnology research or manufacturing can get a good start with B.S. degrees in biology or biological disciplines, such as microbiology, biochemistry, genetics and molecular biology; in chemistry; or in chemical, biochemical or bioprocess engineering. Higher-level research positions require M.S. or Ph.D. degrees. Unit V has links to websites concerning educational opportunities for your students.

The opportunities for your students in biomanufacturing are many and varied. We hope this educational module will expand their horizons and urge them to consider this dynamic, exciting career path.

Unit I

BIOTECHNOLOGY AND ITS APPLICATIONS





A. What is Biotechnology? ¹

Watch any evening newscast for a full week and you're bound to see at least one story featuring biotechnology in action. For example:

- Medical researchers are using biotechnology to develop drugs that will reduce the chances of organ rejection in transplant recipients.
- Biotechnologists are genetically engineering food crops to be more nutritious, more resistant to pests and better able to grow under difficult conditions.
- DNA testing is used to clear a wrongly convicted man of murder and free him from prison.
- Environmental researchers employ biotechnology to create organisms that can reduce the amount of solid waste in landfills.
- Animal scientists are developing new vaccines to improve the health of livestock, making possible better milk and meat production.

Biotechnology affects so much of our lives — but what exactly is it? In its broadest sense, **biotechnology** is the use of living organisms and biological processes to solve problems or make useful products. If you break “biotechnology” into its root words, you have:

- **bio**, which means “living systems,” and
- **technology**, which means “the use of scientific knowledge and tools to solve problems or make useful products.”



From this point of view, biotechnology is as old as the first domestication of crop plants or fermentations to make wine and beer. Humans began growing crops and raising animals 10,000 years ago to provide a stable supply of food and clothing. We have used the biological processes of microorganisms for 6,000 years to make useful food products, such as bread and cheese, and to preserve dairy products. And now, a wealth of sophisticated biotechniques and processes are helping us create a new roadmap for future scientific discovery.

Nowadays we think of **biotechnology** as a collection of technologies that capitalize on the attributes of cells and put biological molecules, such as DNA and proteins, to work for us. Each living cell is like a tiny manufacturing plant. It takes raw materials (such as food, air and water) and uses them to

make products (such as enzymes, some types of drugs and industrial chemicals). Biotechnology companies use living cells to make products, seeking to duplicate or change the function of a living cell to make it work in a more predictable way. A number of biotech companies concentrate on producing medicines, known as biopharmaceuticals, that are made by biological processes rather than by chemical synthesis. In addition, an entire field of biotechnology exists that uses genetic technology for food and agricultural purposes.

As biotechnology research and development firms mature and move into manufacturing and selling their products, they also become defined not only by the technologies employed 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 affect a variety of established industries — both in research and manufacturing.

A glossary of biotechnology terms is available in Unit V and at www.biotechinstitute.org/go.cfm?do=Page.View&pid=21.

B. Biotechnology Timeline^{2, 3}

B.C.E. (Before the Common Era, also known as B.C.)

8000 – 4000	Humans domesticate crops and livestock. Potatoes first are cultivated for food.
2000	Biotechnology is used for the first time when the Egyptians use yeast to leaven bread and ferment beer. The production of cheese and the fermentation of wine occur in Sumeria, China and Egypt.
500	The Chinese use the first antibiotic: moldy soybean curds for treating boils.

C.E. (Common Era, also known as A.D.)

100	The Chinese use the first insecticide: powdered chrysanthemums.
1797	Edward Jenner inoculates a child with a viral vaccine to protect him from smallpox.
1830	Proteins are discovered.
1857	Louis Pasteur proposes that microbes cause fermentation.
1859	Charles Darwin publishes the theory of evolution by natural selection.
1865	The science of genetics begins with Gregor Mendel's studies (although the significance of his discoveries would not be recognized by the scientific community until the early 1900s).
1868	The existence of DNA is discovered.

1915	Phages, or bacterial viruses, are discovered.
1919	The word “biotechnology” is used in print for the first time.
1927	Hermann Muller discovers that radiation causes defects in chromosomes (mutations).
1944	DNA is proven to carry genetic information.
1953	<i>Nature</i> publishes James Watson and Francis Crick’s manuscript describing the double helical structure of DNA. They later would share the 1962 Nobel Prize in Medicine with Maurice Wilkins for this discovery.
1955	Frederick Sanger determines the amino acid sequence of insulin, making it the first protein to be sequenced.
1958	Sickle cell anemia is shown to occur due to the change of a single amino acid. DNA is made in a test tube for the first time.
1966	The genetic code is cracked, demonstrating that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids. Marshall Nirenberg, Har Gobind Khorana and Robert Holley later would share the 1968 Nobel Prize in Medicine for this discovery.
1969	An enzyme is synthesized <i>in vitro</i> for the first time.
1970	Restriction enzymes that cut and splice genetic material are discovered, opening the way for gene cloning.
1971	The first complete synthesis of a gene occurs.

1975	Georges Köhler and César Milstein develop the technology to produce monoclonal antibodies by fusing an antibody-producing cell with a tumor cell. Monoclonal antibodies have become very valuable tools in medicine for diagnosing and treating diseases.
1977	Genetic engineering is done for the first time, when the first expression of a human gene in bacteria occurs.
1981	The first transgenic animals are produced by transferring genes from other animals into mice.
1983	The polymerase chain reaction (PCR) technique is conceived. PCR, which uses heat and enzymes to make unlimited copies of genes and gene fragments, later becomes a major tool in biotech research and product development worldwide. Kary Mullis later would win the 1993 Nobel Prize in Chemistry for this discovery.
1986	The first recombinant vaccine for humans is produced, for hepatitis B. Interferon, the first anti-cancer drug made through biotechnology, is produced.
1987	The first field tests of genetically modified food plants are approved, for virus-resistant tomatoes.
1990	The Human Genome Project, an international effort to map all the genes in the human body, is launched.
1994	Genetically modified tomatoes are sold for the first time in the United States.
1996	Sequencing of the baker's yeast genome is completed.
1997	An animal is cloned from an adult cell for the first time: a sheep named Dolly, in Scotland.
1998	Human embryonic stem cell lines are established.

2002	A draft version of the complete map of the human genome is published.
2003	<p>The genome of the virus that causes SARS (severe acute respiratory syndrome) is sequenced only three weeks after its discovery.</p> <p>A far more precise version of the human genome — one that is 99.999% accurate — is published.</p>
2004	Bevacizumab (Avastin), a recombinant monoclonal antibody, is the first targeted biological therapy of its kind to receive approval from the U.S. Food and Drug Administration (FDA). Based on a theory proposed in 1971, Avastin targets colon cancer by inhibiting the formation of new blood vessels to tumors.
2006	<p>A vaccine against the human papillomavirus, which causes cancer of the cervix, receives FDA approval. The vaccine is made via recombinant DNA technology by inserting of the viral genes into the DNA of baker's yeast.</p> <p>The U.S. Department of Agriculture (USDA) grants Dow AgroSciences the first regulatory approval for a plant-made vaccine.</p> <p>The Wake Forest Institute for Regenerative Medicine, in Winston-Salem, N.C., creates the first laboratory-grown organs by successfully transplanting bladders grown from a patient's own cells. This method greatly reduces the risk of organ rejection.</p>
2007	Scientists discover how to use human skin cells to create embryonic stem cells.
2008	Japanese scientists create the first DNA molecule made almost entirely of artificial parts. This advances the field of gene therapy and brings scientists one step closer to creating an artificial organism.

2009	<p>The FDA approves the world's first human embryonic stem cell study.</p> <p>Canadian-owned Medicigo produces the first plant-based influenza vaccine, in tobacco leaves. Medicigo has built a manufacturing facility in Durham, N.C., to scale up production.</p>
2010	<p>Researchers at the J. Craig Venter Institute create the first synthetic cell.</p>
2011	<p>A trachea derived from stem cells is transplanted into a human recipient.</p> <p>Advances in 3D printing technology lead to "skin printing."</p> <p>European scientists begin clinical trials for an anti-HIV biotech medicine produced using genetically modified tobacco. This increases the potential for cost-effective HIV/AIDS therapy in the developing world.</p>
2012	<p>The FDA issues draft guidelines for biosimilar drugs (follow-on biologics) as a growing percentage of biopharmaceuticals reach the end of patent protection.</p> <p>The pharmaceutical company Novartis receives FDA approval for Flucelvax, the first cell-culture derived vaccine in the United States.</p>
2013	<p>The U.S. Supreme Court rules that naturally occurring genes cannot be patented.</p>

Other Timelines to Explore

- biotechnology.amgen.com/timeline-medical-biotechnology
- www.finbio.net/download/biotech-week_2013/biotech-timeline.pdf
- www.bio.org/articles/timeline-8000-years-mankind
- www.accessexcellence.org/RC/AB/BC
- www.almaz.com/nobel

C. Practical Applications of Biotechnology⁴

Here are a few of the biotechnologies that use cells and biological molecules, as well as examples of their applications in bioprocessing, agriculture, medicine, industrial manufacturing and environmental management.

Tools of Biotechnology

Remember that biotechnology is the use of biological systems, such as microorganisms, whole cells or their molecules, to solve problems or to make useful products. One set of tools in the biotechnology toolbox is **bioprocessing technology**, which uses living cells or the molecular components of the cells' manufacturing machinery to produce desired products. The living cells most commonly used are one-celled microorganisms, such as yeast and bacteria. The biomolecular components we use most often are enzymes, which are proteins that catalyze (increase the rate of) biochemical reactions.

A form of bioprocessing, known as microbial fermentation, has been used for thousands of years to brew beer, make wine, leaven bread and pickle foods. In the mid 1800s, when we discovered microorganisms and realized their biochemical machinery was responsible for these useful products, we greatly extended our ability to exploit microbial fermentation. We now rely on the remarkably diverse manufacturing capability of naturally occurring microorganisms (such as bacteria and fungi) to provide us with products such as antibiotics, amino acids, vitamins, industrial solvents, pigments, pesticides and food processing aids.

In addition to microbial cells, we now use cells isolated from animals or plants and grown in the laboratory (cell culture) to produce desired products. Whole





animals such as pigs and cows, as well as whole plants, also are used.

The second major set of biotechnology tools is based on our increased understanding of genetics, or the science of heredity. We have learned how to use the enzymes that occur naturally within cells to manipulate the genes of any organism and to move genes from one organism to another. This is known as **genetic engineering** (or, more specifically, recombinant DNA technology). A human gene successfully was incorporated into bacteria for the first time in 1977. The result of such manipulation may be called a **genetically modified organism**, or GMO. Using genetic engineering tools, we can:

- genetically modify microorganisms used in bioprocessing to make new products. For example, the gene for human insulin has been inserted into *E. coli*, resulting in bacteria that produce insulin for people with diabetes. Cells from mammals also can be genetically engineered to produce a valuable substance; one example is the production of human interferon by genetically engineering Chinese hamster ovary cells. Once purified, the resulting drug is used to treat multiple sclerosis, a serious disease of the central nervous system. The drug is identical to interferon produced naturally in the human body.
- genetically modify organisms such as crop plants to enhance useful features (for example, resistance to insects and disease). An example is the production of genetically modified corn that is resistant to the herbicide Roundup, which allows farmers to get rid of weeds without harming their crops.

Agricultural Applications

We always have relied on plants and animals for food, shelter, clothing and fuel — and for thousands of years we have been changing these things to better meet our changing needs. Society’s demand for resources provided by plants and animals will increase as the world’s population grows. The world’s population, which numbered approximately 1.6 billion in 1900, was more than 6.4 billion

in 2014 and is expected to reach 10 billion by 2030⁵. The United Nations Food and Agriculture Organization estimates that the quantity of world food production will have to double on existing farmland if it is to keep pace with the anticipated population growth. Biotechnology can help meet the ever-increasing need by improving yields, decreasing crop inputs such as water and fertilizer, and providing pest control methods that are less destructive to the environment.

CROP BIOTECHNOLOGY

Stone Age farmers selected plants with the best characteristics and saved their seeds for the next year's crops. Long before humans understood the science of genetics, the earliest farmers applied genetic modification by selectively breeding wild plants to obtain domesticated crops. For centuries, farmers and plant breeders have relied on traditional crossbreeding to improve the yield and quality of food and fiber crops and to provide crops with built-in protection against insect pests, disease-causing organisms and harsh environmental conditions.

As our knowledge of plant genetics improved, we purposefully crossbred plants with desirable traits (or plants lacking undesirable characteristics) to produce offspring that combine the best traits of both parents. In today's world, virtually every crop plant grown commercially for food or fiber is a product of crossbreeding. Unfortunately, these processes often are costly, time-consuming, inefficient and subject to significant practical limitations. For example, producing corn with higher yields or natural resistance to certain insects takes dozens of generations of traditional crossbreeding, if it is possible at all.





The tools of biotechnology allow plant breeders to select single genes that produce desired traits and move them from one plant to another. The process is far more precise and selective than traditional crossbreeding, in which thousands of genes of unknown function are combined in hybrid crops.

Biotechnology also removes the technical obstacles to moving genetic traits between plants and other organisms. This opens up a world of genetic traits to benefit food production. We can, for example, take a bacterial gene that yields a protein toxic to an insect pest (but not to humans) and transfer it to a plant. The plant then produces the protein and is protected from the insect without the help of externally applied chemical pesticides.

Another agricultural application lies in the rapidly developing field of **biofuels** — fuels such as methane and ethanol produced by microorganisms from renewable resources such as plant biomass and municipal or industrial wastes. Ethanol (now being produced from corn as the raw material) has been shown to reduce the emission of harmful air pollutants, including greenhouse gases linked to global warming. Ethanol also is replacing methyl tertiary butyl ether (MTBE), which can contaminate groundwater, as a gasoline additive. Biotechnology also enables farmers to adopt environmentally friendly growing techniques, known as conservative tillage. In addition, expected advances in biotechnology eventually could make clean-burning fuel from all sorts of organic refuse — including the 280 million tons of lawn clippings, leaves, sawdust, wood pulp and other waste generated every year in the United States. The development of biofuels will help the U.S. reduce its dependence on foreign oil supplies.⁶

FOREST BIOTECHNOLOGY

Throughout the world, wood provides us with fuel, construction materials and paper — and its supplies are dwindling rapidly. Demand for wood products is expected to increase, even as major economies, such as Europe and Japan, are unable to grow enough trees to meet their current demands.



The tools of biotechnology are helping to create disease- and insect-resistant trees and to increase their growth rates. Scientists also are learning how to use biotechnology to improve the efficiency with which trees convert solar energy into plant material and how to shunt more of that energy into wood production (and less into pollen, flowers or seeds). These methods of increasing productivity should decrease the need for wood from natural forests.

Perhaps a more important economic role for biotechnology in this industry will be found in its changing of the way we convert trees to useful products. Extensive research is being conducted to increase a tree's cellulose, the raw material for papermaking, while decreasing the amount of lignin, a molecule that must be removed in papermaking.

Because removing lignin from trees has required harsh chemicals and high-energy costs, changing the cellulose-to-lignin ratio genetically will have important environmental benefits. Increasing the growth rate of trees will help our environment as well. Because trees absorb carbon dioxide, any advance that allows us to increase tree yields without cutting down forest could have significant positive effects on global warming.

Because removing lignin from trees has required harsh chemicals and

In addition, biotechnology is helping to produce enzymes for:

- Pretreating and softening wood chips prior to pulping
- Removing pine pitch from pulp to improve the efficiency of paper-making
- Enzymatically bleaching pulp rather than using chlorine
- De-inking recycled paper
- Using wood-processing wastes for energy production
- Cleaning up soils contaminated with wood preservatives



ANIMAL BIOTECHNOLOGY

Animals, both domesticated and wild, can benefit from biotechnology applications. Studies of the genetics and cellular biology of animals are playing a growing role in the advancement of biotechnology, and animals increasingly are benefiting from biotechnology.

Improving Animal Health

The market for biotechnology-based animal health products and services is more than \$5 billion per

year — and it's growing. The animal health industry invests more than \$400 million per year in research and development.

When it comes to farm animals, biotechnology provides new tools for improving animal health and increasing livestock and poultry productivity. These improvements come from the enhanced ability to detect, treat and prevent diseases and other problems; from better feed derived from transgenic crops (an organism that contains genes from another organism) designed to meet the dietary needs of different farm animals; and from improved animal breeding.

The greatest expense for pet owners are services related to veterinary and health care products, which accounted for more than \$7 billion in 2000. The animal health industry has developed products that contribute to the well-being of companion animals, such as preventive medicines and disease treatments that have been improved through biotechnology. Animal vaccines developed through biotechnology are critical in preventing diseases, such as rabies, distemper, feline leukemia and hepatitis. In addition, researchers have developed biotechnology-based products to treat heartworm, arthritis, parasites, allergies, dental problems, heart disease, kidney failure, separation anxiety, cognitive dysfunction syndrome and other problems.



Enhancing Human Medical Applications

A transgenic animal is one that carries a foreign gene that has been inserted deliberately into its genome (which is its complete set of chromosomes). Transgenic animals such as cows, sheep and goats can be genetically modified so they produce human proteins in their milk. These proteins then can be extracted and purified from the milk and formulated into drugs to treat diseases, including emphysema, cystic fibrosis, burns, gastrointestinal infections and immunodeficiency diseases such as AIDS. Transgenic pigs are being developed that may be used as organ donors. Their organs can be transplanted into humans with less danger of rejection. This process is known as **xenotransplantation**. In addition, a variety of transgenic animals are used in research.

Enhancing Animal Products

Biotechnology can make dramatic improvements to the animal products that humans consume and use. Improved animal health from the use of vaccines, medicines and diagnostic tests results in safer foods for consumers. In addition, transgenic cows, pigs and lambs that have been genetically modified to have reduced fat and increased lean muscle result in healthier meat products.

Improving the Environment and Helping Conserve Endangered Species

Reproductive and cloning technologies, as well as medicines and vaccines developed for use in livestock and poultry, can help save endangered mammals and birds. In addition, several crops improved with biotechnology are helping to decrease farm animal manure production as well as their phosphorus and nitrogen excretion (which contributes to groundwater pollution).

Medical and Health Care Applications

Biotechnology tools and techniques open new research avenues for discovering how healthy bodies work and what goes wrong when problems arise. Knowing the molecular basis of health and disease has led to improved and novel methods for treating and preventing diseases. In human health care, biotechnology products include quicker and more accurate diagnostic tests as well as new and safer vaccines.

DIAGNOSING DISEASES

We now can detect many diseases and health conditions more quickly, with greater accuracy and with lower costs because of the sensitivity of new, biotechnology-based diagnostic tools. A familiar example of biotechnology's benefits is the new generation of home pregnancy tests that provide more accurate results much earlier than previous tests. Tests for strep throat and many other infectious diseases provide results in minutes, enabling treatment to begin immediately — in stark contrast to the two- or three-day delay of previous tests.

TREATING DISEASES

Biotechnology will provide improved versions of today's therapeutic regimes as well as treatments that would not be possible without these new techniques. Biotechnology therapeutics approved by the U.S. Food and Drug Administration (FDA) are used to treat many diseases, including diabetes, stroke, anemia, cystic fibrosis, growth deficiency, rheumatoid arthritis, hemophilia, hepatitis, genital warts, transplant rejection, leukemia and other cancers. These therapies share a common foundation: All are derived from biological substances and processes designed by nature. Some use the human body's own tools for fighting infections and correcting problems. Others are natural products of plants and animals. The large-scale manufacturing processes for producing therapeutic biological substances also rely on nature's molecular production mechanisms.

CHEMICAL AND ENVIRONMENTAL APPLICATIONS

The contributions biotechnology has made to health care and agriculture have received much attention from the press and the public, but now society is beginning to see the benefits of biotechnology's "third wave": chemical and environmental biotech. Applications of biotechnology in the chemical industry often are known as ***industrial biotechnology***.



Chemical companies turn raw materials such as salt and crude oil into products. Crude oil, or petroleum, is a complex mixture of hundreds of chemicals. Chemical manufacturing turns this mixture into a huge range of products, such as plastics (the most common one). Almost everything you use in your daily life, including clothing and much of what you eat and drink, is a direct or indirect product of the chemical industry.

Living systems manage their chemistry more efficiently than manmade chemical plants, and the wastes they generate are recyclable or biodegradable. Living cells and their enzymes operate at lower temperatures, which means they require less energy and produce less toxic waste than conventional chemical processes. They also may use fewer purified raw materials. And just as biotechnology is providing us with new tools for diagnosing health problems and

detecting harmful contaminants in food, it also is yielding new methods of monitoring environmental conditions and detecting pollutants.

Biotechnology in the chemical industry employs the techniques of modern molecular biology to reduce the environmental impact of manufacturing. Industrial biotechnology also works to make manufacturing processes more efficient for industries such as paper and pulp, textiles, and specialty chemicals. Some observers predict biotechnology will transform the chemical manufacturing sector in much the same way it has changed the pharmaceutical, agricultural and food sectors.

Activity

BIOTECHNOLOGY TIMELINE

TEACHER PAGE

LEARNING OUTCOMES

- Students will construct a timeline of key biotechnology events.
- Students will investigate information on a biotechnology scientist/discovery.
- Students will illustrate the importance of a biotechnology milestone and the associated scientist.

ESTIMATED TIME

60–70 minutes

CONTENT

Unit I, Section B

PURPOSE

Two stages are offered for this activity. The **Introductory Timeline** stage serves as an introduction to biotechnology by having students think about and arrange important biotechnology events in chronological order. The **Timeline Investigation** stage gives students a chance to take a closer look at significant events and people in the development of biotechnology.

Stage 1: Introductory Timeline

MATERIALS

- Biotechnology event cards (pages 31–34)
 - » Cut and copy one set for each group of students

TEACHER PROCESS

- Divide the class into groups of 2 or 3 students per group and give each group a set of biotechnology event cards.

Activity

BIOTECHNOLOGY TIMELINE

TEACHER PAGE CONTINUED

- Explain to students that biotechnology is a part of world history. They will be familiar with some of the names and events. They won't be familiar with others. The goal is to have them use logic and reasoning, as well as prior learning, to place the cards in proper chronological order.
- Allow the groups to organize the cards for about 10 minutes. Once the groups decide on the chronological order of the cards, allow each group to share its final decisions and explain some of its reasoning to other groups.
- Share with the class the biotechnology timeline in Unit I, Section B or the *Biotechnology Timeline* PowerPoint presentation that accompanies this section.
- Recognize the group(s) that guessed the correct order (or came the closest).

Stage 2: Timeline Investigation

MATERIALS

- Internet access

TEACHER PROCESS

- If you do not complete Stage 1, have each student read the timeline in Unit I, Section B individually. Afterward, provide additional background on a few milestones or the scientists most closely associated with the milestones.
 - » For example, you could tell the story of Edward Jenner's observation that milkmaids somehow seemed to be protected against contracting smallpox. This observation led Jenner to the discovery that exposure to the cowpox virus appeared to be the factor that protects individuals from getting smallpox. Thus, vaccination, which remains our most effective strategy of disease prevention and protection of public health, was born.

Activity

BIOTECHNOLOGY TIMELINE

TEACHER PAGE CONTINUED

- » Many other great stories are represented in the history of biotechnology, including Gregor Mendel's studies, Alexander Fleming's discovery of penicillin and Leroy Hood's invention of the automated DNA sequencer. (For additional timeline references, see the links at the end of Unit I, Section B.)
- Have students work in groups of 2 or 3 to research an assigned scientist and his or her discoveries on the Internet.
- Explain to the students that they will share the story of the assigned scientist and his/her discoveries. This may be accomplished through an oral presentation, a skit or a visual representation.
- Make sure you probe students' understanding to ascertain that they have at least become familiar with the timeline. Suggested discussion questions are listed below. Example student answers follow in italics.

DISCUSSION QUESTIONS & EXAMPLE STUDENT ANSWERS

- Where and when did biotechnology originate?
 - » *Biotechnology was used thousands of years ago by early civilizations to leaven bread, to produce cheese and to ferment beer and wine.*
- What were some of the first activities?
 - » *Producing cheese, beer, medicine and wine. Early cultures used biotechnology to enhance their lives through food and medicine.*
- Can you think of some examples where we still use these same basic technologies today?
 - » *We still use fermentation in the production of alcoholic beverages. Yeast still is used in baking.*
- How long have humans been improving plants through genetic modification (cross-breeding)?
 - » *For thousands of years, farmers have been planting crops together to encourage the formation of stronger varieties.*

Activity

BIOTECHNOLOGY TIMELINE

TEACHER PAGE CONTINUED

- Explain how a scientist who is tied to a specific milestone used experimentation and data analysis to aid in the discovery/enhancement in question.
 - » *Louis Pasteur, for example, deduced that microbes cause fermentation through his experimentation of bacteria in nutrient broths.*
- How did a specific scientist build on the discoveries of other scientists? For instance, which discoveries helped the Human Genome Project?
 - » *The Human Genome Project was built on several projects. The basis of the research was the discovery of DNA and its structure. The genetic code of DNA is another example of how discoveries served as the foundation of the Human Genome Project.*
- Now that you've seen this timeline, how many of you are surprised that biotechnology can be traced so far back in history?

OTHER OPTIONS

- Assign each group 1 or 2 particular milestones and ask them to identify which preceding discoveries on the timeline were instrumental in making their assigned milestones possible.
- Have each group look up biographical information about the individual responsible for each milestone. ("What is it about the character, knowledge and background of this person that increased the likelihood that he or she would make this discovery?")

Activity

BIOTECHNOLOGY TIMELINE

STUDENT PAGE

<p>Humans domesticate crops and livestock</p> <p>AND</p> <p>Potatoes first are cultivated for food</p>	<p>Biotechnology is used for the first time when the Egyptians use yeast to leaven bread and ferment beer</p> <p>AND</p> <p>Production of cheese and fermentation of wine occur in Sumeria, China and Egypt</p>	<p>Chinese use the first antibiotic: moldy soybean curds for treating boils</p>
<p>Edward Jenner inoculates a child with a viral vaccine to protect him from smallpox</p>	<p>Science of genetics begins when Austrian monk Gregor Mendel studies flowers in his garden to develop the basic laws of heredity</p>	<p>James Watson and Francis Crick describe the double helical structure of DNA, which will lead to them winning the Nobel Prize</p>

Activity

BIOTECHNOLOGY TIMELINE

STUDENT PAGE CONTINUED

<p>Frederick Sanger determines the amino acid sequence of insulin, making it the first protein to be sequenced</p>	<p>Genetic code for DNA is cracked, demonstrating that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids</p>	<p>First complete synthesis of a gene occurs</p>
<p>First recombinant vaccine for humans is produced, for hepatitis B</p>	<p>First field tests of genetically modified food plants are approved, for virus-resistant tomatoes</p>	<p>Genetically modified tomatoes are sold for the first time in the United States</p>

Activity

BIOTECHNOLOGY TIMELINE

STUDENT PAGE CONTINUED

An animal is cloned from an adult cell for the first time: a sheep named Dolly, in Scotland

Human embryonic stem cell lines are established

Draft version of the complete map of the human genome is published

Genome of the virus that causes SARS (severe acute respiratory syndrome) is sequenced only three weeks after its discovery

Avastin, a recombinant monoclonal antibody, is the first targeted biological therapy of its kind to receive FDA approval

Wake Forest Institute for Regenerative Medicine creates the first laboratory-grown organs by successfully transplanting bladders grown from a patient's own cells

Activity

BIOTECHNOLOGY TIMELINE

STUDENT PAGE CONTINUED

Researchers at the J. Craig Venter Institute create the first synthetic cell

Novartis receives FDA approval for Flucelvax, the first cell-culture derived vaccine in the United States

U.S. Supreme Court rules that naturally occurring genes cannot be patented

Activity

CREATE A LOGO

TEACHER PAGE

LEARNING OUTCOMES

- Students will create a fictional biotech company.
- Students will imagine a product that could be produced by the fictional biotech company.
- Students will design a logo for the fictional biotech company.
- Students will defend the logo design for the fictional biotech company.

ESTIMATED TIME

20–30 minutes

CONTENT

Unit I, Section C

MATERIALS

- Blank paper or poster board
- Color markers

TEACHER PROCESS

- Have students read and analyze Unit I, Section C.
- Explain that they are to create the name of a fictional biotech company and a logo for the company. Students can hand-draw their logos or design them on a computer as a homework assignment.
- Hand out copies of the student pages for this activity (pages 37–38), which has links to existing logos for inspiration. Go over instructions or give a demonstration, if necessary.
- Ask your students to invent a product that is manufactured by the fictional company.

Activity

CREATE A LOGO

TEACHER PAGE CONTINUED

- Suggest that students think outside the “biopharmaceutical box.” Consider creating an agricultural, environmental, chemical or veterinary health product for their companies to produce.
- When students finish their logos, have them share their work with the rest of the class.
- When debriefing the activity, ask why they chose the examples they did, what surprised them and what they learned.

Activity

CREATE A LOGO

STUDENT PAGE

Logos can be categorized into four major types, as listed below. The websites offer examples of each type.

1. COMPANY LOGO GRAPHIC DIRECTLY REPRESENTS THE COMPANY'S SPECIALITY

- Cardiome: www.cardiome.com (Electrocardiograph tracing)
- Nutra Pharma: www.nutrapharma.com (double helix)
- Archer Daniels Midland (ADM): www.adm.com (leaf)

2. COMPANY LOGO USES A GRAPHIC THAT IS VERY STYLIZED BUT REPRESENTATIVE OF SOMETHING "BIOLOGICAL" (DNA, A HUMAN, A PILL, ETC.)

- Roche: www.roche.com (company name inside a pill-shaped hexagon)
- Biovest International: www.biovest.com (sphere composed of hexagonal shapes)
- Bayer: www.bayer.com (its famous aspirin pill)
- BD Technologies: www.bd.com (sun and person)
- Novozymes: www.novozymes.com (four-leaf clover)
- AlphaVax: www.alphavax.com/home (spherical molecule)
- Argos Therapeutics: www.argotherapeutics.com (stylized sun)

3. LOGO GRAPHIC REPRESENTS SOMETHING IN THE ACTUAL COMPANY NAME — A TYPE OF "PLAY ON WORDS"

- Jazz Pharmaceuticals: www.jazzpharma.com (musical notes)
- Abeille Pharmaceuticals: www.abeillepharma.com (French for "bee"; name is pronounced "A-Beel")
- Lifespan Technologies: www.lifespantech.com (infinity sign)
- Vertex Pharmaceuticals: www.vrtx.com (triangle)

Activity

CREATE A LOGO

STUDENT PAGE CONTINUED

4. COMPANY LOGO INCLUDES A GRAPHIC THAT DOES NOT RELATE TO ANYTHING BIOLOGICAL OR USES ONLY THE COMPANY NAME/INITIALS

- GlaxoSmithKline: www.gsk.com
- Novo Nordisk: www.novonordisk.com
- VG Life Sciences: www.vglifesciences.com
- Biogen Idec: www.biogenidec.com
- Greer Laboratories: www.greerlabs.com
- KBI BioPharma: www.kbibioharma.com

OTHER SOURCES OF INFORMATION

- Biospace.com: www.biospace.com/company_index.aspx (provides detailed information about more than 300 biotechnology companies and links to their websites)
- NC Biotech Company Directory: directory.ncbiotech.org
- BIO Members & Website Links:
www.bio.org/articles/bio-members-web-site-links

Activity

MAKE A YEAST INCUBATOR

TEACHER PAGE

LEARNING OUTCOMES

- Students will build a simple bioreactor.
- Students will collect data from the balloon inflation.
- Students will compare data with other groups.
- Students will discuss changes that could be made to increase/decrease the rate of inflation.

ESTIMATED TIME

45–60 minutes

CONTENT

Unit I

PURPOSE

The purpose of this experiment is to give students the opportunity to learn about fermentation firsthand by using baker's yeast (*Saccharomyces cerevisiae*). In baking, the purpose of the leavening agent is to produce the gas (carbon dioxide) that makes bread rise. Yeast does this by feeding on the carbohydrates (starches and sugars) in flour. Yeast is a facultative anaerobe — it can survive in the presence or absence of oxygen. When oxygen is present (aerobic respiration), yeast converts sugars and other carbon sources into water, carbon dioxide and 36 molecules of ATP (adenosine triphosphate, a chemical energy source within cells). Under anaerobic conditions (in the absence of oxygen), yeast switches to fermentation and produces ethanol, carbon dioxide and two molecules of ATP. The metabolic activity of yeast cells stops when the limiting carbon source is exhausted.

During this experiment, your students are creating a very simple bioreactor. Strictly speaking, a bioreactor is a chamber in which biological transformation, product formation and/or enzymatic reactions occur. The large-scale bioreactor

Activity

MAKE A YEAST INCUBATOR

TEACHER PAGE CONTINUED

is the heart of the biomanufacturing process, and it is a sophisticated piece of equipment that creates a highly controlled and sterile environment for the cells to grow. The largest bioreactors can be several stories tall, but the “crib” for the cells that grow in those behemoths often is a tissue culture flask or roller bottle that is similar in size to the bottles your students are using.

MATERIALS

For Each Group

- 1 packet (7 grams) of active, dry yeast (not rapid-rise)
- 1 cup (~237 milliliters) of warm water (100° F to 110° F)
- 2 tablespoons (~30 grams) of sugar (sucrose)
- 1 round, rubber balloon (do not use Mylar or water balloons because they do not expand easily)
- 1 small (0.5- to 1-liter) clear, empty water bottle

Other Supplies

- Scissors (to cut open yeast packages)
- Duct or masking tape (to secure balloon onto neck of bottle)
- Thermometer (to measure water temperature)
- Rulers or flexible, sewing-style tape measures (to measure diameter or circumference of balloon as it expands)

TEACHER PROCESS

- Divide the class into groups and have enough of the materials listed above for your groups.
- Hand out copies of the student pages for this activity (pages 44–45). Go over instructions or give a demonstration, if necessary.

Activity

MAKE A YEAST INCUBATOR

TEACHER PAGE CONTINUED

- Have each group prepare its own bottle-balloon yeast incubator. The balloon should begin to expand within 10 minutes. The temperature of the water added to the bottle is an important variable to control. Too-hot water will kill the yeast, while too-cool water will slow down the yeast's growth process (an expansion of the balloon). Brainstorm with your students about ways to keep the incubators from cooling down using easily obtainable supplies.
- Have the students record the size of the balloon at various points in time as it expands.
- Have students complete the discussion questions listed on the student pages for this activity. These discussion questions also are listed below. Example student answers follow in italics.

DISCUSSION QUESTIONS & EXAMPLE STUDENT ANSWERS

1. What product of yeast metabolism is causing the balloon to inflate?
» *Carbon dioxide is a byproduct of yeast breaking down sugar.*
2. How could you change the mixture in the bottle to cause the balloon to inflate more quickly or more slowly?
» *Students may suggest placing the balloon in a warm location to increase how quickly it will inflate or placing the balloon in a cool location to decrease the time of inflation.*

OTHER OPTIONS

- Have students keep a record of each step performed and write a lab report.
- Have each group prepare more than 1 incubator. Each group can prepare a control bottle using the instructions on pages 44–45 as well as 1 or more experimental bottles in which the group changes 1 variable. The groups can compare among themselves the rate of expansion of the balloons that occurs with their control bottles and report to the class on the results of their experimental bottles. Possible variables to change include:

Activity

MAKE A YEAST INCUBATOR

TEACHER PAGE CONTINUED

- » The amount of sugar added
- » The type of nutrient added to the bottle (for example, corn syrup, flour, corn starch or artificial sweetener)
- » The amount of yeast
- » The type of yeast (such as rapid-rise)
- » The temperature of the water
- Have each group write a standard operating procedure, or SOP, for the process. *See Unit II for more information about SOPs.*
- Have students investigate the “kitchen science” of using yeast in breadmaking (such as proofing the yeast to be sure it’s active). Places to look include:
 - » Fleischmann’s Yeast website (www.breadworld.com/FAQ.aspx and www.breadworld.com/Science.aspx)
 - » *How Bread Works*, by HowStuffWorks (science.howstuffworks.com/innovation/edible-innovations/bread.htm)

BACKGROUND

Yeast can be considered humans’ oldest industrial microorganism and one of the earliest domesticated animals. The ancient Egyptians began using yeast to leaven bread and beer more than 4,000 years ago. Much more recently, rapid-rise yeast, (also known as instant yeast or quick yeast) has been improved genetically for rapid-rise processes.

The lowly yeast is held in high esteem among those who study genetics at the molecular level. It is considered the workhorse of molecular genetics, thanks in large part to Nobel Prize winner Leland Hartwell. More than 20 years ago, Dr. Hartwell began conducting key experiments with baker’s yeast that uncovered the genetic basis of cell division. His work revealed that the basic molecular

Activity

MAKE A YEAST INCUBATOR

TEACHER PAGE CONTINUED

mechanisms that govern cell division in unicellular yeast are identical to those at work in more complex multicellular organisms.

Yeast also is used as one type of cellular factory to produce biopharmaceuticals, which are created by incorporating a specific gene into the cells through recombinant DNA technology. The foreign gene becomes part of the organism, the new gene is replicated along with all of its own genes during cell division, and the protein it codes for (insulin, interferon or many other useful pharmaceuticals) is made by the cell's protein-making "machinery." In fact, a vaccine against the human papillomavirus (HPV), which can cause cervical cancer, is made with four different recombinant strains of yeast, each of which has the gene from different strains of HPV in its genome. This vaccine received FDA approval in 2006.

The complete map of the yeast genome, first published in 1996, has proved to be extremely useful as a reference for sequencing human and other higher eukaryotic genes. Furthermore, the ease of genetic manipulation of yeast allows it to be used for conveniently analyzing and functionally dissecting gene products from other eukaryotes. In 2002, the first draft of the yeast proteome — the entire network of protein complexes and their interactions — was completed.

Activity

MAKE A YEAST INCUBATOR

STUDENT PAGE

In this activity you will work with a workhorses of both the genetics lab and the breadmaker's kitchen: baker's yeast (*Saccharomyces cerevisiae*). The ancient Egyptians began using yeast more than 4,000 years ago to ferment beer and wine and to leaven bread. Many consider this the first example of humans using living organisms to make useful products or solve problems — the traditional definition of biotechnology. The same species of yeast you are working with today also is used to produce human insulin via genetic engineering techniques, which involves inserting the human insulin gene into the yeast's DNA.

The yeast is a very adaptable organism. This single-celled fungus derives energy from sugar molecules, just like your cells do. Yeast can break down (metabolize) larger carbohydrate molecules (like starches present in flour) into simple sugar molecules, which then are processed further. In the presence of oxygen (aerobic conditions), they break down sugar into carbon dioxide, water and the chemical energy molecules known as ATP (adenosine triphosphate). In the absence of oxygen (anaerobic conditions), the yeast break down sugar via fermentation. The fermentation process produces alcohol, carbon dioxide, water and ATP (but much less energy than is produced under aerobic conditions).

INSTRUCTIONS

1. Stretch out the balloon, then set it aside.
2. Pour the packet of yeast into the clear water bottle. Add the sugar, then the water.
3. Swish very slowly to avoid coating the sides of the bottle with yeast.
4. Attach the balloon to the mouth of the bottle, tape it on and set it aside in a warm place. Write down the time you start the incubation. Within a few minutes you will see bubbling, and then the balloon will begin to inflate.

Activity

MAKE A YEAST INCUBATOR

STUDENT PAGE CONTINUED

5. Take measurements of the balloon as it expands at regular intervals. Write down each measurement and the time at which you took it.
6. Compare your results with other groups.

DISCUSSION QUESTIONS

1. What product of yeast metabolism is causing the balloon to inflate?
2. How could you change the mixture in the bottle to cause the balloon to inflate more quickly or more slowly?

Activity

DNA EXTRACTION

TEACHER PAGE

LEARNING OUTCOMES

- Students will discuss where DNA can be found.
- Students will extract DNA from the source material.
- Students will observe DNA as a precipitate at the interface of the layers.

ESTIMATED TIME

45–60 minutes

CONTENT

Unit I

PURPOSE

Students hear a lot about DNA (especially if they watch any of the many TV shows about crime scene investigations). They even might have seen drawings or 3D models of the structure of DNA. But they probably haven't isolated DNA themselves, and they will be surprised at how simple it is and that it can be accomplished with supplies from the grocery store.

Point out to your students that many of the substances produced in biomanufacturing are the result of one gene from one organism being transferred into another — such as a bacterium, yeast or mammalian cell. In contrast, the DNA they spool onto wooden sticks contains millions of genes. The extraction of DNA from a cell is often a first step for scientists who need to obtain and study a gene.

MATERIALS

- Plant, animal or yeast sample
 - » *Plant material:* Take a strawberry or a small piece of banana, smash it in a sealable plastic bag and add 2 tablespoons of water.

Activity

DNA EXTRACTION

TEACHER PAGE CONTINUED

- » *Animal material:* Take a small piece of liver and a cup of water, place them in a blender and blend for 30–60 seconds on high.
- » *Yeast:* Mix 1 package of active dry yeast with 1.5 fluid ounces (3 tablespoons, or ~44 milliliters) of 120° F (49° C) tap water to dissolve the yeast in a cup. Keep the mixture covered and warm for about 20 minutes.)
- Adolph's natural (unseasoned) meat tenderizer
- Clear glass or plastic cups
- Distilled water
- Non-iodized salt
- Wooden coffee stirrer, bamboo skewer or glass rod
- Dish detergent
- Liquid measuring cup
- Measuring spoons
- Blender

SOLUTIONS TO PREPARE

Detergent-Salt Solution

- 1 tablespoon (~15 milliliters) of dish detergent
- 1 tablespoon (~15 grams) of non-iodized salt
- 5 fluid ounces (~148 milliliters) of distilled water

Meat Tenderizer Solution

- 1 teaspoon (~5 grams) of meat tenderizer
- 3 fluid ounces (~89 milliliters) of distilled water

Activity

DNA EXTRACTION

TEACHER PAGE CONTINUED

TEACHER PROCESS

- Choose the DNA source material (plant, animal or yeast) to prepare for the students.
- Divide the class into groups and have enough of the materials and solutions listed on the previous pages for your groups.
- Hand out copies of the student pages for this activity (pages 49–50). Go over instructions or give a demonstration, if necessary.
- Have each group keep a record of what it does during each step.
- After the groups complete the assignment, hold a discussion. Discussion questions are listed on the student pages for this activity. They also are listed below. Example student answers follow in italics.

DISCUSSION QUESTIONS & EXAMPLE STUDENT ANSWERS

1. What exactly does the DNA precipitate contain? Which layer contains the other cellular material?
 - » *The DNA precipitate actually is nucleic acid extraction and contains both DNA and RNA. The water layer contains the other cellular materials.*
2. Why do you think it is possible to collect the DNA on a stirring rod?
 - » *Students may suggest that DNA is a long strand of nucleotides.*

BACKGROUND

This procedure is adapted from *Introduction to DNA Extraction* (www.accessexcellence.org/AE/AEC/CC/DNA_extractions.php). The site offers many helpful hints about extracting DNA from plant and animal sources. You also can search online to find many different types of DNA extraction procedures.

You also may check out the well-illustrated *How to Extract DNA from Anything Living* (learn.genetics.utah.edu/content/labs/extraction/howto), especially the Frequently Asked Questions link at the bottom of the page. It explains why the extraction method works and provides helpful hints in case it doesn't.

Activity

DNA EXTRACTION

STUDENT PAGE

All the information required to make a human being is stored in that person's DNA. In fact, the DNA in all organisms provide instructions about how to grow and how to perform millions of cellular processes each day.

To find out how these instructions are communicated, researchers separate the DNA from the rest of the cell and examine how it interacts with other substances in the cell. The isolation, or extraction, can be done in less than an hour in your classroom or your kitchen, but it took many years to learn how to do it.

INSTRUCTIONS

1. Place a sample of the plant, animal or yeast in a cup.
2. Add 1.5 fluid ounces (3 tablespoons, or ~44 milliliters) of detergent/salt solution. Mix thoroughly for 5–10 seconds. Let mixture sit for 5–10 minutes.
3. Add 1 tablespoon (~15 milliliters) of meat tenderizer solution and stir to mix.
4. Pour 4 tablespoons (~59 milliliters) of ice-cold alcohol carefully down side of tube to form a layer.
5. Let mixture sit undisturbed for 2–3 minutes until bubbling stops.
6. You will see a precipitate at the alcohol-water interface. Swirl stirring rod or coffee stirrer at the interface of the two layers. The precipitate is DNA.

Activity

DNA EXTRACTION

STUDENT PAGE CONTINUED

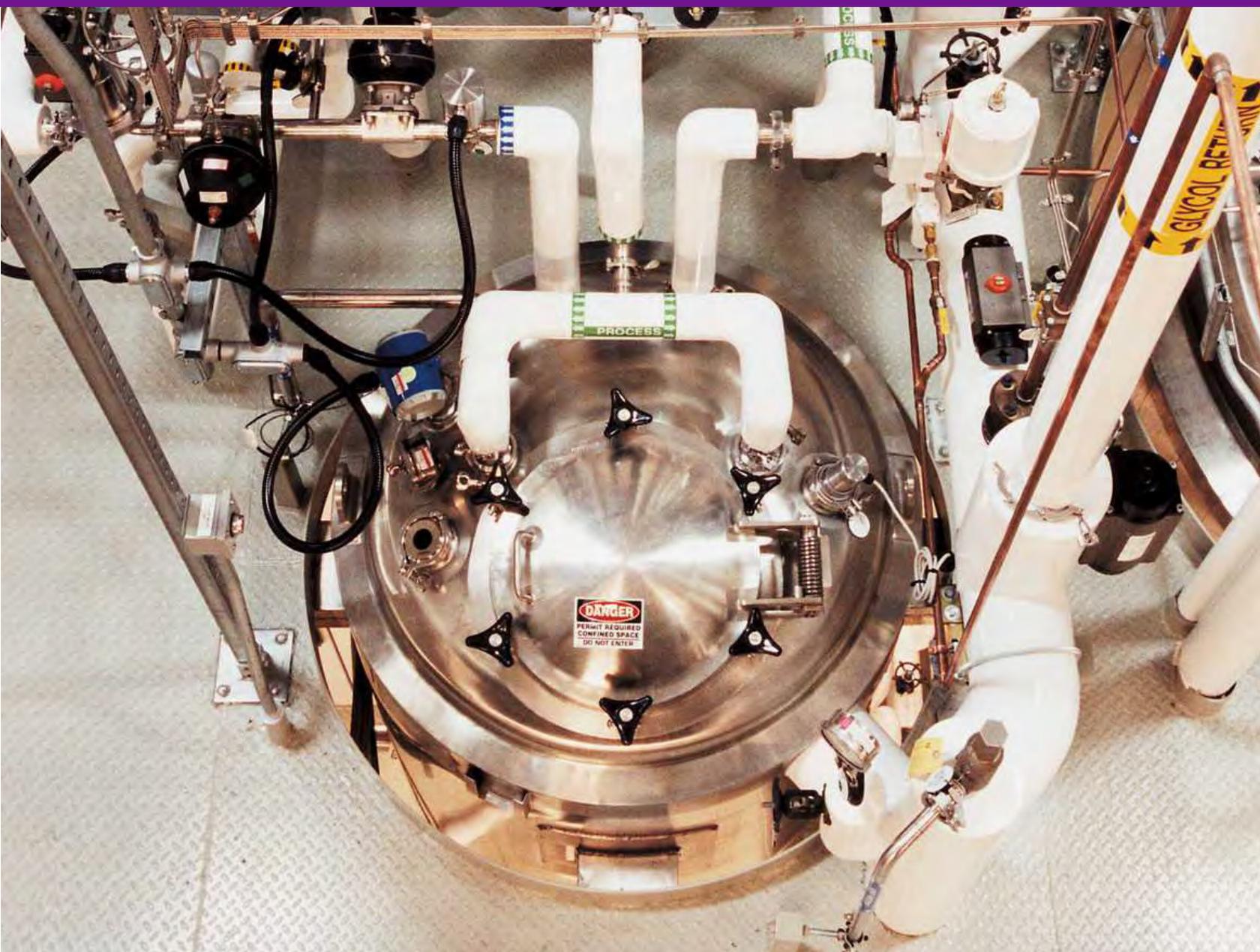
DISCUSSION QUESTIONS

1. What exactly does the DNA precipitate contain? Which layer contains the other cellular material?
2. Why do you think it is possible to collect the DNA on a stirring rod?



Unit II

DRUG DISCOVERY AND MANUFACTURING



A. How a New Drug Gets to Market ¹

Modern medicines are helping people live healthier, longer and more productive lives. Many diseases that once took an early toll on our lives and health now are cured or better managed with the help of medicines. Americans have access to probably the safest and most advanced pharmaceutical system in the world, according to the U.S. Food and Drug Administration (FDA), which is the main consumer watchdog for this system. The FDA evaluates new drugs — prescription drugs as well as medications sold over-the-counter (such as aspirin) — before they can be sold. This ensures these medicines are safe and effective for their intended use. The FDA is focused on protecting the safety and health of the consumer who uses drug products. While this unit will focus primarily on the development process within the United States, it is important to note that similar entities guide the process in other regions of the world, such as the European Medicine Agency and Health Canada.



The development of a new drug is a lengthy and expensive process for both the pharmaceutical and biopharmaceutical industries. This is due to numerous factors, including the length of time needed to screen potential drug compounds and the length of time necessary to build and validate a manufacturing facility.

While these costs are reflected in the cost of pharmaceuticals to consumers, the costs often are significantly lower than the costs of hospital treatment prior to the discovery of the new drug.

Similar to other manufacturing industries, the size of the workforce grows considerably as the process moves from laboratory to manufacturing, creating a great variety of jobs. As described in Unit III, these jobs are available for people coming from a variety of different educational backgrounds. Some companies choose to do all of the work themselves. Other companies rely on the work of still other companies to get the job done. As a result, there are exciting career possibilities at many different types of companies in the broad bioscience industry. In addition to the pharmaceutical and biopharmaceutical manufacturing organizations, this includes research and development (R&D) startups, contract research and testing companies, clinical research organizations (CROs), and vendors specializing in providing contract manufacturing services.



Drug Discovery and Testing

Drug development begins in the laboratory, where scientists look for compounds that treat or prevent disease. In the past this was done through trial and error, but the research tools of biotechnology, which have provided scientists with an increased understanding of life processes, now help the drug discovery process considerably. Chemicals can be designed to interact more specifically with cellular molecules to treat disease. The next generation of human therapeutics includes biopharmaceuticals, which are naturally occurring human proteins or modified human proteins produced from genetically engineered cells grown in culture.

Once a company finds a drug it thinks is promising, it begins preclinical studies that test the drug on animals and in other, nonhuman test systems. Because animals have a much shorter lifespan than humans, valuable information can be gained about a drug's possible toxic effects over an animal's life cycle and on its offspring. The company conducts both short-term animal testing (two weeks to three months) and long-term testing (a few weeks to several years). Some long-term animal testing continues after human testing begins to learn whether long-term use of a drug has the potential to cause cancer or birth defects.

If the preclinical testing looks promising, the drug company may file an Investigational New Drug Application (IND) with the FDA. The IND shows the results of the laboratory testing, explains how the drug is made and provides details about how the drug will be tested in humans.

Clinical Trials

Clinical trials are human studies designed to distinguish a drug's effect from other influences (for example, the effect of a placebo, which is an inactive substance that looks like the test drug). Before a drug receives approval to be marketed in the U.S., it must undergo several phases of testing in humans. If the drug appears to be safe and effective after clinical trials with several thousand subjects, the company files a New Drug Application (NDA) with the FDA. This application requires many months of review before the drug receives FDA approval and can be marketed. *Section C of Unit II describes the clinical trial process in greater detail.*

Manufacturing

The processes used in the laboratory to make small amounts of new pharmaceuticals will not work when it is necessary to generate a large enough volume to sell to consumers. Once new products have been developed, process technicians work under the direction of process development scientists and engineers to perfect the manufacturing processes that are needed to produce the product at a larger scale. Engineers work to design, build and gain FDA approval for the facility. Once the manufacturing facility has been built and approved, the team works to produce the product to meet business needs while engineers and maintenance and instrumentation technicians ensure the manufacturing equipment operates properly. A variety of jobs support the manufacturing

process, including maintenance of the plant and all its utilities (electrical systems, water purification systems, heating, ventilation and air conditioning) as well as a comprehensive quality team that is charged with verifying the quality of the manufacturing process and the product. *Section D of Unit II describes the pharmaceutical and biopharmaceutical manufacturing process in greater detail.*



Sales, Marketing and Customer Service

Once a drug has been approved for sale and has been manufactured, a team of corporate scientific professionals focus on getting new products into the hands of physicians and patients. Technical sales and customer service professionals work with physicians and patients who have questions or problems with new treatments.

B. The Pharmaceutical and Biopharmaceutical Industries: Regulated for Safety and Quality²

From the beginnings of civilization, people have been concerned about the quality and safety of foods and medicines. In 1202, King John of England proclaimed the first English food law, the Assize of Bread, which prohibited adulteration of bread with ingredients like ground peas or beans.

Regulation of food and medicine in the United States dates from early colonial times. One of the earliest food and drug laws was enacted by the state of Massachusetts in 1785. Many tragic events in our history raised concerns about food and drug safety and led to regulations that affect the way we develop and manufacture new products, including new medicines. These changes have resulted in better standardization of clinical trials as well as greater protections for the human research subjects who participate in them.

Notable Events, Laws and Regulations of Food and Medicine in U.S. History

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- | | |
|------|--|
| 1848 | Federal controls over the drug supply begin with the inspection of imported drugs in 1848, after the death of American soldiers from contaminated quinine in the Mexican War. Congress passes the <i>Drug Importation Act</i> , which requires U.S. Customs inspections to stop the entry of adulterated drugs from overseas. |
| 1902 | The <i>Biologic Control Act of 1902</i> gives the government regulatory power over antitoxin and vaccine development. Congress enacts the bill after 13 children, who had received diphtheria antiserum prepared in a horse, die from tetanus. The horse had developed tetanus and contaminated the antiserum. |
| 1906 | The modern era of the U.S. Food and Drug Administration (FDA) begins with the passage of the <i>Federal Pure Food and Drug Act</i> . |
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1937 The FDA successfully removes a product labeled “elixir of sulfanilamide” from the market because it is not an elixir (by definition an alcohol solution), but an antifreeze solution. In all, 107 people — mostly children — die after taking the medication for a bacterial infection. The incident emphasizes the need to demonstrate drug safety prior to marketing and leads to Congress passing the **Food, Drug, and Cosmetic Act of 1938**.

1947 The Nuremberg War Crimes Trials expose the unethical medical experiments performed on concentration camp prisoners during World War II. During the trials, 10 standards are drafted as a method for judging the physicians and scientists who conducted the experiments. These standards, known as the **Nuremberg Code**, become the prototype for future codes intended to ensure that future human research will be conducted in an ethical manner.

1962 Thousands of babies with birth defects are born in Western Europe to expectant mothers taking the new sleeping pill thalidomide. The drug is being tested in American women, and nine women in the United States give birth to babies with the characteristic birth defect (a defective development of the arms and/or legs in which the hands and feet are attached close to the body). The magnitude of this tragedy spurs further regulation and demand that both efficacy and safety be demonstrated before marketing. This mandate is incorporated into the **Kefauver-Harris Amendment to the Food, Drug, and Cosmetic Act**.

President John F. Kennedy proclaims the **Consumer Bill of Rights** in a message to Congress. Included are the right to safety, the right to be informed, the right to choose and the right to be heard.

1964 The World Medical Association produces the **Declaration of Helsinki**, which provides guidelines for the ethical treatment of human subjects. The basic elements are incorporated into the U.S. Code of Federal Regulations.

1974	The National Research Act creates the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Five years later, the commission issues the Belmont Report .
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1979	<p>The Belmont Report, a statement of basic ethical guidelines for the protection of human subjects, identifies three basic principles:</p> <ul style="list-style-type: none"> • Respect for persons and protection of those with diminished autonomy • Beneficence, or an obligation to do no harm • Justice, the fair and equal distribution of clinical research burdens and benefits
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1996	<p>Good Clinical Practices are established as an international standard, providing public assurance that trial subjects are protected.</p> <p>The International Conference on Harmonisation (ICH) guidelines are approved by signatories from the United States, European Union and Japan.</p>
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2000	The World Health Organization issues Operational Guidelines for ethics committees that review biomedical research in order to facilitate and support ethical review in all countries around the world.
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2002	The Best Pharmaceuticals for Children Act is passed, which is designed to improve safety and efficacy of patented and off-patent medicines for children.
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2005	The formation of the Drug Safety Oversight Board is announced. It consists of representatives from nine U.S. government agencies, including the FDA, the Centers for Disease Control and Prevention (CDC), the Department of Defense and the National Institutes of Health (NIH). The board advises the FDA on drug safety issues and works with the FDA to communicate safety information to health professionals and patients.
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- 2011 The ***Food Safety Modernization Act*** is signed into law. The act directs a more proactive approach to food safety (rather than primarily reacting to food safety problems) and it calls for a more science-based approach to food safety concerns.

What are Regulations?

In the United States, the general and permanent rules issued by the various departments and agencies of the executive branch of the federal government are published in the Code of Federal Regulations (CFR). The regulations are “codified” — that is, they are collected and arranged by subject matter. Regulations state what may or may not be done (or how something must be done) and are enforceable by law.

There are 50 “titles” in the CFR. The one that relates to food and drugs is known as Title 21. The CFR contains regulations that are vital to ensuring the quality and safety of drugs marketed in the United States. Specifically, the CFR contains regulations for:

- Good Clinical Practice (GCP), a broad term that refers to the accepted standards for conducting clinical research studies
- Good Laboratory Practice (GLP) for laboratories
- Good Manufacturing Practice (GMP) for manufacturers involved in clinical research and production of marketed drugs.

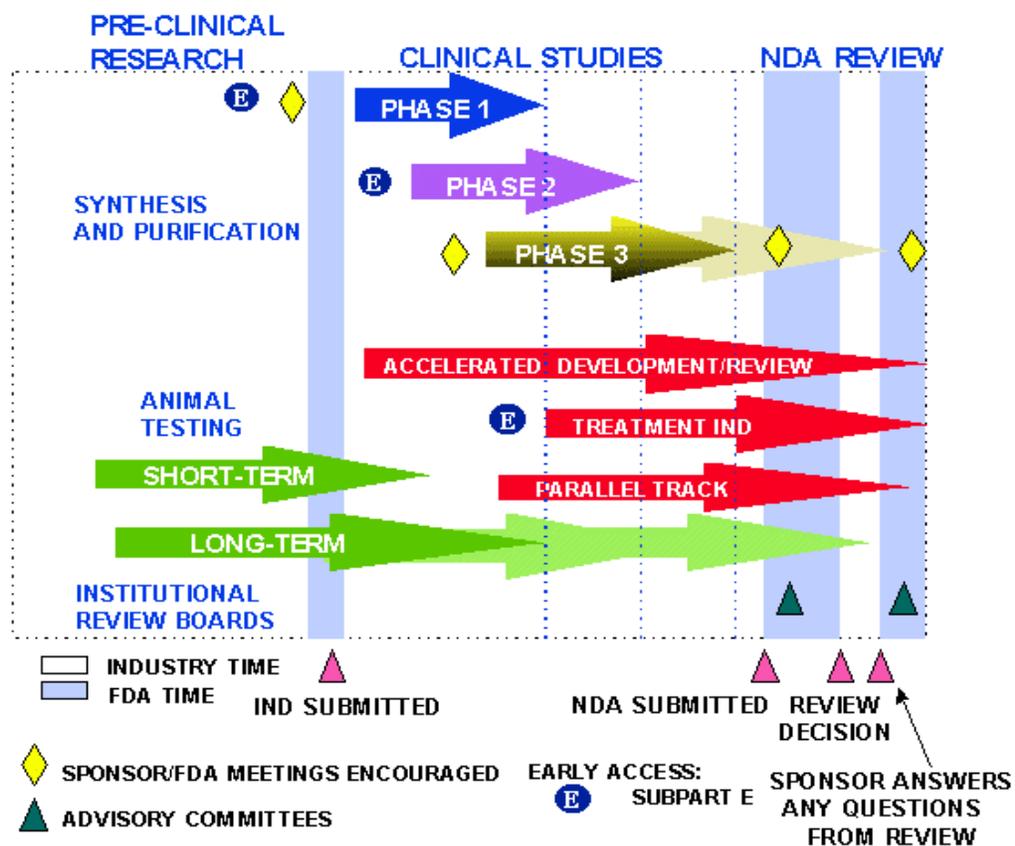
Other regions of the world have similar regulations that govern the development and testing of new drugs. Working with experts from the pharmaceutical industry, the International Conference on Harmonisation (ICH) is a large project focused on bringing together the regulatory authorities of the United States, Europe and Japan to achieve alignment of thought on scientific and technical aspects of pharmaceutical product development.

C. Clinical Trials ³

In Phase 1 trials, the drug is tested for its interaction with the human system, including the way it is absorbed, distributed in the body, metabolized (broken down) and excreted. These trials usually involve normal, healthy volunteers and take about a year to complete.

Phase 2 trials are pilot studies that begin to define the effectiveness and safety of the drug in selected populations of patients with the disease or condition to be treated, diagnosed or prevented. Various doses of the drug and dosing regimens (how often the drug is taken) are evaluated during this phase of testing.

New Drug Development Timeline



Source: FDA/Center for Drug Evaluation and Research

www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm053131.htm

Phase 3 trials are expanded clinical trials intended to gather additional evidence of effectiveness for specific indications and to better understand safety and drug-related adverse effects.

Phase 4 trials are studies that occur after a drug has received approval from the U.S. Food and Drug Administration (FDA) to be marketed. The studies are performed to determine the incidence of adverse reactions, to determine the long-term effect of the drug, to study a patient population not previously studied and for marketing comparisons against other products and users.

Testing in Humans

PHASE	NUMBER OF PATIENTS	LENGTH	PURPOSE	PERCENTAGE OF DRUGS SUCCESSFULLY TESTED
Phase 1	20 to 100	Up to 1 year	Mainly safety	70 percent
Phase 2	100 to 500	Several months to 2 years	Some short-term safety, but mainly effectiveness	33 percent
Phase 3	1,000 to 5,000	1 to 4 years	Safety, effectiveness, dosage	25 to 30 percent

For example, of 100 drugs for which investigational new drug applications are submitted to the FDA, about 70 percent will clear Phase 1 and go on to Phase 2. About 33 of the original 100 drugs will clear Phase 2 and go on to Phase 3. About 25 to 30 of the original 100 drugs will clear Phase 3 and go on to Phase 4. Finally, on average, 20 of the original 100 drugs ultimately will be approved for marketing.

www.centerwatch.com/clinical-trials/overview.aspx

NDA Review: How Long Does This Phase Take?

If the Phase 1, 2 and 3 trials indicate that the drug is safe and effective, the company files a New Drug Application (NDA) with the FDA. The NDA is a comprehensive statement with information about the drug's chemical structure,

scientific rationale and purpose of the drug therapy, preclinical and other laboratory study results, all human clinical testing data, drug formulation and production details, and proposed labeling. The document is thousands of pages long and is submitted electronically — which saves a *lot* of paper!

By law, the FDA has 60 days to conduct a preliminary review and decide if it has enough information to proceed with the NDA review. Then, the FDA is required to make a decision within 180 days of the date the NDA is submitted. This time frame can be lengthened, however, by mutual agreement of the FDA and the company. In practice, the NDA decision-making process can take anywhere from two months to seven years, with an average time of two years. This occurs because the FDA may require minor or major changes to the NDA or additional clinical studies, and may inspect the production, testing and packaging facilities to ensure they are compliant with regulations.

Post-Marketing Surveillance

The goal of the FDA's Post-Marketing Surveillance system is to monitor the ongoing safety of marketed drugs. This is accomplished by reassessing drug risks based on new data collected after the drug is marketed and by recommending ways of trying to most appropriately manage that risk. Surveillance includes adverse reaction reporting by the medical community or the pharmaceutical company that markets the drugs, periodic sampling and testing of the drug, and periodic inspections of the manufacturing and distribution process.



D. Producing a Pharmaceutical or Biopharmaceutical: The Manufacturing Process⁴

Process Development

Even while clinical trials still are underway, 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 from those in the laboratory, and scaling up requires experienced judgment in process or bioprocess development as well as knowledge of scientific and engineering principles.

Production

Once a manufacturing process is in place, it is the job of process technicians and engineers to oversee and operate the equipment that will produce the product. This often consists of large, stainless steel tanks surrounded by a maze of pipes, pumps and computer-controlled hardware. Both pharmaceutical and

biopharmaceutical manufacturing involve many different, complex steps (called unit operations):

SYNTHESIS: CHEMICAL OR CELL CULTURE

The first unit operations are focused on creating the active pharmaceutical ingredient or product.

In chemical-based pharmaceutical manufacturing, the necessary chemicals and reagents are mixed to create the product through chemical synthesis.

In biomanufacturing (bioprocessing), the product is created through cell culture or fermentation (for biomanufacturing) in large tanks called bioreactors. Specialized bacteria, yeast and/or mammalian cells that have been engineered to produce the product are grown in large volumes. In order to ensure harmful bacteria and other types of contamination are not introduced, all ingredients must be sterilized.



PURIFICATION

After the desired product — called the active pharmaceutical ingredient — is synthesized, it must be purified. This means separating it from the other chemicals left over from a chemical synthesis reaction, or separating the living cells from the cellular nutrients and byproducts resulting from biomanufacturing. Purification involves a number of different operations among which often include:

Removal of Solids

Similar to a washing machine's spin cycle (centrifugation) or the way coffee is brewed through a filter, products first are separated from the other solids and waste matter.

Isolation and Concentration of the Product

Once solids and other waste have been removed, the product is concentrated through specialized operations such as chromatography or ultrafiltration that are focused on carefully separating complex solutions.

The end result of production is called the 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

In most cases, several other operations are required to get the bulk product into its final form, which then can be sold. The final forms may be solid (tablets or capsules), liquid, gels/creams or aerosols. Biopharmaceuticals usually are sold as sterile liquids or sterile dry powders. Formulation involves chemical mixing operations to blend the active ingredient with other substances, such as fillers, needed in the final form.

FINAL DOSAGE FORM PREPARATION

The formulated preparation is made into its final form (tablets or sterile solutions, for example), then dispensed into containers. The containers are labeled and packaged.

Quality Control (QC) and Quality Assurance (QA)

The standards are high in this type of manufacturing because the stakes are high. Products of poor quality can harm or even kill consumers. Companies generally ensure quality through their quality control, quality assurance and validation departments. All employees must conform to the guidelines: the Good Manufacturing Practice (GMP), which are regulations established by the U.S. Food and Drug Administration (FDA).

Quality control (QC) employees sample and test both the raw materials and the product during many stages of the manufacturing process. Quality assurance (QA) ensures product quality by setting up and checking the systems of standard operating procedures (SOPs) and of documentation. An SOP guides every task in the manufacturing by defining each procedure in detail so it can be performed exactly the same way every time. This ensures the product meets predefined

specifications. *Section E and Section F of Unit II describe quality and SOPs in greater detail.*

In the manufacturing of pharmaceuticals and biopharmaceuticals, which are regulated by the FDA, companies are required to follow their SOPs. Any deviation from the SOP must be documented and approved by the quality assurance department. Critical deviations that could affect product quality must be investigated to determine impact and disposition of the product. Documentation proves that a company has done what it said, and a company must have a traceable, written record of all process details and checks. The oft-repeated sayings about documentation are: ***“If it isn’t written down, it doesn’t exist. If it isn’t written down, it never happened.”***



Validation

Validation proves that a manufacturing process consistently will produce a product to predefined specifications when carried out exactly, with specified equipment, or that a testing procedure provides accurate results. The operation of every part of the plant that affects product quality — manufacturing equipment, utilities and even the computerized data processing systems used to record and document all aspects of production and testing — must be validated. If the manufacturing process has to be changed or if a new product or process has to be introduced, all steps and parts of the new process that affect product quality have to be validated. Validation scientists and engineers usually need extensive experience in the industry. They must be thoroughly familiar with the FDA regulations and how to implement them.

E. What Quality Means and Why it Matters

The Price of Poor Quality

To be competitive in any industry, companies need to produce high-quality products. When quality is poor, companies pay for it in:

- Damaged company reputation
- Lost customers
- Injured, ill or deceased customers
- Expensive lawsuits
- High production costs
- Loss of potential profit due to bad batches
- Company shutdowns and lost jobs

In biotechnology manufacturing, “quality” is not just a word. It is a way of making sure products consistently are made to the same high standard each time they are manufactured.

The most serious impact of poor-quality products (such as chemicals or drugs) is that they harm or even kill consumers. Consumers need safe products that consistently meet the standards they require. And every employee contributes to the quality of the product.

Five Rules for Quality

How does a company achieve quality? Each company has its own plan, but here are five basic rules:

1. UNDERSTAND CUSTOMER NEEDS

To understand customer needs, a company first must identify external and internal customers and then ask, “What do these customers need and expect?”

External customers are the individuals who purchase the product. Internal customers are company employees. If you are a process technician who works “on the floor” in a biomanufacturing plant, your coworker at the next stage of the manufacturing process is your internal customer. You, in turn, are an internal customer of your coworker who runs the previous stage of the process. You are also the internal customer of maintenance, utilities and other departments that affect your work.

2. SAY WHAT YOU DO (WRITE DOWN PROCEDURES)

A company must have clearly written procedures approved by quality assurance that describe what must be done in a process. Standard procedures and forms are required for every production and testing operation. In addition, batch records define the steps required to manufacture the product, the materials used, testing required and so on.

3. DO WHAT YOU SAY (FOLLOW PROCEDURES)

A company must consistently and exactly follow the procedures that have been developed.

4. PROVE IT (KEEP RECORDS)

To prove it has done what it said, a company must have a traceable, written record of all process details and checks. Technicians in a biomanufacturing facility, for example, must correctly fill out manufacturing records. Remember: ***If it isn't written down, it doesn't exist. If it isn't written down, it never happened.***

5. IMPROVE IT

Following the first four rules goes a long way toward ensuring quality, but it still is not quite enough. Because the product and process never are perfect and because there always is room for improvement, a company continually must evaluate its process and procedures and take steps to make them better while ensuring product quality.

F. Standard Operating Procedure (SOP) and Regulations ⁵

A standard operating procedure (SOP) defines a particular process in detail so it can be performed exactly the same way every time. SOPs guide every task in the manufacturing process. In manufacturing of pharmaceuticals and biopharmaceuticals, which are regulated by the U.S. Food and Drug Administration (FDA), companies are required to follow their SOPs. Any deviation

from the SOP or batch record must be documented and approved by the quality assurance department. Critical deviations must be investigated to determine their impact on product quality.



Companies regulated by the FDA are required to follow lengthy regulations that can be found in the federal government's Code of Federal Regulations (CFR). This is an annually updated documentation of the general and permanent rules by the executive departments and agencies of the federal government. It is divided into 50 titles that represent broad areas subject to federal regulation. Title 21 (Food and Drugs), Chapter 1 of the CFR includes most of the regulations affecting the discovery, approval, manufacturing and marketing of drugs and biopharmaceuticals.

The regulations that most directly affect biopharmaceutical and pharmaceutical manufacturing are known as Good Manufacturing Practice (GMP). GMP regulations describe the methods, equipment, facilities and controls required for producing these products and can be found in Title 21, Chapter 1, Parts 210, 211 and 820.

What is Included in SOPs?

There is no federally approved format for an SOP, but there are expectations within industries about how an SOP should be written. The SOP is written in imperative sentences rather than in a narrative style. A cookbook format is used, and sentences should start with a task-specific verb that tells what to do. The instructions are numbered in the order they will be followed.

Although the headings in a company SOP may vary from those listed below, the type of content will be similar.

EFFECTIVE DATE

Date the SOP takes effect

PURPOSE

Describes the purpose of the procedure

SCOPE

States what the SOP applies to

SAFETY

Informs operators of hazards and necessary protection

RESPONSIBILITY

States who should perform the SOP

REFERENCES

Lists other SOPs or documents needed to perform the SOP

MATERIALS AND EQUIPMENT

Lists materials and equipment needed to perform the SOP

PROCEDURES

Provides detailed steps for carrying out a task

APPROVAL

Shows the persons who have reviewed and approved the SOP

Activity

NEW DRUG DEVELOPMENT

TEACHER PAGE

LEARNING OUTCOMES

- Students will analyze sample advertisements for clinical trials.
- Students will justify where the clinical trial advertisements could fall on the new drug development timeline.
- Students will investigate the drug development process.
- Students will identify advantages and disadvantages of long-term studies for new drugs.
- Students will construct a response to the *FDA Director Experience*.

ESTIMATED TIME

80–90 minutes

CONTENT

Unit II, Sections A–C

PURPOSE

Two stages are offered for this activity. The ***Human Clinical Trials*** stage serves as an introduction to the new drug development process. The ***FDA Director Experience*** provides an opportunity for students to apply critical thinking skills and to research drug development in a role-playing scenario.

Stage 1: Human Clinical Trials

MATERIALS

- *New Drug Development* student pages (pages 77–80)

TEACHER PROCESS

- Divide the class into groups of 2–4 students.

Activity

NEW DRUG DEVELOPMENT

TEACHER PAGE CONTINUED

- Pass out the *New Drug Development* student pages to each group. Have students read the pages and review the sample advertisements. (These were actual advertisements that appeared in newspapers.)
- Have students discuss and respond in their groups to the questions listed below. Example student answers follow in italics.

DISCUSSION QUESTIONS & EXAMPLE STUDENT ANSWERS

- What questions are researchers trying to answer with each study?
 - » *In “Kids Get Anxious Too!”, the trial appears to be in Phase 2 or 3. The researchers want to work with kids who have an anxiety disorder. The researchers want to see the effectiveness of the drug for students while monitoring side effects.*
- What necessary phases must occur before a research study can involve human subjects, and why are those phases important?
 - » *Animal testing occurs in the preclinical research phase. Also, animal testing occurs simultaneously during Phases 1, 2 and 3. (Students should realize that the use of animal models helps reduce the risk of danger to humans.)*
- Would you consider being a participant in a research study? Would there be any circumstances that would make you more likely to participate? (For example, if you were to experience pain, shortness of breath or a lack of energy, would you be more willing to participate in a study that targeted your particular symptoms?)
 - » *Look for answers beyond “yes” and “no.” Encourage students to develop reasons for their choices.*
- What information is common to some or all of the ads?
 - » *Age range of prospective participants, name of the condition or disease under study, purpose of the research, compensation, time commitment*

Activity

NEW DRUG DEVELOPMENT

TEACHER PAGE CONTINUED

OTHER OPTIONS

- Have students check the classifieds or other sections of the newspaper for additional ads.
- Have students write their own ads looking for human clinical trial participants.
- Have students search online for clinical trials that treat a condition that interests them, for clinical trials nearby, etc. Useful websites include:
 - » National Institutes of Health (www.clinicaltrials.gov)
 - » CenterWatch (www.centerwatch.com)
 - » Coalition of Cancer Cooperative Groups (www.cancertrials-help.org)
 - » Duke Medicine (www.dukehealth.org/clinicaltrials)

Stage 2: FDA Director Experience

MATERIALS

- Internet access

TEACHER PROCESS

- This activity is designed to prompt students to research and analyze current information related to new drug development and clinical trials. In this activity, students are divided into groups of 3 or 4 and given the scenario outlined on page 76.
- In a computer lab with Internet access, students should research websites to gather information about the drug development process in order to clearly and accurately respond to the challenges and questions posed by the scenario.
- Have students discuss and respond in their groups to the questions listed on the next page. Example student answers follow in italics.

Activity

NEW DRUG DEVELOPMENT

TEACHER PAGE CONTINUED

DISCUSSION QUESTIONS & EXAMPLE STUDENT ANSWERS

- Why do you think the government regulates the availability of new drugs?
 - » *The government regulates drug development to protect the public from companies that might bring a drug to market after only a small clinical trial.*
- What are the advantages and disadvantages to stringent, long-term studies of new drugs?
 - » *Advantages include increased safety of the drugs that come to market and confidence in the effectiveness of the drugs. Disadvantages include the long wait for promising drugs to reach consumers and the increase in cost because of the long development process.*
- Does the need for an accelerated development review outweigh the risk of developing a drug with serious side effects? Explain.
 - » *Encourage each student to provide clear, logical reasons in defense of his or her answers.*
- Should the number of people affected influence whether the drug is put on a development fast track? Explain.
 - » *Encourage each student to provide clear, logical reasons in defense of his or her answers.*
- Why can't all drugs be put through the accelerated development process?
 - » *It is important to weigh the harms and benefits of drugs. If a drug improves the quality of life but is not life-saving, then the drug should undergo more testing to make sure that it does not ultimately threaten life.*
- What would happen if drug development were not regulated?
 - » *To ensure higher profit margins, companies could bring drugs to market that were not safe.*
- A number of U.S. companies now are running clinical trials in foreign countries. Do you think this is a good idea? What are some of the potential problems that could occur in foreign drug trials?

Activity

NEW DRUG DEVELOPMENT

TEACHER PAGE CONTINUED

- » *The genetic and environmental factors are different and may influence the drugs' performance. (Encourage each student to provide clear, logical reasons in defense of his or her answers.)*

SCENARIO

You are the director of the U.S. Food and Drug Administration (FDA). One Monday morning, you read an editorial in The New York Times written by the president of another nation in which HIV has infected more than 10 percent of all women, with even higher rates of infection predicted. To make matters worse, the most common form of the virus in the population is resistant to all known HIV medications. In his editorial, this president criticizes the “overly cautious policies” of the FDA, which he says unnecessarily delay the approval of promising drugs to fight HIV. This delay in approval in turn blocks the pipeline of potentially life-saving drugs available for import into his country. How might you respond to his charges?

USEFUL WEBSITES

The following sites offer online tutorials and additional information about clinical trials. They can help students and educators better understand the clinical trials process:

- *Clinical Trials*, a basic tutorial written for prospective trial participants (www.nlm.nih.gov/medlineplus/tutorials/clinicaltrials/html/index.htm)
- *Learn About Clinical Trials*, from ClinicalTrials.gov (clinicaltrials.gov/ct2/info/understand)
- Overview of Clinical Trials, which describes the phases of a clinical trial and issues to consider before entering a trial (www.centerwatch.com/clinical-trials/overview.aspx)

Activity

NEW DRUG DEVELOPMENT

STUDENT PAGE

Human clinical trials are a very important component of the biomedical research process and are used in developing prescription drugs. Even after a promising new drug has undergone extensive laboratory research and testing, scientists still need actual human data from controlled studies to answer two key questions:

1. Is the drug effective in humans?
2. Is the drug safe in humans?

There are three major phases of clinical trials that begin after a pharmaceutical firm files an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA). In the IND, a pharmaceutical firm shows the results of testing in animals and explains how the drug is made.

In **Phase 1** clinical trials, researchers determine a drug's interaction with the human system, including how it is absorbed, distributed, metabolized and excreted, and the likely duration of its therapeutic effect. This phase usually includes a small number of healthy volunteers (20 to 100) and takes approximately one year.

Phase 2 trials use controlled tests for the initial evaluation of safety and effectiveness. These studies involve 100 to 300 volunteer patients who have the targeted disease. Simultaneous animal and human tests also are conducted at this stage, as researchers continue to assess the safety of the drug. This phase takes approximately one to three years.

Phase 3 trials are conducted to confirm the results of earlier efficacy tests and to further identify any adverse reactions. Clinical testing at this point is extensive, involving 1,000 to 5,000 volunteer patients in medical clinics and hospitals. This phase takes approximately two to five years.

Activity

NEW DRUG DEVELOPMENT

STUDENT PAGE CONTINUED

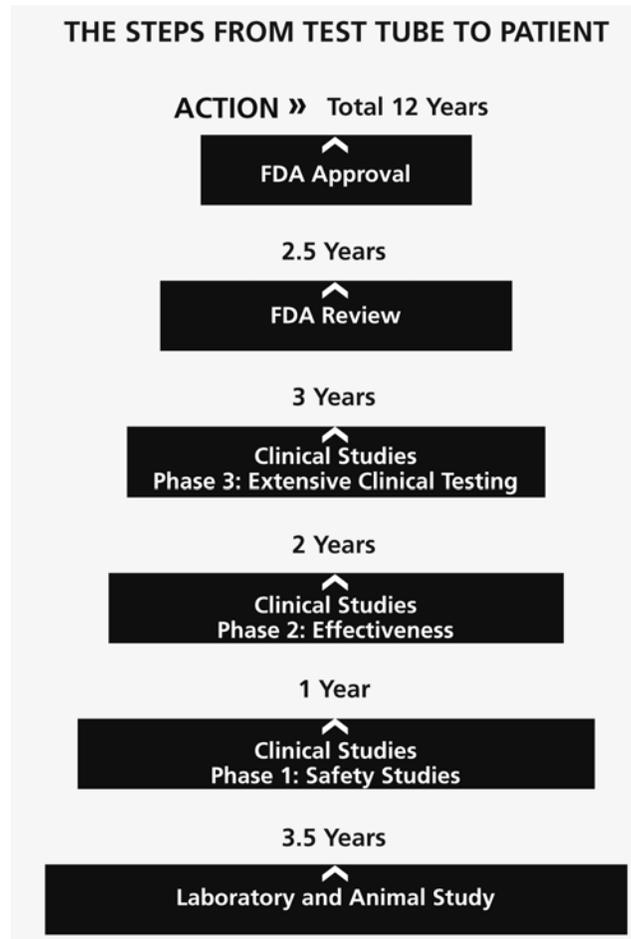
After human clinical trials are completed, firms file a New Drug Application (NDA) with the FDA. The NDA is a comprehensive statement of the information on drug structure, the scientific rationale and purpose of the drug therapy, preclinical animal and other laboratory study results, all human clinical testing results, drug formulation and production details, and the company's proposed labeling. The NDA is thousands of pages long and is submitted electronically — which saves a *lot* of paper! The FDA review is extensive and takes anywhere from two months to two years.

It takes an average of 10 to 15 years from initiation of animal and other laboratory studies through all phases of clinical trials and submission of data to the FDA for approval. For each new medicine approved, the costs are as high as \$800 million to \$1 billion.

Activity

NEW DRUG DEVELOPMENT

STUDENT PAGE CONTINUED



Source: Joseph Dimasi, Tufts University

The time frame for each phase of drug development illustrated above is an approximation and can vary widely. In addition, the FDA has a fast-track program to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. Since 1998, more than 80 medications have been approved via the fast-track program, including drugs to treat HIV, various cancers and even anthrax.

Activity

NEW DRUG DEVELOPMENT

STUDENT PAGE CONTINUED

Actual Advertisements for Clinical Trials

KIDS GET ANXIOUS TOO!

Is your child:

Too afraid to go to school?

Overly worried about bad things?

Afraid to be away from you?

So shy or easily embarrassed that it interferes with his or her school performance or social activities?

If you answered “yes” to any one of these symptoms, your child may be suffering from an anxiety disorder that can be treated. At the Program in Child and Adolescent Anxiety Disorders (PCAAD) at _____ University Medical Center, our doctors can determine if your child needs help. Children aged 7 to 17 may qualify to participate in a research project and receive expert care with medication or psychotherapy.

GENETIC STUDY OF ADHD

Do you have a child diagnosed with ADHD who is between the ages of 5 and 18? If so, your help is needed with an important research study at _____ to find genes that may contribute to ADHD. Participation involves five to six hours of your time, and each family is compensated with \$30 for their time.

SEE YOUR BRAIN

The Healthy Childhood Brain Development Program is recruiting healthy teens to study how their brains look and function. The program will use magnetic resonance imaging (MRI), to create computer pictures of the brain. Eligible participants and one parent will spend approximately one day completing interviews and questionnaires. On a second day participants will return for an MRI scan. Participants are paid \$100 for completing the evaluation and \$70 for the MRI, plus travel expenses.

DO YOU SUSPECT YOUR TEEN IS DRINKING?

Have you noticed any of the following:

1. Problems with school or attendance?
2. Unexplained change in behavior/mood?
3. Difficulties with friends or parents?
4. Suspensions or expulsions?

The Healthy Childhood Development Program at _____ offers a comprehensive day-long evaluation. We can provide diagnosis, recommendations, and referrals. Participants are paid \$50 per day, plus travel expenses. Participants return on a 2nd day for an MRI of the brain.

ARE YOU ALLERGIC TO PEANUTS?

You may be eligible to participate in a clinical study for children and adults (6-75 years of age) to test whether a new drug is safe and effective in reducing allergic reactions to peanuts. If you or your child have a history of an allergic reaction with any of the following symptoms after eating peanuts or foods containing peanuts, you may be eligible to participate: itchy eyes; runny nose; rash; hives; swelling; throat tightness; wheezing; stomach cramps; diarrhea; vomiting. Participation requires visits to your physician every two to four weeks for approximately nine months. Some reimbursement for expenses will be provided.

DOES YOUR CHILD HAVE SEASONAL ALLERGIC RHINITIS?

Physicians at the _____ Department of Pediatrics are studying a new medication to treat seasonal allergic rhinitis (allergies). In this study the medication or a placebo, in the form of a nasal spray, will be given for two weeks. The study involves four visits over one month. Saturday and after-school visits are available. Your child needs to be at least 2 but fewer than 12 years old to enter. Participants will receive:

- Skin testing for allergies
- Compensation for participation and parking

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

TEACHER PAGE

LEARNING OUTCOMES

- Students will plan a procedure for creating a batch of Kool-Aid using the materials provided by the teacher.
- Students will write an SOP for creating a batch of Kool-Aid.
- Students will test another group's SOP for creating a batch of Kool-Aid.
- Students will critique the SOPs and offer improvement.

ESTIMATED TIME

45–60 minutes

CONTENT

Unit II, Section F

PURPOSE

To practice and learn the importance of two of the five rules for quality: **Say what you do** (writing good procedures) and **Do what you say** (following procedures exactly). The focus is on helping students understand that even a simple process must be controlled carefully to ensure a consistent quality.

This activity has two stages. In **Stage 1**, students will work in groups to develop a procedure that tells how to make a batch of Kool-Aid. In **Stage 2**, each group will test another group's procedure while the class observes. By following the procedure exactly, the group will do what the procedure states to make Kool-Aid. As each procedure is tested, the class will identify problems and suggest revisions.

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

TEACHER PAGE CONTINUED

MATERIALS

For Each Group

- *Say What You Do and Do What You Say* student pages (pages 87–88)
- 2-quart (or 2-liter) pitcher (or larger)
- Long-handled mixing spoon
- Measuring cup with minimum volume of 1 cup (or 200 milliliters)
- 2 Kool-Aid packets, all the same flavor (if possible, use packets with different lot numbers)
- 2 cups (~400 grams) of granulated sugar (plus a little extra)

For the Class

- 1 disposable cup per student for sampling the product
- Water (bottled water if the class does not have access to a sink)

Important Safety Note

Make sure to use food-grade, kitchen equipment instead of normal lab equipment.

Stage 1

TEACHER PROCESS

Have students work in groups to develop a procedure that tells how to make a batch of Kool-Aid. Distribute a copy of the student pages to each group. Once they are finished, each group should have listed the materials and equipment needed to perform the procedure.

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

TEACHER PAGE CONTINUED

Materials

- 1 package of unsweetened Kool-Aid that makes 2 quarts (or 2 liters). Students should include the flavor, lot number and expiration dates of the Kool-Aid.
- 1 cup (~200 grams) of granulated sugar. Students should include the brand and any identifying manufacturing codes.
- The source of the water used

Equipment

The equipment below should be listed. Students should number or color-code equipment so they can include this information in the description.

- 1 measuring pitcher
- 1 long-handled mixing spoon
- 1 measuring cup for liquids
- 1 measuring cup for solids
- *Optional: 1 thermometer to record the water temperature*

Suggested Student Procedure

1. Fill pitcher with water to the 2-quart line.
2. Pour sugar into the measuring cup to the 1-cup line.
3. Empty the cup of sugar into the pitcher.
4. Empty the package of Kool-Aid into the pitcher.

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

TEACHER PAGE CONTINUED

5. Use the spoon to stir the mixture until no solid material (sugar or Kool-Aid powder) is visible in the bottom of the pitcher.

OTHER OPTIONS

As an alternative, have students develop the procedure for making peanut butter and jelly sandwiches.

Stage 2

TEACHER PROCESS

- Have each group test another group's procedure while the class observes. By following the procedure exactly, the group will do what the procedure states to make Kool-Aid. As each procedure is tested, ask the class to identify problems and suggest revisions.
- Have students complete the discussion questions listed on the student pages for this activity. These discussion questions also are listed below. Example student answers follow in italics.

DISCUSSION QUESTIONS & EXAMPLE STUDENT ANSWERS

1. Why is such a detailed procedure needed for such a simple process?
 - » *The detailed procedure helps ensure that the process will be performed exactly the same way every time, this creating a high quality, consistent product.*
2. Suppose the Kool-Aid made by your group was a liquid, life-saving drug. Would you trust it to save your life? Why or why not?
 - » *Encourage each student to provide clear, logical reasons in defense of his or her answers.*

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

TEACHER PAGE CONTINUED

Sample SOP

HYBRID-TECH INC	Effective date: 04/11/2014	Review date: 04/10/2015
SOP # 102 Author: Barry Qualified, Ph.D.	Version number: 1	Page #: 1 of 2

SYNTHESIS OF KOOL-AID PROCEDURES

- 1.0 Purpose
The purpose of this SOP is to specify the procedures for making a 2-quart batch of Kool-Aid sweetened with sugar.
- 2.0 Scope
This procedure describes the methods used to make 2 quarts of Kool-Aid, any flavor.
- 3.0 Responsibility
All students and teachers shall be instructed in the correct preparation of Kool-Aid.
- 4.0 References
SOP 100: Obtaining Materials for the Preparation of Kool-Aid
SOP 101: Cleaning Equipment for the Preparation of Kool-Aid
- 5.0 Materials and Equipment
Materials
For each 2-quart batch of Kool-Aid:
 - 5.1 1 package of unsweetened Kool-Aid that makes 2 quarts. Record on the Materials Batch Sheet the purchase date, store and location, flavor of Kool-Aid, lot number and expiration date.
 - 5.2 1 cup granulated sugar. Record on the Materials Batch Sheet the purchase date, store and location, brand of sugar and any identifying manufacturing code.
 - 5.3 2 quarts of water. Record on the Materials Batch Sheet the source of the water. If bottled water, record on the Materials Batch Sheet the brand of water and any other identifying manufacturing code as well as the purchase date, the store and its location.

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

TEACHER PAGE CONTINUED

SOP # 102
Page 2 of 2

Equipment

- 5.4 1 container with lid that holds at least 2 quarts. Record on the Equipment Log any identifying information on the container.
- 5.5 1 long-handled mixing spoon. Record on the Equipment Log any identifying information on the container.
- 5.6 1 measuring cup for liquids. Record on the Equipment Log any identifying information on the container and a description (manufacturer, size of the cup and other identifying information).
- 5.7 1 measuring cup for solids. Record on the Equipment Log any identifying information on the container and a description (manufacturer, size of cup and other identifying information).
- 5.8 Thermometer to measure the temperature of the preparation. Record on the Equipment Log any identifying information on the thermometer and a description (manufacturer, range of temperatures and other identifying information).

6.0 Procedures

- 6.1 Measure the temperature of the water.
- 6.2 Fill container with 2 quarts of water using the measuring cup for liquids.
- 6.3 Measure 1 cup of granulated sugar using the measuring cup for solids.
- 6.4 Empty the cup of sugar into the container.
- 6.5 Empty the package of Kool-Aid powder into the container.
- 6.6 Use the spoon to stir the mixture until no solid material (sugar or Kool-Aid powder) is visible at the bottom of the container.
- 6.7 Secure the lid on the top of the container.

Approvals:

Jack J. Marcus, Quality Control Associate

Date

Good M. Practice, Supervisor

Date

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

STUDENT PAGE

In this activity, you will become familiar with two of the five rules for quality: ***Say what you do*** and ***Do what you say***.

In **Stage 1** of the activity, you will work in a group to develop a procedure that tells you how to make a batch of Kool-Aid. In **Stage 2**, your group will test another group's procedure while the class observes. By following their procedures exactly, your group will do what the procedure states for making Kool-Aid. As each procedure is tested, the class will identify problems and suggest revisions.

INSTRUCTIONS FOR STAGE 1

1. Collect supplies from your instructor.
2. Work with your group to develop a procedure for making Kool-Aid. Make a batch to help you determine the steps.
3. Carefully write out each step of the procedure. Make sure your procedure is precise enough that someone would be able to perform the task successfully by following directions exactly as written. Make sure to also list all materials and equipment needed to perform the procedure, using as much detail as possible.

INSTRUCTIONS FOR STAGE 2

1. Exchange your procedure sheet for the procedure sheet developed by another group.
2. Collect supplies from your instructor.
3. Each group will make a batch of Kool-Aid, exactly following the procedure while the other groups observe.

Activity

SAY WHAT YOU DO AND DO WHAT YOU SAY

STUDENT PAGE CONTINUED

4. When you observe, identify problems with the procedures and be prepared to discuss corrections with the class.
5. Discuss the questions below.

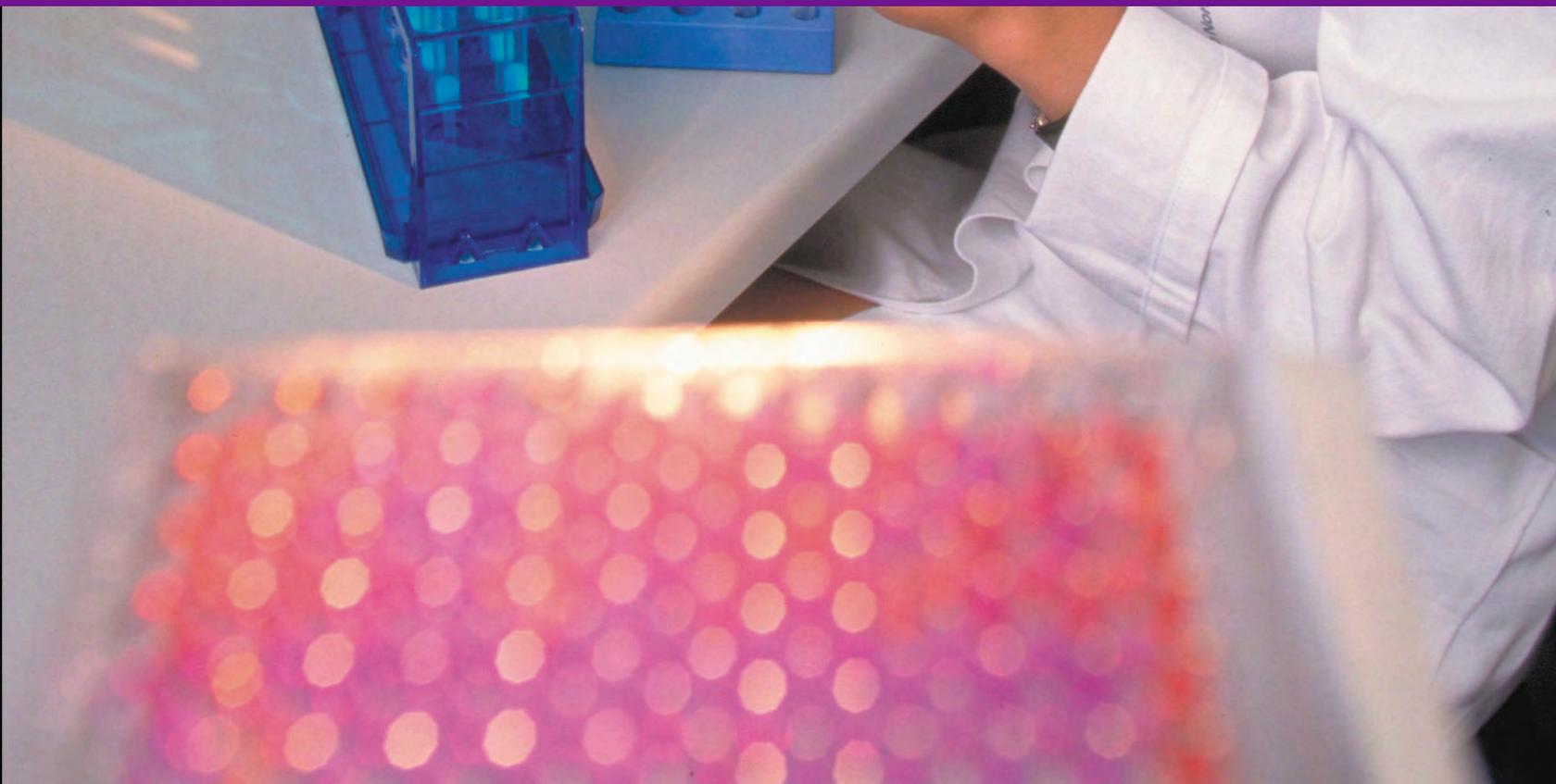
DISCUSSION QUESTIONS

1. Why is such a detailed procedure needed for such a simple process?
2. Suppose the Kool-Aid made by your group was a liquid, life-saving drug. Would you trust it to save your life? Why or why not?



Unit III

CAREER OPPORTUNITIES



A. Biotechnology Generates Opportunities

In the United States

AS A LEADING CONSUMER

The United States is the largest market and leading consumer of biotechnology products in the world and is home to more than 1,300 firms involved in the industry.¹

AS A GROWING INDUSTRY

Between 2001 and 2010, the U.S. bioscience industry grew by 6.4 percent, adding more than 96,000 jobs. By comparison, total employment for all private sector industries in the United States fell by 2.9 percent during that time period, losing more than 3 million jobs.²

AS A HUGE ECONOMY

More than 810,000 people work in the biopharmaceutical industry in the United States, and the industry supports a total of nearly 3.4 million jobs across the economy. This includes jobs in biopharmaceutical companies, jobs with vendor companies in the broad biopharmaceutical supply chain and jobs created by the economic activity of the biopharmaceutical industry workforce.³

AS A CONTINUALLY STRONG OUTPUT

The biopharmaceutical sector directly was responsible for \$63.9 billion in real output in 2003 (up from \$8 billion in 1992).⁴ It is estimated that by 2030, bioscience innovations could contribute up to 35 percent of the output of chemicals and other industrial products, 80 percent of pharmaceuticals and diagnostic production, and 50 percent of agricultural output worldwide.⁵



AS A SOUND INVESTMENT

In 2012, biopharmaceutical companies invested more than \$48.5 billion in the discovery and development of medicines.⁶

AS A HIGH-PAYING CAREER

The average bioscience job paid \$82,697 in 2010 — or \$36,000 more than the average private sector job.⁷

AS A MULTITUDE OF FAST-GROWING OCCUPATIONS

Most occupations within the bioscience industry are expected to maintain average growth of 14 percent between 2010 and 2020, with some occupations, such as biochemist and biophysicist, expected to grow much faster.⁸

AS A GROWING EMPLOYMENT BASE

Employment in pharmaceutical and medicine manufacturing is projected to increase by 13 percent between 2012 and 2022.⁹



In North Carolina

AS A THRIVING INDUSTRY

North Carolina is home to a large bioscience community, which, as of 2011, consisted of more than 58,000 employees at more than 500 companies. This sector has added approximately 8,539 jobs since 2002.¹⁰

AS A GROWING BIOMANUFACTURING CLUSTER

Within this group, approximately 18,700 people are employed in a recognized cluster of “biomanufacturing” companies that share similarities in jobs, process technology and international regulatory oversight. This cluster of companies has grown an average of 2.2 percent per year between 2002 and 2011, a rate of growth much higher than that of many traditional manufacturing industries.¹¹

AS A HOTBED OF CLINICAL RESEARCH ACTIVITY

North Carolina is home to one of the nation’s largest concentrations of contract research organizations (CROs), which account for a large portion of the bioscience industry growth in North Carolina.¹²



AS AN ATTRACTIVE BUSINESS CLIMATE

Citing North Carolina’s infrastructure, business climate and workforce availability, many biomanufacturing companies have not only expanded their manufacturing operations in North Carolina — they also have moved non-manufacturing operations to their sites in North Carolina.¹³

A STRONG TALENT POOL

Biomanufacturing and pharmaceutical manufacturing employers in the Research Triangle Park region are able to recruit approximately 90 percent of their new hires locally rather than importing talent from other states.¹⁴

Broadly speaking, the bioscience industry is a fast-growing field that offers job seekers a great diversity of employer types, company sizes and career opportunities. In addition to the many scientific and engineering jobs, there are many non-scientific jobs — from writers and marketing specialists to financial personnel, project managers and customer service personnel — that do not require extensive training in the life sciences.

Yet in order to ensure that bioscience employers can continue to meet hiring needs as companies continue to grow and expand, it is critical that students and teachers alike recognize the value these jobs bring.

B. Seizing the Opportunity ¹⁵

If you have the qualifications, you will be in a good position to enjoy the unique opportunities and benefits offered by the bioscience industry. Whether you're working for a small startup that is developing a new product, a large bioprocess or pharmaceutical manufacturer, or an international clinical research organization that is focused on managing clinical research activities, you will be part of a growing and thriving industry. It's an industry in which skilled, competent employees are valued and in great demand.

Advantages of Working for Bioscience Companies

PRIDE IN YOUR PRODUCT

You will have the satisfaction of researching, developing and making products that improve lives and boost the economy. These products can:

- increase food production, making it possible to feed the world.
- reduce infant deaths and prevent childhood diseases.
- relieve painful symptoms, fight disease and save lives.

HIGHER WAGES

Employees in the bioscience industry earn a high average wage. In the case of bioprocess, pharmaceutical and chemical manufacturing, this wage is well above the average of many "traditional" manufacturing industries.

STABLE EMPLOYMENT

A rapidly growing industry increases the demand and opportunities for skilled, competent professionals. Your knowledge is your unemployment insurance. Individual companies and whole industries can have their ups and downs in the world marketplace, but your mastery of biotechnology tools and bioprocess manufacturing technology, and your ability to work in a regulated environment are portable. If the particular company you work for downsizes, you are very likely to find a job with a different company.

MODERN AND PROFESSIONAL ATMOSPHERE

Most companies are high-tech, computer-controlled, efficient organizations staffed by well-educated professionals, engineers, technicians and scientists.

Many companies use a team approach and encourage employees to assume higher levels of responsibility for problem solving.

SAFE WORKING ENVIRONMENTS

Bioscience companies provide a very safe place to work because they are highly regulated by the government. One of the first things you will acquire on the job is thorough training in safety.

JOB VARIETY AND CAREER ADVANCEMENT

Employees often have an opportunity for cross training (learning on the job in different parts of the manufacturing process) or even moving out of manufacturing entirely. There is opportunity for career advancement not only in moves like this, but also as employees gain more experience. People often can advance in managerial tracks, with more supervisory responsibility, or they may choose to advance within scientific or engineering specialty tracks.

Bioscience companies often have programs that reward employees for their knowledge and skills. Specifically, they reward employees for completing in-house training and formal academic education. In addition, many companies provide some amount of tuition support for employees to attend college courses.



C. On the Job: Careers in a Typical Bioscience Company¹⁶

A large biomanufacturing company relies on a highly diverse group of employees working to bring a new product to market. In addition to this work happening at pharmaceutical and biopharmaceutical manufacturing firms, it is important to note that these companies often rely on the work of other companies to get the job done. As a result, many of the same exciting career possibilities exist at different types of companies in a broad bioscience industry that spans research and development (R&D) startups, contract research and testing companies, clinical research organizations (CROs), and specialized vendors.

Bringing a new product to market requires all kinds of minds: people who enjoy working in laboratories, people who enjoy working in offices and people who enjoy working on the manufacturing floor. Biomanufacturing and pharmaceutical manufacturing companies value education and rarely hire people straight out of high school. Fortunately, educational options at all levels are available to guide students toward entry-level jobs and rewarding careers in the lab, office and manufacturing environment. These educational options include:

- Certificate programs and short courses (less than a two-year degree program)
- Two-year degree programs: Associate of Science (A.S.), Associate of Applied Science (A.A.S.)
- Four-year degree programs: Bachelor of Science (B.S.), Bachelor of Arts (B.A.)
- Graduate degrees: Ph.D., Master of Science (M.S.), Professional Science master's degree
- Professional degrees: Doctor of Medicine (M.D.), Juris Doctor (J.D.)

While the actual organization of the various departments and jobs may vary greatly from one company to another, the job functions and sample job titles listed on the following pages illustrate the type of positions that exist in a typical biomanufacturing facility (as well as in many of the other companies in the bioscience industry).

Job Type: Scientist

OVERVIEW

Scientists from many different backgrounds are critical in guiding the research, development and manufacturing work central to biotechnology and other industries by developing and leading the innovative thinking around new products.

EDUCATIONAL REQUIREMENTS AND PREFERENCES

Entry-level positions typically require an M.S. or Ph.D. in specialized disciplines such as chemistry (especially organic and medicinal chemistry), cell biology, molecular biology, toxicology, genetics, immunology and biochemistry.

SAMPLE JOB TITLES

Discovery Research Scientist

Works in a team in numerous areas, such as identifying new drug targets, creating animal models to test new drugs and investigating the causes of and treatments for diseases. Disciplines include chemistry (especially organic and medicinal chemistry), cell biology, molecular biology, genetics, immunology and biochemistry.

Process Development Scientist

Designs and executes experiments associated with the development, improvement and scale-up of production processes; interfaces with engineering groups and laboratory groups.

Quality Control Manager

Manages personnel and activities needed to analyze raw materials, in-process samples and finished formulations according to standard operating procedures (SOPs).

Toxicologist

Designs experiments and research studies focused on evaluating the harmful effects of a potential product on human health or the environment.

Other job titles include chemist, microbiologist, biochemist, natural science manager, research and development scientist, research associate, and environmental scientist.

CAREER PATHWAYS

As their careers progress, many scientists move into roles with significant management responsibilities. These responsibilities include overall business planning and overseeing projects and other personnel. In addition, many scientists move out of the laboratory environment into roles as a corporate scientific professional.

Job Type: Laboratory Technician

OVERVIEW

Working under the direction of a scientist or engineer, laboratory technicians essentially are the scientist's hands. They spend much of their time in a laboratory, performing research experiments according to good laboratory practices and collecting and analyzing data.

EDUCATIONAL REQUIREMENTS AND PREFERENCES

Depending on the company and the specific job, entry-level laboratory technician jobs can be found for graduates from both two-year and four-year degree programs:

At the two-year degree level (A.S. or A.A.S.), relevant disciplines include biotechnology, bioprocess technology, laboratory technology and industrial pharmaceutical technology.

At the four-year degree level (B.S. or B.A.), relevant disciplines include the biological sciences, chemistry, microbiology, biochemistry and molecular biology.

SAMPLE JOB TITLES

Research Assistant/Associate

Performs lab experiments and tests according to good laboratory practices under the direction of a research associate.

Process Development Associate

Seeks out new and more efficient ways to use and produce existing products.

Process Quality Inspector

Performs a wide variety of inspections, checks, tests and sampling procedures related to the manufacturing process.

Quality Control Associate

Analyzes raw materials, in-process samples and finished formulations according to SOPs.

CAREER PATHWAYS

Starting a career as a laboratory technician is an excellent stepping stone into the bioscience industry. Because laboratory technicians are able to quickly gain a good understanding of the industry as well as a tremendous amount of scientific and technical skill, they often are great candidates for more senior-level roles in quality control and roles related to quality assurance as a corporate scientific professional.

Job Type: Engineer

OVERVIEW

Engineers are critical to building, optimizing, maintaining and operating state-of-the-art biomanufacturing facilities and are involved in a variety of functions that rely on sophisticated computer software to help them visualize the complex manufacturing environment.

EDUCATIONAL REQUIREMENTS AND PREFERENCES

A basic requirement is a B.S. in an engineering discipline, and some positions require advanced degrees (M.S. or Ph.D.). Some of the engineering disciplines valued by the biomanufacturing industry include biochemical engineering, biomedical engineering, chemical engineering, electrical engineering, environmental engineering, food science, industrial engineering, materials science and mechanical engineering.

SAMPLE JOB TITLES

Process Engineer (Process Development)

Responsible for the design, scale-up and validation of new processes from the laboratory to the pilot-plant stage to large-scale manufacturing.

Process Engineer (Manufacturing)

Develops and operates the current manufacturing process and works with technicians to ensure the product is properly manufactured.

Quality Control Engineer

Develops, revises and maintains standards for converting raw materials into products and devises SOPs for testing procedures. May require a B.S. in engineering or scientific disciplines.

Maintenance Engineer

Manages the design, planning, construction and maintenance of facilities, and oversees repairs to refrigeration, air conditioning, steam boilers, etc.

Process Control Engineer

Designs and installs instruments to monitor and control certain manufacturing processes and helps improve manufacturing techniques.

Environmental Engineer

Develops techniques to recover reusable materials from waste created during manufacturing and designs water storage and treatment facilities.

CAREER PATHWAYS

As their careers progress, many engineers move into roles with significant management responsibilities. These responsibilities include overseeing projects and other personnel. In addition, many take on roles as a corporate scientific professional, such as in quality assurance or validation.

Job Type: Process Technician

OVERVIEW

Responsible for operating the equipment and processes necessary to manufacture batches of product worth millions of dollars. Process technicians

must be highly skilled, dedicated and responsible workers who are willing to work occasional weekend and evening shifts.

SAMPLE JOB TITLES

Process Technician

Responsible for a variety of tasks involved in the monitoring and control of producing the product.

Manufacturing Prep Process Technician

Responsible for washing, drying and sterilizing glassware.

Formulation/Fill Technician

Responsible for preparing the finished product from the purified active pharmaceutical or biopharmaceutical ingredients.

Packaging Technician

Uses packaging systems to label, inspect and package the finished product.

EDUCATIONAL REQUIREMENTS AND PREFERENCES

Biomanufacturing companies rely on people coming from a wide variety of educational backgrounds to build successful process technician teams:

Individuals with proven work experience (retail, military, food service) are attractive candidates for some companies once they have completed certificate courses, such as BioWork. *See page 163 for more about BioWork.*

At the two-year degree level, students completing A.A.S. programs in industrial pharmaceutical technology, biotechnology and bioprocess technology are attractive job candidates.

Students completing four-year degrees in fields such as microbiology and biochemistry can begin successful careers in the industry as a process technician.

CAREER PATHWAYS

Starting a career as a process technician is an excellent stepping stone into the biomanufacturing industry. Because process technicians are able to quickly gain

a good understanding of the manufacturing process and business as a whole, they often are good candidates for laboratory technician roles (such as in quality control) as well as corporate scientific professional roles (such as in quality assurance).

Job Type: Maintenance and Instrumentation Technician

OVERVIEW

Maintenance and instrumentation technicians are valued employees who rarely have difficulty finding work in the biomanufacturing industry. They are vital to the ongoing operation of a manufacturing facility and are responsible for repairing equipment and electrical circuits, calibrating instruments and installing and validating new equipment.

SAMPLE JOB TITLES

Instrumentation/Calibration Technician

Responsible for calibrating, testing, troubleshooting, repairing and maintaining a variety of circuits, components, analytical equipment and instrumentation.

Manufacturing Support Technician

Maintains manufacturing equipment and solves production problems caused by machinery.

Environmental Technician

Performs routine environmental testing and carries out waste treatment operations.

EDUCATIONAL REQUIREMENTS AND PREFERENCES

While many companies occasionally do hire seasoned mechanics and instrumentation personnel who do not have a formal education, educational requirements are increasing over time. At the two-year degree level, students who have completed certificate and/or two-year degree programs in automation engineering, electrical engineering, instrumentation, manufacturing engineering, electronics, industrial systems technology and manufacturing technology are valued highly.

CAREER PATHWAYS

As maintenance and instrumentation personnel develop professionally, many move into roles with significant management responsibilities, including the oversight of projects and other personnel.

Job Type: Corporate Scientific Professional

OVERVIEW

Corporate scientific and business professionals are critical to keeping the bioscience business moving. They come from many different educational backgrounds and may work in the office, may have some business-related travel and still may spend considerable time in the manufacturing or laboratory environment. In addition to quality assurance-related personnel, there are many other roles, including clinical research associates, regulatory experts, patent attorneys, technical writers and graphic designers.

SAMPLE JOB TITLES

Quality Assurance Associate/Manager

Ensures the quality of all manufacturing and laboratory operations by verifying compliance with Good Manufacturing Practice (GMP), writing and updating SOPs, reviewing data for abnormalities and resolving problems that occurred during manufacturing or research. Because they must be thoroughly familiar with the industry and the regulations of the U.S. Food and Drug Administration (FDA), many of these professionals have prior experience in the industry as an engineer, scientist or process technician.

Quality Assurance Auditor

Performs audits of production and quality control to ensure compliance with in-house procedures, standards and regulatory requirements.

Validation Specialist/Scientist/Engineer

Verify that equipment, processes and procedures are working as they are intended by designing and executing experimental protocols. Similar to quality assurance professionals, many of these professionals also have prior experience in the industry as an engineer, scientist or process technician.

Clinical Research Associate (CRA)

Assists in the monitoring and management of clinical trials. This position requires knowledge of drug development, clinical research (studies in humans), federal regulations and Good Clinical Practice (GCP). Many professionals enter careers in clinical research from four-year degree programs, from certificate programs and from other, related careers in the health care industry.

Regulatory Affairs Specialist

Coordinates and prepares a variety of documents to submit to the FDA.

Customer Support Specialist (four-year degree)

Serves as a contact for customers with technical product questions and ensures delivery of product that meets customers' requirements. Companies may require some industry or customer support experience for this position.

Other job titles include project manager, sales representative, marketing specialist, patent attorney, corporate trainer, lawyer and technical writer.

EDUCATIONAL REQUIREMENTS AND PREFERENCES

Many professionals enter these careers by combining a four-year degree in science with additional education in business, law, medicine/health care or communication. Alternatively, professionals often move into roles as corporate scientific professionals after starting their careers in a laboratory or manufacturing environment.

CAREER PATHWAYS

Due to their tremendous breadth and depth of experience, corporate scientific professionals are valued employees and have excellent opportunities for advancement. Because of their comprehensive understanding of the bioscience industry as a whole, they are well-suited for management roles.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

TEACHER PAGE

LEARNING OUTCOMES

- Students will collect facts about different biomanufacturing employment scenarios.
- Students will justify the best and worst aspects of a specific career.
- Students will compare and contrast different biomanufacturing careers.

ESTIMATED TIME

45–60 minutes

CONTENT

Unit III, Section C

PURPOSE

This activity allows students to see that all employees at a biomanufacturing facility have important responsibilities even though the tasks and education of biomanufacturing employees differ considerably. It also is designed to help students see how different jobs appeal to different people.

MATERIALS

- Student pages featuring biographies of six biomanufacturing employees (pages 110–139)
- Flip chart

TEACHER PROCESS

- Have students work in groups and read them the following introduction:
 - » This activity focuses on a typical day in the life of six different biomanufacturing employees. One is a process technician, one is an instrumentation technician, one is a process engineer, one is a quality control associate, one is a research associate and one is a process

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

TEACHER PAGE CONTINUED

development scientist. Although the stories are fictional, they are based on actual job experiences.

- Assign each group a biography and give the groups time to read and answer the questions listed at the end of the biography.
 - » Consider having each student in the group read one paragraph out loud before passing the pages to the next student.
- After groups have completed the assignment, record and discuss answers on the flip chart.

EXAMPLE STUDENT ANSWERS

Example student answers are in italics.

Sue Sanchez, Process Technician

1. What three factors in Sue's work are critical to preventing contamination of the product and harm to the patient?
 - » *(1) Follow strict procedures. (2) Repeat processes multiple times while maintaining cleanliness. (3) Check coworkers' work several times.*
2. Why is Sue so motivated to do her job well, in spite of the painstaking routines?
 - » *Sue likes knowing that what she does helps save lives.*
3. What motivated Sue to enroll in an evening class at a local community college?
 - » *She wanted to learn more about the process, and the education will help her reach the next level of in-house certification and obtain a raise.*

Jesse Farrington, Instrumentation Technician

1. Why did Jesse decide to become an instrumentation technician?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

TEACHER PAGE CONTINUED

- » *Jesse enjoyed working with his dad doing small electronic repairs and wanted to continue his education and work with his hands.*
- 2. What does he like about his job?
 - » *He likes having his daytime free to schedule personal business.*
- 3. Did Jesse's education and previous work experience prepare him to work in the biomanufacturing industry? Why or why not?
 - » *His experience working in the plant and with instrumentation helped him get the job, but he still needed to learn about the documentation and regulation required in the pharmaceutical industry.*

Melinda Wright, Process Engineer

1. Why did Melinda decide to become an engineer?
 - » *She enjoyed tinkering with tools and studying science while growing up.*
2. What does she like about her job?
 - » *She enjoys working with a team of people with different skills and abilities.*
3. Did Melinda's education prepare her to work in the biopharmaceutical industry? Why or why not?
 - » *She feels that her education taught her to think, while on-the-job training has allowed her to apply her knowledge.*

Jack Marcus, Quality Control Associate

1. Why did Jack decide to become a laboratory technician?
 - » *He enjoyed science classes and experimentation.*
2. What kinds of training and experience did Jack have before he went to work at the biomanufacturing facility?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

TEACHER PAGE CONTINUED

- » *He completed an internship and various educational courses at the community college.*
- 3. What does he like about his job?
 - » *He enjoys a challenge and the diversity of tasks he completes in his current job.*

Pat Williams, Research Associate

1. What did Pat like about her job in the medical school research lab?
 - » *She taught skills to those coming into the lab and enjoyed learning and talking about their research projects.*
2. What does she like about her current job?
 - » *She likes the continuing education offered in-house and by local schools.*
3. What is similar about the two jobs? What is different?
 - » *She gets to work with diverse people with various levels of education. She collaborates with colleagues inside and outside the company.*

Mark Jones, Process Development Scientist

1. What undergraduate courses did Mark find to be especially helpful in finding a job?
 - » *Biochemistry and biotechnology courses taught him basic procedures and techniques that have been helpful.*
2. What did Mark find out about his research skills while in graduate school?
 - » *He found out that he excelled at designing experiments and performing the experiments in the most efficient way.*
3. What does Mark like about his current job?
 - » *He likes the variety of people he interacts with and the variety of jobs he gets to perform.*

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE



Biography #1

Meet Sue Sanchez. She's a process technician.

Sue works at a biomanufacturing facility that produces small volumes of high-value pharmaceutical products. The company she works for is a world leader in biotechnology research. The company's research and her work provide treatments for several crippling diseases — treatments that did not exist 10 years ago. She works in an industry that has to follow many government regulations, including Good Manufacturing Practice (GMP).

At the start of her shift, Sue is required to don head-to-toe coverall, booties, hair covering, surgical mask and gloves. "I sometimes get tired of the painstaking

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

routine, but knowing that what I do helps save people's lives keeps me alert," she says. Sue's facility, which runs on a three-shift work day, seven days a week, likes for all of its process technicians to work all shifts on a rotating schedule. This week Sue is on the "graveyard" shift — 11 p.m. to 7 a.m. — something she thought she would dislike strongly. However, it is not as bad as she thought it would be, as the plant is much calmer with fewer interruptions to her work routine.

Sue's job is not for the average worker. It requires a thoughtful, careful, attentive person who takes the purity of the product and the safety of customers and coworkers seriously. This means following strict procedures in exact detail and repeating them over and over without incident. Sue and her coworkers check each other's work several times a day to make sure nothing gets missed. Sue is naturally a tidy, meticulous person and takes pride in doing her work precisely.

One of Sue's jobs involves working with the start-up cultures of genetically engineered mammalian cells, starting with thawing a tiny vial of cells that eventually will grow into thousands of liters of culture to produce the company's product. This one vial will make millions of dollars worth of medicine, and Sue takes care of the process that makes this happen.

More Info About Process Technicians

DEGREE REQUIRED

High school

EXPERIENCE REQUIRED

0 to 3 years

ANNUAL SALARY RANGE

\$30,000 to \$46,000

Note: Additional college work, prior employment and/or military experience also is required by biomanufacturing companies.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

One time, after examining a sample under the microscope, Sue notices that a few of the cells somehow do not look right. She calls her shift supervisor to inspect the sample. As it turns out, Sue was right to take that second look. The culture is growing abnormally and has to be discarded. If she had not noticed and had let the process go on, the company might have lost lots of time and money.

When she was in school, Sue did not like science because she could not relate to it. Now she is eager to learn all she can about what she does and why each part of the process is necessary. She understands the value of her knowledge. Sue becomes motivated to enroll in an evening microbiology class at the local community college. She hopes this will help her reach the next level of in-house certification and obtain another raise.

Already, Sue has become qualified to train other team members in certain aseptic (sterile) procedures and wants to become knowledgeable enough to conduct other types of training. She likes working with people and has discovered training gives her an opportunity to do this. She not only has to pass on the skills and knowledge she has, but she has to find ways to motivate new employees to work in the same careful way that she does.

“Despite the long hours that I work in a controlled environment and the frequent overtime, I feel I’m in a good place right now career-wise,” Sue says. Sue likes the company, her salary and her benefits, and she is positioned to move ahead.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Group Discussion Questions About Sue Sanchez, Process Technician

1. What three factors in Sue's work are critical to preventing contamination of the product and harm to the patient?

2. Why is Sue so motivated to do her job well, in spite of the painstaking routines?

3. What motivated Sue to enroll in an evening class at a local community college?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

4. What do you like *most* about Sue's job? Why?

5. What do you like *least* about Sue's job? Why?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE



Biography #2

Meet Jesse Farrington. He's an instrumentation technician.

Jesse works for a large contract biomanufacturer — a company that carries out process development and pilot-scale drug production for biopharmaceutical companies. This is a critical first phase in bringing a biopharmaceutical out of the research lab and into the marketplace. The plant must follow very detailed, current Good Manufacturing Practice (cGMP) and comply with environmental, health and safety regulations. This is very important, because the facility is producing drugs for humans.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Jesse is part of a crew of instrumentation technicians that maintains, tests, troubleshoots and calibrates the instrumentation and control systems used in the facility. These instruments measure things like pH, pressure and temperature in the tanks where cells grow and in the purification equipment. The instruments are connected to computers that control the manufacturing processes — for example, by opening and closing valves.

Jesse also helps repair instrumentation, technology components and analytical equipment. Like many biomanufacturing facilities, this plant runs on an around-the-clock, three-shift schedule. So even though the bulk of the crew's work is performed during the day (or first) shift, each technician works one week on the second or third shift about once every three months. It's necessary to have several instrumentation technicians present in the facility at all times in case there is a problem with the equipment.

“At first I didn't like having to work the night shift, but now I use those free, daytime hours to schedule personal business, like dentist appointments,” Jesse says.

Jesse's father is an electrician, and as a child Jesse watched and helped his dad perform small electrical repairs at home. Jesse enjoys working with his hands and always was building something in the garage. He thought about

More Info About Instrumentation Technicians

DEGREE REQUIRED

Two-year degree (A.A.S.)

EXPERIENCE REQUIRED

0 to 3 years

ANNUAL SALARY RANGE

\$25,900 to \$46,000

Note: Prior employment and/or military experience are valued highly by bioscience companies.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

getting a construction job after high school but really wanted to continue his education. After considering several options, Jesse decided on the electronics engineering technology program at a nearby community college and earned an Associate of Applied Science degree (A.A.S.) two years later. He graduated with a concentration in instrumentation, which prepared him well for his current position. Jesse worked as an instrumentation technician in a food processing plant for two years before he applied for his current job. With his degree and experience with food products, Jesse quickly was hired for an entry-level position at the biomanufacturing facility. Nonetheless, he had to learn about the extensive documentation and record-keeping required by current Good Manufacturing Practice (cGMP), which are government regulations for pharmaceutical and biopharmaceutical companies.

When he first got the job, Jesse had to learn all about the different types of biomanufacturing processes going on in the facility. Because the company constantly is trying out innovative processes to make new drugs for companies around the world, Jesse feels there is never a dull moment. Plus, a large variety of equipment and instrumentation is present throughout the plant. Because the company performs contract work for many companies, a small batch of mammalian cells may be growing next to huge vats of microbes.

“I really don’t think I could have a full-time desk job,” Jesse says. “As an instrumentation tech, I’m working all over the plant, climbing up and down on equipment and using my knowledge and mechanical skills. I’m doing something different every day and work with a variety of people in different divisions in the plant.” Jesse knows his crew plays a vital role in keeping the facility in good working order.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Group Discussion Questions About Jesse Farrington, Instrumentation Technician

1. Why did Jesse decide to become an instrumentation technician?

2. What does he like about his job?

3. Did Jesse's education and previous work experience prepare him to work in the biomanufacturing industry? Why or why not?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

4. What do you like *most* about Jesse's job? Why?

5. What do you like *least* about Jesse's job? Why?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE



Biography #3

Meet Melinda Wright. She's a process engineer.

Melinda works at a plant that uses specially altered, genetically engineered bacteria to make biopharmaceuticals. To create these bacteria, scientists place a gene for a protein such as insulin into the bacterial chromosome. As the bacteria grow, they produce insulin. This biomanufacturing plant grows the bacteria in huge, stainless steel vats, then isolates the insulin from bacterial culture, which is the nutrient liquid the bacteria grow in.

Melinda is a process engineer in this plant. Engineering is the practical application of science to commerce or industry. Melinda is part of a team that

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

performs many practical tasks for the plant. They design and execute the complex processes involved in going from a tiny vial of bacteria to millions of vials of insulin on the shelves of pharmacies and in the medicine cabinets of people with diabetes. She also helps troubleshoot when problems occur in the biomanufacturing plant and coordinates the introduction of new processes. Her job might involve figuring out the right pump to use in the huge plant, which is filled with giant vats of bacteria and pipes snaked throughout. She also helps train the people who operate the equipment.

Melinda enjoys working with a team of people with different educational backgrounds and likes the diversity of her job. One day she might be climbing to the top of a large tank to inspect equipment. Another day she might be working in her office on a new design for that equipment. The vats where the bacteria are grown need to be tended 24 hours a day, so the plant runs on an around-the-clock, three-shift schedule. The process engineers take turns being “on-call” at night in case of an urgent problem, just as doctors do. Melinda has gotten used to carrying around a pager and staying close to the facility on those nights, just in case she needs to come in to help solve a problem.

Growing up, Melinda always liked to tinker with her dad’s tools, taking apart small, broken appliances and building playhouses in the backyard. She really enjoyed science in high school, so she felt engineering combined her two interests very well. She majored in chemical engineering in college and took

More Info About Process Engineers

DEGREE REQUIRED

Four-year degree (B.S.)

EXPERIENCE REQUIRED

0 to 3 years

ANNUAL SALARY RANGE

\$53,600 to \$64,600

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

courses in biochemistry and microbiology so she could specialize in bioprocess engineering. People with her education are in demand in other industries, including those producing agricultural products, petroleum products and food, so Melinda feels she has job security. To help her in her current job, Melinda would like to take more courses in biotechnology as well as courses about current Good Manufacturing Practice (cGMP), which are government regulations for pharmaceutical and biopharmaceutical companies.

Although she received a good education in college, Melinda feels as if engineers really learn the nuts and bolts of their job once they're hired. "One of my professors used to tell us, 'We can't teach you what you're going to be doing, because it's such a diverse field. We can only teach you how to think,'" she says. "I really like my job because I do think and learn something new every day. And I'm working in an industry that is helping millions of people stay well."

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Group Discussion Questions About Melinda Wright, Process Engineer

1. Why did Melinda decide to become an engineer?

2. What does she like about her job?

3. Did Melinda's education prepare her to work in the biopharmaceutical industry? Why or why not?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

4. What do you like *most* about Melinda's job? Why?

5. What do you like *least* about Melinda's job? Why?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE



Biography #4

Meet Jack Marcus. He's a quality control associate.

Jack works for a biomanufacturing company that produces industrial enzymes. The quality control (QC) division of a biomanufacturing facility is responsible for conducting chemical and biological analyses of raw materials as well as the product during every step of the manufacturing process. It's very important that each batch of a product is made the same way and doesn't vary from the standard operating procedures (SOPs).

Jack's favorite part of his high school science classes was the lab experiments — and he always got good grades on his lab writeups. After high school, Jack

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

earned an A.A.S. degree in biotechnology from his local community college. The curriculum he followed was designed to meet the increasing demands for skilled laboratory technicians in biology, chemistry and biotechnology. Along with a variety of science courses, Jack took several classes in basic and advanced lab techniques and a course that taught professional writing and oral presentation skills. Jack also completed the fieldwork internship he needed for his degree in a university molecular biology lab. The head of the lab offered him a job, and Jack worked there for five years.

Jack greatly enjoyed the challenge of working on a variety of research projects and learning a number of different techniques, but he wanted a change and accepted a job as a quality control assistant at biomanufacturing facility. Although a degree from a four-year college usually is required to become a QC associate, Jack showed great skill and aptitude for his job and received a promotion after two years.

Jack is a jack-of-all-trades in his position of quality control associate. He writes, revises and updates SOPs for the facility; his writing experience in high school, in college and at his first job has served him well. He helps coordinate the activities in the lab and oversees the collection and analysis of the samples during the manufacturing process. Finally, Jack still gets the opportunity to don his lab coat and run some tests when he performs special projects and designs quality control lab protocols.

More Info About Quality Control Associates

DEGREE REQUIRED

Two-year degree (A.A.S.) or four-year degree (B.S.)

EXPERIENCE REQUIRED

0 to 3 years

ANNUAL SALARY RANGE

\$37,200 to \$51,900

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Although Jack is a detail-oriented person, he still thought he would have problems keeping up with all the paperwork and other documentation required at his current job. He really appreciates the in-house training classes that help the QC department members learn more about their jobs. The company also will pay for part or all of his tuition if he takes college courses, and Jack is thinking about working on a bachelor's degree.

“The best part of my job is the variety of work I perform within the QC lab and the opportunity to communicate with people in manufacturing, quality assurance and other areas of the facility,” Jack says. He is especially proud that with persistence and determination he earned a significant promotion within the company.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Group Discussion Questions About Jack Marcus, Quality Control Associate

1. Why did Jack decide to become a laboratory technician?

2. What kinds of training and experience did Jack have before he went to work at the biomanufacturing facility?

3. What does he like about his job?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

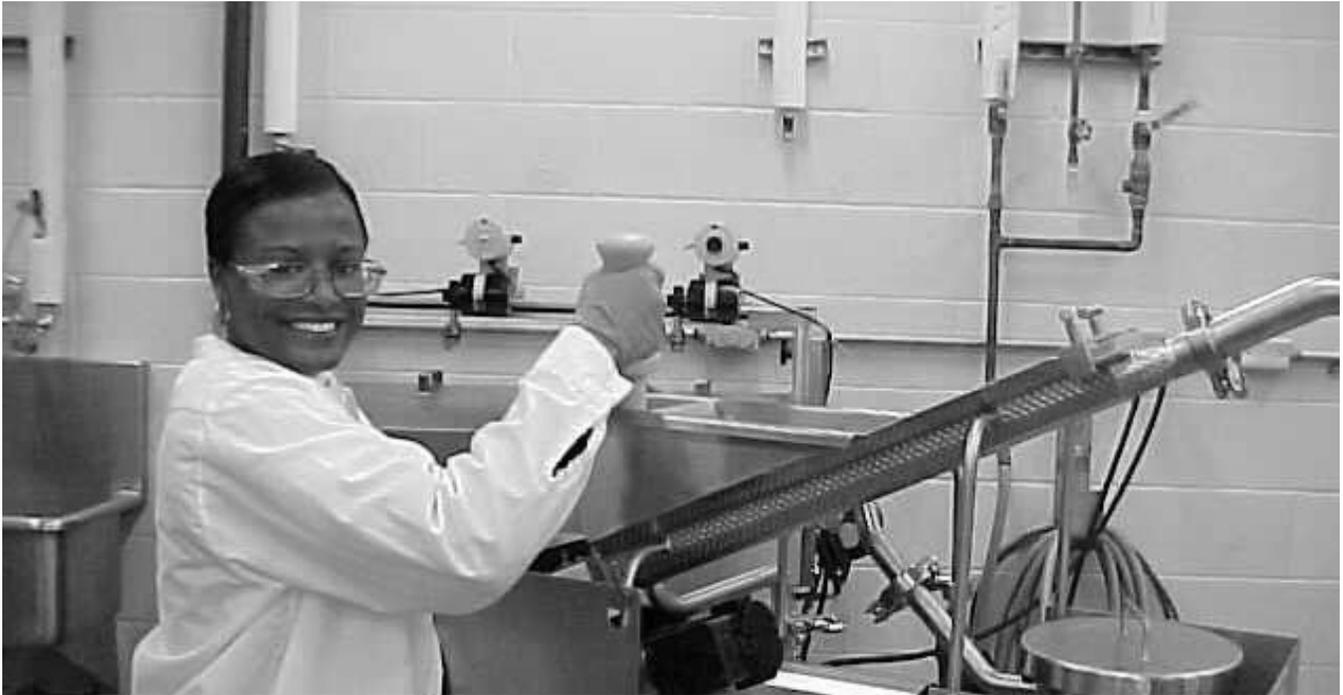
4. What do you like *most* about Jack's job? Why?

5. What do you like *least* about Jack's job? Why?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE



Biography #5

Meet Pat Williams. She's a research associate.

Pat works in the research and development division of a company that manufactures specialty biochemicals used in the life sciences. The company contracts with a number of biopharmaceutical companies to provide them with a dazzling array of substances to purify and identify nucleic acids and proteins, perform cellular analyses and employ viral vectors — the “vehicles” that carry new genes into mammalian and bacterial genomes. Pat works in the Genetic Analysis Group, and her expertise is in the Genetic Identity product line.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

“With the popularity of TV shows about crime scene investigations, everyone seems to know about DNA fingerprinting — and the DNA molecules used in human identification kits are in one of our products,” Pat says.

Pat earned a bachelor’s degree in medical technology and got a job processing patients’ blood samples in a medical school-affiliated hospital laboratory. After about a year, Pat decided she wanted to get involved in research and found a job in the busy lab of a medical school faculty member. Pat really liked the work environment of the research lab, where she worked with medical students conducting short-term projects, with graduate students working on research for their doctoral degrees (Ph.D.s) and with postdoctoral fellows who already had earned their Ph.D.s and were receiving additional research training. She served as the manager of the lab and taught the new students how to perform certain tests and use the lab equipment. They, in turn, taught her about the projects they were working on, and Pat attended the weekly “journal club” meetings along with the students and fellows. At these meetings, they discussed new articles that appeared in scientific journals.

Although Pat very much enjoyed working in an academic research environment, she quit her job when her husband’s company transferred him to another state. Pat accepted a job as a research associate at her current company even though she thought she really would miss working in a medical school lab. However, she has been pleasantly surprised at how much she likes her job. Pat again is working

More Info About Research Associates

DEGREE REQUIRED

Four-year degree (B.S.)

EXPERIENCE REQUIRED

0 to 3 years

ANNUAL SALARY RANGE

\$36,100 to \$44,600

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

with a diverse group of intelligent and dedicated scientists with varying levels of education. There is a lot a variety in her new job, including computer operation, laboratory bench work and collaboration with colleagues both inside and outside of the company. Pat also is responsible for the operating and troubleshooting lab instrumentation, performing experimental design and analyzing data.

Pat says working in laboratories has taught her a lot about problem-solving and has taught her she must be willing to learn new skills and work with a variety of people from different backgrounds. She really appreciates the short, in-house training courses the company offers, which educate employees about activities in other divisions of the company. “My company provides tuition support for employees who take courses related to their jobs, so I’m taking a class about project management that I hope will help me get a job promotion,” Pat says. “And I’m thinking about applying to a master’s degree program next year.”

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Group Discussion Questions About Pat Williams, Research Associate

1. What did Pat like about her job in the medical school research lab?

2. What does she like about her current job?

3. What is similar about the two jobs? What is different?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

4. What do you like *most* about Pat's job? Why?

5. What do you like *least* about Pat's job? Why?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE



Biography #6

Meet Mark Jones. He's a process development scientist.

Mark works for a company that manufactures biopharmaceuticals derived from mammalian cell culture. Biopharmaceuticals are proteins that have therapeutic value for human disease. Proteins such as these usually are produced by cultures of animal cells that have been genetically modified to carry the gene coding for the protein of interest. Mark first learned about the company when he was a graduate student in biochemistry conducting research for his Ph.D. dissertation. "I was always very impressed with the innovative research that led to their products, but I never thought I actually would be working for them someday," Mark says.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

As an undergraduate student Mark majored in biology and minored in biotechnology. He took two biochemistry and two biotechnology lab courses and learned many basic procedures and techniques from all of them. Because he had taken those lab courses, Mark had no trouble finding a job as a laboratory technician in a biochemistry research lab after college. He worked for a university professor who encouraged Mark to apply to graduate school and earn a doctorate (Ph.D.). Mark was hesitant at first, thinking he wasn't "Ph.D. material," so he took a couple of graduate-level courses while working in the lab. He did well in the classes and had a lot of support from his mentor, so he decided to take the plunge and applied to the a doctoral program in biochemistry at another university.

During graduate school, Mark discovered he excelled at designing experiments and figuring out the most efficient way to perform many of the routine tasks in the lab. He became the "go-to guy" — the person everyone turned to when they were having problems with the equipment or an experiment. When he found out about process development scientist positions at a biotechnology job fair, they seemed like a good fit because he likes figuring out how to make things work.

Mark now is responsible for designing and executing experiments associated with the scale-up of production processes for the biomanufacturing company. This means taking a new cell line that makes a new protein product out of

More Info About Process Development Scientists

DEGREE REQUIRED

Graduate degree (M.S. or Ph.D.)

EXPERIENCE REQUIRED

0 to 3 years

ANNUAL SALARY RANGE

\$79,300 to \$97,200

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

the research laboratory and figuring out how to grow the cells in amounts thousands of times greater than the amounts grown in the lab. This requires knowledge of chemical engineering as well as an understanding of how cells grow and how to handle proteins.

He works closely with the facility's engineering group, so Mark has learned a lot of engineering principles since he joined the company. He has a sense of accomplishment, too. He enjoys seeing rows of vials rolling off the filling line, carrying a biopharmaceutical he once studied in the lab to critically ill patients.

Mark's favorite part of the job is the variety it offers. Even though he enjoyed working in a research lab, he spent every day in the same suite of labs and worked with the same people. Now, while still working in a large group of lab personnel, Mark works side-by-side with the engineers and technicians in the manufacturing plant, as well as with quality control scientists. He also is learning about project management from his boss and thinks he might like to be a manager someday.

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

Group Discussion Questions About Mark Jones, Process Development Scientist

1. What undergraduate courses did Mark find to be especially helpful in finding a job?

2. What did Mark find out about his research skills while in graduate school?

3. What does Mark like about his current job?

Activity

A DAY IN THE LIFE OF SIX BIOMANUFACTURING EMPLOYEES

STUDENT PAGE CONTINUED

4. What do you like *most* about Mark's job? Why?

5. What do you like *least* about Mark's job? Why?

Activity

SELECTING A BIOSCIENCE CAREER

TEACHER PAGE

LEARNING OUTCOMES

- Students will investigate three different bioscience careers.
- Students will evaluate personal interests, aptitudes and goals.
- Students will discuss careers and companies that interest them.

ESTIMATED TIME

80–90 minutes

CONTENT

Unit III, Section C

PURPOSE

This activity forces students to think about each career as it relates to his or her personal interests, aptitudes and goals. It also gives students a basic understanding of some of the companies located in North Carolina.

MATERIALS

- *Selecting a Bioscience Career* student pages (pages 142–144)
- Computer(s) with Internet connectivity

Activity

SELECTING A BIOSCIENCE CAREER

TEACHER PAGE CONTINUED

TEACHER PROCESS

- Give each student a copy of the student pages for this activity.
- Have students review, read and analyze the job descriptions in Unit III, Section C as well as the sample job titles for typical bioscience and biomanufacturing careers on the student pages for this activity.
- Have students visit a job search website (www.indeed.com is recommended) and search for 3 specific positions which sound interesting to them.
- As a class, discuss which careers and companies seemed to hold the most interest and why.

OTHER OPTIONS

- Before starting the activity, ask students to write down their personal interests, aptitudes and goals.
- Students can research other job positions in biomanufacturing or biotechnology and even can take some tests to help guide them in their career considerations.
- See a number of links for this activity in Unit V.

Activity

SELECTING A BIOSCIENCE CAREER

STUDENT PAGE

Review the descriptions of the different categories of positions within a typical biomanufacturing or bioscience company in Unit III, Section C and review the sample job titles for each type of position in the table on the next page.

- For each type of job, decide if you can see yourself doing that job in the future. Consider your personal interests (what you like to do), your aptitudes (what you are good at) and your goals (how long you wish to attend college for, etc.).
- Visit www.indeed.com (or another job search website) and search for some of the job titles that you find interesting. Use some of the job titles as keywords. Use other industry keywords as well, such as “bioscience,” “biomanufacturing,” “biotechnology,” “biotech” and “pharmaceutical.”
- Once you have found real positions that capture your interest, place them in the chart on page 144 in your order of preference and describe why you think those jobs would suit you.

Activity

SELECTING A BIOSCIENCE CAREER

STUDENT PAGE CONTINUED

JOB TYPE	SAMPLE JOB TITLES, OR KEYWORDS
Scientist	Discovery Research Scientist, Process Development Scientist, Quality Control Manager, Chemist, Microbiologist, Biochemist, Natural Science Manager, R&D Scientist, Research Associate, Environmental Scientist
Laboratory Technician	Research Assistant, Research Associate, Process Development Associate, Laboratory Technician, Quality Control Associate, Validation Technician
Engineer	Process Engineer, Chemical Engineer, Process Development Engineer, Manufacturing Engineer, Quality Engineer, Facility Engineer, Optimization Engineer, Process Control Engineer, Environmental Engineer
Process Technician	Process Technician, Manufacturing Technician, Manufacturing Associate, Packaging Technician, Formulation/Fill Technician, Manufacturing Prep Technician, Operator, Validation Technician
Maintenance and Instrumentation Technician	Maintenance Technician, Instrumentation Technician, Calibration Technician, Manufacturing Support Technician, General Mechanic, Maintenance Mechanic
Corporate Scientific Professional	Quality Assurance (QA) Manager, QA Associate, Quality Inspector, QA Auditor, Validation Specialist, Clinical Research Associate, Regulatory Affairs Specialist, Customer Support Specialist, Project Manager, Sales Representative, Marketing Specialist, Patent Attorney, Corporate Trainer, Lawyer, Technical Writer

Activity

SELECTING A BIOSCIENCE CAREER

STUDENT PAGE CONTINUED

	Company/Job Title	Why?
1st Choice		
2nd Choice		
3rd Choice		



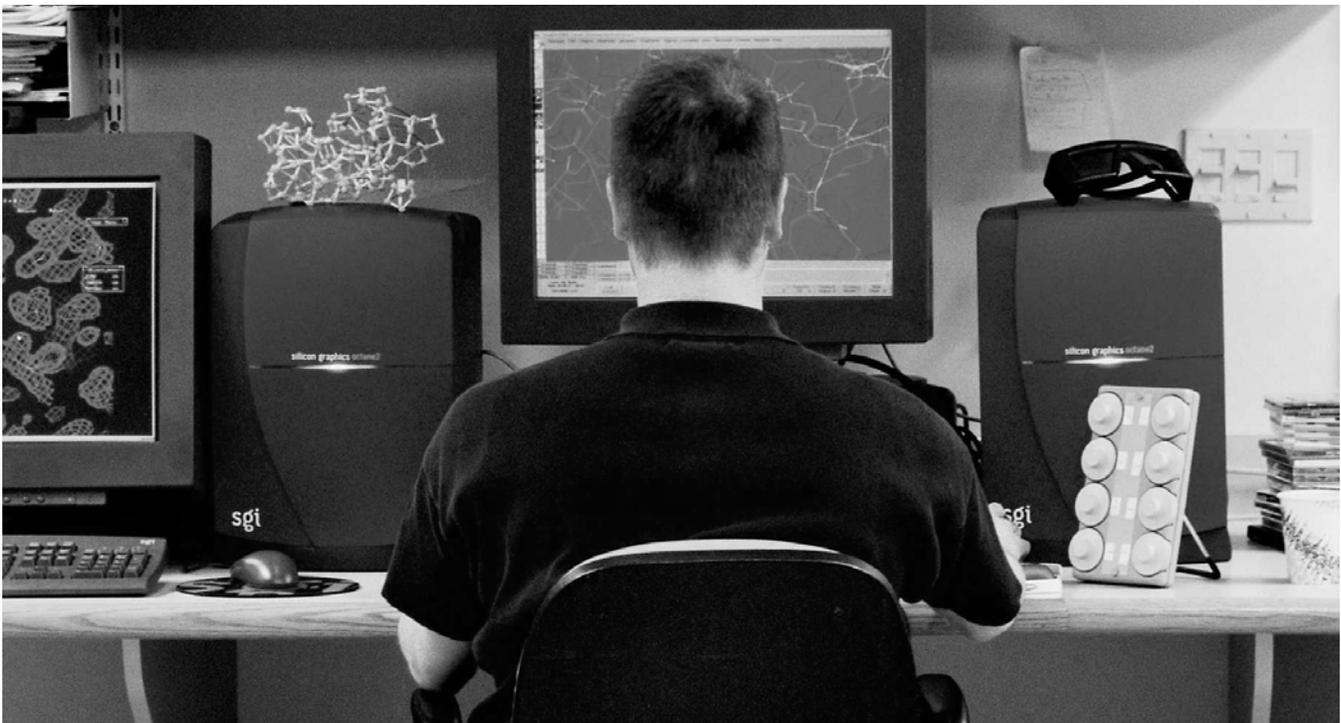
Unit IV

GETTING A JOB AND GETTING AHEAD

A. Taking Charge of Your Future

North Carolina's biomanufacturing and pharmaceutical manufacturing employers recognize the value of the state's educational programs and are able to recruit the vast majority of their new hires from within the state. Because these industries place a high premium on education, industry experience and professional polish, students and educators alike must understand the different factors that drive successful employment in today's competitive job market. And they must, in turn, learn how to apply this knowledge to the education, career planning and job search process.

As discussed in Unit III, the pharmaceutical and biomanufacturing product development process involves a variety of tasks and employs a variety of workers. A variety of entry-level jobs do exist — that is, positions for which companies are willing to hire someone who has the appropriate education but who does not have any prior work experience in the pharmaceutical or biopharmaceutical industries. However, the hiring process still is a highly competitive one, as companies value industry experience for all types of jobs, even entry-level ones.



So what types of skills are needed to successfully compete for jobs in the bioscience industry? Survey data from bioprocess, agricultural, pharmaceutical and chemical companies show the ideal candidate has:

- An appropriate education
- A mastery of basic skills
- The scientific and technical knowledge specific to the job
- A successful employment history and relevant job experience (or military service)

This unit explores some of these needs and identifies strategies students can take now, as they begin preparing for a successful career in the broad bioscience industry.

B. Education ¹

What Do Employers Want?

While Unit III provides specific information about the educational needs for specific positions in the bioscience industry, there also are general trends that students and educators should know!

Like most high-technology industries, the overall education level of the workforce has increased over time. In the last 10 years (since 2004), there has been a notable reduction in the number of employees with only a high school diploma, because most companies require a two- or four-year degree for many entry-level jobs. And even companies that do hire candidates without a college degree place a premium on students who have completed some professional and/or technical education coursework beyond high school. This coursework includes the short courses and certificate programs offered by the community college system.

How Can You Prepare?

It's never too early to begin thinking about your plans for after you graduate high school. It's important to recognize the value placed on education by the bioscience industry. Regardless of your personal and financial situation, opportunities for advancing your education are out there. Both community colleges and universities provide biotechnology-related education and professional development opportunities for full-time students and those students who juggle the conflicting priorities of work, life, family and school.

C. Basic Skills²

What Do Employers Want?

Reading, writing, calculation, problem-solving and computer literacy (including proficiency with general office software) are basic requirements for all positions. Consider what could happen if employees were hired who lacked some of these basic skills. Mistakes would happen that could jeopardize customer safety.

APPLYING BASIC SKILLS ON THE JOB: A FEW EXAMPLES

Reading, Writing and Math Skills

- Reading labels for raw materials
- Reading status reports from previous shifts
- Reading standard procedures and batch sheets
- Reading equipment manuals and diagrams
- Recording procedures and test results
- Keeping a shift log
- Writing reports
- Writing new procedures
- Weighing and measuring raw materials
- Using formulas to make solutions and dilutions or to calculate test results
- Using the metric system, decimals, percentages, algebra and statistics

Computer Literacy Skills

- Reading computer displays to monitor the process
- Using computer systems to control the process from a remote station
- Entering or finding information in a spreadsheet or database
- Writing reports or training manuals on a computer
- Using computers that control laboratory test equipment

How Can You Prepare?

Pay attention in school! Much of what you learn in school now is a critical part of your future success in the bioscience industry.

D. Scientific/Technical Knowledge and Skills³

What Do Employers Want?

In addition to basic skills, employees in the bioscience, pharmaceutical and biomanufacturing industries need technical knowledge — including an understanding of scientific principles — and technical skills that can help them identify, prevent and solve problems on the job.

APPLYING SCIENTIFIC PRINCIPLES AND TECHNICAL SKILLS ON THE JOB: A FEW EXAMPLES

- Controlling the flow of gases and liquids
- Heating and cooling fluids
- Treating waste before releasing it into the environment
- Controlling chemical reactions
- Purifying products
- Operating and maintaining process equipment
- Growing cells
- Identifying microbial contaminants
- Analyzing production samples using chemical methods such as spectroscopy and chromatography
- Interpreting laboratory test results

How Can You Prepare?

By taking this course, you already are headed in the right direction. While still in high school, take any and all available science, biotechnology and higher level mathematics courses available. Students also can obtain valuable experience during college by doing fieldwork or an internship in the pharmaceutical industry. Another option is undergraduate research experience in a university laboratory. For science majors, the more laboratory experience you have, the better your chances of getting hired.

E. Employee Success Skills⁴

What Do Employers Want?

No matter how much education and technical knowledge and how many skills you have, it also is important to maintain good work habits and to get along with your coworkers. When hiring, employers consider these skills to be as important as an applicant's technical knowledge and skills. Knowing how to manage time, projects and people, and having excellent oral and written communication skills are essential for job promotions. Such skills are especially critical for professional positions that require a bachelor's degree or higher.

A successful applicant demonstrates the ability to:

MANAGE TIME

- Shows up for work regularly and on time
- Is willing and able to adapt to shift work when necessary
- Manages personal schedule to meet shift schedules
- Plans and organizes work and sets priorities
- Can attend to several tasks at once
- Completes tasks on time and keeps production on schedule

MAINTAIN A SAFE AND ORDERLY WORK ENVIRONMENT

- Complies with health, environmental and safety regulations
- Follows dress and protective clothing policies
- Assumes responsibility for safety of self and others
- Sets a good example for others
- Handles and maintains equipment and materials with care
- Follows good housekeeping practices

KEEP LEARNING NEW SKILLS

- Shows interest in learning new knowledge, skills and tasks

- Is resourceful and can work with minimal supervision
- Accepts that continuous learning is part of the job

FOLLOW PROCEDURES EXACTLY

- Follows directions exactly as written every time
- Takes no shortcuts

KEEP PRECISE RECORDS

- Keeps records that are accurate
- Keeps records that contain required details

COMMUNICATE EFFECTIVELY

- Communicates clearly and shares information with others in a timely manner
- Understands what details coworkers need to know about a project
- Communicates effectively in person, whether 1-on-1, in group meetings or through formal presentations; and adapts the level of the presentation for the audience
- Writes effectively and clearly, with a concise business style
- Uses scientific and technical terminology precisely

WORK AS A TEAM MEMBER

- Recognizes individual contributions toward a common goal
- Accepts responsibility for team's success or failure
- Accepts own mistakes and is receptive to corrections and suggestions
- Shares concepts, ideas and problems with others
- Coordinates own work and work of others
- Can conduct meetings and helps groups make decisions
- Is eager to share technical knowledge and willing and able to assist and train others

SOLVE PROBLEMS, TROUBLESHOOT AND IMPROVE THE PROCESS

- Is willing to learn manufacturing process and how different units in the plant work together
- Is sensitive to anything unusual in surroundings (sights, sounds, smells) and responds with appropriate action and communication to identify causes and solutions
- Suggests ways to improve manufacturing process through proper channels, even when production is progressing without problems
- Knows and can apply a variety of problem-solving approaches and methods to determine causes and recommend solutions

UNDERSTAND AND ACCEPT THE PRINCIPLES OF GOOD BUSINESS

- Understands need for profit in manufacturing process
- Can identify factors within manufacturing process that determine cost
- Can identify possible barriers to profit in manufacturing process
- Can explain why pleasing internal and external customers is critical to a company's success
- Is willing and able to interact appropriately with internal and external inspectors and auditors

How Can You Prepare?

In addition to seeking out business-oriented coursework in high school and college, there are a number of extracurricular activities that will help propel your career in the right direction.

GET A JOB

Paid and volunteer work experience (including military service) is extremely effective in demonstrating employability and reliability skills, developing a successful work history, and securing professional references.

JOIN A CLUB OR STUDENT ORGANIZATION

Many of these organizations provide fantastic avenues through which students can hone communication and leadership skills while still in high school and/or college.

RESEARCH CAREERS

Knowing the job opportunities that are out there helps you refine your career goals. Use job search and career-related websites to investigate companies and jobs to begin understanding what they value in the employees they hire.

UNDERSTAND THE HIRING PROCESS

Students, educators and job seekers must have realistic expectations about the job search process and must understand how to best navigate the hurdles of applying for a job. When applying for a job, you must learn to develop and use your personal network and must craft a resumé that sells potential employers on your technical and professional contributions.

Activity

THE BIOMANUFACTURING FACILITY

TEACHER PAGE

LEARNING OUTCOMES

- Students will identify the parts of the biomanufacturing process.
- Students will design and test the biomanufacturing process for a desired product.
- Students will develop written procedures for the biomanufacturing process.
- Students will produce the desired product using the approved procedures.
- Students will discuss the biomanufacturing process.

ESTIMATED TIME

30–45 minutes

CONTENT

All of Units III and IV

PURPOSE

This activity is designed as a culminating activity for Units III and IV. Students are required to apply everything they have learned — and more — in walking themselves through the entire biomanufacturing process.

It is extremely important that students understand they should go to great lengths to understand all aspects of the biomanufacturing process and should apply that knowledge to this project.

MATERIALS

- REESE'S peanut butter cups
 - » If any of your students are allergic to peanuts, consider using another type of candy (such as peppermint patties) or sandwich cookies (such as Oreos, Mallomars, etc.).

Activity

THE BIOMANUFACTURING FACILITY

TEACHER PAGE CONTINUED

- Cooking oil
- Saltines
- Disposable gloves
- Instruments for removing the peanut butter, extracting the bulk product, processing the product, dispensing into containers and packaging (forceps, forks, plastic knives, small cups, an optional small blender or food processor)
 - » Make sure to use food-grade, kitchen equipment instead of normal lab equipment.

TEACHER PROCESS

In this activity, students will role-play the different processes in the biomanufacturing facility. The class should be divided into “companies” of 4–6 students. Each company will purify (remove the chocolate from) the bulk product (peanut butter). The company then will formulate (add) the bulk product to the filler (oil) to produce the final form (a semi-solid paste of peanut butter and oil).

Next, the company will package the final form into a container (peanut butter paste between 2 saltines). The company will write the procedures that should be followed. One student per company will serve as the Quality Control, Quality Assurance and Validation Officer. This “employee” will check the company’s compliance with written standards (procedure) as the fellow employees create the final form and report the company’s compliance to the rest of the class.

INSTRUCTIONAL METHODS

1. Divide the students into “companies” of 4–6 students and allow the groups to choose a company name.

Activity

THE BIOMANUFACTURING FACILITY

TEACHER PAGE CONTINUED

2. Explain to students that they will be producing peanut butter crackers by role-playing the biomanufacturing process. Have students brainstorm the parts of the process: research and development, purification, formulation and final dosage preparation.
3. Companies will begin the research and development process. Each company will purify, formulate and prepare a final peanut butter. Students will have access to candy and various supplies. During this process, students should not expect to get it right the first time. There should be failures and improvements during the process. Encourage students to try different techniques to improve production. Once a set of procedures has been established, each company should write the procedures for purification, formulation and final dosage preparation.
Suggestion to aid students: Consider chilling the candy to improve the chocolate removal. Start with a very small amount of oil (¼ teaspoon) to mix with the peanut butter from a single piece of candy.
4. Written procedures should be approved by the teacher. Have each team choose one member to be the Quality Control, Quality Assurance and Validation Officer. Explain that this student will make sure the written procedures are followed throughout the manufacturing process and will collect a small sample of the product (peanut butter) at the end of each step.
5. Each company will follow the written procedures to produce enough bulk product for all its “employees.” If proper equipment and food handling procedures are followed, students may eat the final product.
6. Once the companies have produced their final products, debrief the class by discussing the biomanufacturing process. Suggested discussion questions are listed on the next page.

Activity

THE BIOMANUFACTURING FACILITY

TEACHER PAGE CONTINUED

SUGGESTED DISCUSSION QUESTIONS

Research and Development

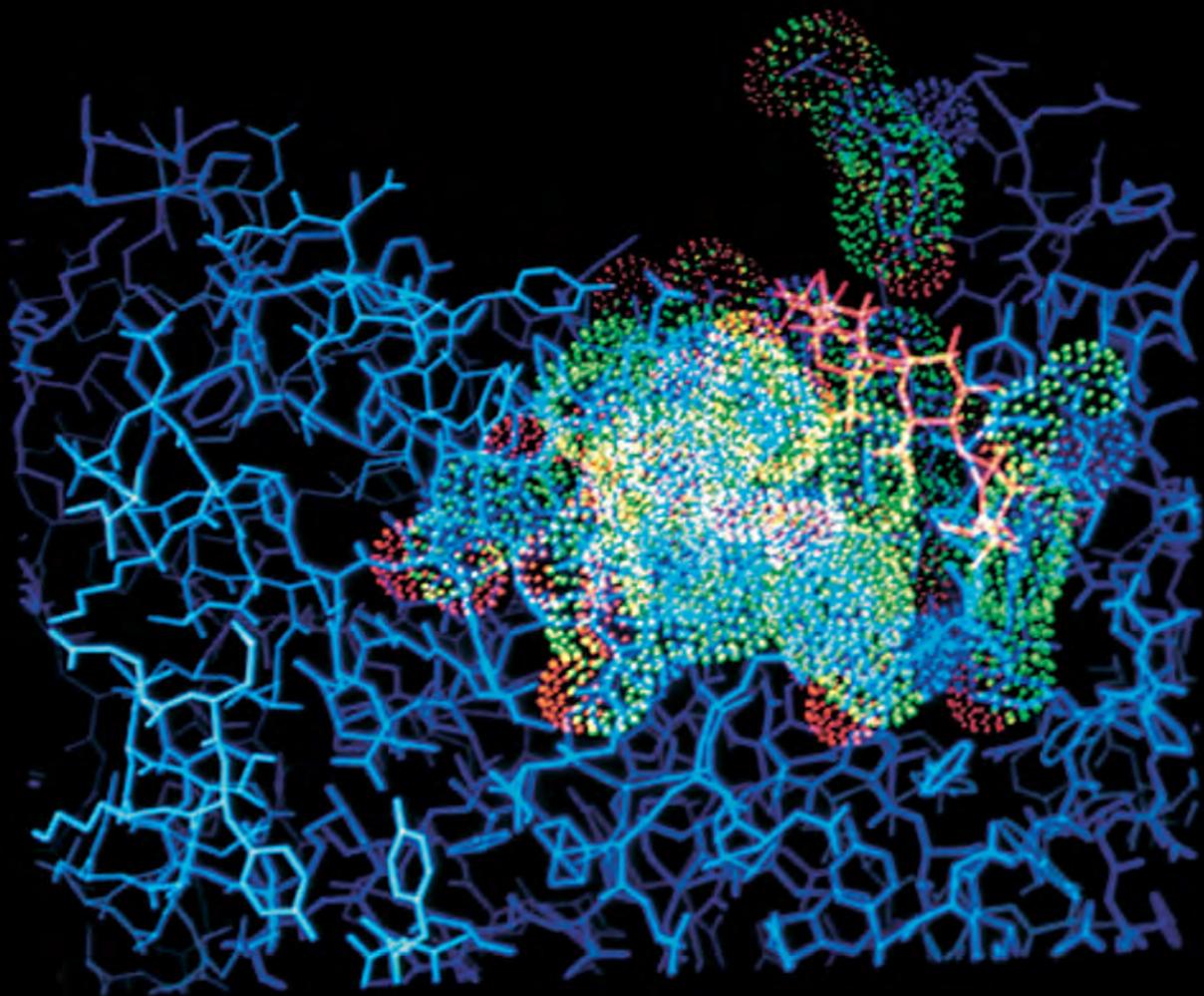
- What method did you develop to separate the impurities (chocolate) from the bulk product (peanut butter)?
- What procedures did you try before finding a method that worked?
- What was enjoyable about the research and development process?
- What was difficult about the research and development process?
- How much peanut butter needs to be extracted for the final product?
- How much oil is needed to mix with the peanut butter to create a spreadable mixture?

Purification, Formulation and Final Dosage Form Preparation

- What would you need to change to purify and formulate enough product for the entire class? For the entire school?
- How would you ensure cleanliness and safety of the product?
- What is the best way to remove the chocolate layer?
- How can you avoid contaminating the peanut butter with chocolate?
- What is the best way to mix the peanut butter and oil together?
- How much of the peanut butter-oil mixture is needed to fill the crackers?

Quality Control, Quality Assurance and Validation

- When are the appropriate times to collect samples for quality control testing?
- What procedures require written SOPs (quality assurance)?
- Which parts of the manufacturing process affect product quality and therefore require validation?



Unit V

ADDITIONAL RESOURCES

A. North Carolina Educational Opportunities

BioNetwork: A website maintained by the North Carolina Community College System with information about educational opportunities and careers.

ncbionetwork.org

BioWork: The website contains an overview of a 140-hour course offered through the North Carolina Community College System. The site provides a list of locations within the community college system where BioWork is taught. Durham Technical Community College offers a pre-BioWork course called *Bio Careers*, a program that provides basic math and science training in conjunction with the career readiness and technical skills development that are necessary to pursue further training in biotechnology.

www.ncbionetwork.org/master-course-list/biowork
durhamtech.edu/noncredit/biocareersfaq.htm

BRITE (Biomanufacturing Research Institute & Training Enterprise) at North Carolina Central University: Created specifically to train the next generation of biotechnology scientists and expand North Carolina's already-booming biotech industry, BRITE offers an undergraduate degree in Pharmaceutical Sciences and master's degrees in Drug Discovery and Biomanufacturing.

brite.nccu.edu

BTEC (Biomanufacturing Training and Education Center) at North Carolina State University: The BTEC was founded to help establish, attract and expand biomanufacturing in North Carolina. The 82,500-gross-square-foot center is the largest of its kind in the United States and the world. It features more than \$12.5 million of industry-standard equipment and a simulated cGMP (current Good Manufacturing Practice) pilot plant facility capable of producing biopharmaceutical products using cell growth and expression, recovery and purification processes in a sterile environment. Undergraduate and graduate programs are offered.

www.btec.ncsu.edu

College Foundation of North Carolina: The site compares more than 100 colleges and universities in North Carolina and permits a search for various programs/courses in biomanufacturing and biotechnology.

www.cfnc.org

NC BioImpact: NC BioImpact is a group of educational, industry and nonprofit organizations dedicated to meeting the workforce needs of North Carolina's life sciences industry. Formerly known as the North Carolina Biomanufacturing and Pharmaceutical Training Consortium (BPTC), the partnership is helping North Carolina achieve international recognition for its innovative biopharmaceutical training and attract major biomanufacturing businesses to the area.

www.ncbioimpact.org

North Carolina Community College System Electronic Education Catalog: The site provides information about the curricula offered by the various community colleges in North Carolina.

www.nccommunitycolleges.edu/programs/education_catalog.htm

B. General Teacher Resources

About Bioscience: This website, by the North Carolina Association for Biomedical Research, has information about more than 35 topics and careers in bioscience for teachers, students and the general public.

www.aboutbioscience.org

Access Excellence @ The National Health Museum

www.accessexcellence.org

Bio-Link: Bio-Link is a National Advanced Technological Education (ATE) Center for Biotechnology that originated in 1998 with a grant from the National Science Foundation. The ATE program was created to improve and expand educational programs that prepare skilled technicians to work in the high-tech fields that drive the U.S. economy.

www.bio-link.org

Biopharmaceutical Industry Contributions to State and U.S. Economies: This 200-page study by the Milken Institute provides a state-by-state examination of the industry's economic impact in four areas.

www.milkeninstitute.org/pdf/biopharma_report.pdf

Biospace.com: The website offers breaking news, career links and other information.

www.biospace.com

Biotechnology Industry Organization

www.bio.org

Biotechnology Institute

www.biotechinstitute.org

BiotechTerms.org: An online glossary of biotechnology terms.

biotechterms.org

Council for Biotechnology Information
www.whybiotech.com

FDA: For Consumers: The consumer home page provides links to a wealth of timely information covering FDA activities, regulated products and health information.

www.fda.gov/ForConsumers/default.htm

goENC.com: A K-12 math and science teacher center.

www.goenc.com

Grocery Manufacturers of America (GMA): The website provides up-to-date information on genetically modified foods.

www.gmabrands.com

Massachusetts Biotechnology Council: The website provides information on jobs, internships and educational programs.

www.massbio.org

The Model Employee: Preparation for Careers in the Biopharmaceutical

Industry: The publication, by the North Carolina Biotechnology Center, provides an excellent overview of pharmaceutical manufacturing, careers in the field, educational requirements and detailed descriptions of six jobs.

www.ncbiotech.org/sites/default/files/TME-EmailFriendly.pdf

National Center for Biotechnology Information: The NCBI advances science and health by providing access to biomedical and genomic information.

www.ncbi.nlm.nih.gov

New Jobs Across North Carolina: A Strategic Plan for Growing the Economy

Statewide Through Biotechnology: The report offers recommendations on ways to attract businesses, train the workforce, strengthen partnerships and improve K-12 education in North Carolina.

www.ncbiotech.org/sites/default/files/Strategicplan_1.pdf

North Carolina Biosciences Organization (NCBIO)
ncbioscience.net

North Carolina Biotechnology Center: The NCBC website offers teacher resources and considerable information on careers, jobs and the biotechnology industry. It also provides links to additional biotechnology resources.
www.ncbiotech.org

Window on the Workplace 2012: Recognizing the strategic job creation potential of North Carolina's biomanufacturing and pharmaceutical manufacturing cluster, this study was undertaken to document the continued growth and hiring needs in the cluster as well as to benchmark progress made in meeting those needs by NCBioImpact.
www.ncbiotech.org/content/window-workplace-2012

C. Teacher Resources for Units I–IV

Teacher Resources for Unit I

Bio Careers: A career hub for postgraduate life scientists.
www.biocareers.com

Biotech Chronicles: The website offers a brief history of biotechnology discoveries that continue to influence the field today. It includes essays on genetics and DNA research, profiles of some of the influential individuals who have helped build the biotechnology industry, and an integrated series of timelines that provide an overview of biotechnology from a historical perspective.
www.accessexcellence.org/RC/AB/BC

Biotechnology Industry Organization: The website of this trade organization provides background information on numerous biotechnology issues.
www.bio.org

Biotechnology Regulatory Services: The BRS, which is part of the U.S. Department of Agriculture (USDA), implements regulations about genetically engineered organisms that may pose a risk to plant health. The website has useful links to other agricultural biotechnology sources.
www.aphis.usda.gov/biotechnology/brs_main.shtml

Children’s Museum of Indianapolis: The webpage also has links to additional information about biotechnology.
www.childrensmuseum.org/themuseum/biotech/timeline.htm

DNai: An interactive timeline about DNA.
www.dnai.org/timeline/index.html

High Growth Industry Profile: Biotechnology: A snapshot of the biotechnology industry by the U.S. Department of Labor’s Employment and Training Administration.
www.doleta.gov/brg/indprof/Biotech_profile.cfm

Teacher Resources for Unit II

Code of Federal Regulations (CFR)

www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR

Clinical Trials, FDA

www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm

FDA 101: Clinical Trials and Institutional Review Boards

www.fda.gov/forconsumers/consumerupdates/ucm134723.htm

Learn About Clinical Studies, National Institutes of Health (NIH): The website also has links to other sites about clinical studies and a glossary.

clinicaltrials.gov/ct2/info/understand

Learn About Clinical Trials, National Cancer Institute

www.cancer.gov/clinicaltrials/learning

Northeast Biomanufacturing Center and Collaborative (NBC2): This website has numerous useful links, including videos about careers in biomanufacturing. The center also sells a biomanufacturing textbook and technical laboratory manuals.

www.biomanufacturing.org

Overview of Clinical Trials, CenterWatch: Written for prospective trial participants, this site provides good information about clinical trials and the questions patients should ask before agreeing to participate. There also is a glossary of clinical research terms.

www.centerwatch.com/clinical-trials/overview.aspx

Teacher Resources for Unit III

BIO Career Guide Introduction, Access Excellence
www.accessexcellence.org/RC/CC/bio_intro.html

Bio-Link Biotechnology Careers: Presents scenarios of individuals who attended community college biotechnology programs, as well as a downloadable book.
www.bio-link.org/home/careers

Biomanufacturing in North Carolina: A brochure by the North Carolina Biotechnology Center.
www.ncbiotech.org/sites/default/files/BiomanufacturingBrochure.pdf

Biotechnology Information Series: This website, from Iowa State University, offers a wealth of information for K-14 educators.
www.cccc.edu/curriculum/majors/bioprocess

Career Guides, Jobstar Central
jobstar.org/tools/career

The Career Key: The site, by Lawrence Jones, Ph.D., of North Carolina State University, offers free and paid information about choosing a career.
www.careerkey.org

Careerplanner.com: The website offers free articles, links to other career sites and career tests for a fee.
www.careerplanner.com

Career Scenarios: Biotechnology
www.bio-link.org/home/careers

Center for the Advancement of Process Technology: Resources for educators, students and industry about process technology.
www.captech.org

Engineering K-12 Center, American Society for Engineering Education: ASEE is home to the popular student-focused eGFI site and teachers' blog.

www.asee.org

Massachusetts Biotechnology Council and MassBioEd Careers in Biotechnology:

The website includes job descriptions, organizational charts for companies of various sizes, a link to current job postings, and more.

www.massbioed.org/students/careers_in_biotech

The Model Employee: Preparation for Careers in the Biopharmaceutical

Industry: This publication, from the North Carolina Biotechnology Center, provides an excellent overview of pharmaceutical manufacturing, careers in the field and educational requirements, as well as detailed descriptions of six jobs.

www.ncbiotech.org/sites/default/files/TME-EmailFriendly.pdf

North Carolina Biotechnology Center: The NCBC has links to classroom resources, biotechnology companies in the state, jobs listings and much more.

www.ncbiotech.org

North Carolina Careers: The site offers career information, planning, workshop information and links to other sites.

north-carolina.careers.org

Occupational Outlook Handbook: The website, from the U.S. Department of Labor, profiles hundreds of occupations and employment projections.

www.bls.gov/ooh

Psychtests.com: The website offers free tests to help with career choices.

testyourself.psychtests.com

Sciencecareers.org: This website, from the journal *Science*, is a source for jobs, funding, meetings and advice.

sciencecareers.sciencemag.org

Teacher Resources for Unit IV

About Bioscience: The comprehensive website from the North Carolina Association for Biomedical Research (NCABR) hosts numerous short videos about biotechnology and biomanufacturing careers, such as Process Development Scientist, Process Engineer, Process Technician, Quality Assurance Associate, Quality Control Associate and Validation Specialist. Each video can be streamed or downloaded in various formats.

www.aboutbioscience.org

BioWork, North Carolina Community System

www.ncbionetwork.org/careers (search “BioWork”)

Enhancing the Biotechnology Workforce: Good Manufacturing Practices

www.bio-link.org/GMPtoc.htm

Northeast Biomanufacturing Collaborative: The website provides information on biomanufacturing programs at community colleges in the Northeast.

www.biomanufacturing.org

What is an SOP? The Parts of a Standard Operating Procedure

www.bio-link.org/GMP/sopparts.html

D. Glossary

Amino acid: The fundamental building blocks of a protein molecule. A protein is composed of a chain of hundreds or thousands of amino acids.

Antibody: A protein produced in response to the presence of a specific antigen.

Antigen: A foreign substance that elicits the production of antibodies.

Assay: A method for determining the presence or quantity of a component.

B lymphocytes (B cells): A type of white blood cell, produced by the bone marrow, that synthesizes antibodies.

Bt (*Bacillus thuringiensis*): A naturally occurring bacterium with pesticidal properties. *Bacillus thuringiensis* produces a protein (Bt toxin) that is toxic only to certain insect larvae that consume it.

Bacteriophage: A virus that infects bacteria. Also called a phage.

Batch record: Documentation that each step in the manufacturing process was completed; it includes very detailed information, such as dates, equipment used, the identity of each component, the sampling performed and the identity of the employees performing and checking each step. This is required by the Code of Federal Regulations Good Manufacturing Practice.

Bioassay: A method of determining the action of a compound by quantifying its effect on living organisms or their component parts.

Biocatalyst: A substance that speeds up biochemical processes in living things. The best-known example is the enzyme.

Biofuel: Fuel produced from renewable biological resources, such as plant biomass, used cooking oil, and treated municipal and industrial waste. Examples of biofuel include alcohol (from fermented sugar) and methane.

Biologic: A medication, vaccine or other type of drug derived from a living source (human, animal or unicellular). Most biologics are complex mixtures that are not easily identified or characterized, and many are manufactured using biotechnology. Biological products often represent the cutting-edge of biomedical research and are sometimes the most effective way to prevent or treat a disease.

Biological control: The use of one organism to control the population size of another organism.

Biological molecules: Large, complex molecules, such as proteins, nucleic acids, lipids and carbohydrates, that are produced only by living organisms. Biological molecules often are referred to as macromolecules or biopolymers.

Biomanufacturing/bioprocessing: A procedure in which microorganisms, living cells or their components are used to produce a desired end product.

Biopharmaceuticals: Products derived using living organisms to produce or modify the structure and/or functioning of plants or animals with a medical or diagnostic use.

Bioprocessing technology: Uses living cells or the molecular components of the cells' manufacturing machinery to produce desired products. The living cells most commonly used are one-celled microorganisms, such as yeast and bacteria. The biomolecular components used most often are enzymes, which are proteins that catalyze (increase the rate of) biochemical reactions.

Bioreactor: A container in which a biological reaction takes place. The term commonly is used to describe the large-scale vessels used in bioprocessing.

Bioremediation: The use of organisms, usually microorganisms, to break down pollutants in soil, air or groundwater.

Biotechnology:

- *Traditional Definition:* The use of living organisms and biological processes to solve problems or make useful products.
- *Modern Definition:* A collection of technologies that capitalize on the attributes of cells and put biological molecules, such as DNA and proteins, to work for us.

Catalyst: A substance that speeds up a chemical reaction but is not itself changed during the reaction.

Cell: The smallest structural unit of living organisms that is able to grow and reproduce independently.

Cell culture: A technique for growing cells under laboratory conditions.

Cell fusion: The formation of a hybrid cell produced by fusing two different cells.

cGMP (current Good Manufacturing Practice): A set of minimum standards established and enforced by the U.S. Food and Drug Administration (FDA) to ensure the safety and purity of drug products manufactured in the United States (see also **GMP (Good Manufacturing Practice)**).

Chinese hamster ovary cells (CHO cells): A cell line originally established in the 1960s that is derived from the ovary of the Chinese hamster. They often are used in biological and medical research and are used by some biopharmaceutical companies to produce certain drugs.

Chromosome: Components in a cell that contain genetic information. Each chromosome contains numerous genes. Chromosomes occur in pairs: one obtained from the mother, the other from the father. Chromosomes of different pairs are often visibly different from each other (see also **DNA**).

Clinical trial: A research study designed to answer specific questions about vaccines or new therapies or new ways of using known treatments by testing them in humans. Clinical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective.

Clone: A cell or collection of cells containing identical genetic material. Clones are produced from a single parent cell.

Codon: A sequence of three nucleotide bases that specifies an amino acid or represents a signal to stop or start a function.

Culture: To grow living organisms in a prepared nutrient mixture or mixtures (known as culture medium or media).

Culture medium: A nutrient system for artificially growing bacteria or other cells.

DNA (deoxyribonucleic acid): The chemical molecule that is the basic genetic material found in all cells. DNA is inherited. Because DNA is a very long, thin molecule, it is packaged into units called chromosomes. DNA belongs to a class of biological molecules called nucleic acids.

DNA fingerprinting (DNA testing, DNA typing): A technique for identifying individual organisms based on the uniqueness of their DNA pattern. The technique has applications in forensics, paternity testing, anthropology, conservation biology and ecological research.

DNA sequence: The order of nucleotide bases in the DNA molecule.

Double helix: A term used to describe the configuration of a DNA molecule. The helix consists of two spiraling strands of nucleotides held together with chemical bonds.

E. coli (Escherichia coli): A bacterium commonly found in the intestinal tracts of most vertebrates. It is used extensively in recombinant DNA research because it has been genetically well characterized.

Embryonic stem cells: Cells that can give rise to any type of differentiated cell. They are derived from the inner cell mass from a blastocyst, the 4- to 5-day-old ball of undifferentiated cells from which a prospective embryo develops. (see also stem cells).

Enzyme: A protein that accelerates the rate of chemical reactions. Enzymes are catalysts that promote reactions repeatedly without being damaged or consumed by the reactions.

Eukaryote: An organism whose genetic material is located within a nucleus. Yeast, fungi, protozoans, plants and animals are eukaryotes.

Expression: The physical manifestation of the information contained in a gene.

Federal regulations: The laws issued by the executive branch of the federal government. They are codified (arranged in a logical order) in the Code of Federal Regulations that is published each year.

Fermentation: A process of growing microorganisms (microbes) to produce various chemical or pharmaceutical compounds. Microbes are usually incubated under specific conditions in large tanks called fermenters. Fermentation is a specific type of bioprocessing.

Food and Drug Administration (FDA): The agency of the U.S. Department of Health and Human Services that regulates the testing of experimental drugs and approves new drugs and medical products based on evidence of their safety and efficacy. The FDA also regulates the safety of foods, cosmetics and other products.

Gene: A unit of hereditary information. A gene is a section of a DNA molecule that specifies the production of a particular protein.

Gene amplification: The increase, within a cell, of the number of copies of a given gene.

Gene mapping: Determining the relative locations of genes on a chromosome.

Gene therapy: The replacement of a defective gene in an organism suffering from a genetic disease. Recombinant DNA techniques are used to isolate the functioning gene and insert it into cells. More than 300 single-gene genetic disorders have been identified in humans. A significant percentage of these may be amenable to gene therapy.

Genetically modified organism (GMO): An organism (plant, animal or microorganism) whose genetic material has been altered using techniques in genetics generally known as recombinant DNA technology. Recombinant DNA technology is the ability to combine DNA molecules from different sources into the one molecule in a test tube. Thus, the abilities or the phenotype of the organism, or the proteins it produces, can be changed through the modification of its genes.

Genetic code: The way genetic information is stored in living organisms.

Genetic engineering: The technique of removing, modifying or adding genes to a DNA molecule in order to change the information it contains. By changing this information, genetic engineering affects the type or amount of proteins an organism is capable of producing.

Genome: The total hereditary material of a cell, comprising the entire chromosomal set found in each nucleus of a given species.

Genotype: The specific genetic makeup of an organism, as contrasted with the actual characteristics of an organism (see **phenotype**).

GMP (Good Manufacturing Practice): Regulations established by the U.S. Food and Drug Administration (FDA) that describe the methods, equipment, facilities and controls required for biopharmaceutical and pharmaceutical manufacturing.

Hepatitis B infection: A chronic inflammation of the liver caused by the hepatitis B virus.

Human Genome Project: A publicly funded international research initiative to sequence and identify human genes and record their positions on chromosomes.

Hybridization: Production of offspring, or hybrids, from genetically dissimilar parents. In selective breeding, it usually refers to the offspring of two different species.

Hybridoma: A type of hybrid cell produced by fusing a normal cell with a tumor cell. When lymphocytes (antibody-producing cells) are fused with the tumor cells, the resulting hybridomas produce antibodies and maintain rapid, sustained growth, producing large amounts of an antibody. Hybridomas are the source of monoclonal antibodies.

Immunoassay: A technique for identifying substances, based on the use of antibodies.

Immunotoxin: The coupling of an antibody and a molecule that is toxic to the cell.

In vitro: Performed in a test tube or other laboratory apparatus (Latin for “in glass”).

In vitro selection: Selection at the cellular stage of individuals possessing certain traits, such as herbicide resistance.

In vivo: In the living organism (Latin for “in the living”).

IND (investigational new drug): The status of an experimental drug after the U.S. Food and Drug Administration (FDA) agrees that it can be tested in people. A pharmaceutical or biopharmaceutical company must file an IND application with the FDA. The application includes information about the way the drug is made, the results of testing in animals and much other information. A drug cannot be tested in humans until the IND application is filed.

Insulin: A hormone produced by the pancreas that regulates the levels of glucose in the blood.

Interferon (IFN): A protein produced naturally by the cells of the immune system of most animals in response to foreign agents such as viruses, bacteria, parasites and tumor cells. It increases the resistance of surrounding cells to attacks by viruses. There are three major classes of interferons. One type, alpha interferon, is effective against certain types of cancer. More than 20 different interferons have been identified in humans.

Interleukin: A protein produced naturally by our bodies to stimulate our immune systems. There are at least 18 known kinds of interleukins.

Leukocyte: A white blood cell (white corpuscle), an important component of the body's immune system. They are classified into two groups: mononuclear cells (lymphocytes and monocytes/macrophages) and polymorphonuclear leukocytes (neutrophils, basophils and eosinophils).

Lymphocyte: A type of white blood cell (leukocyte) found in the blood, lymph nodes and certain organs. Lymphocytes are continuously made in the bone marrow (see also B lymphocytes and T lymphocytes).

Macrophage: A type of white blood cell (leukocyte) that ingests dead tissue and cells and is involved in producing Interleukin 1. They are considered monocytes until they react to a foreign substance, when they become activated and are called macrophages.

Marker gene: Genes that identify which plants have been successfully transformed.

Medium: A substance containing nutrients needed for cell growth.

Microbe: A microscopic organism.

Molecular genetics: The study of the molecular structure and function of genes.

Monoclonal antibody: Highly specific, purified antibody that is derived from only one clone of cells and recognizes only one antigen (see **hybridoma**).

Multigenic: Many genes are involved in the expression of a trait.

Mutagen: A substance that induces mutations.

Mutant: A cell microorganism that manifests new characteristics due to a change in its genetic material.

Mutation: A change in the genetic information.

NDA (new drug application): An application submitted by the manufacturer of a drug or biologic to the U.S. Food and Drug Administration (FDA) after a number of clinical trials in humans have been completed. If the FDA authorizes the sale of the drug or biologic by prescription, it is said to have received FDA approval.

Nucleic acid: A biological molecule composed of a long chain of nucleotides. DNA is made of four different nucleotides repeated millions of times in no obvious pattern.

Nucleotide: A compound made up of these three components: a sugar, a phosphate and a nitrogen-containing base. Found as individual molecules (e.g., ATP, the “energy molecule”), or as many nucleotides linked together in a chain (nucleic acid such as DNA).

Oncogene: A gene thought to be capable of producing cancer.

Oncology: The study of cancer.

Phage (bacteriophage): A virus that only infects bacteria.

Phenotype: The observable characteristics of an organism as opposed to the set of genes it possesses (its genotype). The phenotype that an organism manifests is a result of both genetic and environmental factors. Therefore, organisms with the same genotype may display different phenotypes due to environmental factors. Conversely, organisms with the same phenotypes may have different genotypes.

Placebo: An inactive substance that looks like the drug that is being tested in a clinical trial.

Plasmid: A small, circular piece of DNA found outside the chromosome in bacteria. Plasmids are the principal tools for inserting new genetic information into microorganisms or plants.

Polymerase chain reaction (PCR): A technique for quickly making many copies of a specific segment of DNA.

Preclinical testing: Studies that test a drug in animals and in other nonhuman test systems. Safety information from such studies is used to support an investigational new drug application (an IND).

Prokaryotes: Organisms whose genetic material is not enclosed by a nucleus. The most common examples are bacteria.

Protein: A complex biological molecule composed of a chain of units called amino acids. Proteins have many different functions: structure (collagen); movement (actin and myosin); catalysis (enzymes); transport (hemoglobin); regulation of cellular processes (insulin); and response to the stimuli (receptor proteins on surface of all cells). The information for making proteins is stored in the sequence of nucleotides in the DNA molecule.

Protein engineering: A technique used in the production of proteins with new or artificial amino acid sequences.

Quality assurance (QA): A set of activities that ensures product quality by setting up and checking the procedures in the standard operating procedures (SOPs) and documentation. QA employees evaluate the overall manufacturing process, whereas quality control (QC) employees test the actual product at its various stages of manufacturing (including all of the raw materials).

Quality control (QC): A system to achieve or maintain the desired level of quality in a manufacturing process by inspecting the raw materials and samples at various stages of the process, as well as monitoring the process, so problems can be solved.

Recombinant DNA: DNA that is formed through combining DNA from two different sources. Humans direct the formation of recombinant DNA through selective breeding and genetic engineering.

Recombinant DNA (rDNA) technology: The laboratory manipulation of DNA in which DNA, or fragments of DNA from different sources, are cut and recombined using enzymes. This recombinant DNA is then inserted into a living organism. rDNA technology usually is used synonymously with genetic engineering.

Recombination: The formation of new combinations of genes. Recombination occurs naturally in plants and animals during the production of sex cells (sperm, eggs, pollen) and their subsequent joining in fertilization. In microbes, genetic material is recombined naturally during conjugation.

Regeneration: The process of growing an entire plant from a single cell or group of cells.

Restriction enzymes: Bacterial enzymes that cleave DNA at very specific locations.

RNA (ribonucleic acid): Like DNA, RNA is a type of nucleic acid. There are three major types: messenger RNA, transfer RNA and ribosomal RNA. All are involved in the synthesis of proteins from the information contained in the DNA molecule.

Somatic cell nuclear transfer: The transfer of a nucleus from a fully differentiated cell into an egg that has had its nucleus removed. This is the procedure used to isolate stem cells that is commonly called cloning.

Standard operating procedure (SOP): A document that defines in detail every step of only one particular process so it can be performed exactly the same way every time. In biomanufacturing, there are SOPs for every single step of the process; for example, the correct way to put on a gown before entering the production area. SOPs are required by the Good Manufacturing Practice (GMP) regulations of the U.S. Food and Drug Administration (FDA).

Stem cell: A “generic” cell that can make exact copies of itself indefinitely. In addition, a stem cell has the ability to produce specialized cells for various tissues in the body, such as heart muscle, brain tissue and liver tissue. Scientists are able to maintain stem cells forever, developing them into specialized cells as needed. There are two basic types of stem cells. The first type is the embryonic stem cell, which is obtained from either aborted fetuses or fertilized eggs that are left over from in vitro fertilization. Embryonic stem cells are useful for medical and research purposes because they can produce cells for almost every tissue in the body. The second type is the adult stem cell, which is not as versatile for research purposes because it is specific to certain cell types, such as blood, intestines, skin and muscle.

T lymphocytes (T cells): White blood cells, produced in the bone marrow, that aid B cells in making antibodies to fight bacterial infections. They also are instrumental in rejection of foreign tissue and may be important in the body’s defense against cancer.

Tissue culture: A procedure for growing or cloning cells through *in vitro* techniques.

Transformation: A change in the genetic structure of an organism as a result of the uptake and incorporation of foreign DNA.

Transgenic organism: An organism formed by the insertion of foreign genetic material into the germ line cells (sperm and eggs) of organisms. Recombinant DNA techniques are commonly used to produce transgenic organisms.

Vaccine: A preparation that contains an antigen, consisting of whole disease-causing organisms (killed or weakened) or parts of such organisms, that is used to confer immunity against the disease that the organisms cause. Vaccine preparations can be natural, synthetic or derived by recombinant DNA technology.

Vector: The agent used to carry new DNA into a cell. Viruses or plasmids are often used as vectors.

Virus: An infectious agent composed of a single type of nucleic acid (DNA or RNA) and enclosed in a coat of protein. Viruses can multiply only within living cells.

Yeast: A general term for single-celled fungi that reproduce by budding. Some yeast can ferment carbohydrates (starches and sugars) and thus are important in brewing and baking.

Source: Adapted from Glossary, North Carolina Biotechnology Center
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