Regulatory Approach toward Vaccines against Cancer: The Benefit/Risk Ratio

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Summary

Decisions regarding investigational new drug applications for testing of all biologicals to be used in humans, including those designed to prevent or treat cancers, must be considered in terms of benefit/risk ratios. In order for a regulatory organization to make the appropriate decision regarding the testing of new biologicals in humans, it must have an extremely broad dialog within the critical scientific public and the general public, which are represented on committees functioning in the Bureau of Biologics. There must be a general consensus regarding the benefit/risk ratio of proposed new biologicals for scientific progress and the effective regulation of biologicals.

Everyone is probably aware of the fact that the Bureau of Biologics, located on the NIH Campus, is part of the Food and Drug Administration. The Bureau of Biologics has the regulatory responsibility within the Federal Government for regulating Investigational New Drug applications dealing with clinical investigation that relates to biologicals, and it is responsible for licensing of biologicals. This includes vaccines in general, including anticancer vaccines. In essence, the monitoring during the investigational phase and in the actual certification is the role of this Bureau.

For that reason, of course, we are extremely interested in the type of discussion this group has had at this Symposium, and other similar discussions that have taken place in the past and will occur in the future. We think it is very important that we are part of the interaction and dialog that is going on. This is an area in which there is a great need for dialog between interested scientists, interested parts of the public, and interested people who are providing funds for this type of work. We see ourselves as junior partners, but nevertheless as your partners in this very commendable effort to try to move toward a new type of control of human disease. As such, we would hope that we can play a productive role in interacting with you.

We feel the Bureau operates most effectively, a little bit as a catalyst, perhaps, at the interface between those who are very much involved in the basic sciences in developing new thoughts, new ideas, new concepts, and those who are very much involved in the practical, e.g., manufacturers and clinical investigators. In other words, in this day of great public dialog, we hopefully are at the middle trying to promote the type of discussion and, hopefully, the decision-making necessary in a democratic society.

Turning to the practical concepts, you should also consider several thoughts as to how a regulatory organization like ours operates in today’s world; that is, everything is considered essentially in terms of benefit/risk ratios. There are very few absolutes in the world in which we live. It is easy to say that, but it is true. It is benefit/risk. As such, to evaluate benefit/risk in almost any scientific proposition, one has to have an extremely broad dialog within the critical scientific public. In other words, you must have the best research considered by the best people. There has to be, then, in the ongoing dialog, the development of concepts, the development, if you will, of scientific consensus. But in today’s society particularly, the public also has to be brought into this dialog. When one is talking about benefit/risk, as you realize, we have all the committees that I think all of you are familiar with, similar to your own clinical investigation committees. All of these endeavors are efforts to try to bring as many concerned people as possible into the decision-making process or into the dialog that leads to the decision-making process.

We feel that essentially anything is possible in a benefit/risk proposition, but in arriving at where you are going to be and what you are going to do it is extremely important that one work in as wide a public forum and have as wide a discussion of the issues as possible. Of course, the type of meeting you are having today is exactly that. This is one of the many processes by which the scientific public and the general public move forward to determine in their own minds what specific actions are rational or not rational in terms of evaluating a benefit/risk equation.

In this sort of proposition, we come back to the fundamental thing. The fundamental thing is good ideas. You cannot escape from that. The thing that will make or break any program or make or break any attempt at progress will be the development by people like yourselves of good ideas, practical problem-solving ideas, ideas that are in fact deserving of testing in the laboratory and in man, and ideas with which you can convince your colleagues and the public in general that those ideas do deserve testing in the laboratory and in man. In other words, again, the development of what would be considered consensus is needed to determine whether something is reasonable and desirable to do based upon benefit and risk.

Looking at this concept that nothing is impossible, you should understand how the Bureau of Biologics operates. We have said this to many groups before but we will repeat...
it for this group, because we have not spoken to each of you personally before. Many people, even today, sometimes regard the regulatory organization or the head of a regulatory organization as someone who is sitting somewhere in the closet and making God-like decisions that we will or will not do this or that. You can be assured that nothing is further from the truth. The way a regulatory organization must operate in society today is to try not to make unilateral God-like decisions. Our operation is trying to promote broad public discussion, broad scientific discussion, and the interaction of our group with these groups to be able to identify scientific and public consensus that particular courses of action are logical and reasonable. Now, we can do many things to promote this type of discussion, but our actions must reflect what you yourselves as scientists can come to regard as a basically sound course of action. If you cannot bring yourselves together to decide that a course of action is reasonable, we cannot decide that such a course of action is reasonable. If you decide a particular course of action is reasonable, and for one reason or another we lag behind, we are not discharging our responsibilities. We are saying that in a public agency such as a regulatory agency today, you yourselves are in essence a part of that agency, because all we are doing, in essence, is reflecting the types of benefit/risk judgment decisions that you, the scientific community and the public, make. If we operate in any other way, we are not operating properly.

Looking at benefit/risk then, one says that literally nothing is impossible. If you go through various people's philosophical papers about cancer vaccines, like those of Dr. Maurice Hilleman, Dr. Joseph Melnick, and others, you will find similar ideas. But often people fall into the trap of saying that something cannot be done. You cannot use continuous cell lines. You cannot test attenuated cancer viruses. We would not want to propose that we should go out and do either tomorrow, but in the world we live in, the science world we live in, we would not regard anything as impossible in the indefinite future.

Again, it comes back to benefit/risk, and what is possible is that knowledgeable people will consider a reasonable risk to take on the basis of the type of benefit. This happens every day in the world of cancer, not necessarily for the theoretical, anticancer vaccines being considered today, but in terms of cancer chemotherapy. The types of drug risk that society will take in trying to treat, say, a patient with advanced cancer are entirely different from the types of drug risk that one will take in trying to treat a normal volunteer. So, we regard really nothing as impossible, and it is more a question of deciding what is reasonable and what is proper within the benefit/risk equation.

The final thing we would say is that we all recognize that if we must wait until we completely understand something before we try to deal with it, we will be a long time in dealing with the problems of the world. In manuscripts we have written in the past, I have cited vaccinia and the control of smallpox long before the mechanisms were understood. Others have used the same example. You also can use the example out of this scientific field in terms of bread and yeast. How long have people been baking bread? People were using yeast long before anybody had any concept of what those microorganisms were doing.

Perhaps a more worthwhile comparison with the cancer vaccine might be the use of fire. How long did man use fire before one discovered the processes that are involved in combustion? The other good analogy with fire, too, regarding cancer is that here again with cancer vaccines, one is trying hopefully to make use of something but not to burn one's fingers in the process.
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