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INDUSTRY AND FDA COLLABORATION
TWO ROLES, ONE GOAL

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The FDA and the pharmaceutical firms share a common goal - the assurance of quality, safety, and efficacy of drug products. The roles they assume in achieving this goal, however, may appear to lead them along separate paths. Let us examine these diverse paths which lead to the assurance of product quality.

Certainly a primary goal of any industrial concern is to return a profit on investment. If one considers this goal in depth, one must come to the conclusion that the surest means of favorably affecting the corporate bottom line are by achieving these mutual goals of quality, safety, and efficacy. Certainly, a failure to reach appropriate standards, as in a recall, for example, affect not only the reputation, but the financial health of the firm.

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The goal of assuring the production of high quality products must be approached with practical considerations borne in mind. Some may accuse the FDA of disregard for the practical aspects of expenditures of resources by the firm. Agency personnel must realize that a firm's resources are not unlimited, and that unnecessary expenditures may compromise the firm's ability to compete in the marketplace, or may drain resources from areas requiring additional research expenditures. As an example, sophisticated instrumentation may be mandated for the analysis of a product where less expensive equipment would give equal assurance that the product meets standards. Industry must also guard against internal imposition of impractical instrumental requirements as may occur when laboratory scientists seek to justify the purchase of the latest new and expensive "toy".

The FDA exists in order to assure that firms and their products meet the requirements of federal law. There is usually no real conflict between good science and technology, and regulatory requirements. Where there appears to be a conflict, a closer look at the situation usually reveals a misinterpretation of either the science, the technology, or the law.

Under our governmental systems, the pharmaceutical firm bears the primary responsibility for assuring that its products meet applicable scientific and legal standards. This is both proper and realistic. The firm, thanks to the years spent in

developing each product, has far more intimate and detailed knowledge of all aspects of that product than could ever be gained by the FDA during the course of a review. Both federal law and the laws of the marketplace hold the firm accountable for its actions; its rewards and penalties depend upon its performance.

Industry, then, has the responsibility for assuring that its products meet standards. The FDA has the responsibility of enforcing the federal laws which regulate the standards of the pharmaceutical firms. Differences may arise in the interpretation of legal requirements, and in the judgement of a firm's practices. These differences have been handled in very different ways by different firms.

At one extreme is the type of firm whose policy it is to talk with FDA only when absolutely necessary, such as when approval is needed for a product or a manufacturing facility, and then only at the last minute. They may communicate only when threatened with legal action. In this type of firm, the legal staff, and not the scientists, do the talking.

The FDA has its analogous share of hard-liners, and they have their own, valid reasons for fearing to appear too cooperative. The industry is not generally sensitive to the pressures placed upon agency personnel by consumer advocates and Congressional oversight committees. Mistakes are made very

public, and the decision making process is examined minutely in the glare of much publicity. In such an atmosphere, the rewards may appear to be greater for agency personnel who say "NO" than for those who say "YES". Fortunately, in recent years, the "NO's" have increasingly become "maybes" or "tell me more". This may appear frustrating to those anxious for quick approval, but any atmosphere which keeps the doors of communication open can only, in the long run, aid industry.

How can the pharmaceutical firms take advantage of this new, more open communications policy to improve relations with FDA? In the area of IND's, NDA's and ANDA's, the opportunities to establish a better working relationship exist as never before, due to the proposed rewrites of the IND and NDA regulations. With the FDA having made this initial move, it is now the responsibility of the firms to insure that their submissions are of consistently high scientific quality. Nothing can so easily destroy an atmosphere of mutual respect as poor quality data submitted in support of a proposal. Of course, industry can always quote examples of unbending and unjustified criticism by an FDA receiver, but the groundwork for an over-reaction by the agency in a given situation can usually be traced to a poor submission, not necessarily from the same firm, received at an earlier date. Given the pressures on reviewers, one can understand their reluctance to get burned twice. It is in the best interests of the firm to establish a reputation for consistently high quality sub-

missions, and for a willingness to engage in open scientific discussion.

But what about genuinely excessive and scientifically unjustified demands by a reviewer? It appears to some agency personnel that firms often comply blindly with all reviewer requests, only to complain loudly and longly at industry conferences about the unreasonable demands made upon them. Here it behooves the agency to become more sensitive to the pressures placed upon an industry scientist in this situation. The firm may argue a scientific point for months, and ultimately win the decision, but it is a pyrrhic victory indeed if this scientific argument has delayed the market launch of the product by several months. Every month off the market is a real bottom line loss to the corporation. Viewed in this way, giving in to "unreasonable" reviewer demands makes economic sense.

There is a danger in this approach, however. Not voicing an objection to such a request implies that the request was reasonable and expected. Hardly the truth! Differences such as these, or questions about apparent agency inaction, are best handled if the management of the firm has established a forceful and forthright policy on communication with the agency.

For scientific questions, it is preferable that industry scientists speak to FDA scientists to resolve differences. If resolution of the problem cannot be accomplished at this

scientist-to-scientist level, management should step in to facilitate settlement of the problem.

A second area in which communication between FDA and industry has improved is in the approval process for new plants and facilities. The agency has demonstrated a willingness both at headquarters and at the local level to communicate with industry at the planning stage and throughout construction of such facilities. Firms which have taken advantage of these offers have profited by better communication and marked reduction in time for approval. The old philosophy of "we'll talk to FDA when the building is finished and running" has no place in today's environment.

There are several initiatives the firm can take to expedite the new facilities approval process. The firm should seek the help of the local district office early in the planning and development stage. While FDA may not have all the engineering and subject matter skills at the disposal of the firm, nor does the agency have an obligation to serve as consultants for the firm, they do have a great deal of country-wide experience, and can bring an objective eye to the firm's plans.

Another advantage in involving the FDA at early stages of construction, and throughout a project, is that the FDA has a chance to become thoroughly familiar with the facility by the time final inspections occur and decisions concerning its accep-

tability and approval must be made. This early involvement both saves time, and keeps FDA up to date on the state of the art.

A third area in which industry - FDA relations can be improved is on the occasion of a visit by an FDA inspector. This is the most direct encounter most firms have with the agency. The best way to handle the visit so as to make all participants more comfortable, while yet protecting the rights of the firm, is to have available a well-defined Standard Operating Procedure for handling these visits. This SOP should designate persons from the firm, in various areas of responsibility, who are to deal with the investigator. Wherever possible, unless there is a real legal question involved, scientific or technical people, rather than attorneys, should be assigned to accompany the investigator and to obtain responses to his requests for information. Highly qualified people should be assigned, and their charge should be to respond as completely and concisely as possible. The firm's representatives' should then prepare a report describing the investigator's areas of interest or concern, making an overall evaluation of the visit. They should note all comments made by the investigator, and communicate to him, before he leaves, any disagreement with his findings. These should be followed up with a letter to the local office, describing the disagreements, as well as any corrective measures taken by the firm in response to the investigators' observations. In this manner, most questions can be settled at the local office level, with minimal time

wasted, and without the threat of legal confrontation.

In summary, it should be kept in mind that in all dealings between FDA and industry, the goal of assuring product quality is the same for both participants. Their differing roles may cause divergence in their paths, but there is always room for negotiation. Somewhere between insistence on confrontation, and blind agreement with all demands, lies a middle ground of optimum resolution. It is the task of industry to lead both parties there. FDA and industry can work together to achieve their mutual goal of providing the American public with high quality, safe, effective drugs, while maintaining a healthy pharmaceutical industry within our free enterprise system.