

2004N-0181-Critical Path Initiative: Establishment of Docket

Date: July 30, 2004

GENERAL

As a professional within the life sciences industry who has worked with a number of pharmaceutical, CRO, device, and other life science companies over the past 19 years on process issues related to the clinical development of drugs, biologics, and devices, I am keenly interested in FDA's Critical Path Initiative. I would like to commend the FDA on their work with regard to illuminating some very critical issues related to our pressing medical product development problems as described in the recently released report, "Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products." I completely agree with the content of the report. My comments are to respond to FDA's request for obtaining input on identification of pressing hurdles and activities that would reduce existing problems associated with the design of medical products and their development. The views I am presenting are mine alone. However by way of disclosure, I have offered and do provide consultative services to numerous pharmaceutical, biotech, CRO, SMO, and genomic companies. Also, I am a patient representative to ODAC as well as a patient consultant on the oncology development committee at the FDA.

1. Hurdle Identification. Please describe the product development issue, the nature of the evaluation tool that is out-of-date or absent, how this problem hinders product development, and how a solution would improve the product development process. Please be as specific as possible.

There are many hurdles that exist in the product development cycle. Some of the major hurdles facing sponsors in medical product development reside within the clinical development stage for a product. Namely, sponsors face issues that are 1) of a process nature and 2) also a lack of state-of-the-art technology that can be implemented on a grand scale. The industry (e.g. pharma, CROs, SMOs, investigative sites, and other vendors) would benefit greatly by streamlining some of its business processes and implementing technology tools on a large scale (not project by project). Although not all the hurdles the industry is facing can be addressed in this document, I will attempt to illuminate some important ones below:

- 1) Established and approved product development plans. Many companies today lack sound product development plans before they embark on preclinical and clinical studies. Some companies are able to present their plans to the FDA at pre-IND meetings for feedback; however, this approach would not be feasible for every company as the FDA does not have the current resources to handle this workload. Without product development plans that are sound and approved by the FDA, many programs are embarked upon and fail because of incorrect program development, including study designs, endpoints, etc. Without proper planning upfront, millions of dollars and much time can be needlessly wasted on one product that perhaps would have died early on in trials versus five years down the road when it fails in a Phase III study.

2) Patient recruitment approaches, strategies and screening tools. Since patient recruitment represents one of the largest bottlenecks in the clinical trial process, the issue mainly revolves around the approach, strategy and screening tools. Many trials fail because the requisite numbers of patients are not recruited. Other trials become very costly when sites have to shut down and others are opened because they did not recruit enough patients. In addition, protocol violations occur more and more as investigators want to fill their studies and keep patients on trials as much as they can, especially if the drug is showing promise as is in the case of “complex therapeutic trials” such as oncology, HIV, etc. This overall problem has resulted in the loss of millions of dollars for sponsors over the years and compromised promising trials.

3) Investigator agreements and contracts. This area represents another problem for CROs and sponsors alike. Many times it can take up to 9 to 12 months to get an investigator contract in place thus hampering site initiation, and causing major delays in the recruitment of patients and the overall timeline of the study. By offering a solution to this problem, months and even years could be shaved off of studies as many trials have staggered enrollment, especially oncology and more difficult therapeutic area trials.

4) Budget and contracts with CROs and vendors. This area also represents a bottleneck for sponsors to get their studies started and completed on time. Many times the issues put forth in contracts are not communicated to the development teams or the requirements for final deliverables are not understood. Months are wasted on rework and tracking as well as starting up a study. This all translates to high costs and additional time.

5) Protocol and CRF standardization. Currently within CROs and sponsor companies, CRFs are generated each time a new study begins. Many times these CRFs are developed from scratch. Protocols are also designed and go back and forth with several reiterations before they are implemented. Much time and effort could be saved at both CROs and sponsors if CRFs were standardized and therapeutic or product type protocol outlines were made available. The cost savings for both of these areas would be great.

6) IRB streamlining of processes and informed consent standardization. IRB processes are cumbersome and not standardized. In addition, informed consent forms vary from IRB to IRB and even within IRBs as some reviews are very thorough and others are nearly non-existent. A solution to this problem would translate into the streamlining of the overall site initiation process and offering quality, clean data in studies resulting in more effective and safer products reaching the market.

Overall, a solution to all of these issues above would allow sponsor companies to develop sound medical products in record time, saving millions of dollars. The result would be more effective products reaching the market quicker, that are economically viable, and have an established safety profile. In the end, this would translate to more products meeting unmet needs for many patients.

2. Please rank each hurdle identified in Question 1, above, in priority order according to which hurdles create the most severe product development problems. That is, which problems present the greatest opportunity for improving product development processes? Our goal is to identify those aspects of product development that would most benefit from new evaluation tools.

- 1) Established and approved product development plans
- 2) Patient recruitment approaches, strategies and screening tools
- 3) Investigator agreements and contracts
- 4) Protocol and CRF standardization
- 5) IRB streamlining of processes and informed consent standardization
- 6) Budget and Contracts with CROs and vendors

3. For each problem identified, please indicate the type of drug, biologic, or device to which the hurdle applies.

- 1) Established and approved product development plans-all types of drugs, biologics, and devices with the exception of some diagnostics and other devices that do not have to be tested on humans. Moreover, the more complicated the therapeutic area such as oncology, autoimmune disorders, etc., (“complex therapeutic areas”), the more this hurdle becomes tantamount.
- 2) Patient recruitment approaches, strategies and screening tools-as in number 1 above
- 3) Investigator agreements and contracts-same as number 1 above
- 4) Protocol and CRF standardization-same as number 1 above
- 5) IRB streamlining of processes and informed consent standardization-same as 1 above
- 6) Budget and contracts with CROs and vendors-all types of drugs, biologics and devices.

4. For each problem identified, if a solution would facilitate the development of drugs, biologics, and/or devices for a particular disease or categories of disease, please indicate which diseases would be affected?

Each of the problems identified would have an impact on the development process within any disease or category of disease. However, for more complex trials that are conducted multinationally and for complex studies such as oncology where CRF pages number on average 150 or more versus allergy studies (average 50 pages), solutions would have a greater effect. Moreover, patient recruitment efforts within oncology, for example, require many more resources and have much longer timelines than within simpler therapeutic areas such as respiratory studies, etc.

5. Nature of the Solution. For each problem identified, please describe the evaluation tool that would solve the problem and the work necessary to create and implement the tool/solution. For example, would a solution come from scientific research to develop a new assay or validate a new endpoint? If the solution involves biomedical research, please specify the necessary research project or program. Would a tool be developed through data mining or computer modeling? Would the right tool be a new FDA guidance or industry standard? If work on a solution is underway, what steps remain? Are there other innovative solutions that could be explored?

1) Established and approved product development plans

A guidance document developed by the FDA in conjunction with industry could help guide a company in correctly designing the appropriate program with the requisite number of trials and the appropriate endpoints, target patient population, etc. for each of their trials. The FDA could then establish a review process based on certain criteria such as unmet medical need, etc.

2) Patient recruitment approaches, strategies and screening tools

If a national registry were made available this would help tremendously in connecting the appropriate patients to a trial. Some efforts are underway to do this. Perhaps linking this registry to every patient advocacy group would streamline the recruitment process further. In addition, if all trials run by the sponsor company or CRO were linked electronically to sites, this would also speed up the recruitment process as well as help with the overall quality management and integrity of the trial. Finally, a hand-held tool (e.g. biomarker for rapid genetic, proteomic, metabolomic assessment) similar to a glucometer at each investigator site

for screening would allow rapid patient recruitment with very low screen failures and enhance the overall quality of the trial data, greatly eliminating drop-out rates, etc. This would result in a much better targeted patient population for the trial immediately at the outset. There are some companies developing these currently.

3) Investigator agreements and contracts

The solution to this issue would be to establish a standard agreement or contract for all investigators. The development of such a tool could be spearheaded by various investigators working together to come up with common legalize. This could also be established in collaboration with POMA. Investigators would then generate the agreement with the CRO or sponsor so as to cut down on the back and forth revision process between the two groups.

4) Protocol and CRF standardization

CRFs can be standardized by industry and protocols could also be standardized by industry with input from the FDA based on therapeutic areas and types of products. In other words, a library or database of protocol outlines would exist by therapeutic area or class of compound or product.

5) IRB streamlining of processes and informed consent standardization

Informed consent forms should be standardized across all IRBs and this can be done by industry. Streamlining of IRB processes can be achieved by more oversight on the part of regulatory agencies. Once IRBs have more oversight such as CROs by the FDA, they will begin to standardize their processes leading to the streamlining of this industry sector.

6) Budget and contracts with CROs and vendors

Industry can work to develop in collaboration with POMA and encouragement by the FDA budgets that are more standardized so that they can be compared and quickly negotiated. Moreover, budgets and contracts need to be detailed enough so that expectations are met and rework becomes a thing of the past.

6. For each solution identified, please indicate which could be accomplished quickly, in less than 24 months, and which require a long- term approach?

1. Established and approved product development plans-long-term but not sure-this is an FDA process.
2. Patient recruitment approaches, strategies and screening tools-long term
3. Investigator agreements and contracts-less than 24 months
4. Protocol and CRF standardization-less than 24 months
5. IRB streamlining of processes and informed consent standardization-long term
6. Budget and Contracts with CROs and vendors-less than 24 months

7. For each problem identified, what role should FDA play and what role should be played by others? Should FDA play a convening role, bringing the relevant parties together to discuss an approach or solution? If so, who else should participate? Should FDA coordinate scientific research, the results of which would be publicly available? We are seeking input on ways to target FDA scientific and collaborative activities to help industry bring more safe and effective medical products to us for review.

1. Established and approved product development plans-FDA should play a convening role involving industry, CROs, and patient groups
2. Patient recruitment approaches, strategies and screening tools-long term-FDA should play a convening role bringing groups together such as industry, IT groups, patients, and scientific inventors (biomarkers)
3. Investigator agreements and contracts-FDA can encourage industry to work on this

4. Protocol and CRF standardization-FDA can encourage industry to work on CRF standardization and collaborate with the FDA on protocol outlines
5. IRB streamlining of processes and informed consent standardization-FDA should play a convening role bringing CRO, investigator sites, sponsors, and IRBs together and also set more guidance for this industry sector
7. Budget and Contracts with CROs and vendors-industry can work on this with encouragement from the FDA.

8. What factors should guide FDA in setting priorities among the hurdles and solutions identified?

The factors that should guide the FDA in setting priorities are those related to the safety of the product, its efficacy, and its ability to meet an unmet need for patients. All of these issues are related to cost and time. By analyzing the time and cost issues related to each of these aforementioned hurdles and solutions and then attaching safety, efficacy, and unmet needs parameters to each of these, the FDA will be able to prioritize the list.