# Citizen Petition

The undersigned health care providers, specializing in neurology, headache medicine and/or otorhinolaryngology, submit this petition pursuant to the Food and Drug Administration's ("FDA's") regulations at 21 C.F.R. § 10.30 to request that the FDA require that over-the-counter (OTC) products associating the terms "sinus" and "headache" (e.g., "Sinus + Headache," "Sinus plus headache," and "Sinus headache") be revised given the body of evidence that this association perpetuates the existence of an invalid and imprecise diagnosis which is potentially harmful to consumers. We believe that in current form such products are misbranded, and revised labelling would help to prevent both harms associated with unnecessary interventions as well as the headache-related disability and economic burden associated with misdiagnosed migraine.

## I. ACTION REQUESTED

This petition requests that manufacturers of OTC products associating the terms "sinus" and "headache" (for example, but not limited to: Tylenol Sinus Plus Headache Day (NDC 50580-598-02), CVS Health Maximum Strength Severe Allergy & Sinus Headache Acetaminophen Tablets (NDC 59779-543-09), revise product names and box labelling to remove the direct linkage of these specific terms (e.g., "Sinus + Headache," "Sinus plus headache," and "Sinus headache"). Revision of "headache" to "pain" or "pressure" would be more acceptable. In the current form, we believe that the association of these specific words is misleading and harms consumers given that "sinus headache," as will be described herein, has been established to be an inherently misleading label. In addition, we believe a "Sinus Headache" Warning should be added, alerting consumers that migraine is the most common diagnosis among those with sinus pain and pressure.

## II. STATEMENT OF GROUNDS

### A. BACKGROUND INFORMATION

Sinus headache is a nonspecific and imprecise diagnosis typically referring to facial pain and pressure, which providers and patients assume originates from the sinus cavities. The inaccurate diagnosis of sinus headache may lead to unnecessary diagnostic evaluations (which may be invasive), surgical interventions, medical treatments, as well as the associated morbidity from not treating the accurate cause of the patient's symptoms.[1] The International Headache Society (IHS) and the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) have jointly evaluated the concept of sinus headache and reached consensus on use of more specific diagnostic terms, also highlighting that the overwhelming majority of patients presenting with physician-diagnosed or self-described "sinus headache" have an actual diagnosis of migraine.[1,2]

### B. RATIONALE AND SUPPORTING INFORMATION

We recommend that the direct association of "sinus" and "headache" be removed from over-the-counter product labelling, in addition to a Warning about diagnosis based on the following rationale:

*a. Physician-diagnosed and patient-reported sinus headache is overwhelmingly migraine, and only rarely headache attributed to rhinosinusitis*

At least 6 prospective cohorts applied International Headache Society (IHS) diagnostic criteria to individuals presenting with physician-diagnosed or self-labelled sinus headache, all demonstrating that migraine is overwhelmingly the most common diagnosis in such patients.[3] In the largest cohort, 2,991 patients across 452 sites (predominantly primary care practices) with a physician-diagnosed or self-provided sinus headache label were prospectively assigned a formal IHS diagnosis.[4] Participants reported an average of 3 sinus headaches each month. Final diagnoses in this cohort were migraine (80%), probable migraine (8%), and episodic tension-type headache (8%). Sinus pressure (84%) and sinus pain (82%) were the most common symptoms referrable to the sinus region. In the prospective Sinus, Allergy and Migraine Study, 100 patients presenting for evaluation of sinus headache

were also shown to overwhelmingly have a diagnosis of migraine.[5] In this cohort, patients misinterpreted their pain location involving face as attributable to the "sinuses." Patients commonly misinterpreted symptoms such as nasal congestion and rhinorrhea as due to rhinosinusitis, when in-fact these symptoms are not uncommon in migraine due to cranial autonomic activation.[5]

Recently, the longitudinal CaMEO study (ClinicalTrials.gov identifier: NCT01648530), enrolling a broad cohort of demographically representative U.S. patients with migraine found that sinus headache was the most common misdiagnosis among those not receiving an accurate migraine diagnosis.[6] Finally, a randomized, double-blind placebo-controlled trial found sumatriptan (a migraine-specific therapy) to be effective in patients reporting a diagnosis of sinus headache.[7]

Therefore, there is strong evidence that the label of sinus headache, which patients frequently erroneously self-assign, is both imprecise and misleading.

*b. A label of sinus headache is associated with adverse outcomes and unnecessary interventions*

A label suggesting a relationship of "sinus" and "headache" perpetuates an imprecise and invalid lexicon, potentially confirming a consumer's impression that their impression of "sinus headache" is correct. This may lead to harmful sequelae if their belief in a diagnosis of sinus headache is implicitly validated by OTC product labels. According to Schreiber, et al,[4] "patients may conceptualize these symptoms as "sinus," as advertising of OTC sinus medications has repeatedly conveyed that pounding pain associated with these symptoms are "sinus" headache."

In the largest prospective series of 2,991 patients with physician-diagnosed or self-reported sinus headache, approximately 50% of the patients with what was actually migraine treated symptoms with inappropriate therapies such as decongestants and antihistamines.[4] Antibiotics are frequently inappropriately over-prescribed in this population.[1,8] In the prospective SAMS study, participants presenting with sinus headache had previously undergone at least one unnecessary neuroimaging test (32%), allergy desensitization procedures (27%) and/or invasive endoscopy (11%).[5] Of particular concern, 35% of the participants reported prior surgical interventions, many specifically in an attempt to relieve headache.[5]

Therefore, in the real-world, a label of sinus headache is associated with incorrect, potentially medical therapies and invasive diagnostic and therapeutic treatments, including surgery.

*c. Adverse outcomes of delaying a proper diagnosis of migraine*

For context, care for migraine in the United States is inadequate, with only a small fraction of patients traversing minimum barriers to care including consultation, accurate diagnosis, and prescription of minimally appropriate pharmacological treatment.[6] Migraine affects 1 billion individuals worldwide and is the 2nd leading case of disability in the world.[9] Remarkably, a misdiagnosis of sinus headache represents approximately 50% of cases in epidemiological studies.[6,10]

Sadly, in prospective cohorts specifically evaluating patients with physician-diagnosed or self-reported sinus headache, validated measures of headache-related disability (e.g., HIT-6 and MIDAS) are noted to be in the most severe categories.[4,5]

Therefore, the individual and societal burden associated with misdiagnosed migraine is immense.

## C. SUMMARY

The association of "sinus" and "headache" on OTC products perpetuates a nonspecific, inaccurate, and invalid diagnosis which is misleading to consumers and potentially harmful. Patients carrying an impression of having "sinus headache" are at risk for unnecessary diagnostic evaluations, surgical interventions, and medical treatments. Untreated migraine, which is the most common diagnosis among those diagnosed with sinus

headache, is associated with substantial morbidity and cost. Consumers should be specifically warned about this area of common diagnostic misinterpretation.

We thank you for your consideration.

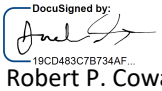
## III. ENVIRONMENTAL IMPACT

We claim a categorical exclusion from the requirement to submit an environmental assessment pursuant to 21 C.F.R. 25.30.

## IV. CERTIFICATION

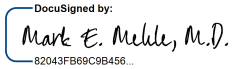
The undersigned certifies that, to the best of the knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and it includes representative data and information known to the petitioners, which are unfavorable to the petition.

1. Jonathan H. Smith, M.D, Headache Specialist, Chicago, IL[1]

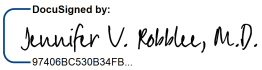



2. Robert P. Cowan, M.D., Headache Specialist, Stanford University

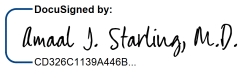

3. Mark E. Mehle, M.D., Otorhinolaryngology, Southwest General Health Center




4. Jennifer V. Robblee, M.D., Headache Specialist, Barrow Neurological Society




5. Amaal J. Starling, M.D., Headache Specialist, Mayo Clinic




6. Roy R. Casiano, M.D., Otorhinolaryngology, University of Miami, Miller School of Medicine


7. Robert E. Shapiro, M.D., Ph.D., Headache Specialist, University of Vermont


8. Frederick Godley, M.D., Otorhinolaryngology, Providence, Rhode Island


[1]*Jonathan H. Smith is a currently an employee of AbbVie. The content of this submission does not reflect the view of AbbVie.*

## REFERENCES

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