

of each proposed provision. For example, answers to questions about testing herbals might have been combined with questions about whether the firms manufactured herbals. Some highlights of the survey are:

- Plant characteristics: Manufacturers account for 62 percent of the total firms and 36 percent of manufacturers produce vitamins and minerals as their primary product.

- Use of published good manufacturing practice model: 65 percent of all firms follow some type of good manufacturing practice model, primarily food good manufacturing practices; 28 percent follow the NNFA good manufacturing practices and 31 percent follow FDA's drug good manufacturing practice requirements.

- Personnel: 67 percent of all establishments maintain records of personnel education, training, or experience.

- Quality control: 85 percent of all establishments have a unit or person responsible for quality control. Almost 80 percent of all manufacturers conduct at least some type of identity tests on incoming components and dietary ingredients and 96 percent of these firms also conduct some type of contamination test; 63 percent conduct some type of potency test. Nearly 70 percent conduct tests on inprocess materials or finished products. Of these firms, 97 percent conduct identity tests, 94 percent conduct contamination tests and 72 percent conduct potency tests. Asked whether firms hold reserve samples of each finished batch, 75 percent answered yes. Of the plants that have production processes, 70 percent use production and process controls that identify the points, steps, or stages in the manufacturing process to prevent adulteration. Almost 68 percent of all incoming ingredient or component lots are tested now and almost 70 percent of inprocess or finished product batches are tested in some manner.

- Warehousing: 70 percent of warehouses have temperature controls and 22 percent have humidity controls.

- Consumer complaints: Only 19 percent report incidents to FDA.

5. Baseline Risk

The current number of illnesses caused by poor manufacturing practices requires data linking illnesses directly to poor practices. Without direct evidence on the number of illnesses caused by poor manufacturing practices, we had to use an indirect approach. There are two indirect ways to estimate the number of illnesses caused by defective products:

- We could take the number of reported cases and multiply by a factor to account for underreporting.

- We could take the number of defective products and multiply by the probability of illness for the given defect.

In an ideal analysis, we would estimate the baseline both ways and then compare them. For the analysis of illnesses from poor manufacturing practices, however, we did not have sufficient data to perform either type of baseline estimate.

We looked at many sources for information, including medical and other literature on adverse events, information from poison control centers, reports to the agency, popular newspaper and magazine articles, and surveys of users. The literature review was conducted using Medline, Healthstar, Aidsline, Cancerlit, and OldMedline (Ref. E12). We found evidence of many adverse events associated with dietary supplements. For example, one recent survey found that 12 percent of consumers (about 11.9 million) who have used an herbal remedy claim to have suffered from side effects or other adverse reactions (Ref. E13). The American Association of Poison Control Centers received 6,914 reports on dietary supplements in 1998 (Ref. E14). In a recent survey, 46 percent of respondents answered that people get sick from dietary supplements "often" or "sometimes" (Ref. E3). In addition, the agency has received many voluntary reports of illnesses caused by dietary supplements (Ref. E15). The vast majority of the illnesses described in the sources we consulted, however, are reported as associated with the ingredients used in the products themselves, not with poor manufacturing processes. We have no direct evidence on what fraction of illnesses can be attributed to manufacturing processes. The anecdotal evidence implies that many illnesses could have been caused by poor manufacturing processes, but with a few exceptions, no evidence explicitly links illnesses to these manufacturing processes.

The agency's recall records are more useful than the reports on illnesses, because the class 1 and class 2 recalls all involve defective products that could have caused illness if ingested. The major public health events that have been linked to poor manufacturing processes show up in the list of dietary supplements recalled. Although the recall data cannot be linked directly to illness data, we have found anecdotes, surveys, and some medical literature on illnesses that could be caused by

avoidable manufacturing mistakes. We have recall data that show that manufacturing mistakes exist, so we can construct a possible link between manufacturing mistakes and potential illnesses or injuries. The number of illnesses associated with a recall is both variable and uncertain, and could be anything from zero to quite large. We concluded that one illness would not be an implausibly high average for a recall, so we assumed that a recalled product could be a proxy for a single reported illness associated with a defective product. We ask for comments on this assumption.

Because there are no well established systems for the notification of adverse health events related to dietary supplements, and some significant barriers to reporting, we assume that unreported illnesses caused by poor manufacturing practices are substantially greater than reported illnesses. We relied on Ref. E16 to estimate a more precise relationship between reported and unreported rates. Based on empirical data for drug and vaccine reporting rates among other studies, the author of Ref. E16 determined that for dietary supplements, reported illnesses represent at best approximately 1 percent of total illnesses (Ref. E16). A similar multiplier of 100 linking known cases of foodborne illness to total incidence is often used. We assume that reporting adverse health events due to poorly manufactured dietary supplements would occur at the same proportion as adverse health events caused for other reasons by dietary supplements. We show the sensitivity of benefits to the choice of multiplier below, in the uncertainty and sensitivity analysis of our results.

The outbreak of eosinophilia-myalgia syndrome (EMS) resulting from contaminated L-Tryptophan resulted in the recall of the contaminated products. In part based on this example, we assume that product recalls can indicate when there are adverse health events. We also assume that the reported class 1 and class 2 recalls that have occurred over the last 10 years represent the number and type of recalls that will occur in the future but for the implementation of this regulation. From 1990 through 1999, the agency received reports on an annual average of 13 class 1 and class 2 recalls of dietary supplements. If each recall is a proxy for a reported illness, then the total number of unreported illnesses per year is approximately 1,300. Obviously, to the extent that products are successfully recalled, illnesses will be avoided. Our assumption is that the recall occurs