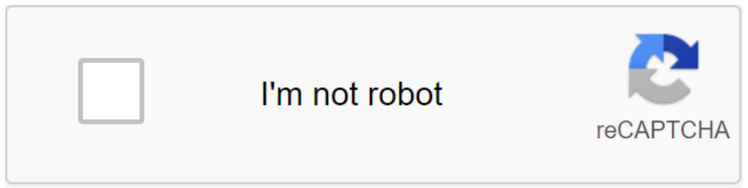

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Sas programming in the pharmaceutical industry second edition 2nd edition

Day. Chapter 1 Environment and Guidelines Statistical Programmer Working Environment Pharmaceutical Industry Vocabulary Statistical Description work Description Drug/Device Process Industry Rules and Standards Your Colleagues Clinical Trial Guidelines for Statistical Programmer Understand The Clinical Research Challenge Program once and reuse your code Everywhere Clinical Trial Data Dirty Use of SAS Macros Reasonably Good Programmer is a good student Of The Aim to Make Your Programming Best to Start With a Learning We then explore the basic principles that should guide you to your day-to-day work. These principles permeate all the tasks that you do on a daily basis, and if you keep in mind, they will keep you from straying from your statistical programming duties. A statistical programmer working the working environment of the pharmaceutical industry Vocabulary Like many industries, the pharmaceutical industry has a vocabulary and language all its own. Our industry is full of abbreviations, medical terminology and jargon that need to be familiarized to become an effective statistical programmer. To help you in defining some of these terms, this book is italicized by the first case of terminology that is specific to SAS programming in the pharmaceutical industry. At the end of the book is a glossary to ask for definitions of these terms. The statistical programmer's description of the work of a statistical programmer usually works in the statistics department of a pharmaceutical or biotechnology research group or contract research organization (CRO). The main role of statisticians is to use their technical and programming skills to enable clinical trial statisticians to perform their statistical analysis responsibilities more effectively. This may include importing and exporting data, working with other it resources professionals on the ground and in other companies, obtaining analytical content and creating analytical data sets, and creating clinical research report materials (CSR), which consist of tables, numbers and lists (TFL). Here is a simplified illustration of the general workflows of a statistical programmer: statistical programmers can perform other roles. They can be an integral part in assisting clinical and other operational staff to better understand clinical data. In addition, as mentioned in the foreword, this book focuses more on the typical role of a statistical programmer. But a statistical programmer can sometimes its work increases the scope for assisting in other areas such as clinical data management operations. Drug/Device Clinical Clinical Development Process industry is primarily concerned with the attraction of new medicines, biologics, devices or treatments for the population and the market as a whole. In the United States, most clinical trials are funded by pharmaceutical companies that want to bring new treatments to market, or the National Institutes of Health (NIH), which fund research to improve the health of all Americans. Since most clinical trials are conducted with the idea of bringing a new drug or device to market, we will take a brief look at the approval process of the U.S. Food and Drug Administration (FDA). More information about the drug approval process and the device can be found on . The FDA's drug approval process is tasked with making sure that all new drugs brought to market are safe and effective. The FDA is helping to do this with a drug approval process that can easily cost hundreds of millions of dollars. And it may take ten years or more to move the drug away from the opening stage at a pharmacy near you. There are several stages of development that are carried out as part of the drug approval process. 1. Preclinical studies are experiments that are conducted in the laboratory and with animals long before a new drug is ever introduced for human use. If these studies are promising, the drug manufacturer usually conducts research on new drug (IND) applications. The application of IND allows the drug manufacturer to conduct clinical trials of a new compound in humans. 2. Phase 1 trials are the first in humans to study a new drug in humans. These studies are usually conducted on small samples of the subjects. The idea here is to determine the safety of the drug in a small and usually healthy voluntary study population. These studies are often very fast-moving projects because they quickly enroll patients and results are needed quickly. This can be a daunting task for a statistician-statistician, and little time to spare when the timing of phase 1 research can be weeks or months in the most. Phase 2 of the trials go beyond Phase 1 studies in that they begin to study and determine the effectiveness of the drug. Phase 2 studies have larger (100-200 patients) population studies than Phase 1 studies and aim to narrow the dose range for the new drug. Safety is also monitored at this stage, and phase 2 trials are usually conducted in target population studies. Phase 2 studies can often take a little longer to complete, because the trial time may be longer, with more evaluations, and with more patients than Phase 1 trials. Phase 3 large-scale clinical trials in populations that range from hundreds to thousands of patients. These are critical trials that a drug manufacturer is working to show that its new drug is safe and effective in targeted population research. If phase 3 tests are successful, they will be Application (NDA). This type of clinical trial can last for months or many years. 5. Phase 4 trials, or post-marketing trials, are usually conducted to monitor the long-term safety of a new drug once the drug is already available to consumers. Stage 4 tests can run for years and they tend to have a reduced sense of urgency than you might see from previous phase trials. The FDA approval process is also responsible for regulating new medical devices. The FDA approval process varies depending on the degree of risk inherent in the device. Class 1 devices do not carry much risk to the patient; they include devices such as elastic bandages and surgical instruments. Class 2 devices have a slightly higher risk to the patient; they include devices such as infusion pumps and motorized wheelchairs. Class 3 devices are high-risk devices and thus require the most rigorous regulatory oversight. Class 3 devices include the replacement of heart valves and implantable defibrillators. Obviously, the requirements for approving a Class 3 device are much higher than for a Class 1 device. Clinical sample studies there are many types of clinical trials, and there are some general concept design trials that you need to understand. One of the key concepts is randomization of trial therapy. When you randomly assign patients to study therapy, you reduce potential bias treatments. Another key concept is blinding treatment. Blinding a patient to treatment means that the patient does not know what treatment is being carried out. In a single-blind trial, only the patient does not know what treatment is being carried out. In a double-blind trial, neither the patient, nor the patient's doctor, nor the staff, the administration of treatment, do not know what treatment is being carried out. Sometimes there may even be a triple blind trial where the patient, the patient's doctor, and the staff analyzing the study data do not know what kind of therapy is being performed. There are other trial design concepts for you to be aware of. A clinical trial can be conducted at one site or it may be a multicenter trial. In one test location, all patients are treated in the same clinical location and, in a multicenter trial, several clinical sites are used. Multicenter research is needed to eliminate bias against a particular site or because more patients are required than one site can register. Tests can be designed to determine superiority, equivalence, or non-inferiority between therapies. The test of superiority is designed to show that one therapy is much better than the other. equivalence is intended to show that there is no clinically significant difference between treatments. The test, not such inferiority, is designed to show that one therapy is not inferior to another therapy. Finally, tests can follow parallel or crossover research designs. In a parallel trial, patients are prescribed that they stay on, and they are compared to patients in alternative therapy groups. In a crossover trial, patients switch or change prescribing therapy during the trial. Industry regulations and standards regulators regulate and direct most of the statistical programmer's work in the pharmaceutical industry. It's important that you're aware of the following rules, guidelines, and organization standards. The International Conference on Harmonization (ICH) International Harmonization Conference (ICH) is a non-profit group that works with pharmaceutical regulators in the United States, Europe and Japan to develop general regulatory guidelines for all three. The purpose of the MUH is to determine a common set of regulations so that the application of pharmaceutical regulation in one country can also be used in another. Over time, the Food and Drug Administration (FDA) typically adopts guidelines developed by ICH, so you can observe the development of the guidance at ICH to see what FDA requirements may be coming. The Clinical Data Exchange Standards Consortium (CDISC) Consortium of Clinical Data Standards (CDISC) is a non-profit group that sets clinical data standards for the pharmaceutical industry. CDISC has developed many data models that you should be familiar with. SDTM identifies data sets of data tables that must be sent to the FDA as part of the regulatory submission. The FDA approved the SDTM in its electronic general technical document (eCTD) guide and document the specification of the study data. SDTM was originally designed to make it easier to produce case report tables (CRTs). Thus, the SDTM is designed to list friendly, but not necessarily friendly to create statistical resumes and analysis. Data Analysis Model (ADaM). The CDISC ADaM team makes recommendations for determining a data set for data analysis structures. These datasets are designed to create statistical summaries and analysis. As a statistician, you can find these datasets as the primary source for your reporting work. You can be very involved in the creation of these datasets. Identify-XML. Formerly known as the case report table data specification, Define-XML is a model for replacing an old data definition file (define.pdf) sent to the FDA with electronic representations. Define-XML is based on the CDISC (ODM) operating data model and is designed to provide a machine-readable version of define.pdf through define.xml. Because define.xml is a machine-readable file, metadata presentation data can be easily read using computer applications. This allows the FDA to work more easily with the data presented to it. It could will allow you to do your job more efficiently and efficiently if you are able to use your metadata. You will export, import and even create data for these models, so it is important that you learn about them. The FDA approves the use of these data models in its data guidelines and documents. There are other CDISC models, such as the Clinical Data Harmonization Model (CDASH) and the Laboratory Data Model (LAB), which may also be of interest to you. The Food and Drug Administration (FDA) Regulation and Guidance FDA is a department within the United States Department of Health and Human Services, which is charged with ensuring the safety and efficacy of drugs, biologics and devices on the market in the United States, as well as food, cosmetics and tobacco. Any work you perform that contributes to the FDA submission is covered by these federal regulations. There are a number of specific rules and guidelines that you should know. 21 CFR - Part 11 Electronic Records; Electronic Signatures 21 CFR - Part 11 is a federal law that regulates the submission of electronic records and electronic signatures to the FDA. Of particular interest to the statistician is the following requirements of Part 11: System Verification to ensure accuracy, reliability, consistent perceived performance, and the ability to distinguish between invalid or altered records. Determining that individuals who develop, maintain or use electronic recording/electronic signature systems have the education, training and experience to carry out their tasks. Proper control over distribution, access to documentation and its use for system operation and maintenance. Review and change control procedures to maintain an audit trail that documents the time-specific development and modification of system documentation. 21 CFR - Part 11 means you have to be qualified to do your job, your programming needs to be tested, you need to have system security in place, and you must have change management procedures for your SAS programming. Additional FDA Recommendations on 21 CFR - Part 11 can be found in the FDA publication titled Guide to Industry Part 11, Electronic Reports; Electronic signatures are the area and application. For more information on how to test your clinical trial programs, see the book SAS Press Checking Clinical Trial Data Reporting with SAS. ICH E3 The structure and content of the clinical reports of the E3 study details what the reporting goes to the clinical report of the study for the FDA submission. This guide has value, because you are often required to create tables, numbers, case report tables, and possibly clinical support for the clinical trial report. ICH E9 Statistical Principles of Clinical Trials E9 discusses statistical issues in the design and implementation of Court. It contains detailed design, trial research, analysis and data reporting. While this guide is most useful for statistics, it provides an excellent overview of how clinical trials should be conducted. ICH E6 Good Clinical Practice: Consolidated E6 Guide (or GCPs) discusses common standards for clinical trials. Anyone working on a clinical trial should understand this document. The following parts of E6 are of particular interest to the statistical programmer. Italics were added for the accent. 5.1.1 Sponsor is responsible for implementing and maintaining quality assurance and quality control systems through written SOPs (standard operating procedures) to ensure that the tests are carried out and the data is recorded (recorded) and reported in accordance with the protocol, GCP and applicable regulatory requirements (s). 5.5.1 The Sponsor must use appropriately qualified persons to monitor the overall conduct of the trial, process, verify data, conduct statistical analysis and prepare court records. 5.5.4 If the data is converted during processing, it should always be possible to compare raw data and observations with processed data. Part 312.33 Part 21 of the Federal Code; Annual Reports and ICH E2F: Development Safety Update Report (DSUR)21 CFR - Part 312.33 discusses what is required for the application of new drug research (IND). Part 312.33 discusses the requirements for annual security renewal reporting for IND. This reporting requires you to create adverse events, death, and the subject of a C SUMMARY dropout annually for any drug under the IND app. ICH recently published the E2F document, which is the international standard for annual security reports. The FDA has since published a guide that will allow the submission of DSUR instead of the traditional INDA annual safety update. The Electronic General Technical Document (eCTD) Specifications and Manual Electronic General Technical Document (eCTD) is a vision of future electronic submissions to the FDA. This specification was developed by the International Conference on Harmonization (IHF) as an open-standards solution for the presentation of electronic materials to regulators around the world. The FDA has adopted eCTD as the standard for how to submit electronic representations to the FDA. Please note that eCTD still relies heavily on sending text documents as PDF files and presenting datasets as SAS XPORT transportation files. The FDA's study data standards provide more detailed information on how to present FDA data in the Study Data Standards document. The requirements in this document apply to data sent to the FDA and applied to the data files provided by the FDA to eCTD as well. It has detailed information on how the FDA expects to get your yours ADaM datasets. This is a document that you want to understand, and the FDA does a good job of keeping it up to date with what their expectations are for electronic data presentation. CDER General Standards Data Issues Document CDER General Standards Data Issues Document provided by the Center for Drug Evaluation and Research (CDER) at the FDA is essentially a continuation of the Study Data Standards document. It contains practical guidance on how to send CDISC formatted data to the FDA and various things that need to be monitored when submitting datasets to the FDA. You should be aware of the current information published in this paper, as well as the document of parental research standards. The CDER Data Standards Program Was founded in 2010 to help improve and improve CDER data standards processes to make electronic presentations more efficient. Under the Pharmaceutical Drug Payment Act, the FDA now has the right to mandate electronic data submissions as well as the format for such submissions. On February 6, 2014, the FDA published three draft guidelines that would require the presentation of electronic data in a standard format. You want to keep a close eye on this group in the future, because that's where the additional data standards mandates and processes will come from. Your clinical trial colleagues at any pharmaceutical company or contract research organization, you work with groups and individuals outside the biostatistics department. Let's look at the functional groups with which the statistical programmer interacts the most. The biostatistics people with whom you work most tend to be in the biostatistics or statistical group itself. Traditionally, this department consists mainly of statisticians and statistical programmers who are responsible for analyzing and reporting on the work of clinical trials. Analysis and

reporting usually consists of obtaining data, creating data analysis structures, and presenting test results through a set of tables, numbers and lists. The division of labor between statisticians and statistical programmers can often be blurred because skill sets can overlap significantly. Sometimes you can also find other roles in the biostatistics group where they may have their own data managers or computer science. The Site Management Group is responsible for the clinical relationship with the site. They recruit doctors in clinics to participate in clinical trials, train their staff to conduct trials, monitor protocols and act as a defender of the clinical facility. Monitoring sites is done by the name of the work called Clinical Scientific or CRA. Site management can be your ally in getting data entered into a clean and easy-to-use form. Form. data at the beginning of the data collection process eliminates the need for additional data requests from data management and helps prevent subsequent data analysis problems. The importance of site management has increased with the creation of electronic data collection technology (EDC), as data entry has shifted from the data management team to the clinical site itself, where the initial data quality is established. Sometimes site management can be included in a larger group called clinical operations, which may include project management and data management functions. Managing data alongside clinical trial statistics, the statistical programmer works most closely with the data management team. The data management team is generally responsible for developing the Case Report Form (CRF), designing and setting up databases, cleaning data, encoding data, monitoring data quality, and providing clinical trial data for analysis by a statistical team. Cleaning up data involves cleaning up data to solve problems through software and manual data verification. Data coding entails the use of common codes to classify freely entered text fields, such as adverse events, medications, and medical histories. Data quality control involves auditing data to make sure it has been entered properly. Finally, the data management team usually provides data to a statistical programmer through some kind of relational database management system (RDBMS), which can then be imported into the SAS. You save time when data management provides a well-cleaned and well-coded clinical database because it means you don't have to program around dirty data. Information Technology Information Technology (IT) group has different responsibilities, depending on the size of your organization. THE IT department is generally responsible for computer system infrastructure, maintenance, and overall computer support support. The IT team can also perform some level of software development. In small and medium-sized organizations, IT can simply use application software interfaces (APIs) between ready-made systems, while in large IT organizations they can be responsible for the full architecture and development of software applications. You need to work with the IT department in your organization, as well as with external sponsors and suppliers. Internally, you can work with IT to manage SAS configuration and installation skills, encryption technologies, and desktop publications or distribution reports. The most common reason to work with external IT staff is usually with regard to information-sharing technologies such as FTP and encryption tools. projects Most contract research organizations and pharmaceutical companies are organized into a matrix management structure. This structure is called a matrix because there are design teams that cover different functional departments. It could to visualize relationships like this: The project manager provides operational oversight in clinical trials. The project manager is responsible for meeting the needs of the trial, with the support of various functional departments. He or she also works with the Principal Investigator, as well as with external suppliers such as laboratories, pharmaceutical companies and contract research organizations. The project manager must work with a statistical programmer during clinical trials. As a statistician, you may find that you respond to (at least) two managers during the trial. Statistical Functional Management acts as a skills-specific manager, while the project manager is your project manager. The quality assurance group (KK) is your internal regulatory reference and they are there to help you. The main goal of the project is to see that operations in your organization meet regulatory standards. They can help you interpret different rules and help you prepare for customer and regulatory audits. A quality guarantee can also perform internal audits to ensure that your business processes meet regulatory standards. Finally, the quality control team usually supports all of your company's standard operating procedures (SOPs). Medical Letter Medical Writing Team can help in creating various documents for your organization. Medical writers can help with writing clinical study reports for the FDA. Medical writers can also participate in writing the NDA presentation. Clinical narrative safety reporting is another task that medical writers help with. Finally, a good medical writer can be a staunch ally in statistical reporting, since he or she can find any last-minute inconsistencies in your analysis before sending it along to the authorities. The guidelines for the statistical programmer below are specific guidelines for SAS programming in the pharmaceutical industry. These are high-level concepts that should be kept in mind when performing any of the widest range of tasks. Understand the clinical study A good statistical programmer takes time to understand the subject. If you were going to have open-heart surgery and you were comfortable with a knife, you wouldn't just roll up your sleeves and get to work. You will receive formal training and first get a medical degree to sas programming in the pharmaceutical industry second edition 2nd edition by jack shostak