The word *vaccine* comes from the Latin *vaccinus*, “pertaining to cows.” But shouldn’t it instead come from a word meaning “pertaining to immunity” or something? The first vaccine was not seen as one of a new class of medicines. It was a fluke. An 18th-century English physician named Edward Jenner was treating milkmaids for cowpox, a minor infection they shared with their dairy cows. One thing he never saw those women get (despite documented exposure) was the deadly smallpox virus. It was a widespread belief in folk medicine at the time that cowpox and smallpox must be related to one another because people who got one were immune to the other. The diseases shared similar symptoms, in particular skin sores. Jenner knew they were both caused by viruses, and he knew something about the human immune system. So he wondered whether the relatively mild cowpox infection somehow lent those young women immunity to smallpox.

Those were adventurous days in medicine, when doctors were beginning to understand about blood transfusions, for example, and learning the hard way about blood types. Some patients were put at risk for the potential benefit to others through the advancement of knowledge — in ways that would never be allowed now (as explained in Chapter 4). Dr. Jenner took a chance and made an educated guess. He injected some fluid from a milkmaid’s cowpox postule (sore) into a healthy young boy who’d never had either cowpox or smallpox. Then some weeks later, after that boy had recovered from cowpox, the doctor introduced him to a smallpox infection. It was a calculated risk, and it paid off. The boy remained healthy. And Dr. Jenner had performed the first-recorded successful vaccination. He also coined the term *vaccine*, named such because the active agent was *Variolae vaccinae*, the cowpox virus.

**Heterologous Vaccines:** That first vaccine was an example of the simplest (and hence, the oldest) type of vaccination: heterologous vaccines derived from different but related species. The modern BCG tuberculosis vaccine also makes use of a bovine equivalent virus (others are in development, however, because it is known to slow progression of the disease more than fully prevent it). Such live vaccines make use of the close relationship between some species of pathogens. Cowpox is a much less virulent form of virus than smallpox, but it carries some of the same antigenic molecules on its surface. An immune system that has fought off cowpox is armed with the necessary antibodies to battle smallpox in the future. Widespread vaccination ultimately led to worldwide eradication of smallpox — declared in 1980 by the World Health Organization (WHO) — except for a few specimens now kept for research purposes in very tightly controlled laboratories.

**Variolation:** Dr. Jenner was not the first to use the physical technique described above, which has since been named *variolation*, to combat smallpox. But he was the first to use a safer virus (a heterologous vaccine) instead of the very infection he was trying to prevent. In China, scabs and pus (both full of immune system cells as well as viruses) from the skin sores of patients suffering a milder form of smallpox were used to vaccinate against the disease — with mixed
results. Some people died; some people got sick but lived, gaining immunity. In Turkey, the wife of a British ambassador saw variolation work, and she told the folks back home about it. Edward Jenner was a lucky beneficiary of the process as a child (1), and his personal experience must have helped him decide to take that calculated risk. He was lucky — as was the boy he vaccinated. In the modern world of vaccine testing, methods such as Jenner’s would not be accepted.

**Whole-Organism Vaccines**

Although it became popular throughout Europe and the Americas in the late 19th century and can be credited with reducing smallpox cases and mortality (2), variolation was a dangerous way to prevent disease — and it didn’t always work. The problem, of course, is that introducing virulent organisms into healthy people is simply infecting them with the disease. If they’re lucky, they’ll get over it and become immune. If not, they can get severely sick or even die. It’s better that they are never exposed in the first place!

**Killed Vaccines:** A better way to trigger an immune response is to use some form of the pathogen — dead ones, for example — that cannot develop into an infection (for example, a pathogen that cannot reproduce). In making the typhoid vaccine and in Jonas Salk’s famous poliomyelitis vaccine (see the Fighting Polio box), the virulent microbes are killed using formalin (a formaldehyde solution). Others are killed with heat or radiation. These vaccines typically come in stable, long-lasting, freeze-dried formulations that can be shipped around the world. Even doctors in remote locations can reconstitute them using water for injection (WFI).

Microorganisms, however, are infamously tough little survivors. Most of us have heard of the bacteria that survived a trip to the Moon and back on one Apollo mission, fully exposed to the vacuum and radiation of space. If just one of millions of poliovirus is able to make it through the formalin process, it could lead to a real infection. Some documented cases of the full polio disease have been related to people who received the vaccination one or more times.

**Live, Attenuated Vaccines (LAVs):** Sometimes dead microbes cannot induce the necessary immune response; or such vaccines can require booster shots in the future because they do not create a strong enough response. Twentieth-century researchers wondered whether it might be possible to simply weaken rather than kill a virulent organism so that it cannot threaten a patient receiving a live form. This technique would most closely mimic an actual infection, so it could elicit a stronger immune response. In some cases, a single dose provides lifetime immunity.

Viruses are weakened (attenuated) by growing many generations of them in hostile cell cultures, making them barely able to survive and reproduce in that type of environment. Scientists thus make use of the viruses’ ability to adapt and mutate so that a strain of the virus is bred to be less capable of infecting human cells. These become the vaccination that provides immunity to the natural or “wild” type of the pathogen. This method has been successful with several viruses, producing among other things the measles, mumps, and rubella (MMR) vaccine that so many of us receive as children. Yellow fever is another, and a researcher named Dr. Albert Sabin used the technique hoped for. Even so, the public and the media called it a cure. But before the year was out, new cases of polio were being reported that were directly linked to the vaccine made by Cutter Laboratories in California. This contributed to the evolving drug regulations of the times, as discussed in more detail in Chapter 3 of this supplement. Connaught continued to make vaccine that proved to be safer.

Meanwhile, several US researchers were working to make a live, attenuated polio vaccine, among them Dr. Albert Sabin, who was the first to conduct a clinical trial. Two others (Hilary Koprowski and Harold Cox) followed, and soon all three were testing independently. The World Health Organization got involved, and eventually the Sabin vaccine was given the green light. Connaught and other companies (including Institut Merieux in France) began to make it as well. After being given to millions of people all over the world, the oral polio LAV was cleared for the US market in 1962.

to create an oral alternative to Salk’s polio vaccine in 1960 (as discussed in the Fighting Polio box).

It’s also how most vaccines for influenza are made. One in particular (FluMist, made by MedImmune, Inc. of Gaithersburg, MD, www.medimmune.com; distributed by Wyeth in Madison, NJ, www.wyeth.com) is formulated as a nasal spray, which eliminates the unpleasantness of a traditional needle injection and more closely mimics how a natural infection happens. This may produce a better immune response, including mucosal immunity. FluMist was licensed in the United States in the summer of 2003 for healthy people 5–49 years old.

Bacteria present more of a challenge. They are more complex organisms than viruses and thus harder to control. There is only one live, attenuated bacterial vaccine on the US market: the Vivotif live oral typhoid vaccine from Berna Products Corporation (Coral Gables, FL), which contains Salmonella bacteria. Some biotechnology companies are using genetic engineering technology to develop vaccines against certain bacteria, Vibrio cholerae for one. If certain genes are removed from the bacterial genome, the microbes can be disabled. They can be made incapable of reproducing, making toxins, or properly metabolizing their food.

LAVs are a more risky proposition than inactivated (killed) vaccines. Again, the toughness and adaptability of microorganisms comes into play. Living viruses or bacteria have the potential to mutate and become virulent. There is some talk of polio, for example, having mutated (perhaps in response to vaccines) to become the Coxsackie virus, which can be found in chronic fatigue patients. And a small number of polio vaccinations have led to the full-blown disease. For this reason, LAVs are never given to people with compromised immune systems, such as cancer patients or those infected with the human immunodeficiency virus (HIV).

A lesser concern with live vaccines is their fragility. Current LAVs must be refrigerated to be kept alive, making them difficult to transport over long distances and presenting storage problems for the doctors and clinics that use them, especially in the developing world. But the benefits often outweigh the risks. LAVs provide both systemic and mucosal immunity — whether intestinal for oral vaccines or respiratory for inhaled ones, depending on the traditional route of infection for the wild type. Killed vaccines give only systemic (blood) immunity and can allow people with immunity to serve as carriers or transmitters of the live disease.

**Acellular and Subunit Vaccines**

As vaccine technology progressed, some scientists asked whether it might be possible to use just a part of an organism (the antigens alone, for example) as a vaccine. An empty viral shell (without its DNA or RNA “guts”) would be incapable of causing disease, but it might trigger the production of valuable antibodies and memory cells. Similarly, the hairlike flagellum a bacteria uses to move around, or merely some proteins from its cell wall, could induce an appropriate immune response. Such an acellular vaccine has been created against the *Haemophilus influenzae* B (Hib) bacterium. Hib is cultured in large numbers, then processed. The purified antigens are formulated into a vaccine, as Chapter 3 explains in more detail. Anthravax (from VaxGen, Inc., www.vaxgen.com) uses the protective antigen of the anthrax vaccine. And some work is being done with the GP120 envelope, a portion of the human immunodeficiency virus (HIV), for use in an AIDS vaccine.

Recombinant DNA technology has made subunit vaccines a viable alternative. Microorganisms certified by regulatory agencies as GRAS (“generally recognized as safe”) are genetically engineered to produce certain antigens or epitopes in large amounts, usually a dozen or so identified in a given pathogen. Fermentation of recombinant yeast, for example, produces a hepatitis B vaccine. Adverse reactions are rare with subunit vaccines, mostly limited to minor irritation of the injection site and so forth, making them safer for use by immunocompromised patients.

Another method of producing subunit vaccines is still under study but is showing promise. Potato,
tomato, corn, and other plants have been genetically modified to produce antigens specific to some viral and bacterial infections. Similarly, *Escherichia coli* has been genetically engineered to produce antigens against hepatitis B and the Norwalk virus. Processing and formulation are then greatly simplified or eliminated. You could be vaccinated simply by eating the fruit of such efforts! Or you might swallow capsules of concentrated antigen-bearing vegetable matter — something like the “herbal” supplements many people in the United States and Europe choose to take. With such vaccines, there is hope for producing cheaper, easier to administer vaccinations for the developing world (as further discussed in Chapters 4 and 5).

Other transgenic vaccines, one for example involving malarial antigens, may be produced in the milk of genetically engineered sheep, goats, or cows. The animals could make a lot of antigens every day, but purifying and processing and formulating the results might be a cost-limiting factor.

**Toxoid and Conjugate Vaccines**

With some bacteria, it is not the infecting microbes themselves so much as the products of their metabolism that present a danger. Diphtheria and tetanus bacteria, for example, secrete toxins that can harm or kill a person. Toxoid vaccines are made when those toxins are inactivated with formalin. They induce an immune response that will protect against the bacterial toxin, but a booster shot is often necessary every 10 years. The immune response to a toxoid is not very strong.

One way to increase the immune response is to include an adjuvant in the vaccine formulation (as described in the Adjuvants box in Chapter 3). Aluminum salts, for example, are said to help macrophages present antigens to lymphocytes in the lymph nodes, thus increasing the immune response. The diphtheria and tetanus toxoid vaccine was found to work better when coupled with a pertussis subunit vaccine, thus giving rise to the DTP combination with which you may be familiar.

Other conjugate vaccines combine toxoids or antigens as adjuvants linked to polysaccharide molecules. Some bacteria use certain polysaccharides (long sugar chains) to disguise themselves so that immature immune systems cannot react to them. *Hib*, *Nesseria meningococcus*, and *Staphylococcus pneumoniae* are guilty of this disguise tactic. Infants and young children are incapable of mounting an immune response against them. Conjugate vaccines can train their immune systems to recognize those polysaccharides as foreign and dangerous by linking them to proteins that cannot be mistaken as such. After only two years of Hib-conjugate use in infants, their incidence of infection dropped from 60 to 1 in 100,000. New conjugate vaccines are in development for *Pseudomonas* bacteria and HIV as well as cancer therapy (see below).

**Combination Vaccines:** The DTP conjugate described above is an example of a combination vaccine. So is the MMR (measles, mumps, and rubella) shot. Other combinations are available, and still more are in development. Combining vaccines can save children from getting more shots than may be necessary. With all the boosters that can be necessary, the chances of missing one or more shots would be much higher without combination vaccines. Missed boosters put everyone at risk, not just the child who misses his or her shot (as discussed in the Community Immunity box).

Some parents wonder whether combining too many vaccines into one shot could overwhelm a child’s immune system. With billions of circulating cells, your immune system can deal with thousands of different antigens at once. It’s been estimated that even an infant could easily handle 10,000 vaccines at once (a). However, combination vaccines are still not a straightforward issue. You don’t just mix the shots together — some require very specific formulations that may be incompatible. A great deal of research goes into determining whether each vaccine is safe and works well with the others.

And there are other concerns: induction of autoimmune reactions, increased risk of side effects, and mercury in certain preservatives.

**DNA Vaccines**

Gene therapy is a process by which to “skip the middle-man” in producing therapeutics or antigens for vaccination. With all gene therapies, the DNA sequence that codes for a particular protein (in this...
antigens are made. Once secreted, those antigens can induce a strong immune response.

The problem with naked DNA techniques is that they’re pretty wasteful: A lot of genetic material must be administered just to get a little bit of it ultimately translated by the cells. Much of it is simply removed from the patient’s system after being dismantled by circulating DNase enzymes. Liposomes (synthetic bilayer lipid membrane vesicles) may present a delivery option, as discussed in more detail in Chapter 4. But recombinant vector vaccines may be a better type of gene therapy — if they can be proven safe. Most currently in development make use of certain viruses’ ability to deliver DNA to human cells.

That’s how viruses reproduce. They latch onto cellular membranes like thorny burrs can latch onto your clothes when you go for a walk in tall grass. Then they inject their own DNA into the cell, forcing it to make more viruses. By removing the viral DNA and replacing it with the code for certain antigens, we can efficiently deliver those genes to the cells. HIV, rabies, and measles vaccines are being developed using adenoviruses, adenoassociated viruses, or retroviruses as recombinant vectors. Another vector showing promise is the Venezuelan equine encephalitis virus, which is being developed by Alphavax, Inc. (www.alphavax.com). Attenuated bacteria can also be engineered to display the antigens of more virulent species, mimicking harmful infection and training the immune system to target it in the future.

**Therapeutic Vaccines**

The newest twist in vaccine technology is immunotherapy. In this case, the immune system isn’t being prepared to fight a future disease; it’s being armed and trained to fight one that’s already in progress. Therapeutic vaccines are being developed to fight allergies, cancerous tumors, and even drug addiction. Some companies are seeking to treat hepatitis, tuberculosis, or HIV. Several peptides (small proteins) are in development for treatment of autoimmune disorders (4). Vaccines against addictive drugs such as nicotine (NicVax in development at Nabi Biopharmaceuticals, www.nabi.com, of Boca Raton, FL) and cocaine seek to block the effects of a drug so that it no longer produces the desired effects.

Cofounded by Dr. Jonas Salk, the Immune Response Corporation (Carlsbad, CA, www.imnr.com) has an HIV vaccine in the works for treating patients already infected with the AIDS virus. Clinical trial results have demonstrated that the drug boosts HIV-specific immune responses and could slow the progression of HIV infection when used alone or in conjunction with antiretroviral therapy. Furthermore, the company believes that its product stimulates the production of specific immune system modulators (cytokines and chemokines) that naturally protect components of the immune system from HIV infection.

Immunotherapy expands the very definition of the word vaccine. Glatiramer acetate (Copolymer 1, marketed under the brand name of Copaxone), a drug/vaccine against the autoimmune disease multiple sclerosis (MS), is an example of a vaccine treatment. It is related to the myelin basic protein, one cause of MS. Studies of antibodies against prions (mutant proteins believed to be infectious) have raised hopes for a vaccine against bovine spongiform encephalopathy (“mad cow disease”) or its human equivalent (new-variant Creutzfeldt-Jakob disease). A preventive (prophylactic) vaccine provokes an immune response directed against a future invader. Therapeutic vaccines do the same thing to current diseases, whether they be pathogens or the body’s own problem (e.g. cancer).

Avant Immunotherapeutics, Inc. (Needham, MA; www.avantimmune.com) is involved in several vaccine research and development projects, from infectious disease and organ transplant vaccines to autoimmune

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**Infectious Diseases Preventable by Vaccines**

- Anthrax
- Bacterial meningitis
- Chickenpox
- Cholera
- Diphtheria
- *Hemophilus influenza* type B
- Hepatitis A
- Hepatitis B
- Influenza
- Measles
- Mumps
- Pertussis
- Plague
- Pneumococcal pneumonia
- Polio
- Rabies
- Rubella
- Tetanus
- Typhoid fever
- Yellow fever

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PHOTODISC (WWW.PHOTODISC.COM)
and cancer vaccines. One product in the works is a tetanus-toxoid–based therapeutic intended to enlist the immune system’s help manage cholesterol.

**Immune Suppression:** When a patient’s immune system is causing problems (as discussed in the **When Things Go Wrong** box in Chapter 1), some aspects of it may need to be suppressed. As scientific understanding of the mechanisms has improved, some researchers have looked at ways to selectively “down-regulate immune responses by vaccinating the immune response against itself” (4). Vaccines are in development that would target certain T-cell antigenic receptors and major histocompatibility complex proteins. Fluctuations in some of those immune system molecules have been shown to associate with autoimmune disease states.

Peptide vaccines for autoimmune diseases tend to be quite small, only 15–20 amino acids long. They need bind only to certain sites on certain molecules to work. Companies working on these kinds of therapeutics include Corixa Corporation (Seattle, WA, www.corixa.com), the Immune Response Corporation (Carlsbad, CA, www.imnr.com), and Avanir Pharmaceuticals (San Diego, CA, www.avanir.com).

**Cancer Vaccines:** Several different treatments are available to cancer patients, from radiotherapy to chemotherapy. All of them have the drawback that they indiscriminantly kill fast-growing cells, whether those are tumor cells or normal ones. Unfortunately, some healthy cells are also fast-growing, among them hair, blood and immune system cells, and the gastrointestinal lining. So cancer treatments can be harsh on patients, disrupting their ability to eat, causing hair loss, and interfering with their immune systems.

Many companies and academic researchers are seeking a better way to kill cancer cells. The immune system is so good at killing things that it is an obvious choice. As with the polio vaccine story, multiple researchers are examining multiple approaches — dozens of them in many stages of development. Cancer centers all over the country have early phase I trials in progress, such as the telomerase peptide being studied as a potential breast cancer vaccine at the University of Pennsylvania’s Abramson Cancer Center in Philadelphia, PA. AVI BioPharma (Portland, OR, www.avibi.com) and CancerVax Corporation (Carlsbad, CA) are among those that have completed phase II clinical trials. Meanwhile, mouse studies at the Maxine Dunitz Neurosurgical Institute (www.cedars-sinai.edu/1043.html) are beginning to suggest ways to improve T cells and make them more capable of fighting late-stage tumors. And Corixa Corporation’s Melanine vaccine for melanoma has been on the market since 1999.

Antigenics Inc. (New York, NY, www.antigenics.com) and Stressgen Biotechnologies Corporation (Victoria, BC, Canada, www.stressgen.com) are focusing on heat shock proteins (HSPs) to stimulate the body’s immune defenses. Also called stress proteins, HSPs are made by many organisms (from bacteria and fungi to plants and animals) in response to stresses such as ultraviolet radiation, viral infection, or a sudden rise in temperature. They are used as adjuvants for tumor-specific antigens, encouraging a vigorous immune response. A gene therapy approach might be to deliver the genes coding for such proteins directly to cancerous cells, forcing them to call attention to themselves.

Some tumor cells express antigens that provoke an immune response. The immune system may deal with some tumors already. But many cancers can disrupt the normal immune response. In one possible therapy, DNA could be delivered to macrophages (away from the cancer site) that would be translated into tumor antigens, which then would be presented at the lymph nodes for creating antibodies and cells against the tumor. This is an approach being pursued by Genzyme Molecular Oncology (Framingham, MA, www.genzymemolecularoncology.com).

AVAX Technologies, Inc. (Overland Park, KS, www.avax-tech.com) is taking a more patient-specific approach. Its autologous cell vaccine modifies a patient’s biopsied tumor cells and reintroduces them to induce an immune system attack on the cancer. In February, clinical researchers working with its malignant melanoma vaccine reported more than doubling the survival rate of patients who received this cancer vaccine with conventional surgery over those who had surgery alone. Timing seems to be key, they said, while also noting that some patients exhibit a stronger immune response than others.

Another form of patient-specific antibodies are antidiotypic vaccines, which then would be presented at the lymph nodes for creating antibodies and cells against the tumor. This is an approach being pursued by Genzyme Molecular Oncology (Framingham, MA, www.genzymemolecularoncology.com).
A Vaccine Timeline

The dates of introduction for the first-generation vaccines for use in immunizing humans against a number of diseases:

1798 Smallpox
1885 Rabies
1897 Plague
1923 Diptheria
1926 Pertussis (whooping cough)
1927 Tuberculosis (BCG)
1927 Tetanus
1935 Yellow Fever
1955 Polio (injectable killed vaccine)
1962 Polio (oral LAV)
1964 Measles
1967 Mumps
1970 Rubella
1981 Hepatitis B

(SOURCE: WORLD HEALTH ORGANIZATION, WWW.WHO.ORG/VACCINES-DISEASES/HISTORY/ HISTORY.SHTML)

such as those in development at Biovest International, Inc. (www.biovest.com) and Genitope, Corporation (www.genitope.com). These monoclonal antibodies mimic the surface antigen of some cancer cells, which when given to patients generate an immune response toward the cancer.

Often cancer vaccines show promising results in clinical trials. One problem that may arise is an insufficient immune response. Immunological effectors may not make it all the way into the tumors, and thus cannot kill all the cancerous cells.

Autologous dendritic cell therapy (such as that practiced by Northwest Biotherapeutics, Inc. of Bothell, WA, www.nwbio.com; and Merix Bioscience, Inc. of Durham, NC, www.merixbio.com) is intended to elicit and stimulate antitumor immune responses. But this technique requires ex-vivo cell processing. Each patient’s treatment is prepared from his or her own cells. This brand new concept of individualized medicine is presenting many regulatory challenges.

Around the turn of the 19th century, a woman with cervical cancer was bitten by a rabid dog, and her cancer shrank. Experiments in the 20th century showed other viruses affecting cancers, including a connection between measles and lymphoma. The same things that make viruses good at infecting and killing their chosen cellular victims make them potentially good cancer fighters. Researchers at the University of Alabama in Birmingham and the Massachusetts General Hospital in Boston, among others, are currently engineering and studying so-called oncolytic viruses as potential tumor therapies. Not really vaccines, these viruses attack cancerous cells and will have to face the immune system as an obstacle like so many therapeutic proteins do.

Some cancers are proving to be caused by viral infections. Hepatitis B and C can lead to liver cancer. Human papilloma virus (HPV) warts are the leading cause of cervical cancer. The Epstein-Barr virus can cause anaplastic nasopharyngeal carcinoma. And a form of leukemia is caused by the HTLV-1 virus. Vaccinations against these viruses could prevent tumor formation in the first place.

Cancer vaccines are an exciting area of inquiry thanks to advancing gene research. Scientists are looking at vectored delivery of tumor antigens, T-cell stimulation, agonist epitopes, and cytokines as adjuvants, among other things. The myriad approaches tend to fall into the categories listed in the Types of Cancer Vaccine box.

Cancer vaccines are also classified by how they are produced. The US FDA classifies them as coming from animal, viral, or cellular (microbial or animal cells) sources. Plant sources (edible or otherwise) have yet to be covered by the regulations.

Animal sources include fertilized chicken eggs, which are used to grow viruses or bacteria in large numbers. Specific pathogen-free eggs (from certified vendors that maintain healthy hens) are injected with the microbe of interest, and then incubated. Transgenic animals present a special case of animal-sourced vaccines. Genetically engineered goats, sheep, or cattle secrete subunit vaccines in their milk, and transgenic hens might lay eggs with antigens already inside.

So-called “virus sourced” vaccines are grown in cell or tissue culture and usually weakened (attenuated) through serial passaging. This technique involves transferring the pathogens from one to another of a succession of animals, eggs, or tissue culture, with growth (or replication) of the virus taking place before each transfer. . . . For example, the rabies virus may be attenuated by adapting it to chick embryo tissues — the virus being serially passaged through a series of hens’ eggs. For use in a vaccine, a successfully passaged pathogen should (a) be nonpathogenic for particular host(s), and (b) retain its specific immunogenicity in order to stimulate the formation of protective antibodies.
Thus, those vaccines described in the guidance as “viral sourced” actually overlap with the other two categories. Most bacteria can be cultured by themselves, although that can be more of a problem with pathogenic species than others.

Yeast, insect, or mammalian cells are used to grow many subunit and therapeutic vaccines. Recombinant cell lines are engineered and adapted to certain cell culture conditions and media, then put into production. Similarly, bacteria (genetically engineered or not) may be cultured in a large fermenter.

The production source of a vaccine, whether it’s a subunit or live and attenuated organisms, makes a big difference in how regulatory agencies expect it to be processed and characterized. Events like the Cutter Laboratories incident described in the Fighting Polio box have led to laws requiring good manufacturing practices (GMPs) on the part of the companies making vaccines and other drug products for sale. For example, cells of animal origin may host adventitious agents that pose a risk if not properly controlled. Measures must be taken to remove, inactivate, or prevent contamination in the first place. And that’s just the beginning.

For Further Reading

Material that is not directly referenced in this article is often the result of combined online research using, among others, the following: The Sabin Vaccine Institute (www.sabin.org), The World Health Organization (www.who.int), the Howard Hughes Medical Institute (www.hhmi.org), and the Toxic Exposure Study Trust Foundation (www.testfoundation.org). Many items came from press releases, which are usually archived on each company’s web site.

References