B. Collections of Information Employing Statistical Methods

The agency should be prepared to justify its decision not to use statistical methods in any case where such methods might reduce burden or improve accuracy of results. When Item 17 on the Form OMB 83-I is checked, "Yes," the following documentation should be included in the Supporting Statement to the extend that it applies to the methods proposed:

1 1. Describe (including a numerical estimate) the potential respondent universe and any sampling or other respondent selection methods to be used. Data on the number of entities (e.g., establishments, State and local government units, households, or persons) in the universe covered by the collection and in the corresponding sample are to be provided in tabular form for the universe as a whole and for each of the strata in the proposed sample. Indicate expected response rates for the collection as a whole. If the collection had been conducted previously, include the actual response rate achieved during the last collection.

The universe of possible respondents includes 191 innovator pharmaceutical companies (those companies that produce name-brand drugs), 60 biotechnology firms (those innovators that produce biologic products), and 181 generic firms[1]. However the focus of the study will be on the top firms in each group, since these firms are likely to be early adopters of new technology and are also most likely to have a larger impact on pharmaceutical quality. The CRADA partner will fax to the top 20 Pharmaceutical companies and Top 20 Biotech Companies a notice of the opportunity to participate in the study. It will send the fax to a Management Level person in each of the offices of Regulatory, Development, and Information Management. Also, the FDA will post the CRADA abstract on its website, once OMB approval is received. Since companies self-select for participation in the study based on the described broadcast of the opportunity, it is not possible or relevant to compute a response rate.

2 2. Describe the procedures for the collection of information including:
3 * Statistical methodology for stratification and sample selection,
4 * Estimation procedure,
5 * Degree of accuracy needed for the purpose described in the justification,
6 * Unusual problems requiring specialized sampling procedures, and
7 * Any use of periodic (less frequent than annual) data collection cycles to reduce burden.

Since the study is not a statistically based survey, the techniques above do not apply.

[1] Based on companies with at least one new drug application or abbreviated new drug application submission during the last five years.

8 3. Describe methods to maximize response rates and to deal with issues of non-response. The accuracy and reliability of information collected must be shown to be adequate for intended uses. For collections based on sampling, a special justification must be provided for any collection that will not yield "reliable" data that can be generalized to the universe studied.

Based on interest expressed during the pilot phase, we do not expect any difficulty in meeting the target of 25 companies as participants in the full study. Participation will be increased after OMB approval by more widespread promotion of the study, including posting of the announcement on FDA's web site and various industry meetings involving the Office of Pharmaceutical Science. Factors which will further promote participation include (1) individualized, confidential feedback to companies on findings that relate to them, to be provided by the CRADA partner; and (2) the opportunity to provide candid comments to FDA while protecting the source of the comments. It is well known that companies are hesitant to provide critical comments to FDA in open forums, fearing possible retaliation (whether this fear is justified or not).

9 4. Describe any tests of procedures or methods to be undertaken. Testing is encouraged as an effective means of refining collections of information to minimize burden and improve utility. Tests must be approved if they call for answers to identical questions from 10 or more respondents. A proposed test or set of test may be submitted for approval separately or in combination with the main collection of information.

As indicated in part A of the Supporting Statement, statistical analysis is not expected to be a significant factor in the study because of the small sample size and the method of data collection. In fact, this study could be characterized as a "qualitative" study under OMB guidelines for surveys (see Question 21 of OMB's January 20, 2006 memo providing Guidance on Agency Survey and Statistical Information Collections). However, objective quantitative analysis will play a role, along with interpretive analysis inherent in focus group interviews involving open-ended questions. That quantitative analysis is expected to be rudimentary, involving the computation of response means by characteristics of company.

Since the top pharmaceutical and biotechnology companies will serve as the sampling universe, the resulting sample will necessarily have relevance for the portion of the industry producing most pharmaceutical and biotechnology products. This is consistent with FDA's goal of impacting the processes and standards used to produce quality pharmaceutical products for the consumer. As part of its statistical evaluation of study results, the CRADA Partner will evaluate the portion of the industry participating in the study, based on product volumes and sales volumes, for the 25 firms selected for the study.

At the conclusion of the study, the findings will be made available to pharmaceutical and biotechnology companies through appropriate published documents. Workshops or

seminars will also be conducted at FDA and other places to disseminate the information gathered during the study. In all cases, study findings will be appropriately qualified as not statistically representative of industry as a whole but only of those companies studied. The findings will be used, as is typical of qualitative studies, to lead to productive discussion in public workshops and possibly to spur more directed, follow-on study. The exact nature of any follow-on efforts will depend on study findings.

Summarized below are preliminary results from the pilot involving seven companies to date. These results were presented to FDA staff by the CRADA Partner and strongly suggest areas to explore further if FDA is to be successful in implementing its pharmaceutical development initiatives (the ‘‘Critical Path Initiative’’, Pharmaceutical cGMPs for the 21st Century—A Risk Based Approach; and ICH Q8--Defining the Design Space).

These results were based on an analysis by the CRADA Partner, taking mean scores of the seven preliminary companies involved in the study pilot. The final report will contain a more detailed analysis, including the distribution of scores and how variations relate to company characteristics, e.g., size of company, type of pharmaceutical or biological product, etc. These results should help FDA to focus its program of implementation by identifying areas that may need further investigation or discussion with industry.

Table 1. Process Analytic Technology (PAT) in Development				
Enabler	**1. Not Enabled**	**2. Emerging**	**3. Partially Enabled**	**4. Fully Enabled**
Awareness of Initiative				●
Understanding/Definition		●		
Examples of Success	●			
Implementation		●		
Management Oversight & Support	●			
Understanding of Required Systems/Tools	●			
Know How to Demonstrate Process Understanding	●			
FDA Commitment	●			

For example, the preliminary results of Table 1 suggest that those surveyed are aware of the PAT initiative but not convinced of FDA's commitment to it.

Table 2. Quality by Design				
Enabler	**1. Not Enabled**	**2. Emerging**	**3. Partially Enabled**	**4. Fully Enabled**
Awareness of Initiative				
Understanding/Definition				
Examples of Success				
Implementation				
Management Oversight & Support				
Understanding of Required Systems/Tools				
Know How to Demonstrate QbD				
Perceived Benefits to Implementation				
FDA Commitment				

Table 3. Design Space/ICH				
Enabler	**1. Not Enabled**	**2. Emerging**	**3. Partially Enabled**	**4. Fully Enabled**
Awareness of Initiative				
Understanding/Definition				
Examples of Success				
Implementation				
Management Oversight & Support				
Understanding of Required Systems/Tools				
Know How to Demonstrate Design Space				
Perceived Benefits to Implementation				
FDA Commitment				

Table 4. Information Management				
Enabler	**1. Not Enabled**	**2. Emerging**	**3. Partially Enabled**	**4. Fully Enabled**
Awareness of Initiative	●			
Understanding/Definition	●			
Examples of Success	●			
Implementation		●		
Management Oversight & Support				●
Understanding of Required Systems/Tools	●			
Know How to Demonstrate PAT, QbD, Design Space, etc	●			
Perceived Benefits to Implementation			●	
FDA Commitment				●

10 5. Provide the name and telephone number of individuals consulted on statistical aspects of the design and the name of the agency unit, contractor(s), grantee(s), or other person(s) who will actually collect and/or analyze the information for the agency.

Since this is a qualitative study, not involving statistical sampling and analysis, it was not necessary to consult with others on statistical aspects of the design.