

Pharma Company Questions and Answers

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ABSTRACT

We've all heard that pharmaceutical companies have two factions, a science directorate that doesn't care about sales and a sales directorate that doesn't understand the science, but there is a third group, the Slartibartfast team. But who are they? Are new hire statisticians any better equipped to deal clinical trials than new hire statistical programmers? Why is the CRA function the only one to avoid when considering dating within your company? What is the difference between project teams and product teams? How did CROs come about? Does anyone ever really adopt an orphan drug? What is so different about the medical writers? What is the difference between PK and PD? Why are the largest pharmaceutical companies in the world mostly US companies? Will MedDRA ever run out of numbers and revert to COSTAR? These and other mysteries of your average pharmaceutical company answered today. Answers to these and other mysteries, along with un-common tidbits of your average pharmaceutical company will be discussed.

THE SLARTIBARTFAST TEAM

. . . from **The Hitchhiker's Guide to the Galaxy** (2005)

Arthur: All my life I've had this strange feeling that there's something big and sinister going on in the world.

Slartibartfast: No, that's perfectly normal paranoia. Everyone in the universe gets that.

Back before major competition appeared in the pharmaceutical world, the CEOs of pharmaceutical companies were the smartest men in the company, typically an M.D / PhD with each degree earned separately. They decided, based on their own intuition, which lines of research would be emphasized and which would be discontinued. This worked during the 1950s but after the Thalidomide tragedy in the early 1960s and the increased cost of meeting the new found regulations for the drug approval process, a specialized function was required to replace one man's intuition.

There are three similar functions, processing quality of life data, cost-benefit analysis of new treatments and market share calculations. These three functions typically respond to similar categories of analysis and frequently can be performed by the same people or small groups of people. Their data processing capacities are all similar, or at least significantly larger than typical clinical trial processing requirements. Therefore they are frequently grouped into the same department or team. Companies may break this by franchise area or indication group, or they may keep it all together. The problem is these teams don't fit well in either the typical clinical science division, nor in the marketing division, they have functions in and for both. Their reporting also tends to be reported to the highest levels of the company and therefore senior management frequently keeps them close at hand.

The name of this team varies by company. I have worked on an Epidemiology team, a Pharmacoepidemiology team and a Pharmacoconomics team. There is also frequently a mix of expertise and backgrounds from economics to epidemiology to pharmacy (Pharm.D.) Although, I've never called this team the Slartibartfast team they do hold power of life and death over your clinical trials and indication and a similar power over sales & marketing plans. In a modern pharma company, a little paranoia goes a long way.

ROOKIE STATS

Are new hire statisticians any better equipped to deal clinical trials than new hire statistical programmers? Of course not. Rookie statisticians are smart people trained in mathematical statistics. Even if they come from a biostatistics department their thesis involved proving lemmas and theorems, finding mathematical certainties and perhaps finding value in other people's error terms. They really don't know that much about clinical trials. They certainly don't know the difference between SDTM 3.1.2 and 3.2.

Rookie statisticians must be groomed in the minutiae of clinical trials. They must learn to work with both senior statisticians and all of the other professions in a pharmaceutical company. Often, they must realize that speaking English and even mediacese, the language of physicians is required of them. Writing specs and shells is a skill which must be demonstrated, studied, practiced and mastered. Most of all statisticians must move from their world of numbers to the world of health care, where words and people are the tokens of exchange.

The FDA mandates that a certain number of statisticians be employed and conduct reviews of certain tasks. This

requirement has greatly increased the demand for people with these skills. Of course, rookie statisticians are no more useful than hockey goalies for this review although presumably they will improve over time.

DATING A CRA

Most people express their greatest fear in dating to constantly being secretly evaluated and compared to standards sans feedback. Men hate being compared to past Lotharios; women dislike comparisons to past flames. We all may be tempted to consider such comparisons of current lovers to past ones.

The clinical research associate is the eyes and ears of the research sponsor. The job of the CRA is to visit a research site, exam their documentation, check record keeping and then evaluate the staff as they progress through all of the processes of research, everything from patient recruitment to inclusion/exclusion criteria interpretation to patient informed consent to medical procedure evaluation to accuracy of record keeping to compliance measurement. All of this is conducted as inconspicuously as possible and the evaluation is not a dialogue, the only feedback comes after all evaluations are complete. In short, the CRA secretly evaluates and compares to standards the entire operation without providing feedback, until the end.

Does that sound familiar? To be fair, the CRAs which I have worked with and who are married and who agreed to answer my questions, all identified a need to put their work down before they took up dating or any encounter with their paramour. Actually, this doesn't sound like a bad strategy for any of us; however, for CRAs it is essential.

OTHER QUESTIONS

What is the difference between project teams and product teams?

Product teams exist to bring a defined product through the stages of development to market, thus a company is fairly certain of their commitment to a molecule before they organize a product team. Project teams exist before that decision is made.

How did CROs come about?

CROs developed for three reasons. First, when the ICH global standards were agreed to in April 1990, this level of expertise was not always available to certain pharmaceutical companies. CROs began by concentrating this expertise to conduct clinical trials. Second, the FDA became skeptical of certain pharmaceutical companies, particularly of their conduct with PIs and therefor a CRO became a buffer. The PI, with expertise in only one _objective_ developed a relationship with the CRO and could test drugs for several companies within this area. Thus, the FDA believes the PI has less incentive towards favoritism toward a particular company or product and the results are more valid. Third, certain hospital networks or university hospitals realized that they had expertise in certain medical areas and could financially benefit by keeping the research operations in house.

Does anyone ever really adopt an orphan drug?

An orphan drug, as defined by the Orphan Drug Act of 1983, is a drug for a disorder affecting fewer than 200,000 people in the United States, that is, currently less than 1 in 1500 Americans. By acknowledging that the drug will never be profitable and applying for orphan drug status, the pharma company acknowledges there are individuals who suffer from this condition and whose lives can be improved. The Rare Disease Act of 2002 expanded the definition of orphan drugs and regularized their exclusive sale without competition for five years. In effect, the FDA conducts an expedited review and approves without complete data, frequently requiring ongoing follow-up. The process can fail however, incomplete safety data can expose individuals to unknown safety complications or a drug with a much larger potential market, such as zidovudine (AZT) an antiretroviral drug for treating HIV/AIDS was approved as an orphan drug.

What is so different about the medical writers?

Medical writers provide the bulk of the material for completing the various written documents required by regulatory agencies. Although most do not possess specific clinical knowledge, at least prior to being medical writers, they complete the sections of the manuscript which require a description of the product, the process and the methods of testing. Most pharmaceutical companies find a way to connect medical writers to the various science teams and often even provide them with a modicum of training. Their employment is a result of the bottleneck in that there are only a set number of statisticians available and only a portion of them are able to grasp all the details of clinical trials. They could either be kept busy writing the SAP, the CSR, the annual update, etc., or they can be kept focused on just the statistical portion of their job. Truth be told, most statisticians think they are also programmers and thus there is really no need for statistical programmers. Generating tables has never been seen as a useful task for PhD statisticians except at a very small number of pharmaceutical companies.

What is the difference between PK and PD?

Pharmacokinetics (PK) is typically defined as what the body does to a drug. Pharmacodynamics (PD) is what the drug does to the body. PK has five stages (LADME), Liberation, Absorption, Distribution, Metabolization and Excretion. PD has seven main possible actions: stimulate action, depress action, block action, stabilize action, exchange substances, and direct beneficial or harmful chemical actions.

Pharma Company Questions and Answers, continued

Why are the largest pharmaceutical companies in the world mostly US companies?

Seven of the top twelve pharmaceutical companies, in terms of sales, are headquartered in the USA. The USA is the only major market without significant regulation of drug prices. Many other countries either specify a fair price or specify a reimbursement price. This tends to restrict the amount of profit which can be made. Many American pharma companies price their drugs in America in order to recoup their investment and then consider any foreign sales to be profit.

Will MedDRA ever run out of numbers and revert to COSTAR?

In short, no. MedDRA expands and revises sections every March and September with the March release containing HLT (High Level Terms) and above changes while the September release is normally restricted to PT (Preferred Terms) and LLT (Lowest Level Terms.) The LLT is the clinical reported term while the PT is the distinct descriptor.

COSTART was the older system, inspired by the FDA but recently officially replaced by MedDRA. While a new disease might receive a provisional numbering in MedDRA, with the March revision, which may include even shifting items between SOC (system organ classes) there is no danger of running out of terms.

Unlike a decimal system, such as the Dewey Decimal System, MedDRA has provision for more than ten items in a category.

CONCLUSIONS

Pharma companies and all the various other companies which support them from CROs to placement agencies to the SAS Institute can be great places to work. Unfortunately, advanced education doesn't seem to prepare anyone for this and because the competition in the industry is fierce there are few sources of answers. For those among us with insatiable curiosity an occasional guide is better than no guide at all.

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