Part B. Statistical Methods

1. Respondent Universe and Sampling Methods

For the PDUFA VI IND communications assessment, FDA needs a sample of INDs that are likely to have activity during a one-year period and that adequately represent IND traits of interest:

- **Sponsor size:** small, medium, large, and private
- **Breakthrough Therapy Designation (BTD):** with and without BTD
- **Regenerative Medicine Advanced Therapies (RMATs):** with and without RMAT status
- **Clinical review office:** in each of the 6 CDER offices, 3 CBER offices, and OCBQ
- **Meeting types:** with Type A, B, B (EOP), and C meetings during the data collection period
- **IND phase:** in pre-IND phase and Phases 1, 2, and 3

The number of commercial INDs with activity each year is approximately 4,000. For this assessment, FDA has selected a target sample size of 150 INDs. FDA's independent contractor for this assessment, ERG, will develop the sample by (1) establishing target distributions for the IND traits of interest, (2) asking FDA's Center for Drug Evaluation and Research (CDER) Performance Analysis Data Services Staff (PADSS) and Center for Biologics Evaluation and Research (CBER) Regulatory Information Management Staff (RIMS) to generate a list of commercial INDs to draw from, (3) removing INDs that do not meet inclusion criteria, (4) randomly selecting 150 INDs that cover the target distributions of traits of interest to the extent feasible, and (5) reassessing the sample at 3 months and 6 months to replace INDs as needed to achieve target numbers and distributions of INDs. See the table below for the target number and distribution of INDs. Where feasible, ERG will oversample in categories where target allocation numbers are small (n<10).

Table 3. Target number and distribution of INDs by trait and category.

IND Trait	Categories	Target Allocation *(+/- 5 percentage points)*
Sponsor size	Small	39% (58 of 150)
	Medium	11% (17 of 150)
	Large	24% (36 of 150)
	Private	26% (39 of 150)
BTD	With BTD	4% (6 of 150)
RMAT	With RMAT	1% (1 of 150)
FDA review office	OAP	11% (17 of 150)
	ODEI	16% (23 of 150)
	ODEII	17% (25 of 150)
	ODEIII	14% (6 of 150)

IND Trait	Categories	Target Allocation *(+/- 5 percentage points)*
	ODEIV	2% (3 of 150)
	OHOP	21% (32 of 150)
	OBRR	2% (3 of 150)
	OCBQ	0% (0 of 150)
	OVRR	4% (6 of 150)
	OTAT	12% (18 of 150)
Meeting type	Type A	4% (6 of 150)
	Type B	48% (72 of 150)
	Type B (EOP)	12% (18 of 150)
	Type C	36% (54 of 150)
IND phase	Pre-IND	TBD
	Phase 1	37% (56 of 150)
	Phase 2	47% (70 of 150)
	Phase 3	16% (24 of 150)

FDA's contractor will send surveys and interview requests to the primary contacts for INDs in the sample (usually Regulatory Affairs managers) because they have expertise and experience with both the INDs being reviewed and the regulatory and communication practices being implemented. Based on experience with previous PDUFA-related assessments, FDA estimates that the response rate for this information collection will be greater than 90%.

2. Procedures for the Collection of Information

FDA's contractor, ERG, will create an initial sample of 150 active commercial INDs as follows:

1. Assign a reference ID to each IND in the list of commercial INDs to draw from.
2. Divide the total number of INDs in the list by 150 (rounded to the nearest whole number), i.
3. Using a random number generator, produce a number between 1 and i.
4. Add the IND with i as its reference ID to the initial sample.
5. From i, add every 150th IND to the initial sample.
6. Create a list of INDs in the initial sample, with flags for traits of interest.
7. Evaluate the list to determine which traits of interest are over- or under-represented.
8. For traits that are over-represented, randomly remove INDs. From the list of remaining INDs to draw from, randomly select INDs from the subset of INDs that have the trait of interest to add to the initial sample. Repeat until target allocations are met.
9. Generate a list of INDs in the initial sample, along with target and actual allocations table.

The contractor will offer surveys and interviews only to sponsors of INDs in the sample that have communication activity. For each IND in the sample, the contractor will email a link to an online fillable survey to the primary contact for the IND directly after a formal (Type A, B, B End of

Phase, C) meeting has taken place; a text version of the survey is attached. In the second half of the data collection period, the contractor will email an interview request to the primary contact for the IND to obtain broader feedback on all types of communications with FDA review staff that have taken place; the interview script is attached. Also attached are templates/scripts for contact emails and calls to IND sponsors to request and remind them of surveys and interviews.

3. Methods to Maximize Response Rates and Deal with Non-response

FDA's contractor for this PDUFA VI IND communications assessment, ERG, has conducted other PDUFA-related information collections with response rates exceeding 95%. ERG will implement the same procedures successfully used with those previous information collections to maximize response rates. These procedures include:

- Before information collection begins, ask FDA staff to notify IND sponsors in the sample that ERG might contact them to request participation in IND meeting surveys and IND communications interviews.
- Where appropriate, ask FDA staff to incorporate reminders about possible survey/interview requests from ERG in the form of notices in routine written communications to IND sponsors in the sample.
- For each IND in the sample, send survey/interview requests to the IND sponsor staff who have been most engaged in interacting with FDA.
- For a first non-response, send a follow-up email.
- For additional non-responses, call sponsor representatives directly to request participation or to identify alternative representatives to participate.
- Continue to follow up until the IND sponsor confirms participation or explicitly declines to participate.
- Send interview reminders before scheduled interviews.

4. Test of Procedures or Methods to be Undertaken

FDA expects only fine tuning changes to the information collection activity. FDA therefore seeks a combined approval of a pretest (consisting of the first five surveys administered for the assessment) and the main survey.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

FDA consulted with the following people on statistical aspects of the assessment design:

- Reza Kazemi-Tabriz, FDA Office of Program and Strategic Analysis, Performance Analysis and Data Services Staff (301) 796-3686
- Louis Nadeau, ERG (781) 674-7316
- Valerie Overton, ERG (781) 674-7398

The people who will collect and analyze the information for FDA are:

- Hannah Busey, ERG
- Marc Goldstein, ERG
- Kuang-Heng (Jason) Hsiao, ERG
- Louis Nadeau, ERG
- Valerie Overton, ERG
- Christopher Sese, ERG