Awareness among those in the serum industry, and among serum users, of some of the pitfalls has risen in recent years.

rindepest-endemic countries, as long as those countries were free from bovine spongiform encephalopathy (BSE). APHIS would, under the proposal, accept serum from USDA-approved abattoirs outside the U.S. On arrival in the U.S., each serum lot would be inspected by an APHIS inspector and then taken directly to an APHIS-approved irradiation facility for treatment. After gamma-irradiation of 2.2 megarads at the temperature of dry ice, the consignment could be released to the importer for distribution.

The USDA's proposal to admit serum from infected regions into the U.S.—if it progresses any further—might provide an additional option: serum irradiated in a USDA-approved way. Kathleen Akin, one of APHIS officials behind the proposal, recognizes that irradiated serum does not have the same growth promotion and maintenance properties as the nonirradiated product. However, she believes that irradiated sera may be able to support certain cell lines that will not grow on serum-free media and might, therefore, be regarded as a product of intermediate nutritional quality. If so, this would go some way to relieving the pressure on nonirradiated serum from acceptable sources. Akin also considered that other forms of serum treatment, including the heat and pH treatments that are outlined in the draft annexes of the EU directive on serum importation, and the commercially developed ultraviolet treatments, would need to be further validated in close collaboration with USDA/APHIS.

In its proposal, APHIS considered that "no action" was not a reasonable option because "it would unnecessarily limit the supply of FBS" in the U.S. This reasoning fails to convince those in the serum

industry who profess to being somewhat bewildered by APHIS' motives. The companies believe that there is sufficient FBS in the U.S. to supply the demand, especially since a number of the biopharmaceutical products that were expected to come on-stream by now have not. The official company responses to APHIS provide detailed technical comments on, for instance, the efficacy of the proposed irradiation treatment or the question of determining "worst case" virus load. However, unofficially, a number of serum suppliers believe that APHIS wanted to "legalize" these serum sources in order to be able to control the legal trade, an argument that is more frequently heard for marijuana than for FBS. Whether such an approach would work is, of course, debatable. But that it should be proposed at all indicates that there may be a serious problem to overcome.

Europe: Slow and Unsure

European regulators seem steadfastly resolved to perpetuate FBS confusion. When *Bio/Technology* last ventured into the mysterious market for FBS,² the Council of (National) Agriculture Ministers from the European Union (EU) member states had just adopted (on December 17, 1992) European Directive 92/118 to deal with the problem. The directive laid down the animal and public health requirements for trade in a broad spectrum of animal products and outlined a set of requirements to which national laws must adhere. It was supposed to be transposed into national law by January 1, 1994.

That this timetable was not kept will come of no surprise to anyone who has watched the European legislative machinery in action. However, it is not—

Technology and Fetal Bovine Serum Purification: A Sisyphean Task?

FBS severely tests the limits of available viral detection technology. These technological solutions tend to deny the sera of the very factors that make it sought-after, and can often significantly affect the serum nutrient quality. With almost three dozen tests run on what is perhaps the world's premium FBS from Australia and New Zealand, there is still a danger of biocontaminant transmission by viral agents that can escape detection if they are not specifically tested for. No FBS supplier can provide a 100% guarantee of safety, and cautious sourcing is but one front in the process associated with providing safe FBS.

The chemical and physical actions of this technology on FBS also tend to cause problems,

according to scientists at various companies, and unacceptable trade-offs occur. As a result, the limits of commonly used methods such as ultrafiltration, for example, may have been reached. Ultrafiltration is used by companies, such as HyClone (Logan, UT), to 40 nm (while the industry standard is only 100 nm), yet even this fine ultrafiltration cannot finally guarantee its safety, and it may even reduce the number of growth factors in the sera, since some are trapped in the filtering process.

Detection methods such as polymerase chain reaction (PCR) are, on a large scale, unfeasible. Further, because most tests are targeted for specific viral particles, unknown viruses can potentially escape detection by PCR, as well as

destruction by methods such as chemical inactivation, heat treatment, detergent washing, and irradiation.

Agents like bovine spongiform encephalopathy (BSE), which defy all technical detection and solutions, have the potential to cause the most damage and are a supplier's worst nightmare. U.S. federal guideline¹ testing does not eliminate this fear. Many companies are not sanguine about the prospects of a technical solution to FBS' problems and see relinquishing the use of FBS altogether as the definitive solution.

—Musa Mhlanga

1. APHIS, Department of Agriculture. 1994. Title 9-Animals and Animal Products. *Code of Federal Regulations*.