

Sent thru Col Bottiglieri

SMUEA-RMC

23 February 1966

Dr. Albert M. Kligman
 Senior Investigator
 Holmesburg Prison
 Medical Research Section
 8215 Torresdale Avenue
 Philadelphia, Pennsylvania 19136

*Mailed
March 6⁵
per Mrs. Wason*

Attention: Dr. H. W. Copelan

Dear Herb:

Col. Bottiglieri sent the revised forms and instructions to me for review and Dr. Kitzes and I have been over them with considerable interest. We both feel that the revisions are definite contributions to the efficiency of the recording system. I personally feel that you have done an excellent job on both forms and, in particular, I was impressed with the manner in which you have solved the problem of combining a rating scale with informal notes and observations on a single page. This is highly desirable for the sake of simplicity and ease of use.

Thank you for conforming with my suggestions about retaining the items on the Behavior Checklist. We have recently made a detailed analysis of the dose levels at which each of these items becomes positive in 50% of the subjects, the ED₅₀, in effect, for each clinical sign. Separate solutions were worked out for mild and severe (1+ and 2+, respectively) and the pattern is very revealing. Most of the signs associated with delirium (for example, hallucinations and non-sensical speech) are rated severe at about the same dose as we have estimated to be the incapacitating dose, using the NF as the criteria for incapacitation. In other words, by analysis of these signs we are able to attach greater meaning to the NF and in a sense validate it.

As you know, many of our medical officers will be leaving this summer and there will be new replacements coming along. Col. Bottiglieri and I feel it desirable to initiate one or two of the newer doctors into the Holmesburg program so that some continuity can be maintained in the year ahead. I hope to arrange a trip within the next month at which time I will try to bring one of these medical officers with me.

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SMUEA-RMC
Dr. Albert M. Kligman

23 February 1966

I believe Dave Kitzes has informed you of the laboratory findings in one of our subjects which showed a transient rise in SGOT, SGTP and LDH values. These are now subsiding but as yet the etiology remains unclear. We would appreciate a list of the subjects that you have tested with this agent (302,368) at each dose level, together with a summary of the pre-and post-exposure liver function values you have recorded. I do not think that there will be any hesitation in the testing program as a result of this single case. We all feel, however, that it is important to review the situation as thoroughly as possible before proceeding.

A number of possibilities have been suggested for further work at Holmesburg and as soon as we have had a chance to sort these out and make a selection we will contact you by phone to recommend additional studies.

I hope all is well with you and yours. Looking forward to visiting you in the near future,

With best wishes,

Sincerely yours,

1 Incl

JAMES S. KETCHUM
Major, MC
Chief, Clinical Research Department
Medical Research Laboratory
Research Laboratories

P.S. I am returning the original of your manuscript. We have made several zerox copies for reference.

JSK

*Copy furnished
Col Battiglen*

DA-18-035-AMC-126-(A)

HOLMESBURG PRISON

REVISION OF EXPERIMENTAL DATA FORMS

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February 1, 1966

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REVISION OF EXPERIMENTAL DATA FORMS

The forms used to record the experimental data have been revised. Some information was eliminated, some was added and the formats were changed. The Medical Research Laboratories were consulted to insure that needed data would not be eliminated. The new forms should guide and simplify the reliable recording of pertinent information. More important, the information will be organized so that interpretation should be less difficult and more valuable.

The data is to be recorded on two forms, a "Subject Data Sheet" and a "Test Behavior and Rating Sheet". The "Subject Data Sheet" replaces the various previous "Experimental Data Sheets". It covers the readily measurable data of the experiment such as vital signs, NF performance and simple subjective indices of peripheral effect. It also details the computation of dosage. The "Test Behavior and Rating Sheet", replaces the old "Test Data Sheet". It provides for the chronological numerical rating and narrative description of altered behavior.

The details of the changes and the respective reasons are listed below in the order that they occur on the sheets. Samples of the new forms are included.

SUBJECT DATA SHEET

1. Height and age are included to allow convenient reference in assessing dosage (as for surface area or age variability) and evaluating effect (as with age and visual blurring).
2. The route of administration is important and is now added to the record.
3. The dosage computation shows every step in the calculation and guides the arithmetical computation from the weight in pounds to the volume injected. (Only the simple arithmetical conversion from micrograms to milligrams is not shown.) The calculated quantities are indicated by double underlining. These changes should minimize errors and simplify checking.
4. The technician is specifically instructed to indicate and explain entries that presented problems. This should decrease the frequency of technical error and allow for interpretation of errors that occur.

5. A column is added for the date. This need be completed only for the initial entry and whenever the date changes. Although the value of a date column is limited for most testing, it should be helpful with long-acting agents.

6. The time of injection is placed in the table of observations as the first entry at zero experimental time. This simplifies calculation of subsequent real times.

7. The observations are arranged in the order they are to be performed during the usual testing procedure. This arrangement guides the technician and simplifies recording.

8. Vital signs are specified as "supine" to guide the technician and the reviewer.

9. Columns for orthostatic pulse and blood pressure are included for experiments where such measures may be important.

10. Simple subjective measures of peripheral effect on salivation and visual accommodation are included. Recording of pupil size alone was inadequate to estimate peripheral effect. Tabulating these measures also allows easy determination of their relationship to central effect.

11. The base-line NF score is included for ease of computation of subsequent NF percentage scores. Subsequent NF raw scores are shown to speed recording and simplify checking.

12. The technician who performs each set of observations identifies himself. This promotes accuracy and simplifies later review of entries.

13. Column width is varied according to the space needed for the respective entries and double lines are used to facilitate entering data in the proper columns.

14. There is no column for "Remarks". This is unnecessary for problem entries, since these are to be handled as described above. Also, "Remarks" are not required for description of behavior because the "Test Behavior and Rating Sheet" will accomplish this. The old "Remarks" column was too small to use well, redundant and confusing since, separate behavior description sheet was also used.

15. The NF low average is included to estimate intensity better than "positive" or "negative" alone.

16. The time for onset and duration of effect are included for ease of review.

TEST BEHAVIOR AND RATING SHEET

1. The records of vital signs, pupil size, NF raw score and inclusive times are eliminated. Simple identifying data for the subject and then the times and NF percentage score for each set of observations are essential.

2. Instructions are included so that the technician will know when to complete the ratings or narrative descriptions.

3. Essential instructions for the content of the narrative description are included to increase the value of these records.

4. The technician is instructed to write across the entire page to conserve space. (The vertical lines do not significantly impair legibility.)

5. The ratings are listed in an order that facilitates the conduct of the observations.

6. Two ratings are added to the former list. The "Lethargic, drowsy" rating will provide one objective measure of simple sedation, and the "Slurred speech" rating will provide a helpful index of coordination, disorganization and sedation.

7. The rating specifics are arranged with spaces between groupings. This facilitates recording in the proper column and groups ratings that are to be made together. If other specific aspects of behavior are later desired these spaces could be utilized for such ratings.

8. The ratings and narrative for each time are immediate to each other and provide a more complete evaluation and easily reviewed description.

9. Several sets of ratings and narrative descriptions of varying length can be included in chronological order on a single sheet. An entire experiment will require few sheets. This reduces the confusion and labor of interpretation.

SUBJECT DATA SHEET

Agent: _____ Surname, Initials: _____ Subject No: _____ Ht _____ In _____ Age _____ Yrs.

Route: _____ Wt _____ lb + 2.2 = _____ kg x dosage _____ ug/kg = Total dose _____ mgm

Concentration _____ mgm/ml = Total volume _____ ml Injection by _____ M.

OBSERVATIONS (Circle problem entries and explain on reverse side)

Date	Exper. Time	Real Time	Temp. Ax. F.°	Supine			Standing		Dry Mouth 0,1,2*	Pupil Size (mm)	Blurred Vision 0,1,2*	N.F.		Test B. (Initi
				Pulse	B.P.	R.	Pulse	B.P.				Raw	%	
	Injection 0000								0		0	Baseline 100		

* 0-absent; 1-slight; 2-marked
Released by: _____ M. D. _____ Date _____ NF Low Average _____ Onset _____ Duration _____ POSITIVE of NEGATIVE

