DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 350

[Docket No. 78N-0064]

RIN 0905-AA06

Antiperspirant Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration, HHS.

ACTION: Request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on two citizen petitions and a response that disagreed with one of the petitions. The citizen petitions request that the rulemaking for antiperspirant drug products for over-the-counter (OTC) human use be reopened to include new information, all aluminum compounds proposed for use in OTC antiperspirant drug products be reclassified as Category III (more data needed) until further studies are done to determine the amount absorbed following topical application and inhalational exposure, and the safety of these aluminum compounds be reevaluated, particularly their potential for skin absorption or toxic effects with long-term use.

DATES: Written comments by July 21, 1993.

ADDRESSES: Submit written requests for single copies of the citizen petitions and the response to one of the citizen petitions to the Freedom of Information Staff (HFI-35), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. These three documents are available at a cost of $94.30 and contain 943 pages. Alternatively, a copy of the citizen petitions containing a bibliography without copies of the cited references, plus a copy of the response to one citizen petition, are available at a cost of $9.70 and contain 97 pages. Submit written comments or new data on OTC aluminum-containing antiperspirant drug products to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857. Requests and comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 10, 1978 (43 FR 46694), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC antiperspirant drug products, together with the recommendations of the Advisory Review Panel on OTC Antiperspirant Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. The agency's proposed regulation, in the form of a tentative final monograph, for OTC antiperspirant drug products was published in the **Federal Register** of August 20, 1982 (47 FR 36492). A final regulation has not been published to date.

The Panel classified the ingredients it reviewed into three categories: (1) "Category I" (generally recognized as safe and effective and not misbranded), (2) "Category II" (not generally recognized as safe and effective or misbranded), and (3) "Category III" (available data are insufficient to classify as safe and effective, and further testing is required). The OTC drug procedural regulations (21 CFR 330.10) provide that any testing necessary to resolve the safety or effectiveness issues resulting from a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph.

The Panel considered aluminum-containing antiperspirant ingredients applied directly to the skin in nonaerosol dosage forms (e.g., lotion, cream, stick, or roll-on) to be safe (43 FR 46694 at 46707 and 46708). However, the Panel had safety concerns about long-term use of aerosol dosage forms and recommended Category III status until further safety studies were conducted (43 FR 46708 to 46711). The agency adopted the Panel's Category I recommendations for nonaerosol dosage forms (47 FR 36492 at 36502) and, based on new data, proposed Category I status for aerosol dosage forms of the various aluminum chlorohydrate antiperspirant ingredients (47 FR 36498).

FDA has been petitioned (Ref. 1) under the provisions of § 10.30 (21 CFR 10.30) to reclassify all aluminum compounds proposed for use in OTC antiperspirant drug products from Category I to Category III until further absorption studies are done to determine the amount of aluminum absorbed following topical application and inhalation exposure. (The petition also requested FDA to amend its regulations to revoke the use of aluminum compounds as food substances; however, this notice addresses only the uses of aluminum compounds in OTC antiperspirant drug products.) Subsequently, the agency received a comment (Ref. 2) that objected to the conclusions of the petition. The comment argued that current scientific information does not support the need to reclassify the safety of aluminum-containing materials, such as foods and antiperspirants. Subsequently, FDA received a second petition (Ref. 3) under the provisions of § 10.30 to reopen the rulemaking to include new information, revoke the Category I classification of aerosol dosage forms, reclassify nonaerosol aluminum-containing dosage forms as Category III, and require reevaluation of their potential for skin absorption or toxic effects with long-term use. Both petitions and the response to the first petition are on public display in the Dockets Management Branch.

I. Current Regulatory Status of Aluminum-Containing OTC Antiperspirant Drug Products

Both the Panel, in its advance notice of proposed rulemaking (43 FR 46694 at 46718), and the agency, in its tentative final monograph (47 FR 36492 at 36502), proposed Category I status for aluminum-containing and aluminum-zirconium-containing antiperspirant active ingredients in topical nonaerosol dosage formulations. The Panel discussed the safety of antiperspirants and stated (43 FR 46707):

> * * * Because of the relatively impermeable properties of the skin to metallic salts and complexes, there is no evidence to suggest that the direct application of antiperspirant products to intact skin has been associated with systemic toxic effects.
>
> Percutaneous dermal toxicity tests have been performed on animals for a great number of antiperspirants. The reported results indicated no ill effects on the animals.

The Panel questioned the safety of the long-term use of these ingredients when applied in an aerosol form (43 FR 46707) and classified all aluminum-containing aerosol antiperspirant products in Category III (43 FR 46725). The Panel stated that the decision to require added testing for aerosol products reflected the fact that damage to the lung, by occurring more insidiously, carries a greater potential for serious illness than damage to the skin (43 FR 46718).

New data were submitted after publication of the Panel's report and were discussed by the agency in the tentative final monograph (43 FR 36492

at 36498). The agency tentatively concluded that the data appeared to be adequate to establish the safe and effective use of OTC aerosol antiperspirants by consumers (47 FR 36498). The agency also proposed the following additional label warning for aerosol antiperspirants in § 350.50(c): "Avoid excessive inhalation." (See comment 22, 47 FR 36498.) However, this warning is not required to appear in product labeling until the effective date of a final monograph. In the interim, OTC aluminum-containing aerosol and aluminum and zirconium-containing nonaerosol antiperspirant drug products currently included in the pending rulemaking for OTC antiperspirant drug products may remain in the marketplace while the agency considers the comments received in response to this notice and develops a final rule for these OTC drug products.

II. Summary of First Petitioner's Views

The following narrative summarizes the information and arguments presented by the first petitioner. The material included in the narrative does not necessarily represent the views of the agency.

The petitioner contended that the use of aluminum in antiperspirants needs to be further studied, particularly the amount absorbed following both inhalational exposure and topical application to the skin. The petitioner mentioned that many published articles that were not discussed by the Panel or by the agency discuss the systemic toxicity and neurotoxicity of aluminum. The petitioner noted that, since the antiperspirant tentative final monograph was issued in 1982, many new studies of aluminum toxicology have been conducted and a growing number of studies show that aluminum is a powerful neurotoxin (Refs. 4 and 5).The petitioner claimed that when taken orally or when inhaled, aluminum can be absorbed and get into the blood; a fraction of aluminum in the blood enters the brain, where it remains and accumulates (Ref. 5). Once in the brain, the petitioner stated, the aluminum can disrupt many normal cellular activities. The petitioner mentioned that animal experiments show that aluminum causes a variety of neurotoxic effects on the brain (Refs. 6 through 11) and in vitro studies show neurotoxic effects on human neurons (Refs. 12 and 13). The comment also stated that human epidemiology studies associate aluminum with neurotoxicity.

The petitioner noted that Perl and Good (Ref. 14) have proposed that inhaled aluminum compounds may be taken directly into the brain by a nasal-olfactory pathway, and this is supported by studies by Pearson et al., who found that olfactory areas of the brain are invariably severely involved (Ref. 15). The petitioner suggested that this may be a mechanism by which aerosolized aluminum compounds in antiperspirants cause Alzheimer's disease. The petitioner stated that a case control study showed epidemiologic evidence of a relationship between aluminum-containing antiperspirants and Alzheimer's disease (Ref. 16).

The petitioner stated that studies show that aluminum can be absorbed when aluminum compounds are inhaled (Refs. 17 through 21). The petitioner contended that there have been no studies measuring the amount of aluminum absorbed systemically by inhalation of aerosolized antiperspirants, and that there has only been consideration of whether aerosolized antiperspirants would cause accumulation of aluminum compounds in the lung, and whether that would cause lung damage (43 FR 46694 at 46708 to 46711). The petitioner also contended that there have been no studies measuring the amount of aluminum absorbed systemically through the skin when antiperspirants are applied on the skin. The petitioner stated that the Panel only mentioned the "relatively impermeable properties of the skin to metallic salts and complexes" (43 FR 46707), but did not quantify the term "relatively impermeable." The petitioner concluded that the use of aluminum in antiperspirants needs to be further studied because it is not known how much aluminum is absorbed, or whether the amounts absorbed are unsafe. The comment added that measurement of absorption is crucial for risk assessment, and that such measurements should be performed before the use of aluminum in antiperspirants receives final monograph approval.

Accordingly, the petitioner requested that: (1) The rulemaking for OTC antiperspirant drug products be reopened, (2) all aluminum compounds proposed for use in OTC antiperspirant drug products be reclassified as Category III until further studies are done to determine the amount absorbed following topical application and inhalational exposure, and (3) the safety of these aluminum compounds, based on the new absorption data, be reevaluated after these studies are done and the compounds then reclassified as Category I or Category II.

III. Summary of the Comment on the First Petition

The comment stated that it had reviewed the published data, including the references cited by the petitioner, and concluded that the data do not support the petitioner's conclusion that the concentration of aluminum in products such as foods and antiperspirants poses a potentially significant neurotoxic risk. The comment contended that the majority of the references cited by the petitioner describe findings from in vitro studies. According to the comment, the studies did not consider the blood-brain barrier, which is the brain's main defense against potentially toxic substances such as aluminum. The comment added that extraordinarily high concentrations of aluminum were used in these studies, and these levels are never approached under physiological conditions or even in pathological states, such as in dialysis encephalopathy. The comment stated that the doses of aluminum that cross the blood-brain barrier must be considered in the aphysiological range. The comment concluded that aluminum from food additives or antiperspirants would not enter the brain in biologically significant concentrations.

The comment also objected to the petitioner's contention that the inhalation of aluminum antiperspirants poses a special risk because this route of delivery bypasses the blood-brain barrier. The comment calculated that an inhalation study (Ref. 19) cited by the petitioner, in which rabbits were exposed to aluminum oxide inhalation for 8 hours per day, 5 days per week for 5 months, would be equivalent to a person using spray deodorants for approximately 10 seconds daily for 789 years. The comment concluded that generalization from this rabbit inhalation study to humans was strained at best.

The comment also disagreed with the petitioner's statement that "aluminum plays a role in Alzheimer's disease * * *." The comment felt that the majority of researchers investigating the etiology of Alzheimer's disease probably would not agree with the petitioner's position. The comment stated that aluminum encephalopathy dialysis patients do not exhibit neurofibrillary tangles or plaques in their brains as do patients with Alzheimer's disease. The comment also stated that neurofibrillary tangles in experimental animals with aluminum injected into their brains differ from the tangles seen in Alzheimer's disease. The comment concluded that current scientific information does not support the need to reclassify the safety of

aluminum-containing materials such as antiperspirants.

IV. Summary of Second Petitioner's Views

The following narrative summarizes the information and arguments presented by the second petitioner. The material included in the narrative does not necessarily represent the views of the agency.

The petitioner agreed with the position taken by the first petitioner that aluminum compounds that are proposed for use in antiperspirant drug products for OTC use need to be reconsidered for safety in view of recent concerns about aluminum neurotoxicity and systemic toxicity. The petitioner also contended that there is a lack of adequate data on the absorption of aluminum from topical or inhaled antiperspirants.

The petitioner requested that FDA revoke its decision in the tentative final monograph to reclassify aerosol dosage forms of aluminum chlorohydrate antiperspirants from Category III to Category I (47 FR 36492 at 36498) because the long-term lung inhalation studies in rats used to support this decision show that aluminum absorption occurs at the peribronchial lymph nodes, and increased aluminum levels are detected in the rat brain and adrenal glands after 12 and 24 months.

The petitioner requested that FDA reclassify non-aerosol dosage forms of aluminum-containing antiperspirants to Category III in order to permit a re-evaluation of their potential for skin absorption or toxic systemic effects following long-term use. The petitioner pointed out that the Panel concluded that because of the relatively impermeable properties of the skin to metallic salts and complexes, there is no evidence to suggest that direct application of antiperspirant products to intact skin has been associated with systemic toxic effects. The petitioner stated that reports show that metal ions do absorb through the skin, and aluminum ions in antiperspirant formulations theoretically appear especially likely to be absorbed. The petitioner further stated that experimental evidence is accumulating to indicate that chronic exposure to low levels of aluminum may lead to neurological disorders, and that there is a reported association between Alzheimer's disease and the exposure to aluminum through lifetime use of antiperspirants.

The petitioner also requested that FDA revise and expand the proposed warning for aluminum-containing aerosols in § 350.50(c)(2), which states "avoid excessive inhalation," to better clarify the safety concern.

V. The Agency's Consideration of Aluminum-Containing Drugs in Other OTC Drug Rulemakings

Since publication of the tentative final monograph for OTC antiperspirant drug products on August 20, 1982, the agency has evaluated substantial additional data on the safety of aluminum compounds used in other categories of OTC drug products. These safety evaluations have some bearing on the issues raised by the petitioners.

A. Topical OTC Drug Products Containing Aluminum

Several other OTC advisory review panels have concluded that various aluminum salts are safe for topical use in other OTC drug products: e.g., acne (March 23, 1982, 47 FR 12430 at 12450), antifungal (March 23, 1982, 47 FR 12480 at 12525), astringent (September 7, 1982, 47 FR 39412 at 39427), and skin protectant (August 4, 1978, 43 FR 34628 at 34634). These conclusions were generally based on the following considerations: (1) Metals are not generally absorbed through the skin. (2) Aluminum salts precipitate protein and may form a superficial protective layer on mucous membranes or damaged skin (Refs. 22, 23, and 24). The Antimicrobial II Panel stated that with protein precipitates, absorption through the skin is probably minimal (47 FR 12430 at 12450). (3) There is an absence of aluminum toxicity reported in the current literature and in standard references (Refs. 24 through 27). (4) There has been a wide clinical usage of aluminum salts topically. (5) There has also been a wide clinical usage of oral aluminum as an antacid, with a minimal degree of absorption of ingested aluminum (Ref. 28).

B. OTC Antacid Drug Products

The agency has evaluated the involvement of aluminum with dialysis encephalopathy and osteomalacia in the **Federal Register** of January 15, 1985 (50 FR 2160 at 2165) and May 11, 1990. In the May 11, 1990 publication (55 FR 19852 at 19856), the agency stated:

When the agency last evaluated this issue prior to publishing the proposed antacid monograph amendment to add professional labeling warnings for OTC aluminum-containing antacids (50 FR 2160 at 2165), the relationship of aluminum to bone disease was not established. There was even some doubt about the relationship of aluminum to encephalopathy (a toxic degeneration of the brain) at that time. Subsequently it has become clear that both encephalopathy and osteomalacia (softening of the bones) can be caused by long-term use of aluminum in renal dialysis patients * * *. Long-term use of aluminum-containing antacids contributes to dialysis osteomalacia * * *. Although only a small fraction of ingested aluminum is absorbed, that amount must be removed by functioning kidneys, bile secretion, or dialysis, or else it will accumulate. Dialysis does not remove aluminum well because the aluminum is bound to albumin and transferrin, which do not cross dialysis membranes. When aluminum accumulates, it tends to be deposited in bone * * * at the mineralization front, blocking mineralization of newly formed bone, increasing calcium loss from bone into serum, and producing osteomalacia * * *. The agency believes that the role of aluminum is significant and that attempts should be made to reduce its contribution to renal osteodystrophy.

The agency further noted that the dialysis encephalopathy, discussed in this section, that was due to aluminum resulted from two factors: (1) Oral aluminum-containing antacids taken as phosphate binders, and (2) aluminum-containing dialysis fluids.

Subsequently, in the **Federal Register** of May 11, 1990 (55 FR 19852 at 19859), the agency added the following warning to the monograph for OTC antacid drug products under § 331.80(a)(4)(i):

Prolonged use of aluminum-containing antacids in patients with renal failure may result in or worsen dialysis osteomalacia. Elevated tissue aluminum levels contribute to the development of the dialysis encephalopathy and osteomalacia syndromes. Small amounts of aluminum are absorbed from the gastrointestinal tract and renal excretion of aluminum is impaired in renal failure. Aluminum is not well removed by dialysis because it is bound to albumin and transferrin, which do not cross dialysis membranes. As a result, aluminum is deposited in bone, and dialysis osteomalacia may develop when large amounts of aluminum are ingested orally by patients with impaired renal function.

The Panel and the agency did not discuss Alzheimer's disease or other neurological disorders in prior publications in the antiperspirant rulemaking. However, the agency did discuss Alzheimer's disease in the **Federal Register** of January 15, 1985 (50 FR 2160 and 2161), covering OTC hypophosphatemia drug products. The agency reviewed the literature available up to 1981, which included some of the early articles submitted by the first petitioner. The agency also noted that Perl and Brody (Ref. 29) studied the aluminum content within individual neurons of brain tissue from three cases of Alzheimer's disease and three nondemented controls. They found that aluminum is frequently present in the nuclei of neurons with neurofibrillary tangles both in the presence and absence of Alzheimer's disease, although neurons with neurofibrillary tangles were found more often in the

Alzheimer's patients. However, the agency pointed out that other investigators found no significant difference in the aluminum content of Alzheimer's patients and normal controls and found no correlation between neurofibrillary tangle formations and aluminum content (50 FR 2161).

The agency noted that aluminum can produce some of the histopathological and clinical features of Alzheimer's disease in certain animal species when aluminum salts are injected into different areas of the brain. However, the agency questioned the relationship of changes induced in these animals to humans, particularly in view of the unphysiological route of administration of the aluminum in the studies (50 FR 2161). The agency quoted a 1980 editorial on Alzheimer's disease in the *British Medical Journal* that "Despite the plethora of hypotheses, however, objective analysis of all the data--immunological, genetic, virological, pathological, and biochemical--shows that we still have no idea of the aetiology of Alzheimer's disease," (50 FR 2161). The agency concluded at that time that a role for aluminum in the pathogenesis of Alzheimer's disease cannot be ruled out, but the evidence supporting such a role is very weak (50 FR 2162).

VI. Request for Comments

The petitions and the comment discussed above raise issues that need to be considered before FDA makes a final decision on the safety of aluminum-containing and aluminum zirconium-containing antiperspirant drug products. At this time, the agency has not decided whether it should grant the petitioners' requests. In an effort to determine whether further study should be required to assess the safety of aluminum antiperspirants before issuing a final monograph, FDA is seeking public comments. In accordance with § 10.30(h)(3) (21 CFR 10.30(h)(3)), FDA is seeking public comments on the following questions before reaching any decision on the petitions:

(1) As described above, there is already a considerable amount of safety data concerning aluminum toxicity. Are these data sufficient to retain aluminum-containing and aluminum zirconium-containing OTC antiperspirants in Category I?

(2) If more data are needed to support safety, what data are needed and what testing should be required? What kind of absorption studies should be conducted to determine the level, if any, of aluminum that is absorbed through the skin and deposited in organs, such as the lungs and brain, from direct application of antiperspirant drug products? What levels of aluminum absorption would be considered low enough to be safe?

(3) If aluminum-containing and aluminum zirconium-containing antiperspirants were found to be unsafe, there would no longer be any ingredients in the OTC antiperspirant drug products monograph. FDA is seeking public comment on whether any ingredients that do not contain aluminum may be suitable for review as OTC antiperspirant drug products.

The agency is currently developing the final rule for OTC antiperspirant drug products. The agency will consider the comments received in response to this notice and then decide whether to grant the petitioners' requests or proceed to publish the final rule.

The complete petitions are on public display between 9 a.m. and 4 p.m., Monday through Friday, in the Dockets Management Branch. Requests for single copies of the petitions may be submitted to the Freedom of Information Staff (address above).

Interested persons may, on or before July 21, 1993, submit to the Dockets Management Branch (HFA–305) (address above) written comments regarding this petition and the comment on the petition. Three copies of any comments are to be submitted except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. The petitions, the comment, other information discussed above, and any comments received in response to this request for comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. After reviewing the comments and other information received, FDA will respond to the petitions.

VII. References

(1) Citizen Petition CP2, Docket No. 78N–0064, Dockets Management Branch.

(2) Comment C42, Docket No. 78N–0064, Dockets Management Branch.

(3) Citizen Petition CP3, Docket No. 78N–0064, Dockets Management Branch.

(4) Boegman, R. J., and L. A. Bates, "Neurotoxicity of Aluminum," *Canadian Journal of Physiology and Pharmacology*, 62:1010–1014, 1984.

(5) Ganrot, P. O., "Metabolism and Possible Health Effects of Aluminum," *Environmental Health Perspectives*, 65:363–441, 1986.

(6) Crapper, D. R., and A. J. Dalton, "Alterations in Short-term Retention, Conditioned Avoidance Response Acquisition and Motivation Following Aluminum Induced Neurofibrillary Degeneration," *Physiology and Behavior*, 10:925–933, 1973.

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(8) Lipman, J. J. et al., "Studies of Aluminum in Rat Brain," *Biological Trace Element Research*, 13:43–53, 1987.

(9) Petit, T. L., G. B. Biederman, and P. A. McMullen, "Neurofibrillary Degeneration, Dendritic Dying Back, and Learning-memory Deficits After Aluminum Administration: Implications for Brain Aging," *Experimental Neurology*, 67:152–162, 1980.

(10) Petit, T. L. et al., "Neurobehavioral Development Following Aluminum Administration in Infant Rabbits," *Experimental Neurology*, 88:640–651, 1985.

(11) Solomon, P. R. et al., "Disrupted Retention of the Classically Conditioned Nictitating Membrane Response in Rabbits With Aluminum-induced Neurofibrillary Degeneration," *NeuroToxicology*, 9:209–222, 1988.

(12) De Boni, U., M. Seger, and D. R. Crapper-McLachlan, "Functional Consequences of Chromatin Bound Aluminum in Cultured Human Cells," *Neurotoxicology*, 1:65–81, 1980.

(13) Nixon, R. A. et al., "Aluminum Inhibits Calpain-mediated Proteolysis and Induces Human Neurofilament Proteins to Form Protease-Resistant High Molecular Weight Complexes," *Journal of Neurochemistry*, 55:1950–1959, 1990.

(14) Perl, D. P., and P. F. Good, "Uptake of Aluminum Into Central Nervous System Along Nasal-olfactory Pathways," *Lancet*, i:1028, May 2, 1987.

(15) Pearson, R. C. et al., "Anatomical Correlates of the Distribution of the Pathological Changes in the Neocortex in Alzheimer Disease," *Proceedings of the National Academy of Sciences, USA*, 82:4531–4534, 1985.

(16) Graves, A. B. et al., "The Association Between Aluminum-containing Products and Alzheimer's Disease," *Journal of Clinical Epidemiology*, 43:35–55, 1990.

(17) Elinder, C. et al., "Evidence of Aluminum Accumulation in Aluminum Welders," *British Journal of Industrial Medicine*, 48:735–738, 1991.

(18) Mussi, I. et al., "Behaviour of Plasma and Urinary Aluminum Levels in Occupationally Exposed Subjects," *International Archives of Occupational and Environmental Health*, 54:155–161, 1984.

(19) Rollin, H. B., P. Theodorou, and T. A. Kilroe-Smith, "Deposition of Aluminum in Tissues of Rabbits Exposed to Inhalation of Low Concentrations of Al203 Dust," *British Journal of Industrial Medicine*, 48:389–391, 1991.

(20) Sjogren, B., I. Lundberg, and V. Lidums, "Aluminum in the Blood and Urine of Industrially Exposed Workers," *British Journal of Industrial Medicine*, 40:301–304, 1983.

(21) Sjogren, B. et al., "Exposure and Urinary Excretion of Aluminum During Welding," *Scandinavian Journal of Work and Environmental Health*, 11:39–43, 1985.

(22) Leyden, J., and A. Kligman, "Aluminum Chloride in the Treatment of Symptomatic Athlete's Foot," *Archives of Dermatology*, 111:1004–1010, 1975.

(23) Blank, I. H., J. L. Jones, and E. Gould, "A Study of the Penetration of Aluminum Salts into Excised Skin," *Proceedings of the Science Section Toilet Goods Association*, 29:32–35, 1958.

(24) Blacow, N. W., "Martindale. The Extra Pharmacopeia," 26th Ed., The Pharmaceutical Press, London, p. 260, 1972.

(25) Gosselin, R. E. et al., "Clinical Toxicology of Commercial Products," 4th Ed., The Williams and Wilkins Co., Baltimore, p. 89, 1976.

(26) Dreisbach, R. H., "Handbook of Poisoning: Diagnosis and Treatment," 8th Ed., Lange Medical Publications, Los Altos, CA, p. 371, 1974.

(27) Sax, N. I., "Dangerous Properties of Industrial Materials," 3d Ed., Reinhold Book Corp., New York, p. 391, 1968.

(28) Casarett, L. J., and J. Doull, editors, "Toxicology. The Basic Science of Poisons," Macmillan Publishing Co., Inc., New York, p. 463, 1975.

(29) Perl, D. P., and A. R. Brody, "Alzheimer's Disease: X-ray Spectrometric Evidence of Aluminum Accumulation in Neurofibrillary Tangle-bearing Neurons," Science, 208:297–299, 1980.

Dated: March 3, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 93–6530 Filed 3–22–93; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF THE INTERIOR

Office of Surface Mining Reclamation and Enforcement

30 CFR Part 938

Pennsylvania Abandoned Mine Lands Reclamation Plan

AGENCY: Office of Surface Mining Reclamation and Enforcement (OSM), Interior.

ACTION: Proposed rule.

SUMMARY: OSM is announcing receipt and requesting comments on a proposed amendment to the Pennsylvania Abandoned Mine Lands Reclamation Plan (hereinafter referred to as the Pennsylvania Plan) under the Surface Mining Control and Reclamation Act of 1977 (SMCRA). The proposed amendment provides for changes to the approved Pennsylvania Plan to allow for the initiation of a State administered emergency reclamation program.

This document sets forth the times and locations that the Pennsylvania plan and the proposed amendment to that plan are available for public inspection, the comment period during which interested persons may submit written comments on the amendment and the procedures that will be followed regarding the public hearing, if one is requested.

DATES: Written comments must be received on or before 4 p.m. on April 22, 1993 to ensure consideration in the rulemaking process. If requested, a public hearing on the amendment will be held at 9 a.m. on April 19, 1993. Requests to present testimony at the hearing must be received on or before 4 p.m. on April 7, 1993.

ADDRESSES: Written comments and requests to testify at the hearing should be mailed or hand delivered to Robert J. Biggi, Director, Harrisburg Field Office at the address listed below. Copies of the Pennsylvania plan, the proposed amendment, and all written comments received in response to this document will be available for public review at the addresses listed below during normal business hours, Monday through Friday, excluding holidays. Each requestor may receive, free of charge, one copy of the proposed amendment by contacting OSM's Harrisburg Field Office.

Office of Surface Mining Reclamation and Enforcement, Harrisburg Field Office, Harrisburg Transportation Center, Third Floor, Suite 3C, 4th and Market Streets, Harrisburg, Pennsylvania 17101, telephone: (717) 782–4036

Pennsylvania Department of Environmental Resources, Bureau of Abandoned Mine Reclamation, P.O. Box 1467, Harrisburg, Pennsylvania 17105, telephone: (717) 783–2156

A public hearing, if held, will be at the Penn Harris Motor Inn and Convention Center at the Camp Hill Bypass and U.S. Routes 11 and 15, Camp Hill, Pennsylvania.

FOR FURTHER INFORMATION CONTACT: Robert J. Biggi, Director, Harrisburg Field Office, (717) 782–4036.

SUPPLEMENTARY INFORMATION:

I. Background on the Pennsylvania Program

The Secretary of the Interior approved the Pennsylvania plan effective July 31, 1982. Information on the background of the Pennsylvania plan including the Secretary's findings, and the disposition of comments can be found in the July 30, 1982, **Federal Register** (47 FR 33079). Effective October 30, 1992, the Pennsylvania Plan was amended to update existing policies and procedures, and to allow for the new initiatives provided under the Abandoned Mine Reclamation Act of 1990 (Public Law 101–508). The Secretary's findings and the disposition of comments relative to the Plan amendment can be found in the October 30, 1992 **Federal Register** (57 FR 49135–49138).

II. Discussion of the Proposed Amendment

By notice dated September 29, 1982 (47 FR 42729–42730), the Secretary extended an opportunity to the States and Tribes to amend their AML Reclamation Plans to allow for a self-administered emergency reclamation program. Until that time, projects declared in emergency pursuant to section 410 of the SMCRA had been administered solely by OSM. To ensure that State/Tribal reclamation plan amendments submitted in response to the notice were consistent and adequately addressed necessary program requirements, OSM established guidelines on March 7, 1983. These guidelines for submission of amendments to State reclamation plans to conduct emergency reclamation contain specific authorizations, policies, and procedures that should be addressed as part of the amendment request. In addition, the March 7, 1983 guidance also contains information on the administration of State emergency reclamation programs.

By letter dated December 30, 1992, the Pennsylvania Department of Environmental Resources (PADER) submitted to OSM a proposed amendment to revise the Pennsylvania Plan to assume responsibility for a State administered emergency reclamation program. The amendment, as submitted, proposes to add a new part F to the current Pennsylvania Plan. Part F is composed of six sections that address AML Reclamation Plan amendment requirements under 30 CFR 884.13. The following is a summary of each section under the new part F:

1. *Governor's Designation of the Department of Environmental Resources:* This section addressed the designation by the Governor of Pennsylvania that PADER is authorized to conduct the reclamation program.

2. *The Legal Opinion Authorizing PADER to Administer the Emergency Program*: PADER has submitted a revised legal opinion from the Assistant Counsel of the Bureau of Legal Services concerning its authorities for conducting an emergency program.

3. *Policies and Procedures in Conducting the Emergency Program*: This section of the amendment contains a discussion of the purpose of the emergency program, coordination activities with other State and Federal agencies, and procedures for entering onto private property and conducting lien evaluations. In addition, this