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**FIN: 0910-AF06**

**HHS—FDA****46. • USE OF OZONE-DEPLETING  
SUBSTANCES: REMOVAL OF  
ESSENTIAL USE DESIGNATION;  
ALBUTEROL****Priority:**

Economically Significant. Major status  
under 5 USC 801 is undetermined.

**Unfunded Mandates:**

Undetermined

**Legal Authority:**

15 USC 402; 15 USC 409; 21 USC 321;  
21 USC 331; 21 USC 335; 21 USC 342;  
21 USC 343; 21 USC 346a; 21 USC 348;  
21 USC 351; 21 USC 352; 21 USC 355;  
21 USC 360b; 21 USC 361; 21 USC 362;  
21 USC 371; 21 USC 372; 21 USC 374;  
42 USC 7671 et seq

**CFR Citation:**

21 CFR 2.125

**Legal Deadline:**

None

**Abstract:**

Under the Clean Air Act, the Food and  
Drug Administration (FDA) within the  
U.S. Department of Health and Human  
Services, in consultation with the  
Environmental Protection Agency, is  
required to determine whether an FDA-

regulated product that releases an  
ozone-depleting substance (ODS) is  
essential. The two agencies have  
tentatively determined that the two  
currently marketed non-ODS metered-  
dose inhalers (MDIs) will be  
satisfactory alternatives to albuterol  
MDIs that contain ODS, and are  
proposing to remove the essential use  
designations for albuterol MDIs. If the  
essential use designation is removed,  
albuterol MDIs that contain an ODS  
could not be marketed after a suitable  
transition period. The proposed rule  
will specifically ask for comments on  
which phase-out period length will best  
ensure a smooth transition and  
minimize any adverse effects on the  
public health.

**Statement of Need:**

Chlorofluorocarbons (CFCs) are organic  
compounds that contain carbon,  
chlorine, and fluorine atoms. CFCs  
were first used commercially in the  
early 1930's and were later found to  
be useful as propellants in self-  
pressurized aerosol products, such as  
MDIs. CFCs are very stable in the  
troposphere—the lowest part of the  
atmosphere. They move to the  
stratosphere, a region that begins about  
10–16 kilometers (km) (6–10 miles)  
above Earth's surface and extends up  
to about 50 km (31 miles) altitude.  
Within the stratosphere there is a zone  
about 15 to 40 km (10–25 miles) above  
the Earth's surfaces in which ozone is  
relatively highly concentrated. The  
zone in the stratosphere is generally  
called the ozone layer. Once in the  
stratosphere, CFCs are broken down by  
strong ultraviolet light, where they  
release chlorine atoms that then deplete  
stratospheric ozone. Depletion of  
stratospheric ozone by CFCs and other  
ODS will lead to higher UVB levels,  
which in turn will cause increased skin  
cancers and cataracts and potential  
damage to some marine organisms,  
plants, and plastics.

The link between CFCs and the  
depletion of stratospheric ozone was  
discovered in the mid-1970's. Since  
1978, the U.S. government has pursued  
a consistent policy of limiting the  
production and use of ODS, including  
CFCs.

**Summary of Legal Basis:**

The Clean Air Act and EPA's  
implementing regulations contain  
general prohibitions on the use and  
manufacture of ODS, such as CFCs.  
Exceptions to these bans are provided  
for specific medical products that FDA,  
in consultation with EPA, has found to  
be essential. FDA's essential use

determinations have been contained in  
21 C.F.R. section 2.125.

FDA published a new 21 C.F.R. section  
2.125 in the Federal Register on July  
24, 2002 (67 FR 48370), (corrected in  
the Federal Registers of July 30, 2002  
(67 FR 49396) and September 17, 2002  
(67 FR 58678)). Section 2.125 provides  
criteria for determining when a use is  
essential and when a use is no longer  
essential. The procedures to determine  
when a use is no longer essential were  
implemented to better carry out  
responsibilities under both the Clean  
Air Act and the Montreal Protocol on  
Substances that Deplete the Ozone  
Layer, (September 16, 1987, S. Treaty  
Doc. No. 10, 100th Cong., 1st sess., 26  
I. L. M. 1541 (1987)).

Fran Du Melle, Executive Vice  
President of the American Lung  
Association, submitted a citizen  
petition on behalf of the U.S.  
Stakeholders Group on MDI Transition  
on January 29, 2003 (Docket No. 03P-  
0029/CP1). The petition requested that  
FDA initiate rulemaking to remove the  
essential use of albuterol MDIs. After  
evaluating the petition, comments  
submitted in response to the petition,  
and other information, FDA has  
tentatively determined that albuterol  
MDIs meet the criteria in section 2.125  
for removal of an essential use.

**Alternatives:**

In the proposed rule, FDA will  
specifically request comments on the  
best effective date for any final rule to  
remove the essential use status of  
albuterol. FDA will consider which  
dates will allow manufacturers to  
obtain the capacity to produce adequate  
numbers of non-ODS albuterol MDIs.  
FDA will also consider which dates  
might minimize any financial burden  
on patients who would have to switch  
to non-ODS albuterol MDIs.

**Anticipated Cost and Benefits:**

The expected benefit from this  
rulemaking, as part of an overall policy  
to eliminate production and use of  
ODSs, is the preservation of the Earth's  
stratospheric ozone.

Currently there are generic versions of  
ODS albuterol MDIs, while there are no  
generic non-ODS albuterol MDIs. This  
rulemaking could force patients to  
switch from lower-priced generic  
versions of ODS albuterol MDIs to  
higher-priced non-ODS albuterol MDIs.

**Risks:**

FDA is concerned about the possibility that some patients might stop using needed drugs because the prices of non-ODS albuterol MDIs might be higher than those of ODS albuterol MDIs.

**Timetable:**

Action	Date	FR Cite
NPRM	03/00/04	
NPRM Comment Period End	06/00/04	
Final Action	03/00/05	

**Regulatory Flexibility Analysis Required:**

Undetermined

**Small Entities Affected:**

No

**Government Levels Affected:**

Undetermined

**Federalism:**

Undetermined

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HHS—FDA

FINAL RULE STAGE

**47. LABELING FOR HUMAN PRESCRIPTION DRUGS; REVISED FORMAT****Priority:**

Other Significant. Major status under 5 USC 801 is undetermined.

**Legal Authority:**

21 USC 321; 21 USC 331; 21 USC 351 to 353; 21 USC 355; 21 USC 358; 21 USC 360; 21 USC 360b; 21 USC 360gg to 360ss; 21 USC 371; 21 USC 374; 21 USC 379e; 42 USC 216; 42 USC 241; 42 USC 262; 42 USC 264

**CFR Citation:**

21 CFR 201

**Legal Deadline:**

None

**Abstract:**

This regulation is one component of the Secretary's initiative to reduce medical errors. The regulation would amend the regulations governing the format and content of professional labeling for human prescription drug and biologic products, 21 C.F.R. 201.56 and 201.57. The regulation would require that professional labeling include a section containing highlights of prescribing information, and a section containing an index to prescribing information; reorder currently required information and make minor changes to its content, and establish minimum graphical requirements for professional labeling.

**Statement of Need:**

The current format and content requirements in sections 201.56 and 201.57 were established to help ensure that labeling includes adequate information to enable health care practitioners to prescribe drugs safely and effectively. However, various developments in recent years, such as technological advances in drug product development, have contributed to an increase in the amount, detail, and complexity of labeling information. This has made it harder for practitioners to find specific information and to discern the most critical information in product labeling. FDA took numerous steps to evaluate the usefulness of prescription drug labeling for its principal audience and to determine whether, and how, its format and content can be improved. The agency conducted focus groups and a national survey of office-based physicians to ascertain how prescription drug labeling is used by health care practitioners, what labeling information is most important to practitioners, and how professional labeling should be revised to improve its usefulness to prescribing practitioners.

Based on the concerns cited by practitioners in the focus groups and physician survey, FDA developed and tested two prototypes of revised labeling formats designed to facilitate access to important labeling information. Based on this testing, FDA developed a third revised prototype that it made available to the public for comment. Ten written comments were received on the prototype. FDA also presented the revised prototype at an informal public meeting held on October 30, 1995. At the public

meeting, the agency also presented the background research and provided a forum for oral feedback from invited panelists and members of the audience. The panelists generally supported the prototype.

The proposed rule described format and content requirements for prescription drug labeling that incorporate information and ideas gathered during this process. The agency has received several comments on the proposal and the comment period was extended until June 22, 2001.

**Summary of Legal Basis:**

The agency has broad authority under sections 201, 301, 501, 502, 503, 505, and 701 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 321, 331, 351, 352, 353, 355, and 371) and section 351 of the Public Health Service Act (42 U.S.C. 262) to regulate the content and format of prescription drug labeling to help ensure that products are safe and effective for their intended uses. A major part of FDA's efforts regarding the safe and effective use of drug products involves FDA's review, approval, and monitoring of drug labeling. Under section 502(f)(1) of the Act, a drug is misbranded unless its labeling bears "adequate directions for use" or it is exempted from this requirement by regulation. Under section 201.100 (21 C.F.R. 201.100), a prescription drug is exempted from the requirement in section 502(f)(1) only if, among other things, it contains the information required, in the format specified, by sections 201.56 and 201.57.

Under section 502(a) of the Act, a drug product is misbranded if its labeling is false or misleading in any particular. Under section 505(d) and 505(e) of the Act, FDA must refuse to approve an application and may withdraw the approval of an application if the labeling for the drug is false or misleading in any particular. Section 201(n) of the Act provides that in determining whether the labeling of a drug is misleading, there shall be taken into account not only representations or suggestions made in the labeling, but also the extent to which the labeling fails to reveal facts that are material in light of such representations or material with respect to the consequences which may result from use of the drug product under the conditions of use prescribed