

## Questions in Site Selection Questionnaires

By Norman M. Goldfarb

Study sponsors and contract research organizations (CROs) distribute site selection questionnaires to collect information for evaluating whether to invite sites to participate in a study. Current questionnaires and the processes surrounding them are clearly inadequate, since most sites underperform their contracted commitments, which are often scaled back from questionnaire estimates.<sup>1,2</sup> Sponsors share responsibility for this underperformance because they design and conduct the site selection process.

Site questionnaires can also:

- Determine the site's level of interest in the study.
- Interest the site in the study.
- Obtain statements and commitments to which the site can be held.
- Impress the site with the sponsor, perhaps for future studies.
- Collect information useful in changing or managing the study.
- Collect information for future studies.
- Help the site think through operational aspects of the study, such as subject recruiting.
- Help the site determine whether it wants to participate in the study.

We cannot expect too much from site questionnaires. They are an efficient way to collect certain types of information for screening purposes and as the basis for a discussion, but they cannot replace the discussion. They are no substitute for the human-to-human interaction and meeting of the minds that are essential to productive working relationships. In theory, a site qualification visit enables these interactions, but the common box-checking exercise is just a slow and inaccurate way to complete questionnaires. The site questionnaire thus needs to be designed as part of a larger process. A thorough site selection process is time-consuming, but the adages "look before you leap" and "measure twice, cut once" clearly apply to site selection.

Just because a question can be in a questionnaire does not mean it should be; asking the question in an interactive discussion may reveal essential subtleties and create person-to-person connections. For example, the site may offer a "war story" as its answer. War stories have little statistical value, but they communicate human values that are difficult to share in other ways.

The last two purposes above are critical. Sponsors can never have complete, up-to-date information about a site. A properly designed questionnaire facilitates the site's decision process. If the site thinks through the study and realizes it is not a good fit, everyone saves time. Empowering the site helps build the relationship and may also elicit more honest answers.

Sites need adequate information to answer questionnaires accurately. An obvious example is asking a site how many subjects it can enroll in a flu vaccination study without specifying the time parameters. The sponsor may not know essential information when distributing the questionnaires, but specificity is more likely to yield results that are comparable from site to site.

Site questionnaires should be designed to accomplish the sponsor's objectives. In particular, the questions should:

- Be necessary to the purpose.
- Be sufficient to the purpose.
- Be clear and unambiguous.
- Be straightforward to answer with readily available information.
- Provide adequate options and space for the answer.
- Allow a broad range of answers.
- Not reveal the "right" answer.
- Accommodate the characteristics of different types of sites.
- Show respect for the site.
- Generate answers that the sponsor can interpret and score.
- Generate answers that the sponsor can validate for predictive ability.

A well-designed questionnaire gives insights into the site's complex, subtle personality. True/false, multiple-choice and numeric answers are easy to read and tabulate, but they do not reveal the site's thought processes. Most sites can figure out the right answer. Elicit comments and allow space to elaborate on an overly simplistic answer. For example, the questionnaire may ask, "How many subjects will come from inside your practice?" The answer is highly dependent on the site's organization: Is the investigator a sole-practitioner? If he or she is in a multi-physician clinic, how are treatment responsibilities shared? Do other departments in a hospital count?

Sloppy questionnaires with typos, ambiguous questions, and inadequate space for answers tell sites that the sponsor is not very interested in the answers and does not respect the sites. Asking the same question in two different ways shows disregard for the site's time or disrespect for its competence. Sponsors should test all questionnaires on a sample of sites, or at least on internal personnel with site experience, before sending them to the entire site pool.

How many questions are sites willing to answer? The number of questions is only one factor in the site's assessment of the cost and benefit of completing a questionnaire. The primary costs are time, effort and aggravation. The benefits derive from the probability of being selected for a study that the site wants to conduct and the use the sponsor will make of the answers. A well-crafted questionnaire addresses both sides of the equation in numerous ways.

The globalization of clinical research introduces even more variety into the suitability of questions and comparability of answers. For example, there is no need for a U.S. sponsor to ask a Brazilian site if translation of the informed consent form is required.

Many answers can be scored automatically or by low-cost labor with clear instructions. Scoring may vary by study. For example, satellite sites may be desirable in some studies, but taboo in others. A precise score for each answer is not important. Use broad ranges to triage sites into essential, possible and unlikely categories for appropriate follow-up. The scores can also be used to identify potential trouble spots at individual sites and for the site population as a whole. In addition, they can be tested for their ability to predict subject enrollment and other aspects of site performance.

Web-based questionnaires with branching questions can efficiently collect required information. For example, it is not necessary to ask sole practitioners about biohazard safety committee approvals. At minimum, create different versions of the questionnaire for large and small sites.

The questionnaire should arrive at the site with a cover letter. A study summary is required to answer many of the most important questions. Sponsors cannot anticipate what a given site needs to know about the study, so the summary should be as complete as possible. For example, a site may not have access to an essential resource at certain times.

Sponsors and CROs also send study feasibility questionnaires to sites for planning a study or preparing a proposal. Study feasibility questionnaires look a lot like site selection questionnaires. Using one questionnaire for both purposes implies either that the feasibility answers will have minimal effect on the protocol or that the selection questions may have to be asked again if the protocol changes. Clearly describe the purpose of a questionnaire so sites are not misled. This article discusses site selection questionnaires, but many of the questions are also applicable to study feasibility questionnaires.

The questionnaire should start with an introduction along the lines of:

Please answer the questions below to the best of your ability. Your answers will help us determine if your site is a good fit for this study and also future studies. Your answers can also help you decide if you want to participate in the study. Please return the completed questionnaire ASAP, and certainly no later than \_\_\_\_\_. If you are uncertain how to answer a question, contact us at \_\_\_\_\_. We hope you can participate in this study, but our highest priority is to build lasting relationships with capable sites. We hope to complete the site selection process by \_\_\_\_\_.

Sites are more likely to provide complete, thoughtful and truthful answers if they believe the sponsor will give due consideration to the answers and not discard the information after sites are selected for the current study. Confirm receipt of questionnaires. Demonstrate with follow-up questions before, during and after the study that the site questionnaire is an important document. When the selection process is complete, inform sites that have not been selected. Explain that the selection process is imperfect and suggest how they can improve their chance of selection in the future. Sites that are offended by these suggestions may not be good sites for future studies.

The most efficient questionnaires are partly completed before the site even sees them. It is not hard to guess the investigator's name and fax number, especially if the questionnaire is faxed to the site. Answers from previous questionnaires can be pre-filled. Sponsors can use low-cost labor to transcribe information from the site's website, at least for the most desirable sites. Inaccurate information can be updated or corrected easily if the questionnaire is online or electronic.

A physically compact questionnaire is preferable, but not if it interferes with the answers. Allow plenty of space for answers and comments.

A question may be more significant than it seems to be on the surface. The answer may also provide information about the site's level of interest in the study, capacity to take on a new study, level of sophistication, commitment to quality, and honesty. For example, thoughtful answers suggest that the site is interested in the study and has time to do the thinking. Neatly written answers suggest that the site will complete the study documentation neatly and produce high-quality results in general.

It is unrealistic to expect a site questionnaire to provide all useful information. For the purpose of selecting sites, the questionnaire is just one step in a process. At minimum, there is likely to be a site qualification visit. It may be worthwhile splitting the questionnaire into two parts and holding the second part for sites that pass the first screen. The tradeoff has to be evaluated: Sequential questionnaires introduce delays, but the first one is more likely to be returned quickly. A two-step questionnaire process may also attract better sites, which can be choosy about the questionnaires they complete.

## Analysis of Site Questionnaires

The author reviewed 72 site questionnaires and found over 200 different questions, not counting many follow-up questions (e.g., "How many?") and numerous variations. The next section presents questions most likely to be useful. The section after that presents alternative and additional questions, which may be useful. The questions below have not been validated for basic properties, such as clarity or ease of answering, much less predictive value. For simplicity, the questions are for a hypothetical study of a new treatment for the willies, a condition that involves feelings of uneasiness, e.g., when entering a haunted cave.

These questions are useful not just for sponsors and CROs, but also for sites. Sites can create a database of answers for future use. The questions suggest what information sponsors would like to see on research site websites, and what site capabilities sponsors are looking for.

### Questions

The following questions are suitable for many studies:

#### Site

1. Site and department name
2. Type of practice or institution: University Hospital, Community Hospital, Group Practice, Private Practice, Stand-alone Research Center, Other: \_\_\_\_\_
3. How many active patients does your [site/department] have (visits within past 12 months)?
4. How many physicians at your site treat patients with the willies?
5. How many clinical research studies are currently active at your [site/department]?
6. How many physicians at your [site/department] are currently principal investigators on clinical research studies?

#### Investigator

7. Investigator name
8. Credentials (MD, PhD, CPI, FACC, etc.)
9. Contact information: Address, phone (back line), fax, email, website
10. Do you have the time and resources to conduct this study?
11. Do you want to conduct this study?
  - a. Why?
12. What are your primary areas of practice with %s? Area A \_\_, Area B \_\_, Area C \_\_, Other: \_\_\_\_\_
13. What % of your work time do you devote to clinical research?
14. What human subjects protection (HSP) and good clinical practice (GCP) training and certifications do you have?
15. Are you affiliated with a site network or SMO?
  - a. Name?
16. How many clinical research studies have you conducted in the past three years?
17. What % of these studies has been industry-sponsored?

18. In what % of these studies have you been the principal investigator at your site?
19. How many clinical research studies are you currently conducting?
20. How many clinical research studies have you conducted in the past three years on the willies?
21. How many clinical research studies have you conducted in the past three years on related conditions?
  - a. Describe

### **Subject Enrollment**

22. How many subjects did the investigator enroll in any study in the past 12 months?
23. How many subjects did the investigator enroll in studies of the willies in the past 3 years?
24. How many studies at your [site/department] will be enrolling subjects with the willies during [time period]?
25. How many active patients does the investigator have (visits in past 12 months)?
26. Of these, how many [had or have/are newly diagnosed with] the willies? (Specify eligible ICD-9 codes in the study summary.)
27. Of these, how many meet the eligibility criteria provided in the study summary?
28. Based on the study summary, how many subjects do you expect to enroll from the investigator's practice in [time period]?
29. How many additional subjects do you expect to enroll from elsewhere in your site?
30. How many additional subjects do you expect to enroll from outside your site?
31. How many patients do you expect to screen for each enrollment?
32. Will this study appeal to your patients?
  - a. Why?
33. Does your site use electronic medical records (EMR)?
  - a. How many active patients does it contain with the willies?
  - b. How will the site monitor access EMR records?
34. Do you have a different database you can use to identify potential subjects for this study?
  - a. Describe
  - b. How many active patients does it contain with the willies?
35. How will you find subjects from outside your site? Advertising \_\_%, referrals \_\_%, other methods (with %s):
36. What is your process for contacting potential subjects and bringing them into your site?
37. Will you need the informed consent form in a language other than English?
  - a. What language(s)?

### **Study Coordinator(s)**

38. How many actively enrolling studies do your CRCs typically manage?
39. How many study nurses/coordinators (CRCs) will participate in this study?
40. Who will the primary study coordinator be?
41. How many years & months has he/she been a CRC at your site?
42. How many years & months of clinical research experience does he/she have?

43. What credentials (CCRC, RN, PA, MD, etc.) does he/she have?
44. What human subjects protection (HSP) and good clinical practice (GCP) training and certifications does he/she have?
45. What % of work time does he/she spend on clinical research?
46. How many studies has he/she managed on the willies?
47. Does the CRC have time for this study?
48. Does the CRC want to manage this study?
49. Contact information: Phone, fax, email

### **Capabilities & Resources**

50. Does the [investigator/team member] have adequate experience with [assessment/procedure/assessment/test]?
51. Who will perform [assessment/procedure/assessment/test]?
52. Do you have access to [equipment, pharmacy, lab, dry ice, secure storage, etc.] with adequate capacity (during the required hours)?
53. Do you actively use clinical research standard operating procedures (SOPs)?
  - a. Describe
54. How many subinvestigators will enroll subjects?
  - a. Describe

### **Site Initiation**

55. How long does it typically take your site to start a study of this type (from receipt of final protocol to site initiation visit)?
56. Does your site pursue IRB/IEC approval at the same time as contract & budget completion?
57. Will you use [the study's IRB/IEC] for this study?
58. If not, what is the name of the IRB/IEC you will use?
  - a. How often does it meet?
  - b. How long does it typically take from submission to receipt of approval letter?
59. Are there additional approvals or review committees?
  - a. Names & approval times?

### **Other**

60. Has your [site/investigator] been inspected by the FDA or similar regulatory agency in the past five years?
  - a. What was the outcome?
  - b. Provide copy of 483 or equivalent document.
61. What challenges and risks, if any, do you see for this study? If so, how will you address them? How can we, the sponsor, address them?
  - a. Study design
  - b. Subject recruiting, screening & enrollment
  - c. Subject adherence & retention
  - d. IRB and other approvals
  - e. Contract & budget

62. Additional comments or questions
63. Which, if any, of the answers above are uncertain?
64. Who completed this questionnaire?
65. Role and contact information (if not above)

### **Alternate and Additional Questions**

The following questions may be suitable for some studies in the initial questionnaire, follow-up questionnaire, or a discussion:

#### **Site**

[none]

#### **Investigator**

66. Do you consider yourself a key opinion leader? Explain
67. How many years of clinical research experience do you have?
68. On average, how many (industry-sponsored) clinical studies do you conduct per year?
69. What % of your studies are investigator-initiated?
70. When was your last study of the willies?
71. List 5 previous trials of the willies, with details: class of compound, indication, phase, # of subjects enrolled, year.
72. Do you have experience with this type of study? (e.g., gene therapy)
73. Are you board-certified? Board-eligible?
74. Do you have a DEA license?
75. Have you conducted a study with a Schedule 1 study drug?

#### **Subject Enrollment**

76. What is the estimated monthly/annual/current number of [potential/eligible] subjects available for this study?
77. What % of patients with the willies are likely to be interested in participating in a clinical trial?
78. Does this study offer your patients an acceptable risk/benefit ratio?
79. What types of patients would you enroll or not enroll in this study?
80. What % of patients with the willies participate in clinical trials?
81. How will you identify potential subjects for this study?
82. How do you typically recruit subjects for studies of the willies?
83. How will you recruit subjects for this study?
84. If your initial subject recruiting plan is inadequate, what is your contingency plan?
85. If your initial subject recruiting plan is inadequate, what is your back-up plan?
86. Are you willing to submit a blinded list of at least nn potential subjects (who have expressed interest in the study)?
87. Would you be willing to work with a centralized subject recruiting program?
88. Do you have access to potential subjects in a hospital/living facility? If so, is traveling to the facility a problem?

89. From what [departments/units/labs/clinics] at your site will you recruit subjects?
90. Can you enroll/screen potential subjects 24/7?
91. What geographical area do you serve and what is its population?
92. What is the [disease/severity/comorbidity/age/gender/race/geography] of potential subjects?
93. What % of new patients previously received [therapy]?
94. What is your standard of care for the willies?
95. What % of patients with the willies normally receive [therapy]?
96. Are you willing and able to use [study therapy]?
97. Do you currently use [therapy] to treat the willies?
98. Are you willing and able to conduct a placebo-controlled study of the willies?

### **Study Coordinator(s)**

99. He/she has experience with EDC in how many studies?
100. Does he/she have a computer with high-speed Internet access for EDC?
101. Does he/she have experience with electronic subject diaries? Describe
102. Who would the other key members of the study team be, and what would their roles be?

### **Capabilities & Resources**

103. Can you use a central laboratory?
104. Do you have a local laboratory? What is its name?
105. What is your site's access to public transportation?
106. Is parking readily available? At what price?
107. What waiting areas are available for family members and during long visits?
108. What food and beverage services are available? During what hours?
109. Do you have a pharmacist to prepare study drug?
110. Do you have a subinvestigator who can do blinded assessments?
111. What is the brand and model of the equipment?
112. Can you administer study drug during [required hours]?
113. Do you have a dedicated, analog, direct-dial fax line?
114. Do you provide Internet access to site monitors with laptops, without special login or configuration requirements?
115. How many satellite sites will participate? Describe

### **Site Initiation**

116. Can you use our standard clinical trial agreement template (with negotiated modifications, if any)?
117. What contracts are needed other than a clinical trial agreement with both the site and investigator?
118. Can you attend a site qualification visit in [period of time]?
119. Can the investigator and CRC attend the investigator meeting on [dates]?



### **Other**

120. Has your [site/investigator] been audited by sponsors in the past five years? When and what was the result?
121. Do you want to participate in the PK sampling part of this study?
122. Do you have experience with PK sampling?
123. What is the primary language at your site?
124. Do the investigator and CRC speak English?
125. Do you have a 24/7 contact available for subjects?

### **References**

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