Comments on Citizen’s Petition #FDA-2013-P-1001/CP-1

Submitted by
Howard M. Druce, MD
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Summary of Petition and Analysis

The Petitioners request that the Commissioner of Food and Drugs add a warning to the labeling of all nonprescription drug products containing an ingredient with “anticholinergic or histamine H₁ inverse agonist effects” noting that the product can cause a confusional state. They also note that older adults may be at risk for impaired cognition, especially in the context of concurrent use of multiple drugs with similar anticholinergic/H₁ inverse agonist effects.

Evidence cited by the Petitioners in the “Statement of Grounds” section of the Petition was reviewed for relevance towards the requested warning. While the ability of antihistamine products to produce sedation is well-known, current labeling for these products reflects the potential for drowsiness to occur.

Justification of a class-related warning should require sufficient evidence of the effect occurring with many, most or all of the drugs in the class. As outlined in more detail below, the evidence provided by the petitioners in support of their request, which includes published case reports, observational and prospective controlled trials as well as other reports in the literature, does not justify the addition of a class labeling statement to all nonprescription antihistamine products with H₁ inverse agonist effects.

Analysis of Scientific References Cited by the Petitioners

This review will follow the chronologic order of the references as cited by The Petitioners.

The Petitioners state that “As early as 1971, case reports were published suggesting that the confusional state following certain medications was due to the anticholinergic effect of the medicines.”

Commentary: Although published, The Petitioners do not cite these case report references. It is thus not possible to assess which medications were involved, the dosage and route of administration, the indication for administration, concomitant medications, and any underlying medical conditions suffered by the subjects of these case reports. This type of information is typically contained in a published case report and is essential to assess the relevance of case reports.

The Petitioners cite Janowsky et al. (1972) who they state “published a placebo-controlled study showing that the confusional state caused by some drugs with anticholinergic effects was not affected by placebo but was improved by physostigmine confirming the anticholinergic mechanism for the confusion.”

Commentary: The reference refers to a letter to the editor in which 3 patient histories are detailed. One received a tricyclic-phenothiazine-benztropine combination product and the other two received phenothiazine-benztropine combinations. Their confusional state was not altered by a placebo injection but was reversed temporarily by physostigmine. No placebo-controlled study is detailed in this reference. None of these patients received any H₁ antihistamines.
The Petitioners report that “Tune, et al, 1992 assessed the 25 drugs most commonly prescribed for the elderly for anticholinergic activity and found 10 had levels associated with impairment in normal elderly subjects.”

Commentary: Tune at al report an in vitro experiment. The authors obtained samples of the 25 medications most commonly prescribed for elderly patients according to a HCFA listing of 225 drugs. They assessed the anticholinergic effects of a standard concentration (i.e. $10^{-8}$ M) of each compound in an anticholinergic radioreceptor assay. They compared the drug levels to an internal standard of atropine sulfate. They expressed each level as nanograms per milliliter of equivalent amounts of atropine. The top 10 drugs in Table 1 of their paper were ranked by frequency of their prescription for elderly patients: furosemide, digoxin, dyazide, lanoxin, hydrochlorothiazide, propranolol, salicylic acid, dipyridamole, theophylline anhydrous and nitroglycerin. No H₁ antihistamines appear in the table.

The Petitioners state that the “American Geriatrics Society 2012 Beers Criteria for potentially inappropriate medications for older adults include 12 first generation antihistamine H₁ receptor antagonists / reverse agonists, many of which are nonprescription drugs.”

Commentary: The 2012 updated Beers criteria include 53 medications or medication classes. Of this large number of specific medications, 12 first generation antihistamines are named. Of these, some are not actively marketed (carbinoxamine), or are only available on prescription for specific indications (cyproheptadine, hydroxyzine). The quality of evidence for all but hydroxyzine and promethazine is moderate. No references are cited in the paper to allow examination of the quality of the supporting data.

The Petitioners state that all H₁ receptor antagonists have central nervous system activity. (Brunton 2011).

Commentary: This reference is taken from the chapter on H₁-receptor antagonists of a standard pharmacology textbook. The reference states…”the first-generation antagonists can both stimulate and depress the CNS. Stimulation occasionally is encountered in patients given conventional doses……Central depression…usually accompanies therapeutic doses of the older H₁ antagonists. ….Patients vary in their susceptibility and responses to individual drugs.” The Petitioners do not refer to the very next page where positive anticholinergic effects are detailed. From P.920 – Many of the first-generation antagonists tend to inhibit responses to ACh (acetylcholine) that are mediated by muscarinic receptors and may be manifest during clinical use. Some H₁ antagonists also can be used to treat motion sickness.

The Petitioners cite Duran et al who reviewed multiple published risk scales and identified 100 drugs as having this activity and “a way to sum the anticholinergic activity of each to determine the anticholinergic burden for a medication regimen of multiple drugs”. They state that many of the high potency anticholinergic drugs on the list are nonprescription antihistamines including chlorpheniramme, cyproheptadine, diphenhydramine and hydroxyzine.

Commentary: Duran et al (2013) published a literature search review. The authors looked in MEDLINE for studies including a finite list of anticholinergic drugs, a grading score of anticholinergic potency and a validation in a clinical or experimental setting. The authors
The authors concluded that there was considerable variation among anticholinergic risk scales in terms of selection of specific drugs as well as of grading of anticholinergic potency. The authors stated that their selection of 100 drugs to be included in a screening software program for anticholinergic burden needs to be supplemented with validated information on dosing and route of administration for a full estimation of the anticholinergic burden in poly-medicated older adults. Cyproheptadine and hydroxyzine are nonprescription drugs in the U.S.

The Petitioners state that “many population-based observational studies have been published showing worse performance in elderly taking drugs with anticholinergic activity than controls who don’t take these drugs.”

Commentary: The Petitioners cite only 2 examples of studies which can be evaluated. Regarding the “many” studies there is no indication of the specific drugs involved, the indications for use, dosage and route of administration of use and underlying medical conditions, all of which need to be considered to assess the validity of the conclusions.


Ancelin et al 2006. The Petitioners do not describe the findings of this study.

Commentary: Ancelin et al performed a longitudinal cohort study which included 372 subjects over age 60, from 63 randomly selected general practices in the Montpellier region of southern France. There was a significant refusal rate of 7%, and 372 elderly subjects without senile dementia were followed for two years. The endpoint for the study was a novel anticholinergic burden classification the authors developed by constructing a table associating known anticholinergic drugs with their serum anticholinergic activity where available, as shown by radioreceptor assays. Also, each participant’s records were examined by a pharmacologist, physician and biologist to classify the burden from 0-3 (0= no anticholinergic drugs used, 1= drugs used with no likely effect, 2= drugs used with low effect, 3= drugs used with high effect). This manuscript does not detail which drugs would contribute to each category. However, Table 1 in the manuscript does contain a list of the anticholinergic drugs used by study participants which had an anticholinergic burden classification of 3. Of the 27 drugs cited, only 2 were given for allergy relief: Dexchlorpheniramine, and Alimemazine, which is a combination product containing a sedative phenothiazine). The authors state that chlorpheniramine was being used for an analgesia and anti-inflammatory application, which is not relevant to U.S. practice. Most of the study participants were taking their anticholinergic medications chronically. 51/372 subjects were taking at least one anticholinergic drug at the start of the study, and at the one year follow up 30/51 were still taking anticholinergic drugs regularly. The list of drugs cited in Table 1 includes prescription medications such as colchicine, digoxin, furosemide, and oxybutynin. Because these were prescribed for chronic conditions, continued adherence is not surprising.

Landi 2007. The Petitioners do not describe the findings of this study.

Commentary: Landi et al reviewed data from a baseline evaluation of 364 subjects enrolled in a study termed iISIRENTE which is a prospective cohort study of elderly subjects age 80 and above in a mountain community in the Sirente area of Central Italy. The goals of the study,
inclusion criteria etc. are not cited in the manuscript. The authors assessed physical performance using a battery of tests including 4-meter walking speed, balance, and chair stand tests. There was no assessment of cognitive or behavioral impairment. The only class of drugs mentioned in the manuscript is “anticholinergic drugs” which the authors define as all medications for which serum anticholinergic activity was previously demonstrated. The authors state that all these physical and functional measures showed significant associations with anticholinergic drug use. After adjustment for potential confounders, the associations were weaker but still statistically significant. Table 4 in the manuscript details the frequency of use of drugs with anticholinergic properties among study participants. The top 5 were: digoxin (21%), furosemide (15.6%), theophylline (4.7%), lorazepam (3.8%) and bromazepam (2.5%). It is inappropriate to extrapolate from use of these prescription medications to “all nonprescription drugs containing an ingredient with anticholinergic or histamine H1 inverse agonist effects” as requested by The Petitioners.

The Petitioners state ”The idea that anticholinergic drugs and especially first generation antihistamines cause cognitive impairment has been so well documented that it is now standard textbook content in geriatrics (Halter JB, et al, 2009), neurology (Roper and Samuels, 2009), and internal medicine (Goldman and Schafer, 2012).”

Commentary: Halter 2009. There is no reference to antihistamines on page 765 as cited by the Petitioners.

Commentary: Roper and Samuels 2009. On P 404 a Table (20-1) is presented of the classification of delirium and acute confusional states. In the large list of disorders of acute confusional states, drug intoxication from multiple classes of drugs are listed – opiates, anticholinergics, barbiturates and other sedatives, trihexyphenidyl, corticosteroids, L-dopa, dopaminergic agonists, serotonergic antidepressants. There is no specific mention of antihistamines. There is no specific mention of nonprescription drugs.

On P. 406 there is a paragraph entitled “confusional states and delirium induced by medications. The authors note that “it must be again emphasized that drug intoxication – predominantly with drugs prescribed by physicians – is among the most common causes in practice. Among the most distinctive syndromes are those from drugs that have direct or indirect anticholinergic properties.” Note here that there is again no mention of antihistamines, and the syndrome is characterized as “distinctive” – as opposed to frequent, severe or other possible qualifiers.

Commentary: Goldman and Schafer 2012. The reference is taken from a standard internal medicine textbook. The reference is apparently directed to a chapter entitled “Acute Poisoning.” Table 110-1 on Page 670 details the signs and symptoms caused by overdose of multiple drug classes. First generation antihistamine receptor antagonists are included in the table, as are many other classes of drugs. There is no specific reference in the text to this class of drug. The relevance of this reference is uncertain to this author.

The Petitioners cite two prospective controlled trials showing “the same thing” (Author’s emphasis).
Sunderland et al (1987) showed that patients with dementia of the Alzheimer’s type had marked impairment to 0.25 mg scopolamine compared to matched elderly control subjects.

Commentary: This was a small study of 10 patients with dementia and 10 control subjects. Three different doses of scopolamine (0.1, 0.25mg and 0.5 mg) were dosed intravenously. The patients were inpatients in a National Institute of Mental Health research ward, whereas the controls were healthy outpatients brought into the hospital for study dosing. The dosing was not completely randomized but as the authors describe it “pseudorandomised” so that lower doses were administered before the highest dose. The battery of cognitive tasks was administered one and two hours after infusion. One issue that the authors discuss is that the two study groups clearly had different cognitive and behavioral measures at baseline. There was no dose-response seen for the physiologic or cognitive effects of the scopolamine. Extrapolation from this small study should be limited and this author would not consider it to be applicable to general populations or for oral dosage.

Pomara et al (2008) showed that normal healthy elderly with the APOE $\varepsilon_4$ gene (carriers) had impaired recall and mental slowness compared to non-carriers when given 2mg trihexyphenidyl orally in a randomized double-blind placebo-controlled study.

Commentary: Trihexyphenidyl is a potent anticholinergic drug available on prescription for the treatment of Parkinson’s disease and tremors of other types. This study comprised 24 cognitively intact, healthy adult adults, 12 of whom were carriers for the APOE $\varepsilon_4$ allele at an outpatient geriatric psychiatry research clinic. The design was randomized, double-blind and placebo controlled. All participants received 1mg or 2mg of trihexyphenidyl or placebo over a period of three consecutive weeks. Cognitive tests were administered at baseline, 1, 2.5 and 5 hr. post-drug administration. Only the highest 2.0mg dose increased subjective ratings of mental slowness. The authors concluded that the $\varepsilon_4$ allele was associated with increased subjective mental slowing after trihexyphenidyl anticholinergic challenge. No data are presented in this paper that suggests that these results could be extrapolated to drugs such as H1-antihistamines.

The Petitioners cite Perry (2003) to state that an “[a]dditional risk of prolonged anticholinergic drug therapy is an increase in the severity of amyloid plaque and neurofibrillary tangles seen in autopsied Parkinson’s disease patients who were receiving anticholinergic drugs compared to those who had not received these drugs…”

Commentary: Perry et al (2003) presented a manuscript in the “Brief Communications” section of the Annals of Neurology. They examined case records for 120 neuropathologically confirmed cases of Parkinson’s disease aged more than 70 yr. at time of death in a teaching hospital brain bank. They recorded the duration of disease and treatment with the following antimuscarinic agents: antiparkinsonian: benztropine, orphenadrine, trihexyphenidyl; bladder dysfunction: oxybutynin, and tricyclic antidepressants amitriptyline and imipramine. Smoking histories were only available for 3 cases. The authors concluded that their data was consistent with the possibility that prolonged use of antimuscarinic drugs accelerates $\beta$ amyloidosis and senile plaque formation in the aging brain in subjects with Parkinson’s disease. The increase in plaque density was not great and far short of that seen in Alzheimer’s disease. Neither plaque nor tangle densities were elevated in Parkinson’s disease patients treated with antimuscarinic drugs for less
than 2 years. There is no mention of antihistamines in this paper and no suggestion that the data can be extrapolated to other drugs such as antihistamines.

In another study, Cai et al (2012) “found that subjects receiving 3 or more months of anticholinergic medications had an increased chance of being mildly cognitively impaired than those not receiving anticholinergic medications”.

**Commentary:** The authors note that their study found an association between anticholinergic burden and the risk of developing cognitive impairment. However, they found that such an association required both a high anticholinergic burden and 2-3 months of continuous exposure to such a high burden. The authors discuss some limitations of their study. The authors did not systematically measure medication adherence, but used drug dispensing as a surrogate. They state that this is an accurate substitute in assessing adherence for antihypertensive medications, but no data are provided for the type of medications under consideration in this study. Also the methodology of this study specifically did not capture OTC medication use. Other potentially confounding covariates of interest were also not recorded, such as depressive symptoms, APOE genotyping and alcohol and tobacco use. An important comment was made by the authors that they were unable to determine the reversibility of the association between anticholinergic exposure and cognitive impairment, but cite a reference which might suggest potential reversibility of the association.

The indications for nonprescription antihistamines are generally short-lived or self-limiting and do not require 3 or more months of medication use.

**Analysis and Conclusions**

The Petitioners request a general class-related warning for nonprescription drugs marketed in the U.S. The evidence they cite does not include any case report or clinical or epidemiologic study of any of the “nonprescription drugs containing an ingredient with anticholinergic or histamine H1 inverse agonist effects.” Diligent literature review has failed to discover any such study. Extrapolation from the data the Petitioners quote is not justified based on the restricted or specialized populations used in the studies they cite, and also based on the anticholinergic drugs taken by the study subjects, predominantly prescription medications such as digoxin, furosemide and theophylline.

In general, the literature on “anticholinergic burden” of medications appears to be based on the pharmacology of the individual medications. There is some controversy on the degree of “anticholinergic burden” that each medication exerts depending on the scale selected for assessment. What appears to be lacking are real-life descriptions of the effects of individual drugs dosed together. Thus, even in the Beers criteria, drug interactions are described as “potentially” harmful. To fully assess these interactions, the patient’s underlying condition(s), dose of drug, drug combinations, route of administration and dosing interval need to be considered. Nonprescription drugs are often administered on “as needed” or “PRN” basis.

The effects of anticholinergic agents on cognitive measures only appear to be evident in acute dosing experiments or after 2-3 months of continuous dosing. Data obtained from clinical studies with 2-3 months of continuous dosing cannot be directly extrapolated.
The effects of short-term intermittent use of nonprescription drugs such as H₁-histamine antagonists on cognitive impairment cannot reasonably be extrapolated from the data submitted by the Petitioners. The indications and labeling for use of these drugs are determined by FDA after careful consideration.

In summary, no data have been produced to warrant change in current labeling.

[Signature]

Howard M. Druce, MD

Dated: June 3, 2014
Appendix 1: Author CV

Curriculum Vitae

Name: Howard Martin Druce

Office Address: 242 E. Main Street
Somerville, NJ 08876-3049
908-704-9696

1. Education
   a. Undergraduate
      Oxford University
      Oxford, England, UK
      Degree: BA with 1st class Honors in Physiological Sciences
      9/1971-6/1974

   b. Graduate
      Oxford University
      Oxford, England, UK
      Degree: MA, Physiological Sciences
      10/1978

University of London, Middlesex Hospital Medical School (Now University College London Medical School)
London, England, UK
Degree: MB, BS. (equivalent to U.S. MD), Medicine with Honors in Clinical Pharmacology and Therapeutics
9/1974-10/1977
2. **Post-Doctoral Training**

   a. **Internship and Residencies**
   
      NY Hospital Queens (formerly Booth Memorial Medical Center affiliated with New York University Medical Center)
      
      Flushing, NY
      
      Internship and Residency: Internal Medicine
      
      7/1979 – 6/1982
      
      United Manchester Teaching Hospitals, University of Manchester
      
      Manchester, England, UK
      
      Residency: ENT, Gynecology
      
      
      University College Hospital (formerly Middlesex Hospital), University of London
      
      London, England, UK
      
      Internship: Medicine
      
      
   b. **Research Fellowships**
      
      National Institute of Allergy and Infectious Diseases
      
      Bethesda, MD
      
      Visiting Associate, Laboratory of Clinical Investigation, Allergy and Clinical Immunology
      
      
      National Institute of Allergy and Infectious Diseases
      
      Bethesda, MD
      
      Fogarty Fellow, Laboratory of Clinical Investigation, Allergy and Clinical Immunology
      
      7/1982 – 6/1983
3. **Military Service**
   N/A

4. **Licensure**
   New Jersey State Medical License (#25MA05938300)
   Medicine, July 1993
   Expiration: June 2014

   Missouri State Medical License (#R4E80)
   Medicine
   November 1984- January 1996

   Maryland State Medical License (#D27910)
   Medicine
   June 1982- September 1986

   D.C. District Medical License (#13387)
   Medicine
   May 1982- July 1985

   New York State Medical License (#143883)
   Medicine
   October 1980- December 1985

   United Kingdom General Medical Council (#2403344)
   Medical Practitioner
   November 1977- November 2003
5. **Certification**
   Diplomate Certified: American Board of Allergy & Immunology
   No. 2570
   October 1985

   Diplomate Certified: American Board of Internal Medicine
   No. 084713
   September 1983

6. **Narcotics Certification**
   New Jersey State
   CDS License # D06284700
   Expiration: October 2015

   New Jersey
   DEA License # BD 3701679
   Expiration: June 2014

7. **University Appointments**
   Department of Medicine, Division of Allergy and Immunology
   Rutgers - New Jersey Medical School (formerly UMDNJ)
   Clinical Professor of Medicine
   July 2008- present

   Department of Medicine, Division of Allergy and Immunology
   University of Medicine and Dentistry of New Jersey - New Jersey Medical School
   Clinical Associate Professor of Medicine
   July 1994- July 2008

   Department of Internal Medicine, Division of Allergy and Immunology
   Saint Louis University School of Medicine, St. Louis, MO
Associate Professor of Medicine
July 1991- July 1992

Department of Otolaryngology, Head and Neck Surgery
Saint Louis University School of Medicine, St. Louis, MO
Assistant Professor of Otolaryngology
July 1990- July 1992

Department of Internal Medicine, Division of Allergy and Immunology
Saint Louis University School of Medicine, St. Louis, MO
Assistant Professor of Medicine
July 1985- June 1991

8. **Hospital Appointments**

Department of Medicine
Robert Wood Johnson University Hospital Somerset (formerly Somerset Medical Center, Somerville, NJ)
Attending Physician, Department of Medicine
July 2009-Present

Department of Medicine, Allergy/Immunology/Rheumatology
University Hospital, Newark, NJ
Attending Physician (Courtesy status)
July 1994- December 2009

Department of Internal Medicine
Saint Louis University Hospital, St. Louis, MO
Co-Director, Comprehensive Sinus Clinic
July 1989- July 1992

Department of Pediatrics
Cardinal Glennon Children's Hospital, St. Louis, MO
Attending Physician
November 1986- July 1992

Department of Internal Medicine
Saint Louis University Hospital, St. Louis, MO
Attending Physician
July 1985- July 1992

Department of Internal Medicine
John Cochran Veterans Administration Medical Center, St. Louis, MO
Consultant, Medical Service/Allergy
July 1985- September 1992

Department of Internal Medicine
Washington Hospital Center, Washington, DC
Junior Attending Physician
May 1984- July 1985

9. Other Professional Positions and Major Visiting Appointments

U.S. Food and Drug Administration
Industry Representative, Pulmonary-Allergy Drugs Advisory Committee
2012-2015
10. **Awards and Honors**

Travel Grant

XII International Congress of Allergology and Clinical Immunology

Washington, DC

June 1985
Travel Grant
American Academy of Allergy and Immunology Annual Meeting
Chicago, IL
March 1984

AMA Physicians Recognition Award for CME

Temple Frere Class Prize in Obstetrics/Gynecology
Middlesex Hospital Medical School, London UK
November 1977

Studentship in Community Medicine
Health Education Council of UK
1977

Third David Moore Class Prize in Obstetrics/Gynecology
Middlesex Hospital Medical School, London UK
November 1977

University of Glasgow
Certificate of Merit: Class of Clinical Obstetrics
March 1976

Nuffield Foundation Exchange Scholarship in Gynecology
University of Glasgow, Scotland
January –March 1976

11. Membership on Boards of Directors or Trustees
12. **Major Teaching Experience**

**a. Lectures**

Rutgers – New Jersey Medical School
Department of Medicine, Division of Allergy and Immunology
Introductory Course on Allergy and Immunology
2002- present

UMDNJ – New Jersey Medical School
Department of Medicine, Division of Allergy and Immunology
Basic Science Immunology Course
2002- 2006

UMDNJ – New Jersey Medical School
Department of Medicine, Division of Allergy and Immunology
Faculty mentor, Allergy and Immunology Journal Club
2002- present

Saint Louis University School of Medicine
Department of Medicine
Preceptor, “Ethics of Death and Dying” Course
2002

Saint Louis University School of Medicine
Department of Medicine
Preceptor, Community Medicine Elective
1986-1992

Saint Louis University School of Medicine
Department of Medicine
Resident Faculty Advisor
1986-1992

Saint Louis University School of Medicine
Department of Medicine
Preceptor, Internal Medicine Course
1986-1992

Saint Louis University School of Medicine
Department of Medicine
Faculty Mentor, Allergy and Immunology Journal Club
1985-1992

b. Research Training

1. Post-Doctoral Fellow
   None

2. Pre Doctoral Students
   Martha Kalasky (Penn State University)
   June 2007 – August 2007

c. Instruction to (unique circumstance)
   None

13. Principal Clinical and Hospital Service Responsibilities
    University of Medicine and Dentistry of New Jersey – University Hospital
    Department of Medicine, Division of Allergy and Immunology
    Allergy and Immunology Service Attending
    Responsibilities: Ambulatory medicine clinical practice, graduate fellow education, resident education, medical student education

Saint Louis University School of Medicine
University Hospital
Department of Internal Medicine, Division of Allergy and Immunology
Internal Medicine and Allergy and Immunology Service Attending
Responsibilities: In-patient and ambulatory medicine clinical practice, graduate fellow education, resident education, medical student education

14. Major Committee Assignments

a. International

WHO Expert Committee on Drug Dependence
Geneva, Switzerland
June 1998

b. National

Member, Taskforce on Practice Parameters for Allergic Rhinitis
Joint Council for Allergy and Immunology
October 2004 – present

Member, Taskforce on Practice Parameters for Sinusitis
Joint Council for Allergy and Immunology
October 2004 – present

New Jersey State Representative, House of Delegates
American College of Allergy, Asthma and Immunology
2011-

c. Medical School

Member, University Faculty Senate
Saint Louis University School of Medicine  
June 1991- June 1992  

Member, Biomedical Communications Advisory Committee  
Saint Louis University School of Medicine  
July 1991- June 1992  

Member, International Services Advisory Board  
Saint Louis University School of Medicine  
January 1987- June 1992  

Member, Institutional Review Board  
Saint Louis University School of Medicine  
July 1986- June 1992  

**d. Hospital**  
Member, CME Committee  
Somerset Medical Center, Somerville, NJ  
December 2009 – January 2013  

Member, Medical Staff Nominating Committee  
Saint Louis University Hospital  
July 1991- June 1992  

Member, Biomedical and Instrumentation Committee  
Saint Louis University Hospital  
July 1991- June 1992
Member, Antibiotic Review Committee
Saint Louis University Hospital
July 1990- June 1991

Member, Laboratory Utilization/Transfusion Practices Committee
Saint Louis University Hospital
July 1988- June 1989

e. Department

Member, Fellowship Review Committee
Division of Allergy and Immunology/ Department of Medicine
Rutgers - New Jersey Medical School
November 1992- present

Member, Faculty Committee
Division of Allergy and Immunology/ Department of Medicine
Rutgers - New Jersey Medical School
July 1992- present

f. Editorial Boards

American Journal of Rhinology
1992-2005

Annals of Allergy, Asthma and Immunology
1990-1995

g. Ad Hoc Reviewer

Journal Reviewer
Allergy (European Journal of Allergy and Clinical Immunology)
Allergy and Immunology Practice
American Journal of Rhinology
American Review of Respiratory Disease
Annals of Allergy, Asthma and Immunology
Diagnostic Cytopathology
Journal of Allergy and Clinical Immunology
Journal of Applied Physiology
Journal of Clinical Investigation
New Jersey Medicine
Pediatric Asthma, Allergy and Immunology
Sentinel Reviewer, American College of Physicians

Grant Reviewer
Medical Research Council of Canada
Cystic Fibrosis Foundation

15. Memberships, Offices and Committee Assignments in Professional Societies

Society for Research on Nicotine and Tobacco (SRNT)
Associate Member
2004-2006

American Academy of Allergy, Asthma and Immunology (AAAAI)
Member, Rhinitis Committee
March 2003- March 2011

American Academy of Allergy, Asthma and Immunology (AAAAI)
Member, Rhinitis, Rhinosinusitis and Ocular Allergy Committee (formerly Sinusitis Committee)
March 2003- present

The Association for Research in Vision and Ophthalmology (ARVO)
Member
2003-2005

Drug Information Association
Member
May 2002- December 2005

American Academy of Allergy, Asthma and Immunology (AAAAI)
Chair, Sinusitis Committee
March 2001- March 2002

Food Allergy and Anaphylaxis Network (FAAN)
Member
1998 - present

Consumer Healthcare Products Association (CHPA) working groups: Decongestant Subgroup, Nasal decongestant, Alcohol Task Groups; Antihistamine, Asthma, Cough/Cold, PPA, Phenylephrine, Theophylline, Dextromethorphan, Pediatric Cough/Cold Dosing
1996- 2008

Mothers of Asthmatics/Asthma and Allergy Network
Member
1994 - present

New Jersey Allergy/Immunology Society
Member
September 1993- present
American Academy of Allergy, Asthma and Immunology (AAAAI)
Task Force on Practice Standards: Sinusitis subcommittee
1991-1999

American Academy of Allergy, Asthma and Immunology (AAAAI)
Chair, Rhinitis Committee
March 1991- March 1993

American Academy of Allergy, Asthma and Immunology (AAAAI)
Workshops Sub-Committee, Continuing Medical Education Committee
March 1990- March 1993

American Physicians Fellowship for Medicine in Israel
Member
1990- present

American Academy of Allergy, Asthma and Immunology (AAAAI)
Program Committee, Asthma, Rhinitis and Respiratory Diseases Interest Section
March 1989- March 1990

American Academy of Allergy, Asthma and Immunology (AAAAI)
Chair, Nasal Provocation Subcommittee
March 1988 – March 1989

American College of Allergy, Asthma and Immunology
Fellow
May 1987 - present

American College of Physicians
Fellow
September 1986 – present
American College of Physicians
Member
September 1984- September 1986

American Thoracic Society
Member
November 1984 – October 2009

American Federation for Clinical Research
Member
March 1984- June 1987

16. Major Research Interests

My initial post-doctoral research focused on the pathophysiology of allergic rhinitis, non-allergic rhinitis and sinusitis. Using novel techniques of laser-Doppler velocimetry, and nasal provocation challenge, I developed new techniques for measurement of nasal blood flow and analysis of chemical mediators. This research extended to studies of nasal reflexes, nasal cytology and olfaction, including work in Alzheimer’s disease. More recently, I have been responsible for designing and conducting clinical studies to obtain regulatory approval for new drugs and to convert prescription drugs to over-the-counter status. These studies are in the areas of allergic rhinitis, non-allergic rhinitis, prevention of sinusitis, tobacco dependence, and symptomatic relief of dry eye conditions. I am particularly interested in developing new and more accurate measures to record and measure cough and other subjective upper respiratory symptoms.

17. Grant History

a. Principal Investigator

Abbott Laboratories.
The effects of clarithromycin on nasal mucus rheology. Co-PI with Bruce Rubin, MD.
Total amount awarded: $31,500.

Glaxo Pharmaceuticals Inc.
A randomized double-blind, placebo-controlled study of the efficacy and safety of aqueous fluticasone propionate given twice daily versus placebo for four weeks in patients with perennial non-allergic rhinitis.
Total amount awarded: $37,500.

Fisons Pharmaceuticals Inc.
A dose ranging multi-center double-blind placebo-controlled, group comparative study of tipredane nasal spray in seasonal allergic rhinitis caused by ragweed pollen.
Total amount awarded: $41,700.

Bristol-Myers-Squibb Pharmaceutical Research Institute.
A noncomparative study of cefprozil in the treatment of acute bacterial sinusitis.
1990-1.
Total amount awarded: $46,900.

Burroughs Wellcome Pharmaceuticals Inc.
A double blind evaluation of DUACT and its individual components administered four times daily for 15 days for the treatment of seasonal allergic rhinitis symptoms.
1990.
Total amount awarded: $78,000.

Syntex Laboratories Inc.
Placebo-controlled assessment of flunisolide nasal spray as an adjunct in the treatment of sinusitis.
1989-90.
Total amount awarded: $16,500.

Muro Pharmaceuticals Inc.
A double blind randomized comparative study of atropine sulfate nasal solution and placebo in subjects ages 18-59 symptomatic for allergic or perennial rhinitis with rhinorrhea as a major symptom.
1989.
Total amount awarded: $40,117.

Boehringer Ingelheim Pharmaceuticals Inc.
Randomized, double-blind, parallel comparison of intranasal Atrovent nasal spray (21 mcg per nostril) versus placebo in nonallergic perennial rhinitis.

1989.
Total amount awarded: $96,709.

State of Missouri.
Physiology of olfaction and etiology of Alzheimer's Disease.
1989.
Total amount awarded: $20,000.

Syntex Laboratories Inc.
Placebo controlled assessment of flunisolide nasal spray as an adjunct in the treatment of sinusitis.
Total amount awarded: $22,788.

Merrell/Dow Research Institute.
Equipment Grant
Total amount awarded: $3,000

Boehringer Ingelheim Pharmaceuticals Inc.
Randomized, double-blind, dose-ranging parallel comparison of intranasal Atrovent nasal spray versus placebo in nonallergic perennial rhinitis.
1987-8.
Total amount awarded: $99,802.
Fisons Pharmaceuticals Inc.
A double-blind placebo-controlled study of the efficacy and safety of nedocromil sodium nasal spray 1% QID in ragweed sensitive rhinitis.
1987.
Total amount awarded: $29,900

Merrell Dow Research Institute
A clinical study of the inhibitory properties of terfenadine on histamine-induced microcirculatory changes in nasal mucosa.
1987.
Total amount awarded: $36,116.

USPHS BRSG (Basic Science Research Grant) 396
Microcirculatory control in chronic rhinitis.
1985-6.
Total amount awarded: $15,295

18. **Major Administrative Responsibilities**

Department of Internal Medicine, Division of Allergy and Immunology
Saint Louis University School of Medicine, St. Louis, MO
Saint Louis University Hospital
Director, Nasal and Paranasal Sinus Research Laboratory
1985-1992

19. **Private Practice**

Ear Nose & Throat Care P.C. & Allergy
242 East Main Street
Somerville, NJ 08876
April 2009- Current

20. **Articles**


**Druce HM.** Sinusitis: Pathophysiology and Treatment. New York, Marcel Dekker, 1993. 336pp


22. **Abstracts**


39. Druce HM, Wheeler A. Use of the national asthma education guidelines (NAEG) to design clinical studies for asthma. 51st Annual Meeting, American College of Allergy and Immunology, Atlanta, GA, November 1993. Ann Allergy 1994;72:94.


23. Reviews


36. **Druce HM.** Diagnostic evaluation in sinusitis: How far should you go? *Masters in Allergy.* 1991;3:11-4


* Publications selected for the Reading List for Board Examination in Allergy and Immunology 1989; Compiled by the Training Program Director's Organization. (Ann Allergy 1988;61:471-82; and J Allergy Clin Immunol 1989;83:495-508), also selected for the 1990 Training Program Directors' Reading List.