

screeener questionnaire, and the 1990 survey questionnaire. The information collected includes the processes and control technologies in use, current control levels, and pollutant releases. EPA also updated survey data through telephone calls and letters to specific facilities in an attempt to ensure that the database reasonably reflects the current status of the industry. The Agency recognizes that the industry is dynamic, and that processes and equipment change over time. Accordingly, EPA will consider information and data submitted in a timely manner by interested parties in response to this proposal for the purpose of updating the database prior to promulgation.

EPA placed information collected about the industry into plant-specific databases. These databases consist mainly of the 1990 survey responses provided by 244 plants but also contain information from EPA's sampling program. EPA then estimated costs of implementing the proposed technology bases in order to analyze the economic impacts of achieving the proposed effluent limitations guidelines and standards. The Agency used the plant-specific databases and other components to calculate wastewater discharges and the costs of complying with the proposed effluent limitations and standards. This comprehensive information provides a strong basis for ensuring that the proposed regulations meet the statutory requirements, and allows consideration of other factors such as multimedia pollutant reduction.

## 2. Summary of Public Participation

Beginning in 1989, EPA met on at least a biennial basis with industry representatives from the Pharmaceutical Research and Manufacturers of America (PhRMA) to discuss the development of the screener and detailed questionnaires that EPA intended to distribute under section 308 of the CWA. The Agency received input from the industry representatives that was invaluable in the development of these information collection instruments. Following the completion of the screener and detailed questionnaires, EPA has continued to meet informally with PhRMA representatives to discuss progress in the rulemaking effort. EPA has also met informally with the Natural Resources Defense Council regarding this rulemaking and has made available to environmental groups and other members of the public the information that was provided to the industry.

On May 23, 1994, EPA held a public meeting on the pharmaceutical rulemaking (see 59 FR 21740, April 26, 1994). Following the meeting EPA sent

copies of revised meeting handout materials to all attendees and to interested parties who could not attend. In addition, by letter dated August 12, 1994, EPA provided written responses to questions submitted by PhRMA concerning issues raised at the public meeting. These documents are in the rulemaking docket.

## 3. Development of Effluent Limitations Control Technology Options

After evaluating a variety of control and treatment technologies and their use in the industry, EPA selected BPT, BAT, BCT, PSES, NSPS, and PSNS control technology options upon which it bases this proposed rule. This process is described in Section IX of this notice.

## 4. Analyses of Regulatory Alternatives

EPA conducted a series of analyses to assess the economic and environmental impacts of various combinations of BPT, BCT, BAT, NSPS, PSES, and PSNS control options. EPA then compared the projected effluent loadings and air emissions resulting from each regulatory alternative to baseline pollutant releases estimated as of January 1, 1991, based on the 1990 survey data. EPA also estimated the costs of implementing the various control options and other environmental and economic impacts for each alternative above the baseline level of control which EPA determined as treatment technologies in place in 1990. EPA evaluated each alternative in order to determine the effectiveness of the control technologies represented and to ascertain the reductions in effluent loadings and air emissions below the baseline that each control technology option could attain. The Agency also determined the environmental effects of these technologies with a goal toward minimizing the cross-media transfer of pollutants between water and air.

EPA also evaluated the possibility of basing BAT and PSES on process changes involving solvent use minimization or elimination. After evaluating information provided in response to the section 308 detailed questionnaire survey regarding pollution prevention measures on-going at pharmaceutical manufacturing facilities, the Agency concluded that no option involving solvent use elimination or minimization is technically available at this time. Nonetheless, the Agency is encouraging the industry to conduct research into eliminating or minimizing the use of solvents for existing processes and to design future manufacturing processes that eliminate or minimize the use of

volatile solvents. See Section XIV, solicitation number 12.0.

## VII. Description of the Industry

### A. Pharmaceutical Manufacturing Facilities

Presented below is a brief description of the pharmaceutical manufacturing industry. Other characteristics of the industry are detailed in Sections IX.B., IX.C., IX.D., and IX.E. of this notice and in Section 3 of the TDD. Based upon responses to EPA's 1989 Screener Survey of Pharmaceutical Manufacturing Facilities, the Agency estimates that there are 566 manufacturing facilities located in 39 States, Puerto Rico, and the Virgin Islands. The major pharmaceutical manufacturing areas in the U.S. are the Northeast, the Midwest, and Puerto Rico.

### B. Manufacturing Processes

#### 1. Fermentation

Fermentation is the usual method for producing most steroids and antibiotics. The fermentation process involves three basic steps: inoculum and seed preparation, fermentation or growth, and product recovery. Production of a pharmaceutically active ingredient begins with spores from the plant master stock. The spores are activated with water, nutrients, and warmth and are then propagated through the use of agar plates, test tubes, and flasks until enough mass is produced for transfer to the seed tank. Following adequate propagation in the seed tank, microorganisms from the seed tank are transferred to a fermenter tank along with the sterilized nutrients and the tank is then sparged with air to begin the fermentation or growth process. After a period ranging from 12 hours to a week, depending on the specific process, the fermenter batch whole broth is ready for filtration, which removes mycelia (i.e., the remains of the microorganisms). The filtered aqueous broth containing product and residual nutrients is then ready to enter the product recovery phase.

There are three common methods of product recovery: solvent extraction, direct precipitation, and ion exchange or adsorption. The most common method, solvent extraction, involves the use of an organic solvent to remove or extract the pharmaceutically active ingredient or product from the aqueous broth. Numerous solvent extractions are usually necessary to remove an acceptable yield of product from the contaminant mixture. Another common recovery method, direct precipitation, involves the use of aqueous solutions of