Is This the Future?

A company we know just had the "pleasure" of a very intense FDA GCP-related inspection. Given the recent news items and agency announcements regarding FDA's revamping of its inspection approach, we wanted to share some first-hand observations related to this inspection:

1. The company is neither a sponsor nor an investigative site, nor was this presented as a directed) inspection. Yet there were two and sometimes three inspectors at the company for a six-week period. In our experience, this level of attention for such a company is not typical unless it would have been a directed inspection, in which case two-three inspectors on site for six weeks wouldn't raise an eyebrow. Will this scope of coverage by the FDA become typical? Will this be the new inspection standard? We, of course, don't know. However, we feel strongly that every company involved in efforts supporting a clinical submission should be prepared to be inspected by the agency.
2. FDA focused heavily on validation- and Part 11-related issues: documentation of all major computerized systems was reviewed for weeks, with volumes of copies being taken off-site for FDA's further assessment and future reference. This seems to be in line with the FDA's announced intention regarding 1) conducting a series of inspections to evaluate industry's compliance and understanding of Part 11 and 2) taking appropriate action to enforce Part 11 requirements for issues raised during the inspections that do not fall under the enforcement discretion discussed in the August 2003 "Part 11, Electronic Records; Electronic Signatures — Scope and Application" guidance.
3. Several FDA-483s were issued and, in some cases, broad statements, rather than specific instances of non-compliance, were cited. Based on these broad statements, general conclusions regarding the company's compliance status were drawn by the inspectors. Lack of detail in FDA-483's and lack of an objective basis against which to compare the response increase the risk of a Warning Letter since FDA-483s without specifics limit the company's ability to respond in a way that FDA would find acceptable.
4. The inspectors asked that the company respond in writing to informal recommendations and observations that were communicated to the company verbally. The reason for this shift in approach is not well understood, and one does not know how this information will be used by the agency (e.g., will it result in a Warning Letter if the responses are deemed to be inadequate?)

In the event that this inspection is representative of a "new" or "changed" FDA, the question becomes whether traditional mock FDA inspections, which are normally limited to three-four days with one to two people, can be effective. We doubt it: as compared to what this particular company experienced, 1) the scope of the traditional "mock" inspection is too limited and 2) companies cannot allocate sufficient time or resources to support a "mock" inspection with several "inspectors" on site for this many weeks.

So what, from a practical perspective, can a company do to compensate for lack of time and resources that would be required to perform a true "mock" FDA inspection exercise? How can a company be as prepared as possible for an unexpected FDA visit of the magnitude described above? We recommend the following: 1) conduct more frequent in-process inspections/internal audits to confirm that processes are being followed, documentation is available, data integrity issues are identified/assessed/corrected as soon as possible, etc., 2) hire third-party auditors to perform at least selected audits for purposes of gaining a fresh and unbiased perspective regarding regulatory compliance, and 3) provide closer oversight regarding areas that may not have received sufficient internal attention in the past (e.g., validation and Part 11-related activities). While these recommendations may not render a company risk-free, they will certainly help to minimize regulatory implications of what may be a "new" or "changed" FDA's inspection approach.

Note: approximately two months after the completion of this inspection, the sponsor received an FDA approval without the "pleasure" of a visit from the agency.

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