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POINTS TO CONSIDER IN THE
DESIGN AND IMPLEMENTATION OF FIELD TRIALS FOR
BLOOD GROUPING REAGENTS AND ANTI-HUMAN GLOBULIN

1st draft 1992

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**POINTS TO CONSIDER IN THE
DESIGN AND IMPLEMENTATION OF FIELD TRIALS
FOR BLOOD GROUPING REAGENTS AND ANTI-HUMAN GLOBULIN
1ST DRAFT 1992**

In response to concerns expressed over the intent in performing field trials on new Blood Grouping Reagents and Anti-Human Globulin Reagents and the subsequent impact on field trial design and implementation, a portion of the November 1990 workshop, "Reagents for the 1990's" was devoted to the discussion of these parameters. A consensus was reached on many elements and the major points of concern have been incorporated into this document. It should be noted that these products have not required the filing of an Investigational New Drug Application (IND) for conducting field trials.

PURPOSE OF FIELD TRIALS - Field trial testing of blood grouping reagents and anti-human globulin reagents is performed after the manufacturer has documented specificity and potency. It is useful primarily to show that the directions for use are adequate, that a broad cross-section of unselected samples give expected results, and that the product performs as expected in the hands of routine users rather than experts.

DESIGN OF FIELD TRIALS - Trials should be constructed to adequately represent the situations and sample mix in which the product will be used.

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I. GENERAL

- A. Field trials should commence only after the manufacturing methods and performance criteria are well established and the manufacturer has determined the recommended methods for use and established that the reagent achieves accurate and reproducible results, i.e.:
1. The reagent has been assessed in-house or through contract by a minimum of 300 tests.
 2. Potency is equal to or greater than the reference preparation.
 3. The reagent is specific by all package insert methods. A panel of appropriate rare cells should have been employed.

II. SAMPLES/SITE SELECTION

A. Reagents

1. Reagent under test
 - a. at least 2 lots
 - b. made by the method described in the application for license
 - c. at least 1 lot must be a batch intended for distribution
2. Approved referee reagent (currently marketed, licensed product or other product approved by FDA¹)
 - a. must meet or exceed an approved polyclonal (unless a new, unique product)
 - b. an approved monoclonal is optional, in most cases
3. Blind coded

¹ If a licensed product is not available for use as a referee reagent, approval from FDA to use an unlicensed product for this purpose may be requested.

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B. Representative Sites

1. Usually at least 3 (excluding the manufacturer's own laboratories)
2. Cover different geographic regions
3. Cover population distributions
4. Cover different facility sizes and procedures
5. Cover different facility functions
 - a. blood collection establishment
 - b. transfusion service
 - c. clinical laboratory
6. Sites outside of the US are acceptable if US standards (i.e., CGMP's) are followed in protocols and recordkeeping.

C. Number of tests

Generally, sample size should be chosen to ensure that, statistically, a minimum of 10% of the samples will be either negative for the antigen corresponding to the antibody under test or positive for the antigen corresponding to the antibody under test with exceptions for very rare specificities.

1. Unselected samples for qualifying new ABO or Rh_o(D) reagents - normal donor samples
 - a. manual or microplate - 3,000 - 5,000 if no problems are encountered
 - b. automated - routine production samples tested for 5 days by at least two operators
2. Selected samples - unusual samples
 - a. additional manual tests - each of the selected samples listed in D. below

² Smaller numbers may be appropriate for reagents other than ABO and Rh_o(D).

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D. Selected samples - must represent the patient/donor population

100 of each of the following

1. Variations in collection and storage

- a. Clotted samples
- b. Anticoagulated samples (cover each that is recommended)
- c. Fresh samples
- d. Frozen/deglycerolized cells³
- e. Stored samples (at 28 days and/or the anticoagulant expiration date, whichever is longer)
- f. enzyme treated cells, if not prohibited by labeling

2. Variations in donor/patient age

- a. elderly people (> age 80)
- b. cord samples

3. Ethnic groups/known variants

- a. Variable, depending on reagent under test
ex. Oriental (B_{sub}) for ABO
Black (D variants) for D
- b. Unselected Caucasian, Black, Hispanic, Asian

³ Fewer than 100 samples may be used if a smaller number can be shown to be adequate.

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10 - 25 of each of the following

1. Disease groups
 - a. acquired antigens, if pertinent
 - b. serum protein abnormalities
 - i. multiple myeloma
 - ii. Waldenstrom's macroglobulinemia
 - iii. pregnant women
 - c. autoimmune hemolytic anemia
 - d. oncology patients
 - i. lymphomas
 - ii. leukemias
2. Interfering substances
 - a. polyagglutinable cells
 - b. positive direct antiglobulin test
 - c. lipemic sample
 - d. hemolyzed sample
3. Other
 - a. Exalted expression of the antigen
 - b. Weakened expression of the antigen

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- E. Methods - all methods/specimens listed in package insert
 - 1. All sites by tube test
 - 2. At least 1 site by slide⁴
 - 3. At least 1 site by microplate⁴
 - 4. At least 1 site by automated method⁴

- F. Records
 - 1. Clearly defined protocol
 - a. define consistent recording procedures
 - b. include detailed analysis of discrepancies
 - c. maintain documentation of known samples and sample sources
 - 2. Complete
 - 3. Consistent with GMP's

- G. Follow-up
 - 1. Discrepancies must be reported to the manufacturer immediately and studied by the manufacturer or a referee laboratory.
 - 2. Aberrant samples should be stored for reference and submitted to FDA if requested.

⁴ If applicable.