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To: FDA, CDER

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Subject: Statement Concerning Non-Sedating Antihistamines Moving to Over-The-Counter Status

Disclosure: My company, MEDTAP International, has conducted health economic research on contract with one or more of the pharmaceutical companies concerning second generation antihistamines and is presently consulting with same on the present OTC conversion issue. This statement is made on my own behalf.

Further, this statement is not a position statement. Rather it is intended to provide a technical review to the FDA and the Committee on a portion of the petition submitted by Blue Cross of California, specifically the summary study abstract entitled "Cost-Effectiveness of Converting Non-Sedating Antihistamines from Prescription to Over-The-Counter Status" by Nichol and Sullivan. In submitting our statement, we are aware that the FDA will *not* be considering health economic arguments in its decision process. However, we also understand that an important safety rationale by the petitioner is that OTC status of second generation antihistamines will increase availability of these drugs, which, in turn, will be expected to avoid unsafe consequences, specifically accidents, associated with first generation products. This projection is based, largely, on economic grounds. The Nicole, Sullivan abstract was submitted in support of the contention of increased safety due, primarily to increased availability of second generation products. Below we provide the Committee and the FDA the benefit of our review.

MODEL CRITIQUE

General

Given the available data and the decision at hand, a decision-analytic model is an ideal tool to assist the decision process and we recommend that the FDA utilize such a tool for decisions such as the present one. However, as noted below, we question whether the present submission is sufficiently refined and whether there is sufficient consensus of key assumptions to assist in the particular deliberation process at hand. In particular, we argue that some key assumptions are unreasonable.

The overall structure of the model seems appropriate.

Specific Mode Elements and Structure:

- The model does not consider the group of allergy sufferers who does/will not receive any medications (i.e., no treatment group). This may be significant in that an OTC conversion of 2nd generation antihistamines will likely result in an increase or decrease of the no treatment group (depending upon assumptions, of course) .
- The only adverse event considered in the model was automobile accidents associated with sedation. Another potential safety issue not considered is the estimated health benefit of the physician visit for diagnosis and prescription, which, presumably, would be lost in an OTC switch.

Model Assumptions:

- The model assumed that after the RX-to-OTC switch of the NSA (non-sedating antihistamines), there would be a 67% price reduction for both the first and second generation antihistamines. This number was derived from the price variations observed in H2 antagonist market. We feel that it is not appropriate to draw a direct analogy between this antihistamine model and H2 antagonists because when the latter medications switched to OTC, they also went off patent. Therefore, a 67% price reduction is unlikely to happen to the antihistamine market since all 2nd generation products still hold patent. Although we do not have a good estimate as to what if any price reduction there may be, 67% seems a gross over-estimate. This estimate is extremely important to develop a reasonable estimate of post-OTC demand (see next note).
- The model assumed that after the switch, the market share of second generation drugs would increase from less than 12% (i.e., those who received NSA in office visits) to 50%, whereas the market share of first generation antihistamines would decrease from 88%+ (i.e. 88% self-treat + those who received RX first generation in office visits) to 50%. This assumption implies a more than THREE fold increase in demand of second generation antihistamines after the switch, which seems extraordinarily high, especially since all present 2nd generation users will likely face a significant out-of-pocket cost increase. This assumption is likely driven by what we believe is an unreasonably low estimate of future OTC prices (see note above) Given a more reasonable estimate of OTC price to the consumer, one would expect a large increase in out-of-pocket expenditures for all patients who now have access through insurance. Economic theory as well as substantial empirical evidence indicate that a consumer price increase will drive demand *down* rather than up for these individuals.
- The model calculates a 'Savings' per QALY. This is a classic dominating scenario, thus does not warrant interpreting the ratio as "Savings" (i.e. negative cost) per QALY. Such interpretation is problematic because if costs were identical but more QALYs had been saved, the solution, after dividing through in the negative ratio, would be expressed as lower savings per QALY. Thus, based on the reported result, one would prefer the first option (same savings, fewer QALYs) than the second option even though the second option actually provides

for same savings and more QALYs. Conceptually, in a ratio, it is not valid to divide a positive number into a negative number, and interpret the results as "savings." (See Gold et al., Oxford University Press, 1996).

- Cost for a physician office visit (\$23) seems much too low. As well, time to see a physician (1 hour) is also too little.

Summary

A decision-analytic model is a useful and valid technique to estimate effectiveness, safety and cost-effectiveness impact of a Rx to OTC conversion of second generation antihistamines and the general approach used in the Nichol and Sullivan model seems correct. However, the model as presently specified seems to contain unreasonable assumptions, and a several technical problems, which call into question the usefulness of the findings. Specifically, we do not believe that the model as presently specified, is predictive of future demand following a hypothetical OTC conversion. The principle driving assumption which seems in error is an assumed 67% drop in price of second generation antihistamines which would lead to a predicted 3-fold increase in demand for these products. We believe, to the contrary, that a more likely scenario is that present users of second generation antihistamine users would face a large price increase which would actually *decrease* demand.