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To: Guideline Task Force Participants

The essays developed by the antianxiety committee were received 11/21/72, have been reproduced, and are now in the mail addressed to 61 designated recipients. It is heartening to see this tangible indication of a strong and pertinent beginning, and I trust that the discussion at San Juan will help us evaluate our efforts and sharpen our perception of our final goal.

Since it may be preferable at San Juan to give first priority to the comments of the non-Task Force recipients, I am forwarding some of my reactions to the essays with the hope that you will consider them as we advance to our later drafts.

The essay on Selecting Subjects is an excellent statement. I wonder, however, if the "considerations," beginning with the second paragraph on page 4 could be translated directly into illustrative courses of action so that the drug house monitor has the benefit of specific suggestions for the incorporation of these considerations into the research he plans and later supervises.

The strengths of the Assessment of Change essay are too numerous for comment. Nevertheless, there are specific features which should be questioned. The words "quantified" and "measures" in the next to last line of paragraph 1 of page 1 are disturbing. All pertinent criteria do not exist in quantified form, and although they can be counted, they cannot be readily measured. For example, the number who are hospitalized during the course of treatment, the number who have improved by any criterion vs the number who have not are all pertinent.

The importance of patients' verbalizations cannot be questioned, but I get the feeling that this essay obscures the difference between the patient's verbalizations, e.g., in the interview, and his responses to a printed self-descriptive inventory. See line 7, paragraph 2, page 1, and line 2, paragraph 3, page 2. Observed verbalizations may be viewed as a symptom, but responses marked on a self-descriptive inventory are not symptoms, and it is more confusing than clarifying (See #2 on page 10) to refer to a self-descriptive inventory under the heading of Symptom Ratings.

Incidentally, how should ratings, using the last visit as a baseline (see paragraph 3, page 9), be analyzed, particularly when there is a lengthy series of visits and there is a correspondingly lengthy series of ratings, each serving as the baseline for the next rating and as a measure of improvement relative only to the last one? Also how should the drug houses be advised to analyze target symptoms, cf. the discussion on pages 10, 11, and 12.

Brief testimonials are offered for the SCL on page 10 and the POMS on page 12. The obvious merit of these two instruments is not to be questioned but published accounts of the use of these instruments in drug studies that have come to me reveal fallibility which would not be anticipated from the present material. (The enclosed comments on self-descriptive inventories illustrate this fallibility.) If specific criterion measures are to be recommended, the list should be lengthy, diversified and described with full documentation of published reports which revealed and failed to reveal drug effects.

There would be little to question in the Clinical Significance essay had the material appeared under some other title. In general, I do not see how most of the material relates to the question of clinical significance. There are some specific questions, however. What is the justification for the last statement on page 3? Cannot a treatment have a clinically significant value on the basis of its ability to ameliorate some manifestations without its being required to ameliorate all of the manifestations in which we are interested?

The correlational approach to the assessment of the size of antidepressant effects (Page 8, paragraph C) relative to the size of placebo effect may have been first used in the early 1960's (Cole and Wittenborn, Pharmacotherapy of Depression, 1966). The Assessment of Clinical Change chapter applied this approach to the reduction of anxiety and phobia in depressed patients.

The reference to an overall test of significance for a set of variables could be misleading (Page 1, paragraph 1). It is possible that the research may reveal that criteria of a given kind and content are consistently significant, while other criteria are not. The drug house monitor should not be obliged to submit all criteria to an obscuring overall test of significance when his data clearly indicate ways in which the treatment is effective and ways in which it is not.

In paragraph C on page 12, care should be taken not to confuse temporary placebo responses with spontaneous remission.

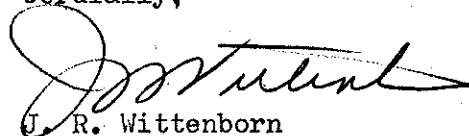
In paragraph D on page 12, the insistence on combining all criteria into an overall judgment is again encountered. On the assumption that we are talking about a state of anxiety and not a discrete symptom of anxiety, it should not be forgotten that a given drug may generate

more than one pattern or symptomatic complex of remission so that different patients may respond in different ways. Factor analyses of sets of improvement scores have suggested this possibility (See Wittenborn and Plant, J. nerv. and ment. Dis. 1963).

The Training Essay is excellent and could be most helpful in its present form. I hope that it will be possible to indicate the sources of appropriate training films, etc.

I look forward to a pleasant and constructive meeting in San Juan. In the meantime, congratulations on the progress you have made.

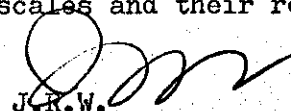
Cordially,



J. R. Wittenborn  
Task Force Coordinating Chairman

JRW:gl

P.S. You will find three enclosures: one, a set of comments urging (most of the substantive issues may soon be settled) that we begin to think about the form and structure which will be most instructive to the drug house monitor. In addition to and in resolving his own uncertainty, this man has the need for some relatively unambiguous authoritative statements which he can cite in defense of some of the procedural decisions that he must make. Enclosed also are some comments on self-report inventories. I hope that they may be seen as indicating the need for detailed documentation for any criteria recommended by the guidelines. The reprint on rating scales and their reliability, etc. is relevant to the general topic.



J.R.W.