



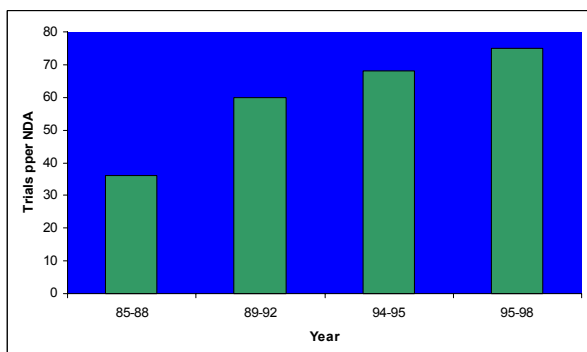
A Marketing-Centric Approach to Patient Recruitment in Clinical Trials

US pharmaceutical companies often miss their deadlines when testing new drugs. Recruiting patients to participate in the trials is the #1 reason deadlines are missed to launch new drugs. A marketing centric approach to manage the recruitment of patients for clinical trials could speed things up considerably.

Testing new drugs is a costly and frustrating headache for pharmaceuticals companies—and the pain is about to get worse. Clinical trials are at best difficult to manage and dogged by delays, and now the genomics revolution and stricter regulatory standards are compounding the problems. For pharma companies, managing the newly increased demands of clinical trials may become the greatest obstacle to realizing the full benefit of the new health technologies.

Matters are made worse by increased number of clinical trials for each New Drug Application or NDA (see exhibit 1).

Exhibit 1 The increased number of clinical trials per NDA places extra burden on pharma companies to take a different approach of patient recruitment

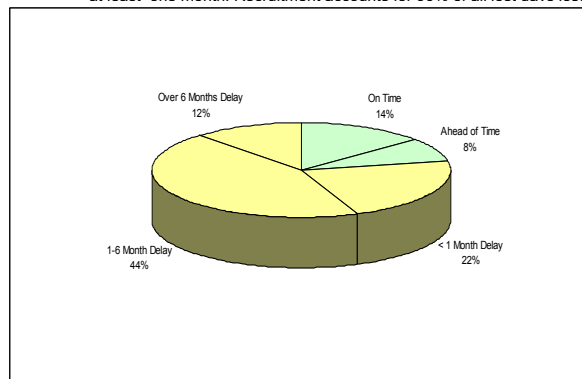


Source: CenterWatch, PhRMA, and Vaxa Inc. analysis

Not surprisingly, it is the clinical aspects of these trials that pharma companies concentrate on: making sure that the research methodology or protocol leads to results capable of standing up to the scrutiny of authorities such as the US Food and Drug Administration (FDA).

But another crucial element—the recruitment of patients—is often overlooked, causing expensive delays that can drain much of the sales potential from any new drug. More than seventy-five percent of all US clinical trials from 1993 to 1998 missed their deadlines by at least a month (Exhibit 2).

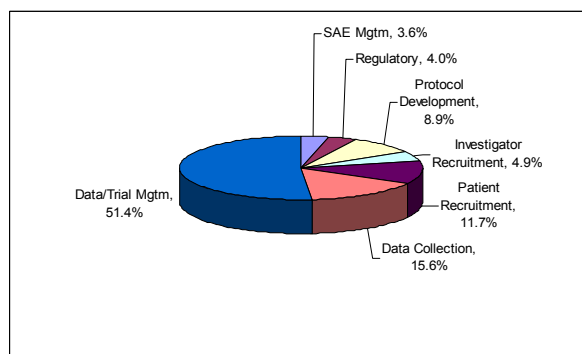
Exhibit 2 Between 1993-98, over 50% of all clinical trials missed their deadlines by at least one month. Recruitment accounts for 90% of all lost days lost.



Source: PhRMA, and Vaxa Inc. analysis

Up to 2001, patient recruitment consistently accounted for about 12% of clinical trials expenses (exhibit 3) but it continued to have the largest impact in terms of trials missing their due dates.

Exhibit 3 In 2001, Patient Recruitment accounted for about 12% of expenses of all US clinical trials but resulted in over 2/3 of all trials being late.



Source: CenterWatch, Vaxa Inc. analysis

The fresh opportunities created in 2000, when the human genome was finally charted¹, are set to increase the demand for patients in clinical trials. Drug research focuses on discovering novel targets: the biological mechanisms, usually receptors or enzymes in human cells, through which drugs work. By mapping the genome, scientists have increased the number of potential targets—to as many as 10,000 from about 500—and the R&D costs associated with developing new drugs could double. As more new drug targets enter the R&D pipeline, poor recruitment could become a bottleneck, hampering a company's ability to bring new drugs to market expeditiously. Delays can cost pharma companies at least \$800,000 a day in lost sales for a niche medication,

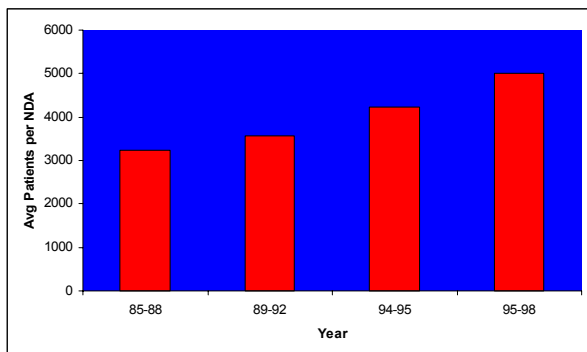
¹ In fact, only about 98% of human genome was mapped at that time but was sufficient enough for it to be used for research purposes.

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such as Amaryl, an oral antidiabetic treatment, and as much as \$5.4 million for a blockbuster like Prilosec, a gastrointestinal medication. If some of this revenue is merely deferred, it may be recouped once a drug goes on the market, but millions of dollars in revenue can vanish if a competitor catches up or, worse, gains the advantage with an earlier debut. Delays can and often affect a company's valuation, since investors closely watch the progress of new drugs: efficient clinical trials put them on the market more quickly, so they take market share more quickly. Pharma companies may also gain a strategic edge by setting a new standard for treating a disease, and speed to market gives physicians and patients a broader, and potentially lifesaving, choice of treatments in less time.

Finding people for trials is always hard, for example, many patients don't realize they can participate. Also, some deaths and questionable practices in isolated trials have made potential participants wary. Moreover, designers of clinical trials are now seeking more narrowly defined sets of patients, in part to distinguish new drugs from rivals on the market. But the most important problem is regulatory change: over the past decade, the number of patients needed for each FDA approval has almost doubled – see exhibit 4.

Exhibit 4 In addition to the FDA, economics is driving pharmas to get their drugs approval in several countries at the same for simultaneous launches.



Source: CenterWatch, PhRMA, Vaxa Inc. analysis

The pharma industry could therefore create enormous value by more efficiently recruiting participants in clinical trials. Taking a single month off a trial by improving recruitment could generate an additional \$40 million in sales for an average drug. But to do so, pharma companies must radically alter their R&D efforts by improving the speed and efficiency of recruitment, and this in turn will streamline the whole clinical-trials process.

Thinking like marketers

To get patients into trials more efficiently, pharma companies must take a marketing campaign view when recruiting patients. By setting a target for the number of patients needed in a trial, the R&D team in essence creates a sales challenge: to get enough patients to buy the "product"—in this case, participation in the trial. To do that job, companies will have to borrow a few marketing techniques.

There are marketing lessons to be learnt from industries outside of pharmaceuticals – e.g., consumer packaged goods, grocery, and regional banking. The challenge faced by these industries is almost the same as that faced by those managing clinical trials – that is, generating interest, getting people to buy the product or service, and providing some level of value.

Planning for a clinical trial begins with the design of a protocol, which sets out the criteria for patients who can be admitted to the trial, maps the treatment they will receive, and establishes how they will be monitored. In addition, the protocol includes such administrative details as the handling of patient consent and the marketing of the trial.

Sites and physicians for the trial are then chosen. Physicians are offered incentives—not only payment for their own time and other expenses but also free equipment, all-expense-paid trips to conferences, and invitations to speak at prestigious events. Physicians and nurses at each certified site get extensive training in the protocol used to administer the trial and in reporting its results properly.

Typically, one of the most crucial clinical phases (Phase III) in the development of a drug ranges from about four months to several years and can involve over 3,000 patients, though the number can vary depending on the disease or ailment targeted. Earlier phases, while also time-consuming, involve fewer patients and whose goals are different. Commonly, for every patient enrolled, four to ten must be screened to determine their eligibility. Pharma companies must also plan for unforeseen events to ensure that recruitment is successful even if they occur.

The recruitment of patients for trials generally follows two paths simultaneously: participating physicians recruit suitable people from their own patient lists while pharma companies advertise

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directly to patients and then pass prescreened lists of candidates on to the physicians.² The efficiency of both approaches to recruitment can be improved.

Segmenting the physicians

Many companies use a one-size-fits-all approach to recruiting and managing the physicians who participate in clinical trials. But just as some salespeople are better at bringing in customers, some physicians are better at bringing in patients for clinical trials. Although many companies recognize this fact, few have tried to identify and manage the top performers systematically.

The first step for pharma companies is to segment physicians on the basis of how well their pools of patients fit the protocol required by a clinical trial and their success in meeting recruitment targets in earlier ones.

A physician whose practice includes a high proportion of targeted patients (people with diabetes, say) could get an above-average recruitment target, greater support, and more attractive incentives. One top US pharma company, for example, discovered that some physicians with superb access to target patients were short of staff to manage the protocols for clinical trials. Providing a part-time nurse to help screen patients increased the rate at which these physicians recruited patients.

Another North American clinical trial enrolled 2,000 recruits in 16 weeks—an exceptional performance—because the company focused on its high performers, who had access to the right patients. Besides segmenting physicians by the number of patients they screen and enroll in a given week and by the number of weeks they take to meet their enrollment targets, pharma companies must track the percentage of patients who pass the initial screenings and complete the trial, for this information permits those companies to develop accurate databases of physicians who have good access to patients, the necessary infrastructure, and the commitment to ensure that enough patients go on to the finish line (Exhibit 5).

Enrollment success can include factors such as dollar spent per patient recruited, number of

² Advertising for clinical trials in the US is generally allowed if the message isn't misleading. Other countries have stricter regulations, and some countries prohibit direct advertising for this purpose, thus forcing the pharma companies to rely on the efforts of physicians.

patients screened/enrolled per week, and the number of weeks it takes to fill the recruitment quota. While, retention success can incorporate number of patients completed the trial.

Exhibit 5 Each Physicians' clinic performs differently and should be supported to fill their capability gap.



Starting from scratch, it could take a company several years to complete such a database. But improvements in the way companies try to find the physicians most likely to meet their recruitment targets are possible even before the process ends, largely through the steady development of deeper relationships with physicians who consistently deliver high numbers of patients.

Marketing to patients

In general, the efforts of pharma companies to market clinical trials are less than effective. One company that was testing an arthritis medication, for example, gave participating physicians a budget for local advertising. With some forethought and guidance, the company should have bought ads aired during cable television shows viewed by the elderly or marketing the trial directly to them. Instead, the physicians purchased space in general-interest local newspapers and got marginal results for the money. Pharma companies need to realize that physicians are not marketers and need help in the most fundamental forms identifying and recruiting patients.

Both the message and the media in which it is disseminated must be chosen wisely if marketing money is to be well spent. First, a pharma company must create a clear profile of the target patient, including age, sex, and ethnicity. Parts of this profile might be implicit in the protocol, but a careful demographic analysis will usually make the profile

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more detailed. Once it is complete, companies need to know how target patients get information about clinical trials and what might serve as an inducement to take part in them.

An example of effective marketing comes from a US company that was researching a drug for Type II diabetes, which disproportionately affects Hispanics. Using focus groups in Hispanic communities, the company set out to learn what would be most likely to motivate these patients to participate in a trial – e.g., free medical care, access to more effective treatment, or a chance to help find a cure for a disease. It found that since many patients in the target population lacked health insurance, free medical care and medication had the greatest appeal. With this marketing data in hand, the company's efforts at recruitment—and the trial—proceeded on schedule.

Indeed, segmenting the audience and targeting the groups with the highest value can also guide decisions about how to convey the message. Television spots, ads in local newspapers, and posters at bus stops, for instance, reach different demographic audiences. It is not which one medium will reach the target audience, but what combination or multi-touch campaign is needed to fill the patient pipeline.

Anticipating problems

By quickly recognizing when recruitment is running behind schedule and pinpointing the problem, pharma companies can avoid days of delay. But first—from the beginning of the trial—the companies should develop early-warning systems and contingency plans.

Companies with successful programs for recruiting patients often overbuild from the start, as one company did in Detroit, Michigan did by qualifying more clinics than necessary as trial sites so they could be activated immediately if needed. A European company produced weekly patient-enrollment reports and monitored responses to particular ads. When problems arose, it was able to bolster its advertising and switch to a different approach, since it had already bought options on media slots in markets where it feared it might miss its enrollment targets. In both cases, contingency plans helped these companies stay on course.

Bringing marketers and scientists together

Once pharma companies recognize that marketing skills are essential for bringing enough patients into clinical trials, it becomes obvious that organizational changes linking marketers with R&D are needed as well. Such changes do not mean substituting brash commercialism for scientific standards, but they do require a better understanding of what motivates people to participate in clinical trials.

To focus on recruitment for these trials, a few of the largest and most successful companies have recently established centers of excellence that include employees from clinical development, marketing, and market research. The marketers have insights that were often missing or overlooked when the trials were being designed: knowledge of consumer behavior and the ability to track the progress of marketing campaigns. Such centers thus help companies complete their studies on schedule.

By contrast, in today's standard approach, the manager of a clinical trial, who has overall responsibility for its success, develops the recruitment procedures. But these managers are evaluated on such criteria as whether the results of a trial stand up to regulatory scrutiny; the timeliness of recruitment plays little if any role.

A manager should therefore be also responsible for recruitment as well for clinical trials, and that manager should be evaluated, to an extent, on the ability to get sufficient numbers of patients enrolled on time—which resembles the kind of accountability that marketing managers bear. By retargeting a part of the recruitment manager's incentive package, pharma companies can raise the level of accountability for recruitment and aggressively challenge the tendency to regard delays as inevitable.

Involving marketers early in R&D also helps ensure that recruitment considerations are included from the outset in the planning for clinical trials. Ideally, the recruitment plan should be based on input from a variety of functions. But many pharma companies, regarding it as unscientific to consider practicalities when they design protocols for clinical trials, do not think, early enough in the planning process, about recruiting patients. Such a lack of foresight is the harbinger of delays and lost potential.

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In one extreme example, a recent trial focusing on the treatment of brain tumors needed patients who had already undergone a rare (and less effective) treatment for their condition. Not enough patients could be found since so few had already gone through this procedure. In another case, the clinical trial for a medication that would be prescribed by general practitioners called for complex screening examinations with equipment that most of them did not have.

Additionally, protocols frequently presuppose an ideal scientific setting, and designers include tests or other procedures merely to cover all contingencies. A more thoughtful design, as we have seen in practice, often loosens up the requirements imposed on participating physicians and patients, without sacrificing any scientific credibility. In both of the cases described above, equally rigorous trials could have been carried out using more practical protocols.

Scientific integrity, far from being compromised, is actually enhanced when practical considerations such as the availability of patients and equipment are dealt with realistically. If a highly specific protocol is necessary, pharma companies must be aware of the inevitable constraints. In the final phase of trials for one diabetes medication, for instance, the protocol called for high doses, which were regarded as essential even though only a few patients could tolerate them. By recognizing this problem early, the company could have anticipated the resulting high dropout rate and recruited a larger pool of participants from the outset instead of enduring delays late in the trial.

New technologies such as biomedicine are opening up vast new horizons for the pharma industry, but they can be reached only through meticulous clinical trials. To deliver value, pharma companies must conduct them safely, thoroughly, and expeditiously. These companies can offer the greatest value to patients, physicians, and investors alike by systematically improving every aspect of patient recruitment. Companies that pursue business as usual face staggering losses. Those that get it right may reap huge rewards.

About Vaxa Inc.

Vaxa Inc. is a strategy & marketing consulting firm that support companies to identify and pursue new growth opportunities.

We were founded in 1996 on the principle that we would provide innovative and fact-based research to help our clients to make strategic choices and decisions.

The industries we serve span Health & Sciences, Technology, Consumer Products, Services and Transportation.

We are located in Ft. Lauderdale:

5448 Estate Oak Circle
Ft. Lauderdale, FL 33312
T: 954-989-2425

www.vaxainc.com

