

Adaptive Clinical Trials

Streamlining and Improving the Development of Medical Treatments

Rely on PPD's proven knowledge and experience in adaptive clinical trials to help you significantly streamline investigational drug and medical device development.

- Implement the most appropriate type of adaptive trial to meet your requirements through the comprehensive knowledge base cultivated by our statistical scientists
- Accumulate and access data quickly and efficiently with our existing global technological tools that offer rapid data handling and sharing
- Maximize the success of your project with our multi-functional team managing the operational, technological, statistical, regulatory, scientific, financial and logistical aspects of your trial

Benefits of Adaptive Trials

Pharmaceutical and medical device companies continue to face intensifying pricing pressures and generic competition, shrinking pools of qualified study participants, and protracted development timelines. Companies feel a greater need to develop medical treatments more efficiently and rapidly.

Adaptive clinical trials offer significant advantages in meeting these industry challenges. They are novel types of studies that use accumulating trial data to decide how to change aspects of the study, while maintaining validity and integrity. By using accumulating data to decide how to change aspects of the study, adaptive trials represent a tool for significantly streamlining drug and device development. They offer significant advantages for trial participants, patients and sponsors:

- **Accelerated timelines:** Seamless Phase II to III trials can significantly reduce the time between completion of Phase II and start of Phase III
- **Fewer treatment failures:** Change inclusion/exclusion criteria if interim results suggest that certain

subpopulations do not respond

- **More precise estimation of dose response information:** Adaptive dose response trials are typically able to investigate more dose levels for the same overall sample size of the trial
- **Appropriately-sized trials:** Sample size redeterminations enable adjustments to the sample size based on data collected so far and can correct assumptions based on incomplete information
- **Better focus on key patient populations, endpoints and hypotheses of interest**

PPD's Proven Expertise

While adaptive trials provide important benefits, they demand extra steps beyond those of conventional trials:

- Additional meetings and coordination with regulatory authorities
- Rapid, repetitive data handling
- Sophisticated statistical methods to account for multiple analyses
- Automated adaptation algorithms

PPD has the global expertise, experience and infrastructure to meet the additional demands of adaptive trials:

- Statistical scientists with a wealth of knowledge and experience in the wide range of techniques that can be employed to conduct adaptive trials
- Interactive response systems for randomization, flexible and reactive investigational product supply management, electronic case report forms and participant diaries
- PPD® Real-Time Analysis (see below)
- All these technologies are joined together by an integrated information platform to enable rapid, accurate data transfers between data systems and decision making

Examples of PPD's adaptive trials experience:

- Sample size redetermination—started trials with modest sample sizes, conducted interim analyses and, where appropriate, increased the numbers of subjects. This technique improved determinations of sample sizes, reducing treatment failures while ensuring statistical power
- Seamless Phase II to III—the data monitoring committee used results from multiple investigative doses within Phase II, to choose a single dose to bring into the Phase III setting Interim analysis with early stopping rule—conducted interim analysis once the primary endpoint on 50% of participants was observed, to provide the potential to close the trial if sufficient evidence about the treatments accumulated
- Adaptive randomizations—specifically the minimization technique, in which each participant was assigned treatment so as to tend to minimize a function of the imbalances between treatment groups in several baseline characteristics, with appropriate adjustment to control type I error and maintain power. This procedure significantly enhanced baseline comparability between treatments and, thus, confidence in the statistical and medical conclusions.

PPD offers a wealth of insights and experience in adaptive clinical trials. We have conducted adaptive trials in oncology, general medicine, nervous system disorders, metabolic disorders, infectious diseases and autoimmune disorders, among others. When you enlist PPD's extensive resources, we will assign a well-orchestrated, multi-functional team to expertly implement and oversee the associated regulatory, scientific, financial and logistical aspects, maximizing the success of your project.

PPD® Real-Time Analysis

This automated production environment, where statistical analysis programs are executed on a pre-defined schedule, provides a critical means of monitoring data accrual from the beginning of a trial, identifying data issues early and monitoring patient safety as the trial progresses. It means clients can conduct adaptive designs, even fully sequential designs, with very little time lag between data accrual and analysis. The system minimizes ugly data surprises and enables rapid closeout of fixed and adaptive trial designs. It dramatically improves quality and efficiencies when compared to studies in which data are first reviewed near the end of the trial.