14.7. REGULATORY CONSTRAINTS ON GENETIC PROCESSES

When genetic engineering was first introduced, there was a great deal of concern over whether the release of genetically modified cells could have undesirable ecological consequences. Reports in the popular press led to fears of "genetic monsters" growing in our sewers, on our farm lands, or elsewhere. Consequently, the use of genetic engineering technology is strictly regulated.

The degree of regulatory constraint varies with the nature of the host, vector, and target protein. For example, consider a scenario where serious harm might arise. The gene for a highly toxic protein is cloned into *E. coli* to obtain enough protein to study that protein's biochemistry. Assume that a plasmid that is *promiscuous* (i.e., the plasmid will shuttle across species lines) is used. Also assume that laboratory hygiene is not adequate and a small flying insect enters the laboratory and comes into contact with a colony on a plate awaiting destruction. If that insect leaves the laboratory and returns to its natural habitat, then the target gene is accidentally released into the environment. Laboratory strains of *E. coli* are fragile and usually will not survive long in a natural environment. However, a very small probability exists that the plasmid could cross over species lines and become incorporated into a more hardy soil bacterium (e.g., *Pseudomonas* sp.). The plasmid would most certainly contain antibiotic resistance factors as well. The newly transformed soil bacterium could replicate. Many soil bacteria are opportunistic pathogens. If they enter the body through a wound, they can multiply and cause an infection. If, in addition, the bacterium makes a toxic protein, the person or animal that was infected could die from the toxic protein before the infection was controlled. If the plasmid also confers antibiotic resistance, the infection would not respond to treatment by the corresponding antibiotic, further complicating control of the spread of the gene for the toxin.

This scenario requires that several highly improbable events occur. No case of significant harm to humans or the environment due to the release of genetically modified cells has been documented. However, the potential for harm is real.

Regulations controlling genetic engineering concentrate on preventing the accidental release of genetically engineered organisms. The deliberate release of genetically engineered cells is possible, but an elaborate procedure must be followed to obtain permission for such experiments.

The degree of containment required depends on (1) the ability for the host to survive if released, (2) the ability for the vector to cross species lines or for a cell to be transformed by a piece of naked DNA and then have it incorporated into the chromosome via recombination, and (3) the nature of the genes and gene products being engineered. Experiments involving overproduction of *E. coli* proteins in *E. coli* using plasmids derived from wild populations are readily approved and do not require elaborate containment procedures (see Table 14.5). Experiments that would move the capacity to produce a toxin from a higher organism into bacteria or yeast would be subjected to a much more thorough evaluation, and more elaborate control facilities and procedures would be required.

The National Institutes of Health (NIH) have issued guidelines that regulate the use of recombinant DNA technology. Special regulations apply to large-scale systems (defined as > 10 l). There are three different levels of containment: BL1-LS, BL2-LS, and BL3-LS. BL1-LS (biosafety level 1, large scale) is the least stringent. Table 14.6 compares the requirements for the three containment levels.