should identify those components that were successful and ensure that they are used for their new study. However, caution should be exercised and due diligence pursued if the new study requires a different subject population or analytical technique. For example, a CRO may specialize in recruiting healthy male and female volunteers but may have difficulty in the recruitment of postmenopausal females. Similarly, a successful bioanalytical project using liquid chromatography does not guarantee success with more complex methods such as liquid chromatography–mass spectrometry. On the other hand, if the firm had a negative experience with a particular CRO, the firm should objectively assess the cause of that experience.

All CRO evaluations should begin with an assessment of information in the public domain. The firm should obtain copies of past FDA inspection reports (483's and Establishment Inspection Reports) through the Freedom of Information. Also, the firm should request any FDA warning letters that may have been issued to the CRO.

The CRO should provide the client with a written and signed statement that neither the CRO nor any of its employees or any subcontractors has been debarred by the FDA (under the provisions of the U.S. Generic Drug Enforcement Act of 1992). The CRO should also provide performance metrics used for tracking timelines and financial metrics. The company should request "references"; these references should include those companies that outsourced studies that resulted in successful ANDA or NDA approvals.

The firm should carefully evaluate any external providers (subcontractors) that the CRO proposes to employ (e.g., clinical laboratories, medical specialists, and specialized assay laboratories). The success of the clinical program (in this case, a BA or BE study) is dependent on the weakest link.

Another important aspect (but one that is difficult to objectively assess) is the support that will be provided by the study program manager. This individual is responsible for overseeing of the various functions within the CRO and often functions as the "program champion" and must be capable of managing a multidisciplinary development team. The program manager also manages timelines and serves as communication facilitator within the CRO team and between team and sponsor. This individual has a focus on overall objectives with eye on the final deliverable and timelines.

The larger CROs have expertise in a number of therapeutic areas and can provide consulting capabilities if needed. Although some CROs provide some limited gratis consulting, the real expertise is usually available on an hourly billing rate. The consulting that is available in the larger CROs covers regulatory, medical, clinical, biopharmaceutics, pharmacokinetic, and statistical issues. Availability of this consulting is key when the "unexpected" happens during the study conduct. The unexpected can include analytical failure or unanticipated adverse events, abnormal pharmacokinetic behavior, or inability to prove BE.

After evaluating the credentials and performance metrics of each CRO, the sponsor should physically visit and audit the clinical, bioanalytical, and pharmacokinetic capabilities of the CRO.

Clinical Site Qualification/Audit

The sponsor should conduct a site qualification visit. In addition to a cGCP site audit, this evaluation should include an assessment of the areas in Table 12.2.