

19. Section 601.12 is amended by revising paragraphs (a), (b)(2)(i), (d)(2)(i) through (d)(2)(v), and (d)(2)(vii); by adding paragraph (b)(4), (c)(6), (d)(3)(iii), and (f)(2)(i)(E); and by removing and reserving paragraph (c)(2)(i) to read as follows:

**§ 601.12 Changes to an approved application.**

(a) *General.* (1) As provided by this section, an applicant shall inform the Food and Drug Administration (FDA) about each change in the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling established in the approved license application(s).

(2) Before distributing a product made using a change, an applicant shall validate the effects of the change and demonstrate through appropriate validation and/or other clinical and/or nonclinical laboratory studies the lack of adverse effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(3) Notwithstanding the requirements of paragraphs (b), (c), and (f) of this section, an applicant shall make a change provided for in those paragraphs in accordance with a regulation or guidance that provides for a less burdensome notification of the change (for example, by submission of a supplement that does not require approval prior to distribution of the product or in an annual report).

(4) The applicant shall promptly revise all promotional labeling and advertising to make it consistent with any labeling change implemented in accordance with this section.

(5) A supplement or annual report shall include in the cover letter a list of all changes contained in the supplement or annual report.

(b) \* \* \*

(2) \* \* \*

(i) Except as provided in paragraphs (c) and (d) of this section, changes in the qualitative or quantitative formulation, including inactive ingredients, or in the specifications provided in the approved application;

\* \* \* \* \*

(4) An applicant may ask FDA to expedite its review of a supplement for public health reasons or if a delay in making the change described in it would impose an extraordinary hardship on the applicant. Such a supplement and its mailing cover should be plainly marked: "Prior Approval Supplement-Expedited Review Requested."

(c) \* \* \*

(2) \* \* \*

(i) [Reserved]

\* \* \* \* \*

(6) If the agency disapproves the supplemental application, it may order the manufacturer to cease distribution of the products made with the manufacturing change.

(d) \* \* \*

(2) \* \* \*

(i) Any change made to comply with an official compendium that is consistent with FDA requirements and provides increased assurance that the drug will have the characteristics of identity, strength, quality, purity, or potency that it purports or is represented to possess;

(ii) The deletion or reduction of an ingredient intended only to affect the color of the product, except that a change intended only to affect Blood Grouping Reagents requires supplement submission and approval prior to distribution of the product made using the change in accordance with the requirements set forth in paragraph (b) of this section;

(iii) An extension of an expiration dating period based upon full shelf life data on full production batches obtained from a protocol approved in the application;

(iv) A change within the container closure system for a nonsterile drug product, based upon a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium;

(v) A change in the size and/or shape of a container containing the same number of dosage units for a nonsterile solid dosage form, without a change from one container closure system to another;

\* \* \* \* \*

(vii) The addition, deletion, or revision of an alternate analytical procedure that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application.

(3) \* \* \*

(iii) A statement by the holder of the approved application or license that the effects of the change have been validated.

\* \* \* \* \*

(f) \* \* \*

(2) \* \* \*

(i) \* \* \*

(E) Any other changes specifically requested by FDA.

\* \* \* \* \*

Dated: June 18, 1999.

**William K. Hubbard,**

*Acting Deputy Commissioner for Policy.*

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**DEPARTMENT OF LABOR**

**Occupational Safety and Health Administration**

**29 CFR Part 1910**

[Docket No. H-371]

RIN 1218-AB46

**Occupational Exposure to Tuberculosis**

**AGENCY:** Occupational Safety and Health Administration (OSHA), Department of Labor.

**ACTION:** Notice of limited reopening of rulemaking record on preliminary risk assessment.

**SUMMARY:** On October 17, 1997, OSHA published its proposed standard to regulate occupational exposure to tuberculosis (TB) (62 FR 54160). Public hearings on the proposal were held in Washington, DC, Los Angeles, CA, New York City, NY, and Chicago, IL between April 7 and June 4, 1998. The post-hearing comment period closed on October 5, 1998. OSHA re-opened the rulemaking record on June 17, 1999 (64 FR 32447) to submit to the record the Agency's report on practices to protect workers from TB in homeless shelter settings and several other studies that had become available after the close of the rulemaking record and to request comments on these studies. In addition to the information requested in the record re-opening published on June 17, 1999, OSHA now requests additional comment and information on issues related to the Agency's preliminary risk assessment for occupational exposure to tuberculosis.

**DATES:** Comments and data from interested parties should be postmarked no later than August 2, 1999.

**ADDRESSES:** Send two copies of your comments to: Docket Office, Docket H-371, Room N2625, Occupational Safety and Health Administration, U.S. Department of Labor, 200 Constitution Avenue, NW, Washington, DC 20210. Comments limited to 10 pages or fewer may also be transmitted by FAX to: 202-693-1648, provided that the original and one copy of the comment are sent to the Docket Office immediately thereafter.

Comments may also be submitted electronically through OSHA's Internet

site at URL, <http://www.osha-slc.gov/e-comments/e-comments-tb2.html>.

Information such as studies and journal articles cannot be attached to electronic submissions and must be submitted in duplicate to the above address. Such attachments must clearly identify the respondent's electronic submission by name, date, and subject, so that they can be attached to the correct submission.

The entire record for the TB rulemaking is available for inspection and copying in the Docket Office, Docket H-371, telephone 202-693-2350.

#### FOR FURTHER INFORMATION CONTACT:

Bonnie Friedman, Office of Information and Consumer Affairs, Occupational Safety and Health Administration, Room N-3647, U.S. Department of Labor, 200 Constitution Avenue, NW, Washington, DC 20210, Telephone (202) 693-1999, FAX (202) 693-1634.

#### SUPPLEMENTARY INFORMATION:

##### Background

On October 17, 1997, OSHA published its proposed standard for occupational exposure to TB (62 FR 54160). Based on a review of the data, OSHA made a preliminary determination that workers in hospitals, nursing homes, hospices, correctional facilities, homeless shelters, and certain other work settings are at significant risk of incurring TB infection while performing certain procedures or caring for their patients and clients. OSHA proposed a standard that would require employers to protect TB-exposed workers by means of infection prevention and control measures that have been demonstrated to be highly effective in reducing or eliminating job-related TB infections.

During the comment period and the public hearing, several commenters suggested that OSHA's estimates of the risk of TB infection, activation to TB disease, and subsequent deaths for health care workers were too high. Although OSHA's risk assessment methodology received little challenge, some commenters objected to OSHA's use of studies showing increased risk to workers in both hospitals and long-term care facilities for the elderly.

##### Request for Comments

In order to obtain the best, most recent data for the purpose of providing the most accurate risk estimates, OSHA requests public comment on any new data or studies that will assist the Agency in determining occupational risk and the reasons why a particular study or set of data should be used. OSHA especially wishes to obtain

studies that could provide estimates of TB infection rates for workers in hospitals, long-term care facilities, in-home health care operations, homeless shelters, and correctional facilities.

This document was prepared under the direction of Charles N. Jeffress, Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, 200 Constitution Avenue, NW, Washington, DC 20210.

It is issued under section 6(b) of the Occupational Safety and Health Act of 1970 (29 U.S.C. 655), Secretary of Labor's Order No. 1-90 (55 FR 9033) and 29 CFR part 1911.

Signed at Washington, DC, this 22nd day of June, 1999.

**Charles N. Jeffress,**

*Assistant Secretary of Labor.*

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## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 52

[CA 210-147b; FRL-6363-1]

#### Approval and Promulgation of State Implementation Plans; California State Implementation Plan Revision, Bay Area Air Quality Management District, Monterey Bay Unified Air Pollution Control District, Placer County Air Pollution Control District, and Ventura County Air Pollution Control District

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Proposed rule.

**SUMMARY:** EPA is approving revisions to the California State Implementation Plan (SIP). This action revises the definitions in Bay Area Air Quality Management District (BAAQMD); Monterey Bay Unified Air Pollution Control (MBUAPCD); Placer County Air Pollution Control District (PCAPCD); and Ventura County Air Pollution Control District (VCAPCD).

The intended effect of approving this action is to incorporate changes to the definitions for clarity and consistency and to update the Exempt Compound list in MBUAPCD, PCAPCD, and VCAPCD rules to be consistent with the revised federal and state VOC definitions. EPA is proposing approval of these revisions to be incorporated into the California SIP for the attainment of the national ambient air quality standards (NAAQS) for ozone under title I of the Clean Air Act (CAA or the Act). In the Final Rules section of this **Federal Register**, the EPA is

approving the state's SIP submittal as a direct final rule without prior proposal because the Agency views this as a noncontroversial revision and anticipates no adverse comments. A detailed rationale for this approval is set forth in the direct final rule. If no adverse comments are received, no further activity is contemplated. If EPA receives adverse comments, the direct final rule will be withdrawn and all public comments received will be addressed in a subsequent final rule based on this proposed rule. The EPA will not institute a second comment period. Any parties interested in commenting should do so at this time.

**DATES:** Written comments must be received by July 28, 1999.

**ADDRESSES:** Comments should be addressed to: Andrew Steckel, Chief, Rulemaking Office (AIR-4), Air Division, U.S. Environmental Protection Agency, Region IX, 75 Hawthorne Street, San Francisco, CA 94105-3901.

Copies of the rule revisions and EPA's evaluation report of each rule are available for public inspection at EPA's Region 9 office during normal business hours. Copies of the submitted rule revisions are also available for inspection at the following locations:

Rulemaking Office (AIR-4), Air Division, U.S. Environmental Protection Agency, Region IX, 75 Hawthorne Street, San Francisco, CA 94105

Environmental Protection Agency, Air Docket (6102), 401 "M" Street, S.W., Washington, D.C. 20460

California Air Resources Board, Stationary Source Division, Rule Evaluation Section, 2020 "L" Street, Sacramento, CA 95812

Bay Area Air Quality Management District, 939 Ellis Street, San Francisco, CA 94109-7714

Monterey Bay Unified Air Pollution Control District, 24580 Silver Cloud Ct., Monterey, CA 93940-6536

Placer County Air Pollution Control District, DeWitt Center, 11464 "B" Ave., Auburn, CA 95603-2603

Ventura County Air Pollution Control District, 669 County Square Dr., 2nd Fl., Ventura, CA 93003-5417

**FOR FURTHER INFORMATION CONTACT:** Cynthia G. Allen, Rulemaking Office [A-4], Air Division, Air Division, U.S. Environmental Protection Agency, Region 9, 75 Hawthorne Street, San Francisco, CA 94105-3901, Telephone: (415) 744-1189.

**SUPPLEMENTARY INFORMATION:** This document concerns Bay Area Air Quality Management District (BAAQMD) Regulation 1, General Provisions and Definitions; Monterey