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December 10, 2008

The Honorable Edward M. Kennedy
Chairman
The Honorable Michael B. Enzi
Ranking Minority Member
Committee on Health, Education, Labor and Pensions
United States Senate

The Honorable John D. Dingell
Chairman
The Honorable Joe Barton
Ranking Minority Member
Committee on Energy and Commerce
House of Representatives

Subject: *Department of Health and Human Services, Food and Drug Administration: Use of Ozone-Depleting Substances; Removal of Essential-Use Designation (Epinephrine)*

Pursuant to section 801(a)(2)(A) of title 5, United States Code, this is our report on a major rule promulgated by the Department of Health and Human Services, Food and Drug Administration (FDA), entitled "Use of Ozone-Depleting Substances; Removal of Essential-Use Designation (Epinephrine)" (RIN: 0910-AF92). We received the rule on November 26, 2008. It was published in the *Federal Register* as a final rule on November 19, 2008. 73 Fed. Reg. 69,532.

The final rule removes epinephrine used in oral pressurized metered-dose inhalers from FDA's list of essential-use ozone-depleting substances that have been exempt from Clean Air Act restrictions on their use.

Enclosed is our assessment of the FDA's compliance with the procedural steps required by section 801(a)(1)(B)(i) through (iv) of title 5 with respect to the rule. Our review indicates that FDA complied with the applicable requirements.

If you have any questions about this report or wish to contact GAO officials responsible for the evaluation work relating to the subject matter of the rule, please contact Michael R. Volpe, Assistant General Counsel, at (202) 512-8236.

signed

Robert J. Cramer
Associate General Counsel

Enclosure

cc: Edwin V. Dutra, Jr.
Director, Regulations Policy and Management Staff
Food and Drug Administration
Department of Health and Human Services

ENCLOSURE

REPORT UNDER 5 U.S.C. § 801(a)(2)(A) ON A MAJOR RULE
ISSUED BY THE
DEPARTMENT OF HEALTH AND HUMAN SERVICES,
FOOD AND DRUG ADMINISTRATION
ENTITLED
"USE OF OZONE-DEPLETING SUBSTANCES; REMOVAL OF
ESSENTIAL-USE DESIGNATION (EPINEPHRINE)"
(RIN: 0910-AF92)

(i) Cost-benefit analysis

The benefits of the final rule include environmental and public health improvements from protecting stratospheric ozone by reducing chlorofluorocarbons (CFC) emissions by roughly 70 tonnes annually, increased returns on investments in environmentally friendly technology, reduced risk of unexpected disruption of supply of over-the-counter (OTC) epinephrine metered-dose inhalers (MDIs), and continued international cooperation to comply with the spirit of the Montreal Protocol.

The costs of the final rule include the costs of increased physician visits, increased use of more expensive reliever MDIs, and potential increases in the use of controller medications, visits to emergency departments, and hospitalizations. Because FDA cannot predict whether over-the-counter epinephrine MDI users will respond to its removal from the market by self-medicating or going to a physician for a prescription, it quantified the costs for two extreme cases. Based on these extreme cases, FDA can estimate that the annualized costs will range from $180 million to $1.1 billion. FDA also notes that depending on consumer willingness to self-medicate, the final rule could result in a potential increase of up to 440,000 annual emergency department visits for asthma, and an increase in hospitalizations for asthma of between 40,000 and 120,000.

FDA states that limits in the available data prevent the agency from quantifying the costs and benefits of the final rule and weighing them in comparable terms. However, if CFCs cease to be available for OTC epinephrine MDIs before December 31, 2011, the effective date of the final rule, then this final rule will have no benefits or costs.

(ii) Agency actions relevant to the Regulatory Flexibility Act, 5 U.S.C. §§ 603-605, 607, and 609

FDA certified that the final rule will not have a significant economic impact on a substantial number of small entities.

(iii) Agency actions relevant to sections 202-205 of the Unfunded Mandates Reform Act of 1995, 2 U.S.C. §§ 1532-1535

FDA determined that this final rule may result in a 1-year expenditure of greater than $130 million by state, local, and tribal governments, in the aggregate, or by the private sector. The FDA incorporated the final rule's cost benefit analysis to meet the Act's requirements, as allowed under 2 U.S.C. § 1532(c).

(iv) Other relevant information or requirements under acts and executive orders

Administrative Procedure Act, 5 U.S.C. §§ 551 et seq.

FDA published a notice of proposed rulemaking in the *Federal Register* on September 20, 2007. 72 Fed. Reg. 53,711. FDA held a required open public meeting to discuss the issues involved at which presentations were made by a pharmaceuticals company and a patient advocacy organization. FDA received 32 comments in response to the proposed rule from consumers, health care providers, a patient advocacy group, professional groups, manufacturers, an international governmental organization, and industry organizations. FDA responded to the comments in the final rule. 73 Fed. Reg. 69,532.

Paperwork Reduction Act, 44 U.S.C. §§ 3501-3520

The final rule does not contain any information collection requirements.

Statutory authorization for the rule

The final rule is authorized by the Clean Air Act, the Montreal Protocol, and FDA's implementing regulations at 21 C.F.R. §2.125(g)(2).

Executive Order No. 12,866

The final rule is an economically significant regulatory action under the Order and has been reviewed by the Office of Management and Budget. FDA prepared a Regulatory Assessment in conjunction with the Order.

Executive Order No. 13,132 (Federalism)

FDA determined that the final rule does not contain federalism implications under the Order.