MEMORANDUM

To: Heinz Schneider

From: Michael Stoto

Re: Phenylephrine meta-analysis

Date: January 27, 2007

I have reviewed the January 23 draft of the CHPH Phenylephrine Task Group’s “Efficacy Meta-Analysis of Single-Dose 10 mg Phenylephrine vs. Placebo in Adults with Acute Nasal Congestion due to Common Cold” and am pleased to report that I find that the task group has addressed all of the issues raised in the December 20, 2006 conference call, and that in my judgment the analysis meets professional standards. As a result, I believe that the conclusions are justified.

There are, however, a number of aspects of the written report that I believe can be improved. They are the following:

p. 6 In presenting the study objectives, it should be noted that (a) individual studies will be reanalyzed in a parallel fashion and (b) a pooled (individual-level) meta analysis will be performed.

p. 12 The footnote to Table 2 is an important point to make, but it should be made in the conclusions section rather than here.

p. 13 The discussion of logs and ratios is overly complicated and confusing. It is well known that the log transformation is appropriate for ratio measures, and that the results of analyses done in the log scale should be transformed back to the original scale for presentation. A geometric mean is indeed equivalent to the retransformed mean of the logs, but this not actually being done in this analysis, so the term “geometric mean” should not be used.

p. 14 The results of study #8, now discussed in the pooled analysis section, should be moved to the conclusions section of the paper.

p. 15, l. 2 Add s to “statistical models”

p. 15 I would have labeled the second model as #1 and visa versa since that way the three would be increasingly complex.

p. 16 The second complete paragraph, beginning with “The results …”, is a result and should be moved to the results section.
Tables 3 and 4 should present the estimated difference or summary difference and a 95% confidence interval, i.e. the information in Figures 1-8.

Units should be given for the horizontal scale.
Comments on Phenylephrine Meta-analysis
M. A. Stoto, December 17, 2006

1. Choice of studies
   a. Why limit studies to before ’76?
   b. Did you search for other studies, before or after ’76?
   c. Complete references should be given for all studies
   d. “Site” looks like it might be the company performing some of the trials

2. Non-included studies
   a. Should list references and specific reason for exclusion
   b. Were results qualitatively consistent with the included studies?
   c. Was lack of individual-level data a reason for exclusion?

3. A priori choices
   a. should be made clear, including reason, at the start
   b. Rationale for excluding study #8 seems to depend on knowing that results would
      be significant without it
   c. Was choice of ΔNAR vs. ΔlnNAR a priori?
   d. Model for individual study and M-A
   e. 30 and 60 minute time points as most important output?

4. Time line
   a. Note at the start that studies tested outcomes at different points
   b. Were there results at other time points not reported here?

5. Data entry
   a. Note more clearly that individual-level data were used.

6. Outcome measure
   a. ln-ratio NAR = ΔlnNAR, which seems like a reasonable measure if NAR is a
      ratio; why was transformation used instead?
   b. ΔlnNAR might help with the departure from normality noted

7. Statistical model
   a. make more clear that this is a pooled meta-analysis (MA-P)
   b. List in text and tables as Model 1.a, 1.b, 2.a, 2.b, 3

8. Results
   a. If ΔNAR was chosen vs. ΔlnNAR a priori, it would be better to present it as such,
      with the alternative as a sensitivity analysis
   b. Report effect sizes and 95% C.I., not P-values
   c. Table 2 is hard to read since it does not make clear which studies has results at
      which levels and which didn’t
   d. Better to present Table 2 in tabular form (e.g. rows = time points, columns =
      study) with effect and 95% C.I. for each available effect estimate. Base on a
      priori choice of statistical model, then indicate differences where they appear
   e. Table 2 (M-A results): Use same format as suggested above, with columns for
      Model 2 and Model 3
   f. Note that time scale on graphs is not equally spaced
   g. Show a forest plot for each key time point, with major analysis only
Abbreviated Curriculum Vitae

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EDUCATION
Science Foundation Graduate Fellowship.

EMPLOYMENT
2006-  Professor of Health Services Administration and Population Health, School of
    Nursing and Health Studies, Georgetown University
2001-2006  Senior Statistical Scientist, RAND
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    Public Health and Health Services, George Washington University
1997-  Adjunct Professor of Biostatistics, Harvard University
1983-1998  Senior Staff Officer, Institute of Medicine, National Academy of Sciences
1979-1987  Assistant, then Associate Professor of Public Policy, J. F. Kennedy School of

TEACHING EXPERIENCE
Pardee RAND Graduate School
2003-  Research Synthesis and Meta-Analysis
Harvard School of Public Health, Harvard University
1997-  Research Synthesis and Meta-Analysis for Public Health and Clinical Medicine
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SELECTED PUBLICATIONS
1. Emerson JD, Stoto MA. Exploratory methods for choosing power transformations. Journal of
2. Hoaglin DC, Light RJ, Mosteller F, McPeek B, Stoto MA. Data for decisions: Information


12. Stoto MA. Doing and understanding meta-analysis and not being misled by the results (Meeting summary). *Current Drugs*, 1997.


Curriculum vitae of Michael A. Stoto


Institute of Medicine/National Research Council reports (with contributions from M. A. Stoto, in addition to those listed above)