Protocol Amendments COME AT A HIGH COST

Trending now: New analysis provides insight into the impact of clinical trial amendments and how to anticipate and manage them.


Ken Getz

RESEARCH SPONSORS implement at least one substantial global amendment for almost 60% of all clinical trial protocols, substantially reducing the number of actual patients screened and enrolled, but leading to significantly longer clinical trial durations and higher costs, a newly completed analysis by the Tufts Center for the Study of Drug Development (CSDD) concludes.

The total median direct cost to implement a substantial amendment for Phase II and Phase III protocols is $141,000 and $535,000, respectively, according to the Tufts CSDD analysis, which defined a substantial amendment as any change to a protocol on a global level requiring internal approval, followed by approval from the institutional or ethical review board or regulatory authority.

In addition, almost half of all substantial amendments — most often undertaken to modify study volunteer demographics, eligibility criteria, and safety assessment activity — are deemed avoidable by sponsor organizations, Tufts CSDD said.

"The positive news is that unplanned delays, disruptions, and costs associated with protocol amendments have spurred the research-based biopharmaceutical industry to identify new approaches to simplify protocol design and reduce the frequency of amendments," says Ken Getz, associate professor and director of sponsored research at Tufts CSDD.

Other findings include:

- Phase II protocols have the highest incidence of substantial amendments (77%), averaging 2.2 amendments per protocol.
- Protocols with even one amendment experience a substantially lower actual number of patients screened and enrolled relative to plan, compared with protocols without any amendments.
- Study conduct durations for protocols with at least one substantial amendment take on average three months longer, compared with protocols without any amendments.
- 38% of changes made as a result of substantial protocol amendments are related to safety assessment activity and 21% are related to efficacy assessments.

Market Access Activities Should Be at Least 18 Months Ahead of Launch


Jacob Presson

A new pharmaceutical industry study found that among surveyed companies, market access teams would prefer to start working on products an average of 4.6 months before they currently start supporting new products. According to research from primary intelligence firm Cutting Edge Information, market access groups would ideally start work on launch sequencing and health economics research at least a year and a half before a product launches.

On average, market access teams would ideally prefer to start conducting products support activities 18.7 months before launch, compared with 14.1 months currently. Payer relationship management is currently only entering market access teams' purview around 4.4 months before launch, on average. The study's data show that ideally these activities would begin at least 10 months before launch. Health economics and outcomes research (HEOR) is a particularly important area to begin work well before launch.

"Getting market access teams involved earlier allows them to begin laying the groundwork for a successful launch," says Jacob Presson, senior analyst at Cutting Edge Information. "Our research has found that allowing more prelaunch time for market access teams to build effective value cases can make the difference in today's price-sensitive pharmaceutical market."

Healthcare CRO Market to Grow

The global healthcare CRO market is expected to reach $45.2 billion by 2022, according to a new report by Grand View Research. With the increasing number of patents expiring, increasing number of partnerships to identify biologics and new compounds and growing R&D costs, drug maker and sponsor companies are under pressure to replace the revenue loss specifically due to generics, which has further made drug development more expensive and complex.

In addition, growing pressure on industry players to follow stringent timelines has increased the demand for outsourcing of research activities. Even government organizations are outsourcing their clinical trial activities to CROs so that they can carry out the clinical trials with the required infrastructure, expertise, and minimize cost and timelines.

North America was the largest regional market with revenue share estimated at over 40% because of the presence of global industries, which invest maximum of their revenue in research activities. In addition, many academic institutes receive grants to undertake these activities.

Europe was the second largest market in 2014. This is attributed to the tax benefits offered to the large and small-scale companies to promote more CRO activities.

Asia Pacific is the fastest growing industry due to the reduced cost it offers in comparison to the U.S and other developed economies. China and India are projected to witness tremendous growth in the CRO market owing to their treatment naïve patient pool coupled with disease prevalence rate. Furthermore, genetically diverse population, highly qualified English-speaking investigators, well-equipped hospitals are other opportunities offered by India for global clinical trials.

Therapeutic trax

Blood Disorders

The market for hemophilia A and B recombinant therapies is set to experience limited growth, rising from $5.4 billion in 2014 to $6.3 billion by 2024. This increase represents a CAGR of 1.52% across Argentina and the seven major markets of the US, France, Italy, Spain, Germany, the UK, and Japan, a product of high treatment rates and market saturation.

Source: GlobalData

Contraceptives

The global oral contraceptive pills market was valued at $13.1 billion in 2014 and is expected to exhibit a CAGR of 6.6% from 2015 to 2023, to reach an estimated value of $22.9 billion in 2023. The combination contraceptive pills segment held the largest share of the market in 2014. The segment is projected to expand at the highest CAGR during the forecast period from 2015 to 2023, due to high efficiency against pregnancy prevention, rising preference toward combination pills, and easy availability. Based on category, the generic contraceptive pills segment dominated the oral contraceptive pills market in 2014.

Source: Transparency Market Research

Infectious Diseases

The global chronic hepatitis B therapeutics market will rise in value from $2.4 billion in 2014 to $3 billion by 2024, representing a modest CAGR of 2.4%. This expansion, which will occur over the eight major markets of the US, France, Germany, Italy, Spain, the UK, Japan, and China, will be slight due to the patent expiration of all existing branded drugs in the chronic hepatitis B therapeutics space during the forecast period, and continued low diagnosis and treatment rates of the disease

Source: GlobalData

The methicillin-resistant staphylococcus aureus treatment market will experience limited growth over the next decade, rising from $1.4 billion in 2014 to $1.45 billion by 2024. This increase, which will occur across the seven major markets of the US, Japan, the UK, France, Italy, Spain, and Germany, represents a very modest CAGR of 0.4%.

Source: GlobalData.

Respiratory Diseases

The pulmonary arterial hypertension therapeutics market will experience modest growth from $3.45 billion in 2014 to $4.75 billion by 2024, representing a CAGR of 3.2%. The increase in PAH treatment sales, which will occur across the seven major markets of the U.S., France, Germany, Italy, Spain, the UK, and Japan, will be driven by new drug launches, the increased use of double and triple combination therapies, and patient assistance programs by manufacturers.

Source: GlobalData

Drug Companies Outsource Clinical Data Management

Clinical development teams now outsource higher percentages of tactical roles, such as data management and trial monitoring, than strategic ones, such as new product planning or medical communications. A recent study of more than 40 clinical development teams found that 83% of Top 10 and Top 50 pharmaceutical companies outsource responsibility for clinical data management compared to 40% of medical device companies.

A clinical outsourcing benchmarking study published by Cutting Edge Information also found that 40% of Top 10 and Top 50 drug manufacturers outsource traditional trial monitoring responsibilities. Additionally, 40% of small pharmaceutical and biotechnology companies outsource trial monitoring.

The frequency of activities outsourced and the percentage of the role that external parties actually handle do not always go hand-in-hand. The extent that teams rely on third parties varies depending on multiple factors, but namely company size and activity type. For example, data management ranks among the top activities that surveyed teams prefer to outsource.

"Activity type may shape a clinical team's willingness to outsource," says Sarah Ray, senior analyst at Cutting Edge Information. "Surveyed teams prefer to retain much of the strategic responsibility for clinical trials in-house."

Half of the surveyed companies report outsourcing some aspect of clinical development. However, teams often report outsourcing smaller percentages of clinical development and other strategic elements than execution-driven or tactical responsibilities.

Among the companies that do outsource clinical development, external teams are typically only responsible for 11% of total clinical development duties.

Developing a strong operational foundation for clinical studies is a necessity for pharma and device organizations alike. Working hand-in-hand with knowledgeable third-party groups can help sponsors' clinical teams fine-tune study protocols and expedite trial timelines.

Oncology Corner...

News and updates around cancer-related R&D, trends, services, and products.

The Cancer Moonshot

A National Coalition has been formed to accelerate the development of new cancer therapies. In January, leaders from pharma and biotech companies — including Celgene, Amgen, NantWorks, NantKwest, Etubics, Altor Bioscience, and Precision Biologics — as well as major academic cancer centers and community oncologists announced the launch of The National Immunotherapy Coalition (NIC), a historic alliance. These companies and others are working in collaboration with Independence Blue Cross, one of the nation's largest payers, and Bank of America, one of the largest self-insured companies in the United States, with a singular focus: accelerating the potential of combination immunotherapies as the next generation standard of care in patients with cancer.

This collaboration will make access possible to more than 60 novel and approved agents under exploration in the war against cancer and will enable rapid testing of novel immunotherapy combination protocols, forming the basis of The Cancer MoonShot 2020.

One program under the collaboration is the QUILT (QUantitative Integrative Lifelong Trial) program, which is designed to harness and orchestrate all the elements of the immune system, including dendritic cell, T cell and NK cell therapies, by testing novel combinations of vaccines, cell-based immunotherapy, metronomic chemotherapy, low dose radiotherapy, and immunomodulators.

The QUILT Program will be stratified across multiple Phase I and Phase II trials, addressing up to 20 tumor types including breast, lung, prostate, ovarian, brain, head and neck, multiple myeloma, sarcoma, pancreatic cancer, among others. Pharmaceutical and biotechnology partners have made an unprecedented commitment to make more than 60 novel immunotherapy, targeted therapy, and chemotherapeutic agents available to be combined across multiple tumor types.

"There are unique times in history when events and advancements in technology converge to elicit a quantum leap in medical care," says Patrick Soon-Shiong, M.D., founder and CEO of NantWorks and the Chan Soon-Shiong Institute of Molecular Medicine. "This is not only a unique time, but also a unique inflection point in the history of cancer. The era of immunotherapy has taken the oncology world by storm. For the first time in 40 years there is a glimmer that we may be able to win this war against cancer."

The goals of the Cancer MoonShot 2020 Program were first presented at a meeting hosted by U.S. Vice President Joseph Biden in December 2015 and highlighted by President Barack Obama in his State of the Union Address in January 2016.

Ogilvy CommonHealth Worldwide Joins Forces With Cancer Support Community

Ogilvy CommonHealth Worldwide has formed a partnership with the Cancer Support Community (CSC) and healtheo360 to launch the #4Chords4Cancer initiative, a campaign created to ensure all people impacted by cancer are empowered by knowledge, strengthened by action, and sustained by community.

Through the #4Chords4Cancer campaign, the CSC will send a Martin D-28 acoustic guitar, courtesy of Martin Guitar on a tour around the United States to be played, signed, and photographed with some of the top artists in the music industry including Sara Bareilles, Laura Benanti, Jay Jay French, cast members from ABC's show Nashville, and cast members from Andrew Lloyd Webber's School of Rock.

The guitar will then be auctioned off at the CSC's annual Spring Celebration gala in New York City. Funds raised will help increase cancer awareness.

Cancer Death Rates Continue to Drop

Steady reductions in smoking combined with advances in cancer prevention, early detection, and treatment have resulted in a 23% drop in the cancer death rate since its peak in 1991. The drop translates to more than 1.7 million cancer deaths averted through 2012. The findings are included in Cancer Statistics, 2016, the American Cancer Society's latest annual report on cancer incidence, mortality, and survival.

Overall cancer incidence is stable in women and declining by 3.1% per year in men (from 2009-2012), with one-half of the drop in men due to recent rapid declines in prostate cancer diagnoses as PSA testing decreases. Cancer mortality continues to decline; over the past decade of data, the rate dropped by 1.8% per year in men and 1.4% per year in women. The decline in cancer death rates over the past two decades is driven by continued decreases in death rates for the four major cancer sites: lung, breast, prostate, and colon/rectum.

Cancer Trax

Brain Cancer

The blioblastoma therapeutics market will grow dramatically from $659 million in 2014 to $3.3 billion by 2024, as promising new therapies are introduced.

Source: GlobalData

Breast Cancer

The global breast cancer therapeutics market is set to increase in value from $10.4 billion in 2014 to $17.2 billion by 2021, at a CAGR of 7.3%. This growth will be primarily due to substantial increases in the prevalence of breast cancer.

Source: GBI Research

Gastric Cancer

The treatment market for gastric and gastro-esophageal junction adenocarcinoma (gastric cancer) will experience rapid growth, from $1.13 billion in 2014 to reach $4.39 billion by 2024, representing an impressive CAGR of 14.6%. This rise, which will occur across the eight major markets will be driven by the introduction of premium-priced therapies for advanced gastric cancer.

Source: GlobalData

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