BY IRA ASHERMAN

Ensuring Success In The Regulatory Process

The measure of a pharmaceutical company's success is the number of drugs it gets approved and into the market. This is what the *Wall Street Journal*, *Barrons* and every other financial journal writes about. It is what drives the price of stock and is, therefore, the greatest concern of every pharmaceutical company. Every drug in the pipeline is important, but only as an indicator of drugs that might eventually come to market.

Getting regulatory agencies to say yes becomes crucial, since it is their decision that allows the drug into the marketplace. And with most issues in drug development, some companies get that "yes" easier than others, who are in a continual struggle with the agencies to get their compounds approved. The question that everyone wants answered is: *What can I do to get "them" to approve my drug more expeditiously?*

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There are three sets of skills critical to a company's success in dealing with regulatory agencies:

- An understanding of the regulations;
- Good science and high quality data; and
- High quality working relationships with agency staff.

For the past several years, I have conducted negotiation workshops for industry, as well as FDA. It is my experience that most companies know the regulations and most companies have highly capable scientists who understand what they need to provide if a drug is to successfully navigate the regulatory process. I believe there is one issue that distinguishes the more successful firms from their less successful counterparts: the quality of the relationship maintained with agency staff and, most notably, the degree of trust that exists between the company and agency personnel.

Trust derives from two places. First, and probably most important for regulatory personnel, is their company's reputation. The second is how they, individually, are viewed — their individual reputations with regard to trust. There has been much research looking at trust and its impact on communication and negotiation. These studies suggest that when trust is high, the quality of the interaction is different. In "Beyond the Walls of Conflict," David Weiss stated: "Trust allows the negotiating parties to communicate honestly about their problems and to explore mutual gains solutions jointly. Trust allows you to understand alternatives and make effective choices."[1] In their 1985 study, which looked at trust in buyer/seller transactions, Paul H. Schurr and Julie L. Ozanne reported: "There is reason to believe that tough postures fail when trust is absent from an exchange or bargaining relationship."[2] In a 1972 *Administrative Science Quarterly* article, Dale E. Zand wrote: "In high trust groups, there is less socially generated uncertainty and problems are solved more effectively."[3] In his 1978 book entitled — interestingly enough — "Trust," Jack Gibb brought it all together when he wrote: "Trust makes it unnecessary to examine motives, to look for hidden meanings, to have it in writing. As trust ebbs, we are less open with each other; we look for strategies in dealing with each other; we seek help from others; or, we look for protection in rules, norms, contracts and the law."[4]

While none of these studies directly relate to the regulatory process, the evidence is persuasive in suggesting the importance of trust in the negotiation process, as well as its potential for impacting the negotiations between company and agency personnel.

Should the quality of the relationship really make a difference in the drug approval process where the science and data are the ultimate issues? The answer is

a resounding YES. We all act and behave differently with people we trust, and data have a totally different impact when presented by a highly trusted individual. Trust does make a difference. I found this to be true during my own employment with the New York City Human Rights Commission, where I was charged with looking into the employment practices of the retail industry. I behaved very differently towards those companies I trusted than those I did not. I would suggest that the reviewers at FDA, EMEA and other agencies throughout the world do not behave any differently. I am not suggesting that a good relationship can take the place of poor data, only that, all things being equal, a strong relationship can and will make a difference. Creating and fostering trust is not a one-way street. Although it is not solely the company's responsibility, it is the company that wants its drugs approved and it is the company that needs to take the initiative if relationships are to improve and trust is to increase.

Low trust companies behave differently. As a former official at one of the European agencies noted to me, "low trust companies often have less robust data." If you have any doubt that there are differences, you need only look at CDER Ombudsman Jim Morrison's article in the December 1999 and January 2000 issues of *News Along the Pike*.[5] In the article, Morrison attempted to answer the question: "What most bugs the center's staff about industry?" Morrison surveyed FDA staff for comments and among the items identified were:

- Calling very frequently regarding the status of a document review;
- Failing to control anger, making inappropriate and demeaning statements to staff;
- Bypassing several levels in the supervisory chain to bring problems to senior management that could be solved at a lower level;
- Ignoring advice on protocols and other input from previous meetings and correspondence;
- Doing only the minimum with regard to what is requested;
- Seeking immediate answers to complex regulatory issues at meetings or on the phone; and
- Being less than forthright about safety issues with investigational or marketed drugs.

Morrison details a number of other inappropriate behaviors. Based on my experience with FDA staff, I would suggest that all of Morrison's Pet Peeves will have a negative effect on the quality of the relationship. In discussing the safety issue, he notes: "Nothing destroys working relationships and trust so much as appearing to be willing to trade public safety or corporate reputation for financial advantage. In the long run, strategies that attempt to hide information, even for a short time, cause much more damage than they can ever avoid." He continues, adding "the most difficult aspects of any type of law enforcement or regulatory work are how to recognize who is trustworthy and who is not — and to deal with each accordingly."

In addition to being the industry's greatest strength, science is also its greatest weakness.

High trust companies behave very differently. For example:

- When asked for information by the agency, they respond quickly and appropriately;
- When there are problems with the data, they let the agencies know early;
- They don't hide things, hoping they will not be discovered;
- They don't blame the agency when problems arise. They take responsibility for their behavior;
- They don't come to the agency with minimally acceptable packages; and
- When dealing with agencies in other parts of the world, they bring someone who speaks the local language.

Will increasing the trust and the quality of the relationships really make a difference? I believe it will, in a variety of very subtle, but important ways. When agency staff trusts you, they look at your data differently. They are more willing to take things at face value instead of looking for hidden motives. In addition, when trust is present, people are more willing to look for creative solutions to difficult problems. As Morri-

son notes in discussing the Pet Peeves: "There are certain behaviors to avoid, and if avoided, one can significantly increase trust and improve interactions."

Engaging in low trust behavior has far reaching implications, and is internalized differently, depending both on the behavior and how frequently it or similar behavior has occurred in the past. By engaging in the type of behavior Morrison lists, you also send the reviewer a message about how you see them. I would suggest that the message is not a flattering one and is seen for what it is — namely that you believe the reviewer is not as smart as you are and that you can put something over on them. This is clearly seen and understood. In addition, agency staff talks to each other and your reputation (particularly if it is negative) will be affected. As with all large organizations, the agencies have excellent informal communication networks.

The remainder of this paper will detail our view of the internal corporate factors that affect the quality of agency relationships, and give rise to many of the behaviors detailed above. I also will suggest a comprehensive approach that I believe can improve a company's success in working with all regulatory agencies, not just FDA. The factors are in no particular order.

Overemphasis on the Science

Probably the greatest strength of any pharmaceutical company is its scientific competence. *If we have the best scientists, in time we will have the best compounds.* Science is what it takes to get compounds approved: it is essential. This industry has at its very core, high quality science conducted by outstanding scientists. However, in addition to being the industry's greatest strength, science is also its greatest weakness. When it comes to working with regulatory agencies, an overriding concern with science can limit a company's ability to look at and explore options. All attention is focused on the data, the science, and the more data the better. This emphasis on science also is seen in the vast array of courses and programs offered by such organizations as RAPS, PERI and DIA. A brief review of their offerings and the sessions at their national conferences reveals an almost singular focus on the technical side of the equation.

Although the science is critical, it is not the only currency available. To focus exclusively on it is a serious mistake. Rarely do we find companies looking at the quality of their agency relationships or asking what they can do to improve interactions with agencies. Yet, when we conduct our agency workshops, a major topic of discussion is always how reviewers feel they are treated by company personnel. If companies are to build high trust relationships, they need a better balance between the content (the science) and the relationship (trust).

Lack of a Long Term Strategy

Most companies approach regulatory agencies on a drug by drug basis. *What will it take to get today's compound approved and how fast can it be accomplished?* Although focusing on today should not be overlooked, companies must begin to look at the big picture, to think strategically and in the long term. In a recent *Harvard Business Review* article,[6] Danny Ertel, looked at the negotiation process and suggested, "companies rarely think systematically about their negotiating activities as a whole. Rather they take a situational view, seeing each negotiation as a separate event, with its own measures of success." In short, companies must develop an overall strategy for dealing with regulatory bodies.

Only with a strategic view can a company effectively answer the tactical questions that constantly need to be addressed. This issue of strategy is of particular importance, since regulatory staff frequently is not the only ones interacting with the agency. There are a variety of stakeholders, constantly pushing to take action. Having an approach that is clearly understood and accepted by everyone gives regulatory leverage in dealing with individual stakeholders, as well as with agency staff.

Demonizing the Agency

I ask participants in our programs to describe the conversations that take place about regulatory agencies at their companies. I ask if the conversations are generally positive or negative. Almost without exception, people report that the conversations are negative; rarely is something positive said. The problem is further complicated by the fact that people rarely talk about the people involved, but about "the agency." This makes it very easy to demonize. *The agency is just a group of people who don't understand what we are trying to accomplish. They make unreasonable demands that only delay our drugs reaching market.* When individuals are discussed, it is also mostly in negative terms. The general sense in most companies is *the agency is a negative outside force making our life unreasonably difficult.* It is interesting that when I ask if their actual experiences are so singularly negative, most say that they have had some very positive experiences working with agency staff. Our follow-up question is always the same. Do

you share these experiences with your co-workers? The typical response is usually a resounding no, because there is too much personal risk involved in defending the agency. As many participants have suggested, *you run the risk of losing credibility with your co-workers if you are seen as someone who defends the agency.* The long-term implication of this behavior is that it paints and sustains a very negative picture of the agency and its staff. The same series of questions get very similar responses, when asked during our agency programs.

Understanding the Agency

Agency personnel are, at best, in a very difficult position. Companies are so focused on their own needs that they rarely take the time to think about and understand the person representing the agency. To paraphrase a former FDA employee: *"We're between a rock and a hard place. On the one side are people telling us to speed up the process — that we don't approve drugs quickly enough and on the other side are those concerned that we're approving drugs too quickly and unleashing dangerous drugs on a unsuspecting public."* Agency personnel are faced with trying to find the balance between these competing needs. And, if you are to work effectively with the agency, then you need to understand and appreciate this dilemma and the pressure it creates for the reviewer. The choices are not as simple or as clear as we sometimes make them sound. We need to put ourselves in the reviewer's shoes and perhaps *not* make that extra call or push for one more meeting.

Inability to Admit Mistakes

Companies seem almost totally unable to admit that they may have made a mistake in their dealings with the agency. If anything goes wrong: *"It's not our fault, we did everything they asked. They changed the requirements,"* or, *"They changed reviewers who looked at things differently."* It is never considered that the data was not as good as it should have been or that they never fully answered the reviewer's questions. Since no one from the agency is there to share the agency's view of events, blaming them comes very easily.

Internal Constituents

Regulatory personnel play a unique role. They are not just "liaison personnel," but "boundary people" who span the boundary between the company and outside agencies. Being a boundary person presents some very unique issues and problems. Regulatory people serve as the company's representative to the outside world and, as a result, are faced with balancing competing needs and interests — those of the agency and those of the company. Internal negotiations can seriously affect one's effectiveness with the agencies. It is urgent for regulatory staff to maintain their relationship with the agency. Yet, other departments (Marketing and Clinical, for instance) are driven by competing needs that are more short term in nature and these needs may require the regulatory person to take actions that are not compatible with maintaining agency relationships. While regulatory personnel acknowledge the involvement of other departments, they may not fully appreciate the impact these groups have on their behavior. Relationships with Marketing and Clinical, as well as with senior management, are critical — they are your clients. Regulatory personnel do not negotiate in a vacuum, but within a constellation of complex, intertwined relationships.

Regulatory personnel are "boundary people" who span the boundary between the company and outside agen-

Willem F.G. Mastenbroek, a Dutch consultant, writing in *Group And Organizational Studies*[7] in 1980, highlighted the complexity of this relationship when he discussed what he calls, the "Representation Dilemma." He suggests: "Yielding to the pressure of the rank and file often means that the chance of the negotiators to achieve results is reduced. Constituents tend to be more radical than their representatives. They not only want a larger share of the benefits, but they also see their adversaries in more negative and stereotyped ways. If a representative goes along with these tendencies, his or her position as a representative

is often strengthened. Members approve a tough stand. It gives them confidence in the credibility and leadership of the representative." He added: "It can be difficult for negotiators to resist this kind of pressure from the rank and file, especially when yielding to it strengthens their own position" with their constituents. The degree to which constituents trust the people in Regulatory, the greater degree of freedom they will have in dealing with the agencies. Unfortunately, this degree of trust does not always exist and "they" are frequently pressuring us to take action we feel to be inappropriate. Yield to that pressure and you run the potential of compromising your agency relationships. Resist and your internal clients will lose confidence in you.

Industry's continual refrain is that the agencies need to be more transparent but how transparent is industry?

It is important for regulatory groups to recognize that they span the boundary between their companies and the authorities. To do the job well requires an understanding of not only the regulations, but of how to navigate the complex series of relationships that impacts their effectiveness. How well that is accomplished will affect the company's success with the agencies.

Next Steps

Strategy Meetings

Where do we go from here? The first step in addressing the issues outlined above is to look at the issue of strategy and develop a vision as to how to be viewed by both the agencies and internal clients. Not looking at both creates a very incomplete picture. In conducting this type of meeting, you would be attempting to reshape your firm's culture as it relates to working with regulatory agencies. The questions that need to be answered at a meeting of this type are:

- How are we now viewed by our internal clients?
- How are we now seen by the agencies that we work with?
- If they were here today how do you think they would describe us?
- What do we do well?
- What do we need to improve?
- How would we like these groups to describe us in three years?
- What steps do we have to take to achieve the above?

If a meeting like this is to be successful, it should be held off-site and critical internal clients should be invited. To ensure that senior management fully supports the plan, appropriate representatives should be asked to attend the meeting. The results of this meeting should be shared throughout the company, so it is seen as company policy and not the exclusive province of the regulatory group. If possible, data should be collected from the various agencies you deal with and brought to the program.

Assess Pet Peeves

Using Morrison's list of "Pet Peeves," look at your company's behavior and ask: *"If we were on the receiving end of our behavior, how would we rate us?"* Try to place yourself in the reviewer's shoes. If you are not sure or have doubts about the answers, ask an impartial outsider or invite one or more of the many ex-FDA officials who are now working as consultants to participate. If appropriate, you also might ask some of the reviewers you deal with to rate you. This activity could easily be integrated into the above strategy meeting.

"How transparent are we when dealing with the agencies?" Industry's continual refrain is that the agencies need to be more transparent. But how transparent are we with regard to our data, our actions and our motives? Based on my own experiences, I doubt sponsors always meet the same high standards they set for the agencies.

Build Negotiation Capability

Concurrent with developing a strategy, it is critical to develop the capability to implement that strategy. If a company is to be successful, questions need to be answered and strategies implemented. First, identify those people you consider your premier negotiators. What is it that they have done that distinguishes them? What traits have they demonstrated? As a second step, analyze and reduce what the top negotiators do to a

series of behaviors that can be taught to others. Experience suggests that this can be done. Going through this process allows you to identify the core competencies that are critical to being a successful negotiator in a regulatory environment. Once the competencies have been identified, training programs can be developed that teach these skills. By implementing this process, you send a very strong message: negotiation is a skill and it can be taught. The process should not stop at this point. Unfortunately however, most corporate learning is seen as a series of isolated events — employees attend a training program and that is where the process ends. Negotiation, particularly as it relates to the regulatory process, cannot be treated in that manner. If a company is to be successful and sustain that success, it must develop approaches to institutionalize its successes and to learn from its failures.

To that end I suggest:

- Regular meetings at which people are asked to present particular negotiations — what they accomplished, their approach and anything that others can learn from. These should be meetings in which peer feedback is valued.
- Preparation must be seen as a process that requires a particular format and the involvement of others.
- Criteria should be developed against which you can measure negotiator success. At a minimum, this should include both content and relationship issues.

Danny Ertel, in writing about the companies he studied, summarized the importance of taking these steps saying, "by creating a broadly supportive infrastructure, they produce powerful results. They don't just improve the outcomes of individual negotiations; they break down the assumption that every negotiation is unique and immune to coordination and control. They form the basis for more collaboration, creativity and efficiency — not to mention more accountability — throughout a company's negotiation activities."

Conduct Lessons Learned Sessions

"Lessons Learned" meetings should be conducted on a regular basis throughout the development process, not only at the point that a compound is approved or disapproved. To wait until the end means that too much time will have elapsed and memories become very selective. More significantly, periodic reviews allow for adjustments to be made in what you are doing. Make sure that you invite everyone who has been involved. It does you no good if the meeting is restricted only to the regulatory staff. As part of this process, it might be interesting to involve the agency. At a minimum, outside consultants familiar with your drug and what you are trying to accomplish should be a part of the process.

Create New Stories

New stories about agency personnel should become part of your company's culture. The importance of stories in creating a more collaborative environment cannot be underestimated. There are a number of ways that this can be accomplished, including, but not limited to:

- Positive articles in the company newspaper or magazine about the agency staff and the agency in general. Many years ago, one of our clients did a multi-page article in their company magazine on FDA, its staff and its role.
- Be realistic in your assessments of agency staff and their dealings, both with you and other company personnel. Be willing to talk about the positive experiences.
- Involve critical stakeholders in Lessons Learned meetings.

New Educational Activities

Educate your stakeholders about what you do and the role of the regulatory department in the drug development process. You have a positive and critical role to play that needs to be communicated and understood. This can be accomplished by:

- Conducting training programs for staff about what the department does. This doesn't have to be a major program — a half-day is probably more than enough. This activity could be done at team meetings.
- Inviting stakeholders to attend agency meetings with you. Take the initiative, don't wait until they ask. Once they ask, it is too late.
- Publishing a newsletter that brings people up to date about what is happening — generally and specifically — with regard to individual compounds. In today's environment this can be accomplished easily electronically. Establish your own Web Site — everyone else is doing it.
- Attending meetings of your stakeholders so they see that you care about their concerns and understand their business and the pressures they are under. Let them know that you are not the enemy.

Conclusion

Success with regulatory agencies is a complex process. It requires attention to both the science and the relationship. There needs to be balance. One without the other will ensure that you will always be less effective and your internal clients rarely satisfied. Improving the quality of the relationship — to improve the degree of trust — will require both time and attention. I believe this will be time well spent. Can I guarantee that if you do all of the above your drugs will be approved more quickly? I wish that I could. What I can guarantee is that if you do not pay attention to the quality of your agency relationships, the compounds you submit will face a more rigorous and demanding review process.

NOTES:

1. Beyond the Walls of Conflict, David W. Weiss, Irwin Professional Publishing, Chicago, IL, 1996; p.51.
2. Influence on Exchange Process: Buyer s Preconceptions of a Seller s Trustworthiness and Bargaining Toughness, Paul H. Schurr and Julie L. Ozanne, Journal of Consumer Research, Vol. II, March 1985.
3. Trust and Managerial Problem Solving, Dale E. Zand, Administrative Science Quarterly, Vol. 17, 1972; pgs. 229 239.
4. Trust, Jack R. Gibb, The Guild of Tutors Press, Los Angeles, CA, 1978; p.14.
5. CDER s Pet Peeves, Part 1 & 2, James Morrison, News Along the Pike, Vols. 5, 6, December 1999 and January 2000; pgs. 2, 3.
6. Turning Negotiation into a Corporate Capability, Danny Ertel, Harvard Business Review, May June 1999; p. 55.
7. Negotiating a Conceptual Model, Willem F.G. Mastenbroek, Group and Organizational Studies, September 1980; pgs. 324 329.

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