THE CANCER LETTER INTERACTIVE

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Cancer Center Directors Contemplate The Role Of Centers In The 21st Century

PHILADELPHIA—What do current trends in demographics, technology, and health care tell us about the cancer centers of the 21st century? What will be the mission of these institutions? What can be surmised about their form, function, and funding? What sorts of perils—and opportunities—lie ahead?

Some trends are worrisome, cancer center directors said at a symposium titled "The Future of Cancer Research Centers," held April 12, at the annual meeting of the American Association for Cancer Research. As the U.S. population ages, cancer incidence can be expected to rise. At the same time, reimbursement for cancer care will continue to be subject to downward pressures, and, surely, there is an economic downturn on the horizon.

However, the 21st century is likely to bring advances in basic science and informatics that could lead to major improvements in mortality and morbidity from cancer—provided that research institutions such as centers are there to translate laboratory findings to clinical interventions, the center directors said.

"Cancer research centers have many of the same problems that all

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In Brief:

UT-Southwestern Wins BMS Grant; ONS Gets $1.6M; Unilever Chair In Diet Formed At CINJ

HAMON CENTER for Therapeutic Oncology Research at University of Texas Southwestern Medical Center at Dallas received a $500,000 unrestricted cancer research grant from the Bristol-Myers Squibb Foundation to support the center's work in identifying genetic changes leading to lung and breast cancer. **John Minna**, director of the center, will supervise the five-year grant. . . . **ONCOLOGY NURSING SOCIETY** received a pledge of $1.6 million from Bristol-Myers Squibb Co. for research and educational programs. The funds will be used for the ONS Foundation's Center of Leadership Information and Research, grass roots educational programs, and Living With Lung Cancer: The Women's Perspective, a study to document the quality of life of women with lung cancer. . . . **UNILEVER**, the global consumer products company, donated $1.25 million to the **Cancer Institute of New Jersey** to create the Unilever Chair for the Study of Diet and Nutrition in the Prevention of Chronic Disease. The institute is seeking nominations for the position. Contact William Hait, UMDNJ-Robert Wood Johnson Medical School, CINJ, 195 Little Albany St., New Brunswick, NJ 08901.

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Center Directors Discuss Challenges, Opportunities

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academic medical centers have today and some problems that are unique," said Joseph Simone, medical director of the Huntsman Cancer Foundation and Institute, University of Utah, and organizer of the symposium. "We are in a changing environment, economically, academically, and in the influence of industry in our world."

At the symposium, five current cancer center directors and one director emeritus provided insights into their concerns, plans, and hopes for the future.

Excerpts of their remarks, and portions of the symposium discussion, follow:

Robert Young, president of Fox Chase Cancer Center, on "Comprehensive Cancer Centers in the 21st Century."

What are the huge influences we are going to run into over the next century that will change every single cancer in the country?

—Demographics: Currently there are 34 million people over 65; by 2080, there will be 87 million, a 150 percent increase. For those above age 85, now 3.8 million; by 2080 there will be 18.3 million, a 400 percent increase. The frequency of people above age 85 will double by 2025.

There are 80 million baby-boomers heading to senior citizenship, that's 30 percent of the U.S. population. Currently, 13 percent are above age 65, and by 2030, 20 percent will be over age 65.

Cancer is projected to replace heart disease as the No. 1 cause of death by 2005.

In 1995, 75 percent of our population were non-Hispanic whites. In the next 10 years, only 25 percent of U.S. growth will be in this population. Highest population growth rates will be Hispanic and Asian. By 2030, the non-Hispanic white population will be less than 50 percent of the population under age 18. By the middle of the 21st century, two out of five births will be non-Hispanic white, one-third Hispanic, one-fifth African-American, and one-tenth Asian.

The cancer patterns in our institutions will shift. Patterns are likely to change over the generations, but for a couple of generations we are going to be seeing more stomach cancer, more pancreatic cancer.

There is also confusion in cancer demographics going on which is difficult for the public to sort out. On the one hand, we have the good news that the age-adjusted mortality for cancer began to decline in 1990 and has declined every year since then at about 1 percent a year. At the same time, because of the aging of our population, between 1995 and 2050, the aging population will cause a 75 percent increase in total deaths, 2.3 million in 1995, and 4 million in 2050.

With the elderly population the most rapidly growing segment of our society, total cancer deaths will increase annually unless there is a dramatic decrease in the age-specific death rates.

—Computers and informatics: It's projected that by 2010, the average PC will have the capacity of our current supercomputers. It's likely that in the next 20 to 30 years, it will be possible to both store and retrieve all clinical information on all patients treated. With microprocessors, miniaturization, we can make multimedia information exchange common and inexpensive. This brings the capacity for advanced home healthcare systems, self help, information, health coaching, electronic house calls, image-guided surgery, and robotics.

—Genetics and genomics: No one in this meeting would suggest that this is not going to revolutionize everything we do. Cautionary notes: Straightforward genetic explanations likely to occur at best in 5 to 15 percent of cancers. The genetics of complex traits which influence the other 85 percent, this array of genetic interplay with environmental causes may simply become too complex to sort out in any clinically relevant way.

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Our concept of genomics over-promises. All that the genomics information is going to give us initially is a picture of the cards we hold in our hand, not the capacity to either correct the cards we hold in our hand or even reshuffle the deck.

The potential political backlash if we don't do this kind of research correctly is always present.

Having said that, the promise is incredible. It will clearly be a tool for discovery of novel drugs. It will promise new diagnostic tools. It will allow us to do disease risk profiling in ways we have never been able to do in the past. It opens the world to strategies related to the genetics of pharmacology and the metabolism of new pharmacologic agents and the specificity of pharmacologic agents to individual patients. Way down the road in this century is the genetic re-engineering to eliminate disease risk.

What's the role of cancer centers in this changing environment? First, they need to remain the discovery engine for cancer research in this country. Over 50 percent of all of the NCI grants are in cancer centers. At the same time, there is increasing competition for novel infrastructure funding mechanisms. We've seen the birth of Specialized Programs of Research Excellence, of Cancer Genetics Networks, of tobacco centers for excellence. Since 1992, the centers funding has increased about 7 percent and SPOREs 77 percent.

I'm not saying SPOREs aren't good. They are. What I'm saying is, there are more and more mechanisms out there competing for research dollars with the cancer center.

The informatics revolution will create a new center-based potential for regional and national networks. One of the most important and powerful tools for the future will be the capacity to link genetics and genomics with carefully defined patient populations and outcomes.

What else will be changing? We will see an increased focus on population-based research, because it's now more possible than ever before because of the informatics and genetics capacities that are emerging. We will see a shift from high-tech, end-stage intervention to prevention-oriented research. We will see an increasing role of cancer centers in brokering science between academic health centers, industry, payers, and different health care settings. Hopefully, we will also see an increased focus on compression of morbidity in addition to our focus on prevention and cure.

Unless centers are successful in dealing with all of these issues, their relevance will progressively diminish in the next century.

We are all going to have to face the issue of where the money comes from. Societal demographics make the viability of the present health care funding suspect. That's the most charitable way I could express that statement. I don't see any way, given the demographics, that anything we have in place is capable of dealing with the reality of the health care bill in 2030 to 2050. Medicare is supposed to be bankrupt by 2015. The philanthropic support for our centers, which is one of the most flexible of all our funding mechanisms, rests on this extraordinary economic boom. If it goes bust, the philanthropic support for these efforts will decline as well.

You have seen the institution of a wide variety of important new NCI funding mechanisms, and I support them. One of the realities is that as these are created, it creates the need to continue to increase funding. The reality is that a 10 percent per year increase in the NCI budget is needed to keep the investigator-initiated research funding pool level.

New technology and prevention increases, not decreases, the total health care costs. That's one of those dirty little secrets people don't want to talk about. But in fact, the easiest and most cost-effective way to deal with health care bills of people is to have them die in infancy. Anything you do that prolongs their survival and their disease-free survival ultimately increases total health care costs.

Furthermore, society keeps expanding our definition of health. We now lobby to have our tennis elbow repaired by the Medicare funding mechanism. That certainly was not considered 100 years ago.

One of the most extraordinary pieces of information [comes from] 1990 Medicare data [showing] this extraordinary maldistribution of health care consumption. Four percent of the Medicare population consumed 32 percent of the Medicare dollars. Fifteen percent consume 80 percent of the Medicare dollars, and 24 percent of the Medicare population consume 92 percent of Medicare dollars.

If you are a wise Medicare HMO, these are the patients you want in your HMO because you get reimbursed at somewhere around 90 percent of the average Medicare reimbursement. So if you run a successful HMO and you care for the patients who don't need care and you shunt all these into the present Medicare system, the total health care costs of Medicare patients goes up, not down.

What are going to be the key roles for centers

in the 21st century? They must remain the centerpiece for cancer research and discovery. If they don't, they shouldn't be around and we probably don't need them. We need to implement the technology advances in genetics and informatics. We need to be a part of a serious dialogue about the reality of health care funding. We need to encourage the definition of appropriate coverage limits. We need to develop new paradigms for population-based research. We need to develop systems to demonstrate and deliver quality cancer care. We need to participate in demonstrations that define what works and give up what doesn't.

Some practical hints for survival in the 21st century:

—If centers are not engines of quality science, there will not be cancer centers.

—One of the realities of the demographics is you may end up needing those beds you have closed as more and more elderly people have cancer.

—We need to be honest about what works if we ever want a fighting chance to control uncontrollable health care costs.

—We need to think seriously about outcomes and how to demonstrate quality care within our cancer centers.

—We need to focus on prevention research opportunities.

—We all need to learn how to speak Spanish.

Paul Marks, president of Memorial Sloan-Kettering Cancer Center, on "The Challenge of 'Health Care Reform' for Comprehensive Cancer Centers."

The challenge of health care reform for comprehensive cancer centers has been primarily related to the fact that reform has focused on health care costs. This focus has dominated the health care scene for the past six years following the effort to reform by the Clinton Administration beginning in 1992. The Health Security Act introduced by the Administration in 1993 and the debate that it stimulated focused more on health care cost reform than either the quality or the accessibility of health care, especially cancer care.

The failure of that legislation simulated very rapid expansion of so-called managed care. In most areas of the country, managed care has not so much been about managing the quality or access to care as it has been about containing or trying to reduce the costs of that care.

Another aspect of the challenge of health care reform for comprehensive cancer centers which has its root in the failed effort of passing comprehensive health care legislation has been the spate of mergers among academic health centers and between academic health centers and community-based health care providers. The networks being formed in this manner often do not focus sufficiently on the quality of the cancer care provider brought in to such a network. This has to be a source of concern because comprehensive cancer centers should be the hallmark of high-quality cancer care, as well as institutions for basic and clinical cancer related research and health professional training. This role of comprehensive cancer centers could be undermined by efforts on the part of academic health centers of which they are part to become dominant providers in their regions or to achieve greater penetration in their market. These were goals not previously perceived to be central to the mission of comprehensive cancer centers. Indeed, if cost containment continues to drive our cancer care providers, then cancer care will become a commodity as medicine was before the Flexner report (Carnegie Foundation for the Advancement of Teaching, 1910) in the first decade of this century. It's appropriate to recall the impact that report had on U.S. medical education and medical practice. The report concluded that there were too many medical schools providing too inferior an education, leading to inferior health care providers. The report led directly to making quality a central issue in medical education and health care.

We must recognize that there are factors that are driving up health care costs. Bob Young has already eloquently touched on the great challenge of the aging population. Another factor he touched on were new technologies. I don't think all new technologies increase health care costs. Clearly, some like laparoscopy, to avoid exploratory abdominal surgery, or drugs such as G-CSF to avoid the complications of chemotherapy, have led to reduced costs in the caring for patients. As Bob indicated, unfortunately, we have experienced an overuse of expensive new technologies that have not necessarily been proven to be worthy of their costs.

A third factor is increasing the costs of health care owing to errors in diagnosis or treatment. I was unable to find any accurate statistics with respect to estimating the costs of medical mistakes in cancer care. But there is a 1991 report from the Harvard School of Public Health on the costs of medical

mistakes in the state of New York, which estimated that about $1.8 billion per year and the additional costs of lost worktime of about $0.5 billion per year were directly related to medical mistakes or malpractice. I think a further insight into this problem can come from data that have been reported with respect to second opinions on surgical pathology. At Memorial's department of pathology, something over 15 percent of all specimens referred in for second opinion following review resulted in a change of diagnosis or staging that required refinement or basic change in the approach to the treatment of patients. Similar reports with regard to the percent of second opinions that led to altered care have been reported in the last three or four years from Johns Hopkins, M.D. Anderson, and Southwestern Medical School.

A fourth factor that contributes to increased health care costs is the relatively inadequate emphasis on programs of prevention and early detection, including the fact that in many instances, managed care programs fail to adequately reimburse for these procedures.

It is clear that we are entering a period of rapidly emerging new knowledge about cancer, particularly the genetics of cancer. With it comes very promising, complex opportunities, as well as challenges for comprehensive cancer centers.

As we know in just a few years, we anticipate the deciphering of the precise structure of the human genome and with it, previously unavailable opportunities for approaches to cancer care. There is no question that genetic research will impact every aspect of cancer research, health professional education, and cancer care through better understanding of the causes of cancer, the development of predictive tests for risk to cancer, new and better diagnostic and prognostic tests, and better targets for prevention and therapy. With this will come very complex ethical, social, and public policy issues, which, if we do not properly handle, will not only stifle research, but more importantly, will prevent the appropriate application of these advances to improve health care.

With the rapid advances in health care comes another challenge to comprehensive cancer centers. That is the integration of these new therapeutic modalities into the care of patients. This will be facilitated by information systems and new medical technology. Outcomes will become the primary basis for decision with regard to both the appropriateness of cost and the quality of our care. Above all, care will become increasingly patient focused.

Over the past several years as part of a comprehensive quality-oriented approach to health care, various innovative disease management programs have been developed that cover both standard and investigational diagnosis and therapy, taking into account both the quality of care as well as the cost. Disease management is an approach to patient care which integrates patient care services, provides standard treatment practices to reduce variability, evaluates treatment in terms of various endpoints, as well as financial and patient oriented quality of life outcome. As we increasingly move to this approach to cancer care, in most traditional academic health centers, we will face the challenge of the departmental disciplines and integrating that approach to academic governance, and education, and research, with the disease management approach, which clearly must cut across multiple disciplines.

Disease management teams share a focus on a disease or a closely related group of diseases. At Memorial, 17 such teams have been organized, related to specific cancers. They include experts in surgery, medical oncology, etc., dealing with that disease. Every member of the staff is a member of one or more disease management team of their own choosing and perception of their own expertise. Supporting the disease management system, a software program has been developed which permits, first, a systematic approach to designing treatment pathways used in the care of each cancer patient, and secondly, an ability to analyze clinical and financial outcomes and identify the best and most cost effective approaches to delivering cancer care.

A great challenge to comprehensive cancer centers will be not only the education of our own staff with regard to best practices and the ongoing clinical research programs, but to extend that education of the state-of-the-art cancer care to community-based cancer care providers.

At the present time, useful outcome data from which to base judgements as to best practices are limited. The situation clearly is improving. Recently there was an article in Lancet reporting an outcome data of cancer care in the United Kingdom that indicated that the greater the experience of the provider, the better the outcome. This relationship was strongest for patients with breast cancer, ovarian cancer, and gynecological malignancies. In this country over the past couple of years there have been a number of studies reported focusing on surgical

outcomes comparing the experience of surgeons and/or hospitals with particular procedures and the mortality data. Data from New York institutions based on New York state's SPARCS database analyzed the impact of hospital and patient volume on inpatient mortality rates. The data clearly show a direct relationship between the high volume hospital and physician, which has the lowest mortality rates of about 2.2 percent, compared to the low volume hospital and physician, which is 9.9 percent. That's more than a four-fold difference. These data carry through several analyses which have been made based on the Medicare data, and have very profound public policy implications and carry profound challenges to our comprehensive cancer centers.

As you might suspect, postoperative in-hospital mortality rates do relate both the length of stay, and cost of care. The better the outcome, the better the stay, the less costly the therapy for the disease. These outcome data indicate that quality of care need not been more expensive, and in fact, may be less expensive than care that leads to less desirable outcome.

This is the obvious message from where we stand today and where comprehensive cancer centers are going to be challenged in years ahead. The emphasis must be on quality and not quantity, and the best cancer care requires an environment in which excellent research and teaching are going forward.

Max Wicha, director of the University of Michigan Cancer Center, on "The Challenge and Promise of University-Based Cancer Centers."

I think its fair to say the strength of the national Cancer Centers Program is based on the diversity and the strength of individual centers. Certainly, no two centers are alike, because each center takes advantage of their particular strengths. University-based centers have challenges and opportunities that are somewhat unique.

The obvious advantages or opportunities of a university-based center results from the fact that these centers are part of research universities. The strength of a university-based cancer center is largely dependent on the strength of the research and educational activities of the university, and it's the challenge of the cancer center leadership to figure out how to take best advantage of those opportunities. I will talk about departments from the point of view of what are the problems of academic departments, but I want to point out that they also have strengths, and having strong academic departments greatly increases the ability of the cancer center to marshal all of its resources in cancer care and research.

The managed care issues for university-based cancer centers are equally important, but somewhat different, than freestanding cancer centers, in that much of our business is total cancer care in a contract in which we can subcontract cancer care, but it's not quite as urgent to have carve-out contracts as it is in freestanding cancer centers. We all have a large alumni base in training and students.

At the University of Michigan, we are situated in the middle of a university that has strong schools in the health sciences and in other disciplines. Our cancer center has members from all of the health science schools who actively participate in our research programs, as well as other schools in the universities, particularly the engineering and biology departments, in a number of our basic science programs.

What tangible benefit does one get from being part of a university? A benefit is illustrated by a new program that is just being undertaken at our university. The Life Sciences Initiative will spend about $200 million to build an infrastructure for basic science that will link the medical campus with the rest of the university. The cancer center leadership has played a key role in this life sciences commission, and we plan a new research building that will be right between the medical center and the university. What's interesting is, some of the topics we've chosen for the life sciences involve this issue of biocomplexity, really a the center of trying to understand cancer, since it is clear that cancer is not the result of defects in a pathway but in branching networks of pathways, and complex information theory will be necessary to piece this together with the major inputs into genetics and biotechnology, including imaging. So I dare say that virtually all of our programs in the cancer center will greatly benefit from being part of the university. We also think this will have an advantage in educational activities.

I can't talk about the University of Michigan without talking about football. At the Michigan vs. Michigan State game, during The March last year, we brought in 100 cancer survivors. The new scoreboard listed messages about the importance of cancer research. The athletic department has been a major supporter, raising over $300,000 a year for the cancer center.

There are many different models for how

university cancer centers have been established and what structure and governance that they use. One is a departmental based model, like Johns Hopkins University, in which there is department of oncology. There are now more and more of these around the country. They have the advantage of a simple structure, with the authority of the director more clearly defined. There are matrix centers, the way we function at the University of Michigan. What mainly distinguishes these is whether the cancer center director has authority to make academic appointments, or whether this needs to be shared with existing departments. Duke is one university that has the hybrid model, and again, there are more and more of the hybrid model, in which most appointments are made in departments, but a limited number of appointments, particularly in the basic sciences, are made in the cancer center. All of these models have worked in different institutions.

The major challenges to university cancer centers are the departmental structure and resistance to change. Those are the two biggest obstacles to overcome in establishing successful university-based cancer centers. It's up to us as leaders of these centers to figure out how we can work with the existing structure to change it into structures that make more sense in the future. The departmental structure of academic health centers made sense in the era before managed care, and when science made more clear distinctions between different disciplines.

As we are aware now, science has evolved. The distinctions between different basic science departments have disintegrated. For instance, somebody working in signal transduction could be in any one of the basic science departments. Similarly, clinical care is becoming more and more multidisciplinary. So the barriers between departments don't make sense on the clinical side either. Even education initiatives, which were the main reason to establish academic departments, have now become more interdisciplinary. This relates to the authority of the cancer center director. In many centers, even though there are new opportunities in philanthropy created by being part of a medical center of a university, there also is competition for donors. It is important to have a structure set up and agreements so that this can be handled fairly.

Another problem that many academic centers run into is the issue of indirect costs from grants, who gets that? How are the grants administered, by the cancer center or by departments? In talking to many department chairman not only from our university but others, what's interesting is that the most important thing to many of these department chairs is not so much the control of these grants, because after all, they don't really get much other than a percent of the indirect cost, but the credit for grants, because the success of academic departments is measured by their NIH funding.

We are now initiating at Michigan a new system where grants can be managed by the cancer center, but they will be credited to academic departments. That removes one of the major hurdles to setting up some of these interdisciplinary centers.

Change is the biggest problem to overcome. One irony of health care reform, as bad as it has been for many areas of financing, one of the things that it's done is it's forced medical centers to look at how they do business. If it wasn't for that, there would be very little impetus for change.

Cancer center directors, in order to be successful, need to have resources. These four areas of resources—space, budget, appointments, and philanthropy—all successful university-based cancer centers have the ability to have at least three or three and a half out of these four. Many don't have the authority to make appointments independent of academic departments, but I don't think there is an example of a cancer center nationally that has been successful without the cancer center director having some of this authority. NCI has been very useful in assisting some of the cancer center directors with their leaderships of the medical centers to convince them that this is clearly important.

The design of our center and its opening two years ago gave us the chance to completely rethink the way we did cancer care at the University of Michigan. We set up committees to work on how the structure of the center and our patient care activities would work. We have an executive committee that has department chairs on that, and the most important committee is a steering committee, which has the leaders of the traditional disciplines. Virtually all other cancer centers have moved away from this in their core grants, which are truly multidisciplinary. But it's very important to involve the leadership of the existing structures in order to take best advantage of the resources available.

In 1996, before we planned and moved into our new building, we had 13 different cancer clinics, but they were all run independently by each department. Each had a completely different system, and the

cancer center had made a small inroad into getting four multidisciplinary clinics started with a lot of resistance from the departments. There were 10 different locations, and six main clinical departments.

We completely re-engineered the way we deliver cancer care into multidisciplinary teams. These teams run both multidisciplinary clinics as well as single discipline clinics in an integrated fashion. Each of the teams has a physician team leader, but has members of multiple disciplines in addition to physicians, nurses, social workers, and clerks. These teams meet regularly and we think have improved the care of cancer patients. We have 10 multidisciplinary clinics. The lesson we learned about these clinics is, in order to be efficient, you need to have very tightly controlled scheduling and you need to have flexible ways of mixing multidisciplinary clinics and single discipline clinics.

We have immediate tumor board so that patients can get the opinion of the group as soon as possible. We are being hooked up for telecommunications to be able to communicate with affiliates.

Being in the Detroit area, we took advantage of the car companies, and General Motors had a program in management efficiency. For example, we had them plan how an infusion area would work. Instead of five different departments giving chemotherapy, it's now centralized with very tight scheduling, and our efficiency has doubled—the time required for patients has been reduced by half, with greatly increased patient satisfaction.

There is a special area designed for pediatrics. We made the decision in our medical center that pediatric oncology would be part of the cancer center, clinically, and not part of the pediatric hospital.

Virtually all cancer centers are in various stages of development of networks. In setting up these networks, the overall driving force has to be the quality, and the quality of data obtained on clinical trials. In setting up a network, one can have competing interests between the financial interests and the interests of the hospital, versus the academic interests of the cancer center. I believe that the best centers take advantage of their academic potential. The chief reason most of our affiliates have wanted to work with us was because of the potential for academics and to extend clinical research to the community.

After we moved into the new building, our volume of new cancer patients has more than doubled. One of the issues we face is how big do we really want to be? We believe that our patient population should serve our academic mission, and that should be what determines the size of the clinical enterprise. To give you an example of the power of a multidisciplinary organization, before we had a cancer center organized, we saw about 100 new melanoma patients a year. Last year, we saw about 900 new melanoma patients coming from all over the Midwest, because of the multidisciplinary team.

One of the biggest issues in running a cancer center like this is, what about the revenues? We are all aware that the clinical margins have gotten smaller and smaller, and in the future, there probably won't be much of a margin. Nevertheless, in order to have an efficient operation, the cancer center has to have some ability to reallocate resources and to invest in the development of future programs.

Different centers have used different models to try to figure out how to deal with the needs of departments and the needs of cancer centers, which are often competing. At the University of Michigan, we are in the process of setting up a structure. Right now, all of the personnel in these cancer clinics are employees of the cancer center, not employees of departments. But what about the clinical revenues? How does one ensure that physicians are meeting the needs of the cancer center? There are several different models that have been used and we are exploring these. The most complete model is a pooled model where all of the income from cancer goes to the cancer center, and it has complete control over these resources. Needless to say, this is the most threatening to the department structure and most department chairmen are not very willing to do this, although there are a few examples.

Our chairmen have agreed that we will work toward this over the next few years, but they are not ready to leap into that yet. A much simpler model which one can institute much quicker without radical changes in structure, but one can view as a transitional model, is essentially a taxation model, where a percent of the cancer income weighted also for efficiencies of cancer care, and you can use other things such as patient satisfaction, result in an overall taxation of the cancer business, which flows back to the cancer center to use as discretionary money. The argument for doing this at a time when departments are already financially strapped, and asked how could they give more money to the cancer center? The answer is that the volume and the business can increase significantly, much more than the tax would be.

Finally, a number of centers including our own

have set up endowments to provide discretionary dollars.

At the heart of all this is the ability of cancer centers to change with the environment as we move into the 21st century. We've heard of some of the scientific challenges we face ahead, but I think we also have great opportunities, and the cancer centers are in an excellent position to continue to be the translational engines that will drive research and deliver the best patient care.

Robert Day, president emeritus of the Fred Hutchinson Cancer Research Center, on "The Cancer Centers' Research Mission and the NCI."

I have been fortunate to have had some experience to write a brief paper on this subject. The first such experience being a member of the National Cancer Advisory Board for a term that ended last year, which led to my serving on the review committee that [NCI Director] Rick Klausner appointed to review the Cancer Centers Program. [The report is available at http://deainfo.nci.nih.gov/ADVISORY/bsacactrprgmin.htm]

There has always been a tension between the cancer centers and NCI. That tension has to do with accountability, the kinds of research that are conducted, perhaps the mission that NCI sees for itself. On the other hand, the cancer centers are often presented as an extension of NCI. I recall a map that [former NCI Director] Vince DeVita used to show the activities of NCI. It began in Bethesda and involved the cancer centers, the cooperative groups, and other types of efforts. As this map was elaborated, it covered the entire country.

Those who have preceded me on this program have presented some very provocative and interesting approaches to what we face ahead: the aging of the population. Being among the group that's aging rapidly, I am particularly concerned about how we deal with things like Medicare and how we are treated in these cancer centers. Unfortunately, these demographic facts are facts, and we will have much more cancer in the future than we've had in the past. We have a great deal to do.

I've summarized some of the data from the NCI website dealing with the centers and also received some information in response to my request. These are very broad estimates. In 1997, approximately $1.5 billion went into the extramural research program of NCI. The intramural program was about 25 percent of the total [NCI budget]. The difficulty I have in interpreting is how much of this is direct cost and how much is indirect cost, and since the federal government tends to build their buildings on a cash basis, while centers tend to bond these out and pay for them over time. So there are some big differences probably. I am not that aware of the intramural program of the NCI. I have chosen the figure of 2,250 as the number of NCI employees that were shown for 1997, and from that I abstracted about one in 10 would be what I would call regular scientific staff members. These would be individuals on a tenure system who would have space and resources in their own right and run laboratories or intramural programs of some magnitude. Again, I may be off by some amount, but the relative proportions are what's important. In addition, I would estimate that of that total of 2,250, probably a quarter have doctoral degrees.

If we break that down, divide the $600 million by 550, we get about $1.1 million for each of the intramural investigators who has a doctoral degree, and the figure is much larger, $2.7 million, for each of the senior investigators. That, I'm sure, does include the indirect costs of running the Institute, and of course, there is great variation in the amount of money that's needed to support a laboratory compared to a major epidemiological study, and compared to some of the clinical research efforts.

Of the 58 cancer centers in 1997, 10 are basic science, 13 clinical centers, and 35 comprehensive centers. These account for about two-thirds of the research, not counting contracts, that were awarded by NCI in 1997. That's about $1 billion out of the $1.5 billion that went into the R01-P01 related pools.

The space available to the NCI research program is about 600,000 square feet. I don't know if that includes common space, or if that includes clinical space, but again, that would be about 2,700 square feet per senior investigator, which in my experience is probably not far off the mark. That would allow a number of laboratory modules for laboratory investigators and some shared space. Here again, I plead ignorance of the intramural program and how space is assigned, but based on having run a cancer center for a number of years, I think that's a reasonable amount and accounts for the fact that some people are office-based.

The [NCI] Cancer Centers Program budget for 1997 was $132 million, and an additional $28 million for the SPOREs program. Most of the SPOREs are conducted in the cancer centers. Summarizing from

the experiences I've had in the past, I would like to draw your attention to some unfinished business in the review of the cancer centers, and perhaps some different ways of doing things.

As a result of the program review that Joe Simone chaired and a number of the center directors were involved in, there was great concern that the focus of the cancer centers and the review of the cancer centers go to the quality of science. Everyone on the committee agreed that this was important, and that a great deal of the database that was used to allocate funds to the cancer centers or approve requests based on quantitative information could be handled in a much less rigorous fashion. However, I would point out that the review of a cancer center for the purposes of cancer center support or core grant, though it may focus on the quality of science, really does not review the science. It reviews the infrastructure, the leadership of the program, the programs of the center, the shared resources, how the clinical activities of the center utilize the patient base, etc.

I have some alternatives to suggest.

One way to support the cancer centers that would certainly be a different way than we are doing now would be to agree upon some basic allocation to the cancer center because it meets certain minimum criteria, that is, it has a certain NCI grant base. This would form the core grant, and in addition, there would be some increment added for the increased amount above that floor that each cancer had as a result of being competitive for NCI grants and contracts. So that each cancer center would be able to count on a ready amount of support and some variable amount that would reward its competitiveness.

There is another way to look at supporting the cancer centers in relation to the NCI intramural program. Because in a sense, the NCI intramural program and the programs of the many of the cancer centers really are quite similar. One way to do this is as follows: NCI has a tenure system, which is not dissimilar to that found in many of the extramural institutions. There is a rigorous review process that has been instituted of about an every four year cycle of reviewing the intramural program investigators. If they meet standards which I don't believe are dissimilar from the extramural community, they continue to receive budget, space, and resources for their research. The cancer centers do have tenure systems. However, the amount that goes to basic salary support of the core investigators in a cancer center has been reduced systematically over the years. When I became director of the Hutchinson center in 1981, essentially all of the basic science group received all of their salary support through the core grant. This wasn't necessary in the clinical division because of the clinical income, but could have been at that time since most were funded, peer-reviewed investigators. That amount has been reduced progressively so that relatively few of the centers use the staff investigator award, which is the way in which members of the cancer center who were not program leaders, who were not in administrative capacities did receive support before under the core grants.

The core grant today primarily supports shared resources, development funds, and all in all is a very important grant, but it is not directed necessarily at supporting the core science of the cancer center, which of course is a strength of the investigators individually and collectively.

When the cancer centers were formalized under the National Cancer Act of 1971, some of the existing centers at that time such as Memorial, Fox Chase, Roswell Park, M.D. Anderson, received a fairly large core grant that included support for the basic investigations of the center, for the R01/P01 type of investigations, as well as other elements of support from a cancer center core grant.

If we go back to the model of how the NCI investigators are supported, which is a package, the tenure system, and reviews leading to direct support for their research activities as well as the indirect support their achieve through the Cancer Institute and NIH overall, the cancer center support grant could be changed and could include a tenure system for the cancer centers. In other words, go back to the days when the staff investigators were supported and that support would come from the cancer center support grant as it used to. It would be on par then with the way the intramural program at NCI works.

One alternative to that would be to compete both NCI investigators as well as the extramural community investigators for their support using the R01/P01 mechanism. It would be a level playing field in that respect and the pool of grant and contract activity would be broader, and everybody would compete for it.

Another alternative would be to take some of the $1 billion in 1997 that went to the cancer centers and use this in the same fashion that used to be used in the days of these very comprehensive core grants

and make available to the cancer centers an amount of money for each of the investigators. Their review would be similar to the review that is provided members of the NCI intramural program, every four years. Each of these investigators would be reviewed, as well as the cancer center overall. That, indeed, would be reviewing the science of the cancer centers.

The standard of research and education in the medical and biological sciences in this country, particularly since World War II, has been very decentralized. The cancer centers are part of a very major academic enterprise that includes education as well as the primary source of new knowledge through investigations. This is somewhat different from another approach, something that I understand about the British approach, where there tends to be a focus at certain places in certain areas, in depth. There might be several centers of excellence in gene therapy, for example. De facto, that occurs to some degree. But a mechanism that provided for core support for a cancer center could also include some flexible support for both the investigators and their research as well as the customary core grant support, and allow more concentration of science.

We are entering a big science era in biology which is different from what we've known before. It may have analogies to physics where the experimentation requires a great deal of effort and is very expensive and so requires a coordinated effort of a number of people. Particularly if you are going to look at genotype, clinical histories, follow people over time, collect other information about them, their relatives, their clinical course, correlating that with population samples. All of this gives rise very quickly to a large array of data points. To do that efficiently and effectively, in fact to do it at all, may require concentrations of investigators around resources that will need to be develop that's very different from what we've known in the past, where most of the science is conducted by relatively small groups or by individual investigators. That does not necessarily relieve us from the responsibility of assuring that the imagination of the individual investigator is still available to bring forth new ideas that can be translated into effective practices.

Looking forward to the next century, it may be that we will need to re-examine this issue of the cancer centers in their relationship to the research programs of NCI. Although it is a very good instrument currently, it can be perfected further, and in so doing will get us down to what our fundamental business is, and that is to find something new and better to do about the burden of cancer.

Umbrella Grants Vs. "Contrivances"

In a discussion session following Day's remarks, Simone asked the center directors about "umbrella" grants once used to pay staff investigator salaries.

"I think those umbrella grants proved too difficult to control for the quality," Marks said. "You gave a lump sum to a cancer center, but the quality issue became too big. I think that's one of the problems with umbrella grants, you don't have the opportunity to evaluate a group of investigators."

SIMONE—At one time a considerable amount of money from core grants went for salaries of investigators. Was that a good thing or a bad thing?

MARKS—I think it was a necessary thing, because salaries became a big issue. You couldn't see a uniform scale of salaries throughout the National Cancer Program. That became a big issue. Before removing the salaries, we went to a percentage or a ceiling on the contribution from a core grant. Then it became an area where it was possible to lay off to the institution some of the costs of the cancer centers as budgetary constraints became more and more of an issue, particularly during the late 1970s.

SIMONE—On the funding structure of your center, Max, what do the chairmen tell you?

WICHA—The chairmen pay lip service in public to how it will benefit them, but in private it's hard talk. I think it requires decision at the top. The dean really has to want to do this. If they make that clear to the chairs and if the chairs are convinced they won't lose money over the long run, then I think they will go along with it.

SIMONE—Is there anyone in the audience from a center that has shifted to a service model, where all cancer revenues come to the center?

DAVID TARIN, director, University of California, San Diego, Cancer Center—We are in the process of doing that. The departmental chairs have been remarkably helpful and have gone along with the oncology faculty who could see the benefits of the oncology service line because of the efficiency of it.... The revenues are going to come into what we call the oncology business administration.

The benefit of this is that if the service line really improves and it attracts more patients, it of course benefits clinical research because there are many more patients coming in to put into clinical trials. It flows from there that the better clinical trials you've

got, the more patients are going to want to come. So it's almost a self-fueling engine once it starts to work.

JOHN MENDELSOHN—We've had multidisciplinary clinics at M.D. Anderson for a decade, but they have always been resourced through the departments. We are doing an experiment now. Each multidisciplinary clinic is going to develop its own budget, these will be reviewed by a group of division heads who will try to put in balance the overall desires of these multidisciplinary clinics, and then when we distribute our budget funds, they will go directly to these clinics. It's going to be a challenge, but I think it's the right way to go.

DAY—There's a real disconnect between what the cancer centers are here for, which is primarily to train a new generation of physicians and find a better way to deal with cancer, and the Cancer Institute, which has its intramural programs that are well supported. I think there needs to be a redistribution of the cancer centers' dollars so that the research mission of the cancer centers is paid for and we don't have to go through all these contrivances to find ways to do it.

John Mendelsohn, president of M.D. Anderson Cancer Center, on "Cancer Centers As Translational Research Engines."

I have a little different opinion than what was presented by Dr. Day. I feel that the funding to the cancer centers should be to support the infrastructure of the center to support the ways it facilitates getting physicians, scientists, and others, social workers, working together on the cancer problem. It might not be wise to ask NCI to support the full salary structure of those individuals because it would draw money away from what the main function of the NCI is, which is to support research. The cancer centers are very effective at supporting research, and with these added infrastructure dollars which wouldn't include to my thinking paying full salary for all the investigators in the center. It puts the centers in an advantage to get the research dollars. That's the way I look at it.

The goals of cancer centers are three-fold. First, research-driven cancer care, and I want to emphasize the research-driven part. We are building data, sometimes in formal trials and sometimes collecting data retrospectively to continually try to improve care. A second goal is the translation of research discoveries into improved detection, treatment, and prevention of cancer. A third major goal is the education of the public and professionals to improve cancer care for the patient and for the people delivering the care.

Cancer centers enhance and focus both expertise and experience in the scientific and medical disciplines and departments to carry out translational research in a number of targeted areas—pathology and lab medicine, diagnostic imaging, the traditional surgery, medicine, and radiation oncology, the basic sciences of genetics, biology, immunology, developmental therapeutics, and prevention and population studies. This collection of expertise and experience focusing on cancer is what I think we bring to the table that justifies the resources that are brought to the centers.

As a result, all but one of the SPORE grants that NCI has offered in open competition are awarded to academic institutions that have cancer centers. Clearly, the cancer center being there has something to do with the SPORE grant being captured. The NCI estimate is that about 75 percent of phase I trials with new cancer drugs are performed by academic medical centers which have NCI designated cancer centers. The great majority of phase I trials are occurring in centers that are supported by core grants.

More than half of all NCI research grants, both basic and clinical, go to institutions with NCI designated cancer centers. That doesn't mean all the money goes to the cancer center, but those institutions which have cancer centers have more than 50 percent of basic and of clinical research grants from NCI.

Cancer centers also provide the faculty, the infrastructures and the patient populations that enable systematic, data-driven testing of new hypotheses bearing on the detection, treatment, and prevention of cancer. These large numbers of faculty infrastructure units and patient populations result in the fact that cancer centers can provide investigators, both clinical and laboratory, with research-driven hypotheses relevant to cancer. Non-cancer center universities and academic centers can do this too, but I think cancer centers have this critical mass that does it better. The center tends to get together colleagues who are willing to work in multidisciplinary, collaborative research programs and in multidisciplinary clinics. The centers are a source of developmental funds that come directly from the core grant and from philanthropy and other sources. The centers provide critical, core resources which are very important for developing new translational

research. Some examples are the nude mouse facilities, analytic pharmacology, vector-producing laboratories, biostatistics, and monoclonal antibody production facilities, which I would guess are present in one form or another in about half of the cancer centers in the country.

These are very valuable resources that allow faculty interested in translational research to get access to these types of resources without having to independently develop them.

Cancer centers can also provide large numbers of well-staged patients with banked tumor specimens. Usually the data are available to follow and document responses to therapy. We are being constantly called upon by drug companies as well as by academic units to draw on this resource of data on patients with their banked tumor specimens.

The cancer centers do facilitate access for scientists to partners. Access to NIH and NCI are enhanced by being a cancer center. Access to industry and biotechnology—they are drawn to cancer centers. Usually cancer centers provide help and a lot of expertise in patenting and licensing products that are produced, more than many universities can do in general. Cancer centers can support technology transfer. Entrepreneurs looking for areas where they would like to invest or develop new products are drawn to cancer centers. We'll look at new technologies and new drugs that are being developed. This can speed the process. Venture capitalists often work the same way.

The cancer centers become the conduit for faculty and others that are trying to develop new forms of therapy.

Here is an example of one investigator's portfolio. It happens to be Dr. Waun Ki Hong, from M.D. Anderson. In head and neck cancer, he has a P01 grant and a NIDR grant. [One] grant is looking at the molecular and genetic causes of head and neck cancer, using that to try to develop diagnostic approaches, better therapies, and early detection methods. [The other] grant is looking at chemoprevention, an area in which he has an expertise and in which they are trying to take former smokers and reduce the incidence of cancer in the head and neck area.

Another is a lung cancer grant, where we are looking at chemoprevention of lung cancer. [He has a] lung SPORE which is in collaboration with UT-Southwestern, looking at the molecular and genetic causes of lung cancer, and how this will lead to earlier detection, diagnosis, and better therapies. Finally, there is a cooperative radiotherapy study with a radiotherapist, looking at better ways to improve the toxic therapeutic effect of radiation therapy.

Together, there are probably 100 people collaborating in this from 10 different departments, and it's the kind of thing that can be done anywhere, but that being in a cancer center greatly facilitates.

Technology transfer is something we are talking about in depth at M.D. Anderson. Our goals and objectives in this initiative are to accelerate and increase the cancer therapy discoveries that are being made, to create new opportunities, either through an investment pool where we are going to take some of our monies and make them available to scientists who have ideas, or to raise funds from investors in the community to create a research endowment for basic research, which would be targeted toward technology transfer into new treatments. We certainly would like to have financial returns to the institution. We would like to reward the participants for their efforts, and the University of Texas has a very generous policy of sharing revenues from patents and licenses with the inventor. It's 50 percent going back to the inventor—very high compared to most universities. There is an impact on local and regional economic development as new products are developed and spin off companies.

The track record at M.D. Anderson for the past decade: In 1998, there were $3.4 million brought in in license income. This is from companies to which we have licensed products. They are now contributing to the research directly. There is one FDA-approved drug, Abelcet, an anti-fungal encapsulated in liposomes, and seems to be very effective when amphotericin resistance occurs from standard use of that drug. There are 11 drugs in development in phase I, II, and III at M.D. Anderson, which came primarily from our own research. Twelve companies have been formed in the past decade where M.D. Anderson scientists have collaborated with entrepreneurs and venture capitalists in Texas and outside of Texas to form companies. The equity portfolio for the institution, mostly in options, is now at $14.8 million from these efforts.

We have filed 895 patents [in the past decade] and have acquired and had issued 267 patents. This is a complicated and expensive process, but we feel it's important in order to generate some of the revenues and in order to control the development of these agents.

On the one side, there is research that produces and designs new drugs, and on the other side, there is the testing and the delivery to the patient. There is often a gap between these and that is an area that we would like to decrease. We want this gap to be minimized. The smaller the gap, the greater the chance for us to bring new treatments for cancer to the clinic. Because of that need, we are focusing on five area where we think there could be added value to the process provided by the cancer center as infrastructure. I want to emphasize that we're not going to set up and pay for all of these at M.D. Anderson. We are talking with people with whom we could collaborate. These five areas, if we succeed in setting them up and making them available for investigators, will achieve the goal of increasing translational research.

First, basic screening services. This includes a way to assess the cell cycle effects of different compounds, with a shared resource with flow cytometry. It also may involve a tissue bank where someone that's developed a compound in their own laboratory often tested against only one or two cell types can have access to cells and nude mice and do some simple screening, something that's hard to do in one's own laboratory, but given the resources and the skills already present at the center, we should be able to set up.

Second, analytic services. That includes developing extraction methods. If you have developed a product and you are going to start studying it in animals and eventually in people, somebody has to figure out how to get it out of the blood, how to assay it, how to validate the assay, and setting up proper quality controls so that this product does move forward and one can accurately measure it.

Third, small-scale manufacturing scale-up. We have investigators who would like to have peptides made, antibodies made, low molecular weight drugs, antisense molecules, and vectors for gene therapy. We're not going to get into all of these, but in some of these areas, we will be able to provide product formulation and packaging and quality control so that a reproducible product can be made, with GMP-like quality, initially, up to the phase I area, and eventually, we hope, turning it over to an independent, outside source by the time we get to GLP quality for more advanced studies.

Fourth, toxicology. For any new product being developed, there are FDA requirements in toxicology, and drug metabolism needs to be studied. These are the types of resources that are available in our center in scattered laboratories. By pulling them together, we think we can help this process, and that part could be done internally quite well.

Fifth, clinical pharmacology, which includes being able to assess pharmacokinetics and pharmacodynamic parameters as agents are studied in animals and then on to people, allowing us to arrive at the proper and safe dose of drugs.

We feel that technology transfer and the development of new therapies is a special skill of cancer centers. We are taking a very careful look at ways we could facilitate this process. We are fully aware that many drug companies are in the process of trying to streamline these very same processes, and we are talking with some of them about collaborating in such efforts.

The new area now of targeted drugs is exploding already, but it's going to reach the point where there are far too many compounds ready for phase I trials than all of us can handle. It's just amazing, because five years ago, all of us were worried that we had reached the asymptote in the development of new drugs for cancer, and now that the targets have been identified, often as oncogene or suppressor gene products, we are just pouring out new ideas that will need to be tested and efficiently worked up through this series of steps. I believe that the cancer center investigators should have a major role in this and should have the tools to do it.

At M.D. Anderson, our goal is making cancer history, and this is one way we are approaching it.

Albert LoBuglio, director of the University of Alabama at Birmingham Comprehensive Cancer Center, on "How Should The National Cancer Institute View Cancer Center Collaborations With Industry?"

I believe that cancer centers should partner with private industry in translational, early clinical trials, using their NCI-supported infrastructure. When I mention this to people, they either respond that that's so patently obvious that it's hard to know why we need to talk about it, or they respond that this sounds like a topic better left undiscussed. As I go around the country and visit various centers, there is a considerable variation in their perspective of industry interaction, particularly in the translational sphere. As John has mentioned, we are entering a phase of clinical research and translational research where there is an enormous number of options for potential

agents and interventions in neoplasia. Certainly, a more important role for the cancer center is to be generating the novel pathways or molecules or targets, but NCI has spent substantial resources helping us to be in a position to play an important role in that initial interface of a novel therapeutic intervention entering the clinical trial for the first time. This is a very difficult and challenging area, and one in which can often kill a program or a drug right in its tracks when the first clinical trial does not show the miraculous outcome which was hoped for.

Is there a conflict or a problem in this interface between NCI-supported infrastructure and industry early clinical trials? There is a potential for difficulty. Obviously, it is not the intent for industry to supplant expenses on their part by using NCI funds to carry out their specific programs per se. On the other hand, it certainly seems reasonable that the kind of infrastructure that we have that is often dealing with three, four, five in-house developments for early clinical trial, and has not reached anything like our maximum capacity to do this, to go ahead and use that infrastructure in a scientifically sound way in the interface with patients in the initial phase I or proof-of-principle kind of trial. I believe this represents an important opportunity on our part.

If there is a problem, who has the problem? NIH and NCI? I called some notable leadership in the NCI and asked if they have any policy documents on how cancer centers or funded entities should behave in relationship with industry. There don't appear to be any written documents in this regard. It is somewhat of a shifting objective at NCI, but it's reasonably clear that if the intent of the effort is sound scientific investigation and it fits within the portfolio of research interests and expertise of the center that there shouldn't be a problem, whether that agent is derived from an NCI source, a drug company source, or an internal source.

Congress is constantly reminded how the Cancer Centers Program provides ready access of novel, new therapeutics to patients and that this kind of support provides an important leg up on our biomedical industry here in the U.S. as compared to other areas of the world. Certainly, the public or our patients don't have a problem with this. They are anxious to have informed, scientifically sound early trials going on with novel agents being available to them.

If anybody, I think the site visitors seem to have more problems with this topic than any of the preceding groups, and I think it's important that we do have the ability to discuss this openly and provide an opportunity for industry to develop technology in terms of early clinical application through our infrastructure.

Why partner with industry? Willy Sutton's retort to why he robbed banks was, "That's where the money is." I don't mean money necessarily per se; it's where many of the drugs and reagents are. There are certainly agents that can be developed within a cancer center, might in fact be brought to GMP level of production in early phase I studies, but many more opportunities exist if one is going to interact with industry to develop those agents, since that's where the resources for much of this development exist.

The companies have the developmental machinery and expertise to carry out many of the toxicology studies and other developmental, formulary, etc., kinds of things. It's also where the resources for that intent actually exist. I think the company orientation provides a motivation toward getting the job done, the protocol activated, and the science accomplished, since they are trying to get the application into clinical use as efficiently as possible.

What infrastructure are we talking about? We have a clinical trial shared facilities of very expert individuals who can carry out difficult and complicated clinical trials. We have tumor procurement services that can provide high-quality materials so that one can do proof-of-principle kinds of studies. We have laboratory correlates funded from a variety of mechanisms in terms of grants and contracts that can bring cutting-edge scientific technology to the bedside to ask whether there is, in fact, a proof-of-principle in a strategy or not. We have recruitment and retention units that can provide adequate number of patients for these high-quality studies. We have increasingly expanded into community networks so that early phase II trials where we need more substantial numbers of patients can be readily accomplished. We've worked hard at building our informatics and communication system both for identification of patients, for cataloging of information about them, and for follow-up.

There is quite a bit of infrastructure that NCI and our cancer centers have put in place in regards to this translational interface that I think industry finds quite attractive and results in the interface of companies with our cancer centers.

Is industry particularly interested in interacting with us? I think the answers are sort of yes and no.

It's certainly true that the smaller companies, the gene therapy companies, the targeted immunotherapy companies, some of the small molecule signal transduction inhibitor companies are quite interested in interacting. The larger companies have very large staffs and often feel that they do not need the expertise of cancer centers or universities in order to carry out early clinical trials. It's true the interest is much higher in early trials, first-time ever in demand, documentation that in fact the strategy is taking place or not taking place in individual patients, and the recognition of the hurdles and the need for second-generation and third-generation reagents.

Most importantly, as the shift in reagents have gone to novel agents that cannot use traditional guidelines—that is, we no longer are simply going to be able to give a drug in a dose that finally makes the patient sick and then test that dose—we have to develop novel endpoints that allow us to determine whether a particular dose and schedule of an agent is having a bearing on the pathway or molecule that in fact is intended.

The experience of cancer center clinical investigators and translational researchers in battling these kinds of major hurdles is an important strength that is often neglected. These companies have large numbers of agents, they are interested in getting them into early clinical trial, but they know that the trial has to either have a positive result clinically, which is usually unlikely, or a positive result that allows them to move to the next stage of studies with some information that makes it more likely to be beneficial. One only needs to look at the monoclonal antibody area, which we now have a great resurgence of interest, with two approved products for cancer therapy. But when you look at the long history of the development of those two agents, we basically had to waste a company for every generation of reagent.

The companies that came out with murine antibodies went under before the genetically engineered antibodies came along. Many of those companies have gone under while we are looking at more preferred targets and objectives of the antibodies. This inability for companies to be maintained through first, second, and third generations is a real shortcoming of development.

Are cancer centers capable? Many of them are. There certainly is an attitude that maybe the cancer centers do high-quality research and industry is there to slug it out in the trenches, not very sophisticated. The attitude and the quality of research in industry have undergone substantial changes in the last decade, and there is a great deal to be gained in both directions.

The IRB issue is a recurring problem in dealing with industry. Our institutions are struggling with trying to provide an efficient mechanism. We still have experiences of some cancer centers signing up to do a clinical trial, and the trial is almost completed by the time the IRB approval takes place. The centers need to address the ease of getting protocols activated and completed. Certainly it's true for contracts. Adequacy of patient populations and quality of data, in many of the NCI-supported capabilities in cancer centers have produced dramatic improvement in data quality at those institutions.

Many centers are already fully embarked on partnering with industry for the ability to move agents from the animal model system to the human setting. There is a huge gulf between positive mouse studies and clinical efficacy. It is important that the cancer centers' capability address this, regardless of whether the agents are coming from industry or from NCI or other sources.

NCI Position On Center-Industry Interaction

In the final discussion period, Robert Wittes, NCI deputy director for extramural science and director of the Division of Cancer Treatment and Diagnosis, said the Institute endorses the efforts of centers to work with industry. "I don't think the NCI position here is equivocal," Wittes said. "I think we have made it clear in any number of ways, including by explicitly amending the guidelines for the core grants, that we support this.

"The slight proviso is that if a company comes to you with a shiny protocol that's been written at the company and says, 'Here, cancer center, we want you to do this,' we think that's fine, but we think they ought to pay you the full freight of doing that, because then you are sort of acting as a contractor to them," Wittes said.

"On the other hand, when you work with a company and you help conceptualize the protocol and you are actually part of formulating the experiment, the guidelines are quite clear. The funds you get from NCI can be used in support of that effort."

NCI's new grant program for clinical translational projects, called Quick-Trials (http://www.nih.gov/grants/guide/pa-files/PA-99-070.html) makes no distinction between industry drugs, NCI drugs, and drugs discovered in academia, Wittes said.

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