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Opinion

Practical Pointers for Drug Development and Medical Affairs

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January 2023

Drug Development

• It is absolutely an essential part of the clinical research process in providing informed consent, and having the potential participant sign the forms (ICF).[1] It may help foster enrollment by also explaining to potential study participants not only why the research is being conducted, but also how their individual participation will help in product development and what this product has the potential to accomplish.

• It is more difficult than ever to enroll patients in Phase I oncology clinical trials.[2] One partial solution, when feasible, is to make this a multi-center semi-decentralized clinical trial rather than one inhouse unit.

- o Making some of these visits home visits may further enhance enrollment.
- o This will open up a wider enrollment area.
- o This may decrease subject travel time and costs.

• The Food and Drug Administration (FDA) will now start in-person meetings.

- o This gives companies the ability to have face-to-face dialogue with the agency.
- o Such meetings may provide a better chance for companies to present their data and reasoning.
- o Proper preparation with an experienced team is critical to success at these meetings.

Medical Affairs

• Writing medical case studies is an excellent method to demonstrate your products' attributes in an actual clinical example. It shows clinicians the practical aspects of the diagnostic or therapeutic intervention.[3]

• According to Erica Dankiewicz, "*The promotional review committee is a multi-disciplinary group with representatives from Medical, Legal, and Regulatory and is often referred to as MLR. Together, as a team, they ensure materials are fair balanced and meet function-specific standards while achieving marketings' goals. In the US, the Federal Food, Drug, and Cosmetic Act (FD&CA) and Title 21 of the Code of Federal Regulations (CFR) predominantly govern prescription drug advertising and promotion.*"[4] When conducting Legal, Medical, Regulatory Review (LMR), it is important to be conservative and follow the exact wording of the package insert.

• Clinicians frequently come up with new potential uses for approved products. Allowing these physicians to conduct an investigator-initiated trial (IIT) may be a cost-effective way to test these concepts in a pilot study.

February 2023

Drug Development

• Up to 50% of subjects have poor medication adherence in clinical trials. This can be a significant factor affecting the efficacy of the results. In order to prevent this, it may be worthwhile to do a placebo screening for 2-4 weeks to determine if the potential participant will demonstrate adequate medication adherence to be enrolled in the study.[5]

• The constant change of regulations, introduction of new technology, and the modifications of best clinical trial practices, makes the need for continuing staff education and training essential. This type of guidance will help maintain the highest clinical practice

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standard for your company and may also prevent staff turnover.[6]

• The signing of an ICF is not totally adequate in obtaining a potential participants informed consent for a pharmaceutical clinical trial. The process should also involve a careful, meaningful explanation of potential risks and a commitment to attend all required patient visits and procedures. These procedures should be clearly defined so that the potential subject understands their actual commitment. This is not only a regulatory requirement but an ethical, moral, and medical obligation. If potential study participants better understand the risks and their obligations it should also aid with patient retention.[7]

Medical Affairs

• A practical method to demonstrate the application of a biopharmaceutical product may be to publish a case history or series about this topic. Through these articles, healthcare providers are able to identify the example with their own patients and how this product may fit in with their practice.[3]

• The use of n-1 clinical studies is another cost-effective manner of conducting small pilot clinical studies.[8] They are especially useful in patient-centric research and to re-evaluate chronic therapies.[9]

• Medical Affairs teams frequently want to work with established experts, Key Opinion Leaders (KOLs), in specific therapeutic areas.[10] These teams should have an ethical synergistic plan that provides benefits for both the clinical scientist's research and/or patient care (as well as addressing their own needs) allowing for a prudent exchange of ideas. Rather than compensating a physician only for their time, a more useful activity will help establish a better relationship. An example is a medical liaison (working for a company that sells allergy products), contacting a prominent allergist to determine what pollens seem to cause nocturnal allergy symptoms in July in San Diego.

March 2023

Drug Development

• In order to prevent inappropriate subject enrollment, obtaining a past medical history via medical records can prevent protocol deviations based on concomitant medications or ineligible medical history. A subject may also use inappropriate terms, such as 'arthritis' when in reality they have polymyalgia rheumatica, a potentially more serious disorder. It frequently occurs because many patients forget, don't understand or may think that the information contained in their past medical history is irrelevant.

• Sponsors of clinical trials should ensure that they have an adequate amount of clinical trial insurance to cover unplanned, unexpected related serious adverse events.

• The use of randomized double-blinded therapeutic withdrawal of the investigative product may be a useful way to also demonstrate efficacy.

Medical Affairs

• When attempting to obtain true informed consent from a potential clinical trial subject, it would be useful to administer some standardized questions to see if the subject is able to correctly answer basic questions after having read information pertaining to the trial. For example, if the subject was given a list of potential side effects, would they be able to correctly verbalize one or more side effects of the medication.

• The promotional review committee should review your digital social media before it is posted (X, Instagram, Meta, LinkedIn, etc.) to ensure all information is accurate and that all rules and regulations are being followed. In addition, biopharmaceutical personnel should not use their own social media account when they are discussing any of their companies' products.

• When conducting comparative pharmacoeconomic studies, it is important to include the comparative cost of adverse events from the competitive product. For example, if the competitive drug or device has a 5% chance of causing a complication that necessitates an expensive medical procedure, this calculation may show a large differentiator in the cost of the two products.

April 2023

Drug Development

• It is often difficult to locate academic clinical research sites that are not already filled to capacity or who are so short-staffed that they cannot take on new projects. This provides an opportunity to work with and help educate and train the lesser-known medical institutions that have both the medical expertise and specific patients but lack substantive experience in clinical trials.

• Currently, there is a greater emphasis on enrolling additional populations that have not adequately participated in clinical trials such as minority, geriatric, and pediatric populations. Investigators should ensure that these potential subjects fully understand the risks and benefits (the informed consent process) of participating in these studies. It. may be useful to have them answer a series of standardized questions to demonstrate that they understand the essential elements of the ICF (Institutional Review Board (IRB) approval should be obtained for the questions if in written form).

• The following are links to FDA webpages and documents relating to the pre-Investigational New Drug (IND) and IND process that should be reviewed when developing your pre-IND submission briefing package:

- o Small Business and Industry Assistance: Frequently Asked Questions on the Pre-IND Meeting[11]
- o Investigational New Drug (IND) Application[12]
- o IND Applications Prepared and Submitted by Sponsor-Investigators[13]
- o Guidance for Industry: Content and Format of INDs for Phase 1 Studies of Drugs, Including Well- Characterized, Therapeutic, Biotechnology-Derived Products.[14]

Medical Affairs

• New AI tools, ChatGPT for example, may be helpful in writing journal articles. This is especially true for providing an outline of the topics that you want to cover in the article. It may also be useful in finding references to help produce your original material, but they should be checked for accuracy.

• When launching a new product or introducing a new indication of an established product, we recommend that you have multiple review articles discussing your product from not only an efficacy and safety standpoint, but also from a pharmacoeconomic standpoint and potential position in the Health Care Provider (HCP) therapeutic regimen.

• When promoting your product, you may want to emphasize the importance of the individual patient reaction to a specific medication. Just because they reacted poorly or insufficiently to one drug in a specific class, does not mean they will react the same way to all drugs within that class.[15]

May 2023

Drug Development

• Informed consents have grown much larger, more complex, and often times uses terminology that may be difficult to understand for persons with limited language skills.[16] It is imperative to make these forms shorter, simpler, and easier to understand. Studies have demonstrated poor patient comprehension of the essential elements of the informed consent process not just in the United States but globally.[17-19]

• The definition of a laboratory adverse event is usually described in the protocol as a value that is clinically significant in the investigator's judgment. One frequent protocol guidance for this is having a lab test reported as clinically significant if repeated. However, many results are repeated just to ensure that the results are insignificant or are due to a procedural error (hemolyzed blood). We recommend removing "repeat laboratory testing" as an indicator of a significant adverse event.

• Removing all patient identification is important for sites to remember when they send patient hospital records or other medical records to the sponsor or contract research organization (CRO). In addition to name, it also includes items such as home address, telephone number and medical record number.

Medical Affairs

• Making the most out of poster presentations

  o Place on social media

  o Solicit comments and questions

    - Answer appropriate questions and communicate these to a wider audience
    - Broadcast current and future work in this area when applicable.

  o Write up and disseminate pertinent questions and answers

  o Create a white paper and journal articles from the data

• Commercial booths at scientific conferences

  o Verify that a promotional committee consisting of LMR has reviewed your booth and all material in detail. This includes the following:

    - Booth location
    - All banners
    - All printed material, videos, handouts, etc.
    - Labels, headers, designs, etc. on the booth wall
    - Location of medical science liaisons (MSLs) in relation to the commercial team

  o Detailed examination of all items is critical to maintain compliance with the regulations

• Product feedback is an important way to learn how health care providers are actually using your product

  o Having MSLs talk directly to clinicians is a way to gather this information. In addition, you can learn why and when they are actually using the product in this manner.

  o What difficulties or drawbacks are there to the product?

  o Can the patient experience be improved, such as administering a drug at bedtime?

June 2023

Drug Development

• When developing a medication that will be administered by an inhaler, one has to understand that many patients have difficulty coordinating this device with their inhalation. It is extremely important for the study coordinator to repeatedly educate and check on the participant's technique.[20,21]

• Many subjects will develop adverse events secondary to the use of a placebo, known as the nocebo effect. It is, therefore, not possible to discern which patients are on the investigational product vs. the placebo so the incidences of adverse events that patients develop does not mean that they are on the experimental product. Hence, the blind is not broken.[22]

• It's vital to patient safety that an emergency crash cart be immediately available when biopharmaceutical clinical trials are taking place because symptoms of anaphylaxis need to be treated immediately.[23] This includes having a well-stocked crash cart that contains injectable epinephrine and inhaled bronchodilators. As medical monitors we have, unfortunately, seen this unnecessary and potentially dangerous situation where investigational sites have erroneously claimed that they were close to an emergency care center and didn't need a complete crash cart.

Medical Affairs

• When producing promotional material, the font size and location

of the Important Safety Information (ISI) is required to be the same size as the advertising statements and prominently displayed for drug products. This is to remain in compliance with federal regulations.[24]

• The most successful Medical Science Liaisons are usually the ones that are well prepared to discuss the basic science of their product with healthcare personnel (HCPs).[25] This not only helps the HCP to better understand the product, its applications, and potential adverse events but may also stimulate them to do their own investigation of the product in such activities as investigator initiated clinical trials or conducting literature reviews and analysis.

• To obtain optimal benefit from attending scientific conferences attendees should plan for the following:

- o Direct knowledge from scheduled talks
- o Competitive intelligence
  - Information about your company's product
  - Information about competing products and companies
- o Networking[26]
- o Developing partnerships
- o Obtaining educational credits (Continuing Medical Education (CME), nursing credits, etc.)
- o Gaining new marketing ideas and concepts[27]

CONFLICTS OF INTEREST

I hereby affirm that the content of this article is the result of our independent research. No potential conflict of interest, financial or otherwise, has influenced the outcome of this article or the conclusions drawn herein.

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