



September 2008: Cancer Clinical Trials – Funding & Finances
"Government Laws and Funding"
by Amanda R. Dinsdale, CCRC, Program Coordinator,
Montana Cancer Consortium

The National Cancer Institute (NCI) is a component of the National Institutes of Health (NIH). The NCI was established under the National Cancer Act of 1937 as the nation's principal agency for cancer research. The NCI coordinates national research programs on cancer causes and prevention, detection and diagnosis, and treatment through a variety research projects and clinical trials. As a Federal Government research agency, the NCI receives its funding from the US Congress. The National Cancer Program established in 1971 gives the director of the NCI authority to submit budgets of full funding needs directly to the President.

Grants are a Federal financial assistance mechanism used to support and stimulate research. Congress influences NCI program and grants administration decisions by controlling the amount of funds authorized annually and by setting conditions on the use of funds. The NCI budget development cycle for a fiscal year is about 30 months. Research accounts for 70% of the NCI's budget.

The first cancer research grant funded by the NCI was awarded in November 1937 to investigate chemical structure and carcinogenic activity. This grant was for \$27,550. Since that time the NCI has funded nearly two hundred thousand grants totaling over \$40 billion.

When an institution applies for a grant the institution must agree to administer the grant in accordance with the regulations and policies that govern the grant program. The application process is a long and involved process with an end result of hundreds of pages of forms, tables, and dialog describing in depth the research activity for which funds are being requested. The NCI releases funding opportunities throughout the year. Each grant is designed for specific research activities and has strict guidelines as to who is eligible to apply. Individual guidelines exist for certain types of grants and those guidelines must be followed. The application window is fairly short, often only a month or two, so the applicant institution must be organized, plan accordingly, and work quickly.

Once an application has been submitted to it goes through a variety of reviews and processes. The Code of Federal Regulations contains the regulations for reviewing and administering NCI grants. The review and selection process for applications takes approximately 8-10 months. The application is first reviewed for completeness to ensure all sections and components have been included and are complete. Then the application goes through a scientific review. The scientific review is done by a panel of reviewers consisting of NCI personnel as well as expert peer reviewers. Summary statements are generated reflecting the judgment of the reviewers. The summary statements include a concise statement of the application and an evaluation of its merit.



Based on the scientific review a priority score and percentile rank is given. The priority score and percentile rank helps to prioritize all applications being reviewed for that review cycle. The application then goes to the National Cancer Advisory Board where data gathered from the scientific review is analyzed. Those applications to be funded are selected and budgets are generated. A final review of the completed application and budget is done before notification is sent to the appropriate congressional liaison. Finally the grant award is issued and a notification letter is sent to the applicant institution. The Notice of Grant Award is the official notification to the applicant that a project has been funded. Specific terms and conditions for the grant are incorporated in the Notice of Grant Award. Funds are not distributed in whole but rather managed through the Payment Management System where funds are drawn down by the institution as needed. This process is governed by the US Department of the Treasury and is in place to minimize the impact of cash withdrawals on the public debt level.

The NCI constantly oversees and manages all grant awards through audit reports, progress reports, financial reports, site visits, correspondence, and peer review. When problems or weaknesses are found, the NCI staff works with the grantee intuition to resolve the issues.

There are numerous cross-cutting public policy requirements applicable to Federal grants such as age, sex, and race discrimination. The NCI upholds high ethical, health, and safety standards in the conduct of research it funds. The public policy requirements set many of the standards held by the NCI.

September 2008: Cancer Clinical Trials – Funding & Finances
"Private Funding for Research (Including Pharma)"
by Patrick G. Beatty, MD, PhD; Medical Oncologist,
Montana Cancer Specialists; President, Montana Cancer
Institute Foundation; Missoula, MT

Over the past few decades, governmental funding for clinical research has declined. It is now difficult to maintain an active clinical trials program in private (e.g., non-University) practice settings using only public funds. For instance, funding for clinical cancer research from the Southwest Oncology Group (SWOG), in which most Montana cancer programs participate, is not sufficient to pay for the support staff necessary to compile the necessary data.

This problem has led either to practices ceasing to participate in clinical research, or to look for alternative sources of funding. This essay will focus on private sources.

One source of private funding is charitable contributions from individuals or foundations. In relatively small (and poor) states such as Montana, such gifts are much appreciated, but rarely are large enough to sustain a full program.



Another source has proven more promising, which is large Pharmaceutical Companies. Many of the large companies have started looking to non-Academic cancer programs to participate in their testing of new anti-cancer drugs. Such centers usually can do the trials faster, and more cost-effectively, than the big University Centers. In return, the local cancer centers have access to new and promising medications, and in addition, often receive enough compensation to subsidize the expense of putting patients on cancer protocols sponsored by government agencies, such as SWOG. These trials provide the drug in question, money to pay for the support staff to gather the data, with usually some money left over.

The challenge for the cancer programs is to choose protocols wisely: it is essential to keep in mind that the number one objective is to provide the best possible care to every individual patient. The centers must therefore screen every proposed protocol to be certain that they would provide that, ignoring any financial incentives. Furthermore, there are some trials, called "Phase IV", which sometimes are thinly veiled marketing schemes: the idea is to gather data on a particular drug after the FDA has already approved it. Some of these trials can be valuable, but some simply want to get the participating physicians used to using the drug in question, and thus prescribe it more often.

The rapid growth of such Company sponsored trials has led to concerns at a number of levels about possible abuses, some of which are alluded to above. There are governmental agencies exploring this, but the best bulwark against such potential problems is the responsible treating physician.

September 2008: Cancer Clinical Trials – Funding & Finances
"The Cost of Clinical Trials"
By James M. Burke, MD, Director of Clinical
Research, Billings Clinic Cancer Center, Billings, MT

Americans want new drugs developed quickly and safely. This is an expensive expectation. In the oncology arena, the FDA (Food and Drug Administration) attempts to target **expedited** review and approval of drugs. However, by some estimates, the average drug takes approximately 10 years and 1 billion dollars to develop. The cost of clinical trials takes up the vast majority of this time and money but preclinical development, and FDA filing fees are also factored into the equation.

Why the expense? First, drug company fixed expenses in terms of full time employees accumulate as long as the company is open. Second, the cost of paying for patient enrollment, drug administration, response evaluation, data collection and review, and submission to the FDA is trial and drug specific. The average clinical trial per patient costs are in the 30-50 thousand dollar range ... the more complicated the trial, the higher the cost. For a typical phase 3 trial



enrolling 800, the patient costs alone are 24 million dollars. This just for one phase 3 trial ... at times 2 pivotal trials are needed to establish a drug as being useful ... not taking into account the fixed costs to the company running the trial, preclinical, and early phase clinical development. Finally, this average cost per drug of 1 billion dollars is an average of both drugs that receive approval and those that do not. In the field of oncology only 1 in 10 to 15 drugs entering the clinic are ultimately approved.

So, how about some more math to summarize?

For an average development program lasting 10 years with one Phase 3 trial of average size and complexity:

- 1- \$ 24,000,000 for patient costs for the phase 3 trial
- 2- \$120,000,000 fixed operating costs (1 million dollars/mo x 120 mos)
- 3- \$ 10,000,000 the phase 1 and 2 trials and preclinical development

The cost for this single drug development program sums to approximately 150 million dollars-not a billion – yet. Now, multiply this by 10 to include the 9 other drugs that went through development and did not achieve FDA approval and we're over the billion dollar mark. As a disclaimer, recall this is a broad estimate based on the average costs for a program projected to take 10 years. The estimates obviously will slide up or down depending on the complexity and size of the program as well as the company's fixed operating costs.

Given the costs and the low frequency of approvals for drugs entering the development pipeline, why would anyone ever embark on such long term, high risk venture? From a purely economic perspective, ignoring the humanitarian goal of curing disease and improving outcomes, once a drug is approved the manufacturer has the opportunity to recoup losses and profit by having exclusive rights to sell the drug nationally and most of the time internationally as well, for approximately 10 years. It is this exclusive opportunity to profit that drives the continued investigation for new drugs ... and the cost per drug. Without this profit incentive built into the system, the development of new drugs, as you can appreciate by looking at the numbers above, would come to nearly a stand still. Thus, in America if we want the best and the safest drugs as fast as possible, we have to realize there is a price to pay.

September 2008: Cancer Clinical Trials – Funding & Finances "Third Party Payers"

by Grant W. Harrer, MD, Co-Principal Investigator of the Montana Cancer Consortium and Medical Director of the Sletten Cancer Institute, Great Falls, MT

The September Forum will consist of four essays addressing the economic issues involved in cancer clinical trials. This one is devoted to "third party payers". This phrase refers to the three



parties at the proverbial table when healthcare costs are the issue ... the patient (the first party), the provider (the second party), and the payer (the third party). The third party payers include not only private insurance companies, but also certain government organizations, e.g., Medicare.

Currently, there is an incredible patchwork of coverage for cancer clinical trials by third party payers. As a physician investigator, on any given day, for the same disease, stage, and clinical trial, I may see everything from complete coverage of the trial to an absolute denial of coverage. The latter often includes denial of even conventional care IF it is provided in the context of a clinical trial and even if the investigational drug(s) is/are provided by the sponsors of the study.

Let's look at the relevant portion of a standard consent form for a contemporary NCI-approved Phase III clinical trial involving standard care plus or minus an investigational drug that has shown promise in early phase trials:

"What are the costs of taking part in this study?"

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

(The study drug) will be provided free of charge while you are participating I this study. ...

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web Site at:

<http://cancer.gov/clinicaltrials/understanding/insurance-coverage>

(I recommend this site as required reading on this topic)

You can print out a copy of the 'Clinical Trials and Insurance Coverage' information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy."

At very least, the uncertainty of clinical trial coverage as highlighted above is a barrier to participation, let alone the possibility that coverage will not be available at all!

A major irony in all of this is that most clinical trials do not cost third party payers more than standard care, and may well cost even less (the details are the stuff of another essay). However, third party payers are reluctant to allow patients to enroll in trials due to the perception of risk of incurring additional costs. One of the "bottom lines" (pun intended) is insurance companies that do cover clinical trials have not been driven into bankruptcy due to excess costs of the studies.

313 West Mendenhall
P.O. Box 6446
Bozeman, Montana 59771



Phone: 406-587-8080
Fax: 406-556-1050
www.CancerFamilyNetwork.org

A final but incredibly important point in this essay relates to this statement on the NCI "Clinical Trials and Insurance Coverage" page: "A growing number of states have passed legislation or instituted special agreements requiring health plans to pay the cost of routine medical care you receive as a participant in a clinical trial."

First, although under discussion, Montana is not one of those states. Second, Montana has many larger employers whose health insurance is self-funded. These policies fall under the purview of federal and not state laws. Hence, even if Montana passed such a law, it would not apply to many of the third parties in our state who currently deny coverage of clinical trials. Third, we need a federal mandate for clinical trials coverage ... and somewhat unbelievably, there is a good template for doing so ... called Medicare ... more on this in October.