

habitats. (Earth BioSciences petition from the requirement of a tolerance for *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24, dated May 3, 2002.) In addition, the potential for transfer of *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 to surface or ground water during run-off associated with intended use applications is considered minimal to non-existent, due in part to its percolation through and resulting capture in soil. Most importantly, though, the risk from consumption of drinking water containing *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 is considered minimal as there is no evidence of adverse effects from oral, dermal, or inhalation exposure to this microbial agent. (See Unit III.) Accordingly, it is not considered to be a risk to drinking water.

#### B. Other Non-Occupational Exposure

Based on the proposed use patterns, the potential of non-dietary exposures to *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 pesticide residues for the general population, including infants and children, is unlikely. Accordingly, the Agency believes that the potential aggregate non-occupational exposure, derived from dermal and inhalation exposure through the application of *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24, should fall well below the currently tested microbial safety levels. (MRID Numbers 447581-10, 447581-11, 447581-12, and 456725-02).

1. *Dermal exposure.* Dermal exposure via the skin is a potential route of exposure resulting from applications of *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24. Unbroken skin is a natural barrier to microbial invasion of the human body. Dermal absorption could occur only if the skin were cut, if the microbe were a pathogen equipped with mechanisms for entry through or infection of the skin, or if metabolites were produced that could be dermally absorbed. Acute dermal toxicity/pathogenicity data resulted in irritation that persisted 72 hours, and slight irritation persisted for 10 days, and all resolved by day 11. No deaths were observed. The acute lethal dose (LD<sub>50</sub>) is greater than 2,000 mg/kg. (BPPD Review - December 20, 1999). Accordingly, the risks anticipated for this route of exposure are considered minimal.

2. *Inhalation exposure.* Inhalation would be an additional potential route of exposure resulting from applications of *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24. However, because the pulmonary study showed no adverse effects (MRID Numbers 447581-12 and 456725-02)

the risks anticipated for this route of exposure are considered minimal.

#### V. Cumulative Effects

The Agency has considered available information on the cumulative effects of such residues and other substances that have a common mechanism of toxicity. These considerations included the cumulative effects on infants and children of such residues and other substances with a common mechanism of toxicity. Because there is no indication of mammalian toxicity to *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24, the Agency is confident that there will not be cumulative effects from the residues of this product on all agricultural commodities. (See Unit III.)

#### VI. Determination of Safety for U.S. Population, Infants and Children

1. *U.S. population.* *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 is a naturally occurring microorganism and *Bacillus subtilis* var. *amyloliquefaciens* is widespread in the environment. Based on the very low levels of mammalian toxicity associated with *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24, which is demonstrated by the data summarized above, and the history of safe use of *B. subtilis*, the Agency has concluded that there is a reasonable certainty that no harm will result from aggregate exposure to residues of *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 to the U.S. population. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. Accordingly, exempting *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 from the requirement of a tolerance should be considered safe and pose no significant risk.

2. *Infants and children.* FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base on toxicity and exposure unless EPA determines that a different margin of exposure (safety) will be safe for infants and children. Margins of exposure (safety) are incorporated into EPA risk assessments either directly through the use of a margin of exposure analysis or by using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. Here, EPA concludes that the toxicity and exposure data are sufficiently complete to adequately address the potential for additional sensitivity of infants and children to residues of

*Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 and that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 residues. Also, for food use of microbial pesticides, the acute toxicity/pathogenicity studies have allowed for the conclusion that an exemption from the requirement of a tolerance for *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 is appropriate and adequate to protect human health, including that of infants and children.

#### VII. Other Considerations

##### A. Endocrine Disruptors

EPA is required under section 408(p) of the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there is no scientific basis for including, as part of the screening program, the androgen and thyroid hormone systems in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP). When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

Based on available data, no endocrine system-related effects have been identified with consumption of *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24. It is a naturally occurring bacteria that is widespread in the environment. To date, there is no evidence to suggest that *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24