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May 15, 2013

VIA Hand Delivery

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Submission of Citizen Petition on behalf of Allergy & Asthma Network Mothers of Asthmatics Docket No. FDA-2012-N-0171

Dear Sir or Madam:

Please accept the attached citizen petition (in four copies) submitted on behalf of Allergy & Asthma Network Mothers of Asthmatics pursuant to 21 C.F.R. § 10.35.

Sincerely,

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Mothers of Asthmatics
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FDA-2013-P-0711

2013-4520
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May 15, 2013

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Re: Citizen Petition re Using Innovative Technologies and Other Conditions of Safe Use to Expand Drug Products Considered Nonprescription Docket No. FDA-2012-N-0171

CITIZEN PETITION

Dear Sir or Madam:

The Allergy & Asthma Network Mothers of Asthmatics ("AANMA") and the undersigned petitioners (collectively, "Petitioners") hereby submit this Citizen Petition under 21 C.F.R. § 10.30 to request that the Commissioner of Food and Drugs take action requested below. AANMA is joined in this petition by the American Academy of Allergy, Asthma and Immunology ("AAAAI"), the American Association for Respiratory Care ("AARC"), the American College of Allergy, Asthma & Immunology ("ACAAI"), the American Latex Allergy Association ("ALAA"), the American Thoracic Society ("ATS"), and the American Chronic Obstructive Pulmonary Disease Foundation ("COPD Foundation").

I. Action Requested

Petitioners request that the Food and Drug Administration ("FDA") promulgate regulations, pursuant to section 505 (21 U.S.C. 355), of the Federal Food, Drug and Cosmetic Act ("FDCA") to exempt from compliance, modify or waive the requirements for compliance under sections 503(b), 505(d)(1) and (d)(4) for OTC monographs, and specifically exempts asthma and anaphylaxis medications from OTC non-prescription drug status. As such, health care professional organizations representing a variety of patient and health care professional sectors are signatories to this petition and are supportive of the request to exempt asthma and anaphylaxis medications from consideration in FDA's new Paradigm, "Using Innovative Technologies and Other Conditions of Safe Use to Expand Which Drug Products Can Be Considered Nonprescription, " announced February 28, 2012.

II. Statement of Grounds

A. Background

In an effort to address under-treatment of many common chronic diseases and conditions in the United States the FDA is considering a new paradigm [hereinafter referred to as Paradigm] whereby, FDA would approve certain prescription drugs for nonprescription use under certain conditions of safe use specific to the drug and setting in which it is sold. FDA's goal is to reduce the amount of time and attention physicians need to give for routine appointments related to prescription refills so they can attend to more seriously ill patients and reduce the burden on the already overburdened healthcare system, and reduce health care costs.

The Petitioners contend, however, the FDA 's Paradigm is overbroad, runs contrary to well established national guidelines for asthma and anaphylaxis, has unintended public policy consequences and lacks demonstrated safety and efficacy data for the proposed asthma and anaphylaxis medications in the OTC setting.

The FDA Paradigm is inconsistent with state and federal programs and guidelines.

This Paradigm heightens the problem of poorly managed diseases by undermining National Institutes of Health ("NIH"), National Heart Lung and Blood Institute ("NHLBI), National Asthma Education Prevention Program ("NAEPP)" asthma and National Institutes of Allergy and Infectious Diseases ("NIAID") food allergy guideline-based care. The guidelines clearly demonstrate routine care reduces the need for medication, improves outcomes and reduces healthcare costs. FDA's Paradigm focuses on symptom control with medication alone and, therefore, could increase the use of asthma and anaphylaxis medications, and potentially transfer the complex diagnosis, treatment and management of life-threatening allergy and asthma from physicians to pharmacists and kiosks in retail outlets.

FDA's Paradigm assumes patients, parents and caregivers possess all the necessary decision-making tools and independent self assessment, monitoring, prevention and emergency management skills consistent with NAEPP asthma guidelines and NIAID food allergy guidelines.

Federal and state funded programs such as CDC's National Asthma Control Program, Medicare, Medicaid and Children's Health Insurance Program ("CHIP") clearly state the standard of care for managing asthma long-term should be physician-directed with at least annual visits. Furthermore, professional medical societies such as ACAAI, AAAAI, American Academy of Pediatrics ("AAP"), AARC, ATS, National Association of School Nurses ("NASN") all endorse practice parameters and guidelines based care anchored in the physician-patient relationship. The guidelines focus on stepping up and stepping down medication

under the monitoring and management of symptoms by a physician. The FDA Paradigm, as applied to asthma and anaphylaxis, lacks focus on symptom identification and environmental remediation of the cause of symptoms. In asthma and anaphylaxis care, risk assessment, prevention and emergency preparedness is what saves lives.

Increasing use of quick-relief medications is a sign of progressively worsening disease in asthma and anaphylaxis. A physician must address this concern sooner rather than later if the patient is to reduce medication, remain productive and reduce the burden on the healthcare system. Delay of treatment, for any reason including access to too much medication, is faulty and could be life-threatening.

<u>No actual use studies exist to support OTC use of asthma and anaphylaxis medications.</u>

This petition seeks relief limited to the class of asthma and anaphylaxis medications—specifically asthma medications that are oral or inhaled and epinephrine auto -injectors for the treatment of severe life-threatening allergic reactions. These medications are intended for patients whose chronic conditions require a physician's initial diagnosis and subsequent care. While there are numerous safe and effective OTC drugs that have been approved by the FDA, asthma and anaphylaxis medications have not demonstrated safety and efficacy for approved OTC use.

B. The FDA Paradigm is inconsistent and at odds with the National Asthma Education and Prevention Program's (NAEPP) Asthma Guidelines Expert Panel Report 3 ("EPR 3").

The NAEPP coordinated by the NIH/NHLBI is the leading organization to (1) raise awareness about asthma as a major public health problem, (2) develop clinical practice guidelines and other supportive materials based on the latest scientific evidence, and (3) use multiple strategies to enhance guidelines implementation. A coordinating committee composed of professional, medical, and lay health organizations as well federal agencies (such as the FDA), work collaboratively to address the growing problem of asthma in the United States.

In 1991, NAEPP presented its first set of recommendations for the management of asthma aimed at helping clinicians and patients make appropriate decisions about asthma. The NAEPP updated its guidelines in 1997, 2002 and 2007. In all four publications the guidelines consistently advocate (1) asthma cannot be properly self diagnosed, (2) a physician should make the initial diagnosis of asthma and (3) the patient should receive continued care from a physician because, (4) asthma is a chronic and progressive disease.

Asthma currently affects an estimated 25 million people in the United States and the number is expected to rise significantly by 2025. Patients with asthma have been shown to underestimate the severity of their airway obstruction. [1] Many patients fail to recognize the difference between mild, moderate and severe asthma symptoms. A variety of health conditions may coexist or be mistaken for asthma. The NAEPP Guidelines recommend that a primary care physician or a specialist diagnose asthma based on the patient's medical and family histories, a physical exam, environmental allergen and irritant exposures and test results. [2] Procedures attempted by a kiosk will be a less than thorough interpretation compared to a physician's analysis and below the NAEPP standards.

The guidelines stipulate that asthma is a chronic and progressive disease. Improperly treated, asthma in most cases will worsen at various rates. Even when well managed, asthma is a disease of variability; however, this complex, chronic disease can be slowed and even halted by treatment under continued physician's care. Inhalation drug/devices must be matched to patients by the physician according to the needs of the patient and progression of the episode. Medications can be inhaled as micronized powders, aerosolized mists over a period of several seconds or minutes to ensure airway deposition, an aerosolized mist without propellant, and a pressurized mist with or without a holding chamber. A physician may prescribe long-term control inhaled and oral drugs for asthma used to prevent attacks. These medications need to be taken daily to achieve optimal outcomes, even in the absence of symptoms. In addition, a physician may prescribe short-acting bronchodilators for quick relief used early to interrupt the progression of an attack or episode. Moreover, bronchodilators are not all the same. Bronchodilators have different mechanisms of action, methods of use,[3] duration of action, and forms. Whether a patient would benefit more from using a nebulizer, or a metered-dose inhaler (MDI) are treatment decisions that currently rest with the physician. The physician is the health care provider best qualified to determine which delivery method is best for the patient. The most effective strategy embraces and advances the proposition of a physician's initial and continued care in order to halt the progression of asthma and long-term damage to the airways.

Most children and adults with asthma recognize symptoms and experience warning signs before the actual attack occurs. However, the problem is they tend to treat symptoms only when the feel or their caregivers witness symptoms and rely heavily on the quick-relief bronchodilators (which do not treat the underlying

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[1] Dawson, A Reproducibility of Spirometric measurements in normal subjects. Am Rev Respir Dis 1966; 93, 264-268 [PubMed]

[2] NIH, National Heart, Lung and Blood Institute. How Is Asthma Diagnosed? http://www.nhlbi.nih.gov/health/health-topics/topics/asthma/diagnosis.html

[3] The method of using a nebulizer or MDI with an accompanying spacer that has been chosen by a physician is presently taught by a qualified trained health care provider, e.g. a nurse trained in asthma education.

inflammation). The FDA Paradigm actually reinforces such uninformed behavior and is inconsistent and contrary to NAEPP guidelines. [4]

FDA's Paradigm states that in some cases "a visit to a practitioner would be required for the initial prescription, but a certain number of refills could be authorized beyond those that would normally be authorized without a return visit...[t]his paradigm might be useful for certain quick-relief medicines, such as inhalers used to treat asthma or epinephrine for allergic reactions."[5] Petitioners assert this is already the standard of care for asthma and anaphylaxis patients. A prescription is written for the number of refills that fill the conditions of safe use before the next routinely scheduled visit. The goal of managing asthma and life-threatening allergies is to minimize the need for medications.

The FDA's Paradigm is narrow in scope and fails to fully address the NAEPP's guidelines for asthma control. In 2007, the NAEPP issued its most recent and comprehensive guideline update. The new approach emphasizes that four important factors should be considered collectively, in order to strengthen one's ability to achieve quality asthma care and control. That is, (1) physician assessment and monitoring, (2) address environmental factors, (3) provide appropriate medication and (4) emphasize patient education.[6] The FDA Paradigm only addresses one of the four required key components (provide medication) for asthma management and thus conflicts with NAEPP guidelines and patient-centered outcomes.

The policy direction outlined in the FDA Paradigm document has unintentional and profound negative consequences. Approximately 20% of patients with severe persistent asthma symptoms rely exclusively on quick-relief bronchodilators, and do so, to their detriment. They unknowingly neglect the fundamental underlying long- term root cause of their chronic and often progressive condition and may not notice a gradual deterioration of symptoms by refilling their short- acting, quick-relief bronchodilators without seeking medical advice. This has lead to death by asphyxiation since over use of short acting bronchodilator leads to receptors desensitization and patients no longer respond to asthma medications. By allowing asthma inhalers to become a commonplace, OTC long-term solution FDA is endorsing a practice of poor asthma control and, an increased risk of mortality.[7] Moreover, the anticipated cost savings articulated in the Paradigm, that stems from

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[4] NAEPP Guidelines summarizes that treating mild, moderate and severe persistent asthma with mono-therapy with short acting beta agonists is contraindicated and could cause harm.

[5] Utilizing Innovating Technologies and other Conditions of Safe Use to Expand Access to Nonprescription Drugs

[6] U.S. Department of Health, NIH, NHLBI, 2007 NAEPP Guidelines for Diagnosis and Management of Asthma (EPR-3).

[7] Each day nine Americans die from asthma. There are more than 3,300 deaths due to asthma each year, many of which are avoidable with proper treatment and care. "New Asthma Estimates: Tracking Prevalence, Health Care and Mortality," NCHS, CDC, 2001

the reduced number of routine visits for asthma and allergy is simply not justified by the risks presented. The Petitioners strongly believe, and are supported by all clinical practice guidelines, managing asthma with bronchodilators alone is unsafe and misguided.

C. The FDA Paradigm is inconsistent with the National Institute of Allergy and Infectious Diseases (NIAID) Food Allergy guidelines.

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. For more than 60 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States and around the world. NIAID is one of the 27 Institutes and Centers of the National Institutes of Health (NIH). [8] NIAID worked with 34 professional organizations, federal agencies, and patient advocacy groups to develop concise clinical guidelines for healthcare professionals on the diagnosis and management of food allergy and the treatment of acute food allergy reactions. NIAID is a trusted source of food allergy information. The guidelines define food, food intolerance, food allergy, food allergens, and specific allergic conditions associated with food.

Anaphylaxis does not meet FDA's criteria for OTC products because (1) life-threatening allergies are conditions that cannot be self-diagnosed without initial and ongoing engagement with a practitioner, (2) epinephrine is a synthetic form of adrenaline and is associated with toxicities that require an evaluation of the benefits and risks by a practitioner; and (3) the device requires a practitioner's input for use. Anaphylaxis kills more than 450 Americans each year.

Parents commonly misdiagnose children with suspected food allergies. Statistics show 15 percent of parents who believed their child had food allergies actually did not. Food allergies have been confirmed in only 1 to 3 percent of all Americans[9]. Food allergies are difficult to self diagnose. Food allergies often tend to coexist with asthma and other diseases or conditions, and symptoms are frequently confused.

Furthermore, an individual's allergic response to certain foods will evolve throughout life and requires monitoring and periodic testing. Parent and caregiver education and childhood self -management skill development are all part of the routine care provided by allergists. Selecting the appropriate epinephrine auto-injector and teaching the patient and parent how to use it is important, however, it

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[8] U.S. Department of Health and Human Services, National Institutes of Health, National Institute of Allergy and Infectious Diseases; http://www.niaid.nih.gov.

[9] Time Magazine, New Guidelines Help Doctors Diagnose Food Allergy, December 6, 2010. Alice Park.

is even more compelling to ensure both are prepared to recognize an anaphylaxis emergency, use the device early enough to be effective, seek emergency help at a hospital and obtain a refill of the device(s) just used. They must be taught the importance of carrying two epinephrine auto-injectors everywhere everyday.

NIAID guidelines dictate food allergy is a life-threatening disease requiring ongoing physician-patient dialogue and care. The need for ongoing monitoring and assessment is paramount to assure patients are utilizing the medicines properly and with optimal disease control. Allergists are trained to separate true food allergies from food intolerance, food dislikes, and other conditions that mimic food allergy. The guidelines advise, that physicians confirm the presence of four factors: a report from the patient (or from the parent, in the case of children) of an adverse reaction such as a rash, intestinal difficulties, difficulty breathing or other reactions after consuming a particular food; a blood test that measures antibodies indicating an allergic immune reaction, a skin prick test with the allergen that shows an adverse reaction; and finally, the gold standard, a positive oral challenge test, in which the patient ingests a small amount of the food allergen under direct physician supervision. The guidelines also urge doctors to follow up with all food allergy patients at least once a year which affords patients the opportunity to obtain prescription refills and necessary patient education aimed at trigger avoidance, anaphylaxis action plans and emergency preparation.

The NIAID is a trusted source of allergy related information for both the public and medical community. The FDA's proposed policy is contradictory to the NIAID guidelines. Petitioners emphasize self- diagnosis is dangerous. Life-threatening food allergies require physician diagnosis and ongoing care pursuant to treatment selection and avoidance measures. In addition, therapies for life-threatening allergies require epinephrine, the only drug that can simultaneously stop the progression of the allergic cascade while stimulating receptors to keep the heart beating and stabilize blood pressure during anaphylaxis. Epinephrine is a well-known drug with great potential for good, and like all other drugs, also houses the potential for misuse. Self-treatment would make a nonprescription transition of these medications unsafe, unfeasible and undesirable.

D. No Actual Use Data to Support the Use of Asthma and Anaphylaxis OTC Medications

The process of reclassifying drugs from prescription to OTC status is referred to as an "Rx to OTC switch." FDA states drugs are commonly switched one of two ways: under the OTC drug review, or by a manufacturer's submission of additional information to the original new drug application. Currently, asthma and anaphylaxis medications would not classify for an OTC drug review. Therefore, they

must advance under the switch process as a new drug application.

The New Drug Application (NDA) is the vehicle in the United States through which drug sponsors formally propose that the Food and Drug Administration (FDA) approve a new pharmaceutical for sale and marketing. The goals of the NDA are to provide enough information to permit FDA reviewers to establish the following:

- Is the drug safe and effective in its proposed use(s) when used as directed, and do the benefits of the drug outweigh the risks?
- Is the drug's proposed labeling (package insert) appropriate, and what should it contain?
- Are the methods used in manufacturing (Good Manufacturing Practice, GMP) the drug and the controls used to maintain the drug's quality adequate to preserve the drug's identity, strength, quality, and purity?

The legal requirement for approval is "substantial" evidence of efficacy demonstrated through controlled clinical trials. This standard lies at the heart of the regulatory program for drugs. It means that the clinical experience of doctors, the opinion of experts, or testimonials from patients, even if they have experienced a miraculous recovery, have minimal weight in this process. Data for the submission must come from rigorous clinical trials.

The trials are typically conducted in three phases:

- Phase 1: The drug is tested in a few healthy volunteers to determine if it is acutely toxic.
- Phase 2: Various doses of the drug are tried to determine how much to give to patients.
- Phase 3: The drug is typically tested in double-blind, placebo controlled trials to demonstrate that it works and is safe. Sponsors typically confer with FDA prior to starting these trials to determine what data is needed, since these trials often involve hundreds of patients and are very expensive.
- (Phase 4): These are post-approval trials that are sometimes a condition attached by the FDA to the approval.

The legal requirements for safety and efficacy have been interpreted as requiring scientific evidence that the benefits of a drug outweigh the risks and that adequate instructions exist for use, since many drugs are toxic and technically not "safe" in the usual sense. Even relatively safe and well understood OTC drugs such as aspirin could be dangerous if used incorrectly. Data for the submission must come from rigorous clinical trials.

Petitioners assert that OTC asthma and anaphylaxis medications lack critical clinical data necessary and thus fail to meet the FDA's own rigorous legal and regulatory standard of care for safety and efficacy given the intended use described in the FDA Paradigm.

Actual use study is required to show the proposed labeling for OTC use is effective in enabling patients to use the drug properly. Moreover, additional actual use study considerations need to address specific factors obstructing the drug from present OTC use or the ability to keep the product out of the hands of children who are too young or ill prepared to self manage. For example, if the question as to whether the prescription indication will now be taken OTC is self-diagnosable, and then a study of self-diagnosis would be required.

The key issue is can conditions of safe use be established for asthma and anaphylaxis medications without routine medical care from physicians and work as well in the real world context given the inherent randomness that exists. Actual OTC use studies are legally required and necessary. A precedent set by one particular prescription to OTC switch could be damaging in terms of overall public policy.

E. Conclusion

Pursuant to section 503(b), 505(d)(1) and (d)(4) of the Federal Food, Drug and Cosmetic Act ("FDCA"), the FDA has considerable latitude to exempt from compliance, modify or waive the requirements for compliance prescription to non prescription medications. We respectfully request an exemption for asthma and anaphylaxis medications from the list of over the counter (OTC) medications in the proposed new FDA Paradigm.

III. Environmental Impact

This petition is categorically exempt from the requirement for an environmental assessment or an environmental impact statement pursuant to 21 C.F.R. § 25.30(j).

IV. Economic Impact

As provided in 21 C.F.R. §10.30(b) economic impact information is to be submitted only when requested by the Commissioner following review of the petition.

V. Certification

The undersigned, on behalf of AANMA and the additional undersigned associations, certifies, that to the best knowledge and belief of the undersigned, this

petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioners, which are unfavorable to the petition.

Respectfully submitted,

Nancy Sander, Founder & President
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Petitioners' Interests

Asthma and Allergy & Asthma Network Mothers of Asthmatics (AANMA) is a national membership organization dedicated to eliminating suffering and death due to asthma, allergies, and related conditions through education, advocacy, community outreach, and research.

The American Academy of Allergy Asthma & Immunology (AAAAI) is the largest professional medical specialty organization in the United States, representing allergists, asthma specialist, clinical immunologists, allied health professionals, and others with a special interest in the research and treatment of allergic disease. Its mission is the advancement of the knowledge and practice of allergy, asthma and immunology for optimal patient care.

The American Association for Respiratory Care (AARC) is a 37,000-membership organization of respiratory therapists and others involved in pulmonary health. Respiratory therapists work in the hospital, doctor's offices, and sleep clinics, with patients of all ages to diagnose, treat and manage lung disease and illness.

The American College of Allergy, Asthma & Immunology (ACAAI) is a professional medical organization comprised of qualified allergists/immunologists and related healthcare professionals dedicated to the clinical practice of allergy, asthma and immunology through education and research to promote the highest quality patient care.

The American Latex Allergy Association (A.L.E.R.T., Inc.) (ALAA) is the lay organization affiliated with AAAAI and ACAAI that provides education and support to individuals with natural rubber latex allergy. ALAA supports the doctor/patient relationship in the treatment of individuals with latex allergy.

The American Thoracic Society (ATS) is a membership organization with more than 15,000 physicians, research scientists, and nurses and other allied healthcare professionals dedicated to improving health worldwide by advancing research, clinical care, and public health in respiratory disease, critical illness, sleep disorder, infectious disease, pediatrics, allergy/immunology, thoracic surgery, behavioral science, environmental and occupational medicine.

The Chronic Obstructive Pulmonary Disease (COPD) Foundation is a 501(c)(3) not-for-profit organization designed to develop and support programs that improve the quality of life through research, education, early diagnosis, and enhanced therapy for persons whose lives are impacted by Chronic Obstructive Pulmonary Disease.

Petition signatories follow.

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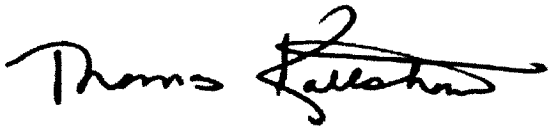

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End of Petition Signatories.