020321

Minnesota Department of Health and Minnesota Department of Commerce

February 28, 2002

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2001 Minn. Laws First Spl. Sess. Chap. 9 Art. 16 Sec. 9

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FINDINGS AND RECOMMENDATIONS OF THE WORK GROUP TO CLARIFY HEALTH PLAN COVERAGE OF THE COST OF ROUTINE CARE PROVIDED IN CLINICAL TRIALS

Pursuant to Laws of Minnesota (2001 Special Session) Chapter 9, Article 16, Sec. 9 (Exhibit A), the Commissioners of Health and Commerce, in consultation with the Commissioner of Employee Relations, convened a work group to study health plan coverage of clinical trials. The Work Group met as a whole seven times between September, 2001 and January, 2002. An additional working session of medical doctors associated with clinical trials was held on November 16, 2001 to obtain their technical assistance in completing the task.

Exhibit B is a list of the participants and persons invited to meetings of the Work Group. Invited participants include those who monitored 2001 legislative consideration of the issue and additional representatives of consumers, patient advocates, health plan companies, purchasers, providers and other health care professionals. In addition, persons in attendance at the first two meetings were invited to submit additional names of people who should be invited to subsequent meetings. The Work Group worked with the Minnesota Working Group on Cancer, various health plan companies, the Council of Health Plans and other interested persons. Staff of the Departments of Health and Commerce conferred with staff of Commissioner of Employee Relations. All meetings were open for anyone to attend.

Recommendations

After extensive discussion of definitions and alternative approaches as specified in the statute, the Work Group recommends a Voluntary Program to Clarify Health Plan Reimbursement of the Costs of Routine Care Provided in Cancer Clinical Trials (Exhibit C). The Work Group believes that a Voluntary Program is preferable to legislation because it better accommodates changing science, technology and medical practices in a timely manner and it ensures that patients have access to best care available.

The Work Group further recommends that the learning and experience gained in discussing coverage of routine health care costs in cancer clinical trials be used to improve and facilitate further discussions between the persons interested in clinical trials other than cancer and health plan companies. Individual health plans are encouraged to address reimbursement for clinical trials in other life-threatening diseases as soon as possible.

Scope and Limitations

The Voluntary Program attached to this report does not add new benefits to the coverage currently offered by health plan companies. Instead, the Voluntary Program recommends payment of existing routine care costs according to the following definition:

> *"Routine Care Costs"* are those costs incurred through the administration or performance of items or services that are (a) required as part of the Protocol Treatment in a High-Quality Clinical Trial, (b) usual, customary and appropriate to the patient's condition, and (c) would be typically provided to that patient when cared for outside of a clinical trial, including those items or services needed for the prevention, diagnosis or treatment of adverse effects and complications of the Protocol Treatment.

While the language contained within Special Session Chapter 9, Article 16, Section 9 directs the Work Group to consider health plan coverage of all types of clinical trials, the Work Group found that most complete information exists among provider organizations conducting cancer clinical trials. The lengthy and successful history of cancer clinical trials has developed with extensive quality control mechanisms.

The Work Group further believes that more time is needed to effectively analyze and study the type and amount of data available for clinical trials for other diseases so as to facilitate a discussion on definitions that distinguish between routine care costs and protocol driven costs. The same level of coordination and collaboration simply is not present in the broader clinical trial provider community that would permit the Work Group to responsively develop recommendations around clinical trial coverage for routine care in clinical trials for other life threatening diseases. More time is needed to reach agreement on what constitutes a high quality clinical trial among the other trials.

The Work Group process has led to a healthy dialogue on the issue of health plan coverage in clinical trials. Both the cancer clinical trial community and the health plans have learned a great deal about the complexity of the clinical trial process for cancer trials and issues relating to decisions on health plan coverage. This learning was greatly facilitated by the presence of broadly coordinated and shared information on the protocols of cancer clinical trials and the costs associated with the trial protocol. More importantly, these costs can be openly identified and shared through common web-sites that have permitted both the cancer clinical trial community and health plans to more readily identify and discuss each others concerns around coverage. In the area of cancer clinical trials, there are also resources for patients to more freely, and appropriately access information on these trials.

Due to these factors, the Work Group believes that the knowledge gained in cancer clinical trial coverage decisions will assist all parties in developing a strategy and process to facilitate a more informed discussion around clinical trials focusing on other life threatening disease. Time simply did not permit the level of information that would be needed to effectively discuss a similar process for trials in treating other life-threatening diseases.

While the Work Group agreed that cancer clinical trials are extremely important, there was some opposition to limiting coverage to cancer only clinical trials. It was the sense of some members of the group that other trials, such as, cardiovascular, diabetes, neurology, AIDS, and epilepsy, are all important and should be included in the agreement.

Since implementation part of the program is still unfinished, some providers were also concerned with the administrative burden of implementing any mandated coverage provisions that differ from Medicare's coverage of clinical trials, pursuant to the National Coverage Decision.

This recommendation should be perceived as an opportunity to move into discussions of clinical trials in the future using reliable and informed information to make decisions around a complex set of issues. Due to the success in arriving at a better understanding of each party's processes and definitions, the work group expressed a desire to continue this discussion around clinical trials for other life threatening diseases. The cancer clinical trial discussion is believed to provide the opportunity to use cancer clinical trials as a successful pilot project to reach an understanding as it relates to other trials.

An important principle in the Voluntary Program is that this agreement to pay for routine care when a patient is participating in a cancer clinical trials must not be construed to alter, bypass or otherwise negate existing coverage or current business practices and participating provider relationships of health plans and insurers. Within the scope of contract coverage, most health plans are currently paying, on a case-by-case basis, for routine care when a patient is participating in any clinical trial. This will not change with regard to clinical trials other than cancer.

While the Voluntary Program attached to this Report has received consensus agreement from the Work Group in most issues, there are still some issues in which the Work Group has not completed the program. For example, the Work Group recognized that further clarification is needed to determine trial eligibility in advance for "Other Trials and Sponsors" in section 3.2 c, page 10 and 11 of the Program document.

Another unresolved issue is coverage of costs associated with population-wide screening trials in which an investigative tool (e.g. test, procedure or device) screens asymptomatic individuals for the presence or precursor of a disease or condition. That tool itself is a protocol-induced cost generally paid by the research sponsor. Other associated costs for monitoring and follow-up of such investigative screening trials are not addressed in the Voluntary Program document. The purpose of population-wide screening should be more clearly assigned to governmental sponsorship and funding as compared to the purpose of prevention, symptom management or treatment trials for patients based upon their disease, condition and risk factors.

Process for Implementation

The Work Group supports implementation of the Voluntary Program in four phases:

1. This report to the Chairs of the Health Policy and Finance Committees of the Senate and the House communicates these findings and recommendations to the Legislature. No formal action is recommended by the Legislature.
2. If there is no formal legislative action encouraged by committee chairs, the Voluntary Program found in Exhibit C will be recommended to be adopted through signature by representatives of all health plan companies and self-funded employers in Minnesota. The Program will be completely voluntary for each company and employer and there will be no implied regulatory intent.
3. Health plans are urged to communicate with purchasers to provide information about the Program and to answer any questions or concerns about the Program. The benefits to health plan and self-funded enrollees should be emphasized and the expectation of no or minimal cost impact should be described.
4. The Program will be implemented through clarification of contract terms and provider agreements. While no new benefits are added by this Program, contracts may be amended to describe how standardization of definitions and procedures will assist patients who may participate in clinical trials.

Exhibit A

Laws of Minnesota Chapter 9 (2001 Special Session)

Article 16, Sec. 9. [COVERAGE OF CLINICAL TRIALS.]

The commissioners of health and commerce shall, in consultation with the commissioner of employee relations, convene a work group to study health plan coverage of clinical trials. The work group shall be made up of representatives of consumers, patient advocates, health plan companies, purchasers, providers, and other health care professionals involved in the care and treatment of patients. The work group shall consider definitions of routine patient costs, protocol-induced costs, and high-quality clinical trials. The work group shall also consider guidelines for voluntary agreements for health plan coverage of routine patient costs incurred by patients participating in high-quality clinical trials. The commissioner shall submit the findings and the recommendations of the work group to the chairs of the health policy and finance committees in the senate and the house by January 15, 2002.

L:mcs/report/exhibitA.doc

LIST OF WORK GROUP PARTICIPANTS AND PERSONS INVITED TO MEETINGS OF THE WORK GROUP

Participants

Geoff Bartsh, HealthPartners
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David Benson, American Cancer Society
Tom Berg, Minnesota Working Group on Cancer
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R. Craig Christianson, U-Care Minnesota
Ann Deshler, MN-CCOP, Metro
Stacie Emberly, Medica Health Plan
Mary Fahey, Fairview Health Services
Matt Flory, American Cancer Society
Patrick J. Flynn, M.D., Minnesota Oncology Hematology, P.A.
Keith Folkert, M.D., Blue Cross and Blue Shield of Minnesota
John Frederick, M.D., Preferred One
Stephanie Frost, HealthPartners
Anna Geary, Allina Hospital and Clinics
Cindy Goff, Blue Cross and Blue Shield of Minnesota
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Chris Reisdorf, Minnesota Department of Human Services
Robyn Rowen, Insurance Federation of Minnesota
Bob Schmitt, American Cancer Society
Michael Scandrett, Minnesota Council of Health Plans
Mark Skubic, Park Nicollet Health Services
Harold Windschitl, M.D., CentraCare Clinic

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Lee Beecher, M.D., Minnesota Physician-Patient Alliance
Bill Conley, Mental Health Association of Minnesota
Mary Jo George, Minnesota AIDS Project
David Haugen, Department of Employee Relations
Mike Hicke, National Federation of Independent Business
Bob Johnson, Insurance Federation of Minnesota
Carolyn Jones, Minnesota Chamber of Commerce
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Maureen O'Connell, Legal Services Advocacy Project
Carolyn Pare, Buyers Health Care Action Group
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A VOLUNTARY PROGRAM TO CLARIFY HEALTH PLAN REIMBURSEMENT OF THE COSTS OF ROUTINE CARE PROVIDED IN CANCER CLINICAL TRIALS

January 2002

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A VOLUNTARY PROGRAM TO CLARIFY HEALTH PLAN REIMBURSEMENT OF THE COSTS OF ROUTINE CARE PROVIDED IN CANCER CLINICAL TRIALS

1.0 Preamble

1.1 *General.* In the course of its 2001 Special Session, the Minnesota State Legislature directed the state Commissioners of Health and Commerce to convene, in consultation with the Commissioner of Employee Relations, a work group for purposes of studying health plan coverage of clinical trials. The 2001 1st Special Session, SF 4, Article 16, section 9 stated the following:

> "The commissioners of health and commerce shall, in consultation with the commissioner of employee relations, convene a work group to study health plan coverage of clinical trials. The work group shall be made up of representatives of consumers, patient advocates, health plan companies, purchasers, providers, and other health care professionals involved in the care and treatment of patients. The work group shall consider definitions of routine patient costs, protocol-induced costs, and high-quality clinical trials. The work group shall also consider guidelines for voluntary agreements for health plan coverage of routine patient costs incurred by patients participating in high-quality clinical trials. The commissioner shall submit the findings and the recommendations of the work group to the chairs of the health policy and finance committee in the senate and the house by January 15, 2002."

The Work Group met on a number of occasions and has developed the Voluntary Program on Coverage of Clinical Trials (Program) described herein. The Program includes definitions of high-quality clinical trials, eligible trial sponsors, approved investigators, and qualified performance sites. The Program also includes recommendations for apportioning costs of care provided in a clinical trial to the responsible party. Furthermore the Program outlines

methods and systems for operational aspects, for evaluation of performance, and for generation of ongoing reports.

1.2 *Initial Program Scope Limited to Cancer.* Clinical trials play a crucial role in improving disease management as they are the optimal way to generate statistically valid health outcome data. This data is crucial for the development of new treatments, establishing the relative efficacy of existing treatment alternatives, and elimination of outdated treatments. Clinical trials may also offer direct benefits to patients by providing access to the latest treatments before these become generally available.

Although all diseases are equally reliant on clinical trials for improving health outcomes, and clinical trials in all areas of medicine are based on the same principles of science and scientific methods, the applied aspects of clinical research vary greatly across the range of medical specialties. Of all patient-oriented trials open at any particular time in the U.S. and in Minnesota, the single largest proportion is related to cancer. These trials are designed to develop newer or better strategies in all aspects of the detection and diagnosis, treatment, prevention or quality of life of cancer patients. The infrastructure that allows the performance of cancer clinical trials is arguably the most highly organized, and has a longer track record of successful performance, than any other area of medical research. Given this the Work Group focused on cancer as a model for resolving coverage issues related to clinical trials. The solutions developed for cancer research can then be expanded to address other diseases and life-threatening conditions.

1.3 *Goals.* The goals of the Program are to (a) recognize that patients and society derive benefits from participation in clinical trials, (b) support the pivotal role of clinical trials in maintaining a high-quality care delivery, (c) increase participation in clinical trials among patients who are citizens of Minnesota, and (d) appropriately allocate costs between health plans, clinical trials sponsors and investigative sites. These goals are realized only when treatment is provided to a **Program Participant** in the setting of a **High-Quality Clinical Trial** by an **Approved Investigator** practicing at a **Qualified Performance Site**. Provisions for all of these Program parameters must be met in order for a patient's trial-based care to be considered eligible for consideration under the Program. The Program also suggests operational considerations for

guiding implementation; communication, awareness and education; and resolving disputes.

The Work Group recommends that this Program be adopted by each health plan and group purchaser (including HMOs, indemnity insurers, nonprofit health service plans, self-insured employers, purchasing alliances, etc.). Once adopted, it should be incorporated into the health plan and group purchaser policies and contracts. After this Program document has been completed and disseminated, each health plan or group purchaser will be asked to publicly state whether they will adopt the Program and incorporate it into health plan policies and contracts.

1.4 *Principles.* In implementing this Program the following principles apply:

Principle 1. Trials must be of the highest quality and offer therapeutic intent to the participant. Treatments and procedures that are both investigational and the subject of a high-quality clinical trial should be provided only in the setting of that high-quality clinical trial.

Principle 2. Available clinical or pre-clinical data must provide a reasonable expectation that the treatment will be at least as effective as the non-investigational alternative. There must not be a clearly superior non-investigational treatment alternative.

Principle 3. Trial-based care must be provided only at performance sites and by clinical investigators that are qualified and who adhere to all accepted standards practices and principles ensuring the health and safety of their patients. The primary responsibility of these clinicians and researchers must be to the health and safety of their patients.

Principle 4. The costs of items and services provided in the clinical trial must be identified to, and borne by the appropriate party: Costs of routine care is the responsibility of the health plan or insurer, and protocol-induced costs are the responsibility of the trial sponsor. Clear allocation of costs improves the ability to forecast and manage costs by clinical trial performance sites, health plans or insurers, and patients as well as provide a clearer understanding of funding needs.

Principle 5. Provision of treatment in a clinical trial must not be construed to alter, bypass or otherwise negate existing coverage or current business practices and participating provider relationships of the health plan or insurer.

2.0 Definitions

For purposes of this Program, the following general definitions apply. Details on how these defined terms are included within the Program follow in the Parameters section.

"High-Quality Clinical Trials" means those trials that have been subjected to independent peer-review of the rationale and methodology; are sponsored by an entity with a recognized program in clinical research that conducts its activities according to all appropriate federal and state regulations and generally accepted standard operating procedures governing the conduct of participating investigators; and whose results will be reported upon completion of the trial regardless of their positive or negative nature.

High-Quality Clinical Trials generally have the following characteristics: (a) the Protocol Treatment is appropriate for the patient's disease, condition and risk state, and is undertaken with therapeutic intent; (b) the trial is based on a peer-reviewed written protocol with clear definitions and statements on study objectives; (c) the trial includes clear criteria for patient eligibility including inclusion and exclusion criteria; (d) the trial specifies study size (target accrual number and rate), study duration, statistical requirements, and endpoints; (e) it is approved by a federally registered IRB; and (f) it is overseen by a group or review committee experienced in data monitoring and management that is provided regular updates.

Improving the overall outcome of cancer care and management is not based strictly on improving treatments; it requires parallel improvements in strategies for prevention. Accordingly High-Quality Clinical Trials that address treatment and prevention and approved by an Eligible Trial Sponsor are considered equally important and all are included in the Program.

"*Institutional Review Board*" (IRB) means a duly constituted board, committee or other group formally designated by an institution to review, to approve the initiation of, or to conduct periodic review of, biomedical research involving human subjects to ensure the protection of the safety, welfare and rights of those subjects and which meets or exceeds the requirements of Title 21, Parts 50 and 56, and Title 45, Part 46 of the U.S. Code of Federal Regulations (CFR), and is registered with the Office of Human Research Protection (OHRP) of the U.S. Department of Health and Humans Services.

"Program Participants" are those individuals who have been diagnosed with a disease or are at increased risk of developing a disease based on the presence of biological or disease factors shown to be associated with that disease; and who (a) are enrolled in a health insurance plan; (b) have signed an informed consent to participate in a clinical trial; (c) have signed the necessary authorization or other appropriate privacy consent to allow for release of information to allow communication among the parties for payment, statistical analysis, and administrative issues related to the clinical trial program; and (d) are receiving the Protocol Treatment. If during the course of being treated on a clinical trial the Program Participant ceases to be enrolled in a health insurance plan, payment for subsequent services related to continued treatment in the clinical trial shall become the responsibility of the Program Participant in accordance with state laws regulating continuity of care and continuation of benefits.

"Protocol-Induced Costs" are those costs incurred in the administration of any item or service that is required for the completion of the Protocol Treatment but are not usual, customary and appropriate for the patient's condition and would not typically be provided to that patient when cared for outside of a clinical trial; would be incurred by performance of tasks directly related to data collection, reporting or analysis for purposes of the Clinical Trial; or that would be provided by the Trial Sponsor or Performance Site and not otherwise charged to the health plan or insurer. Some examples of Protocol-Induced Costs that might occur in the current system for design, conduct and management of High-Quality Clinical Trials are:

(i) items or services specified as necessary in the protocol document but delivered solely to satisfy data collection and analysis needs of the clinical trial and not used in direct clinical management of patients;

(ii) items or services provided by the Trial Sponsor without charge and the cost of the investigational item or service itself;

(iii) costs associated with fulfillment of regulatory requirements or contractual processes; and

(iv) costs incurred during development of publications or travel to meetings to report protocol results.

(c) Examples. The following are examples of how costs of care might be apportioned in different trial scenarios:

(i) For a device trial: Consider a trial that compares delivery of an Food and Drug Administration(FDA)-approved chemotherapeutic agent by intravenous infusion to the same agent delivered through a surgically implanted reservoir still subject to an Investigational Device Exception. In this case the cost of the reservoir implant surgery is protocol-induced and therefore not covered by the health plan or insurer. In the alternate case, a study may be comparing administration of a drug that is the subject of an Investigational New Drug by intravenous infusion or by a surgically implanted, but FDA-approved reservoir. In this case the cost of a non-FDA approved drug is Protocol-Induced and therefore not covered by the health plan, but both routes of administration are considered usual and customary care so related items and services would be covered by the health plans.

(ii) For a prevention trial: A protocol using a non-FDA approved drug requires a screening mammogram every six months as opposed to an annual screening mammogram that is usual and customary practice. In this study the second screening mammogram each year would be a Protocol-Induced Cost as would be the non-FDA approved drug. If the clinical trial uses a tool (e.g., test, procedure, device) to evaluate individuals for the presence or precursor of a disease or condition, and that tool itself is the focus of the investigation, this would be a protocol-induced cost.

(iii) For a symptom management trial: Comparing the efficacy of two approved drugs administered continuously for analgesic control in patients with terminal cancer. All costs would be routine care costs except for expenses directly related to the study including items and

services customarily provided by the research sponsors free of charge for any enrollee in trial, and items and services provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the patient

(iv) For a treatment trial: A study compares two FDA-approved chemotherapy agents for treatment of advanced breast cancer. Drug A, is the older more established agent and is to be compared against the newer agent, Drug B. In both cases there is a significant risk of severe or fatal cardiac toxicity so tests of ventricular function are performed every six months in both arms. The generally accepted medical practice for monitoring treatment effects of Drug A is to perform ventricular function tests every twelve months. In Arm A, therefore, one of the ventricular function tests would be considered Protocol-Induced. Drug B is known to be associated with much greater risk of cardiac toxicity so the generally accepted medical practice is to monitor the patient more closely by performing ventricular functions tests much more frequently (for example every three months) in which case all of these tests are considered Routine Care.

"Protocol Treatment" means those items, drugs, procedure, services and schedule for administration described or specified in the IRB-approved protocol document. In the case of comparative studies, Protocol Treatment refers to all arms in the protocol document (e.g., the 'standard' arm and the 'experimental' arm).

"Routine Care Costs" are those costs incurred through the administration or performance of items or services that are (a) required as part of the Protocol Treatment in a High-Quality Clinical Trial, (b) usual, customary and appropriate to the patient's condition, and (c) would be typically provided to that patient when cared for outside of a clinical trial, including those items or services needed for the prevention, diagnosis or treatment of adverse effects and complications of the Protocol Treatment.

"Therapeutic Intent" means High Quality Clinical Trials that "provide some benefit to improving a subject's condition (*e.g.*, prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given

to an individual with the hope of inducing some improvement in the patient's condition as well as assessing the safety and pharmacology of a drug."[1] Therapeutic intent includes prevention trials, for example the use of a drug traditionally used to treat cancer being used to prevent that cancer. Therapeutic intent does not include clinical trials intended to solely test toxicity.

3.0 Program Parameters

3.1 *General.* Program Participants enrolled in a **High-Quality Clinical Trial** as described in Sec. 3.2, which is approved and overseen by an **Eligible Trial Sponsor** as described in Sec. 3.3, and is conducted by an **Approved Investigator** as described in Sec. 3.4, at a **Qualified Performance Site** as described in Sec. 3.5, will be covered by the Program.

3.2 *Eligible Trial Sponsors.* (a) General Eligible Trial Sponsors have a clear and stated policy regarding sponsored cancer research and approve clinical trials according to all applicable laws and published rules regulating human subject research (e.g. scientific peer-review, human subject protection, institutional compliance, conflict of interest, and data management) such as found in the NIH Guide for Grants and Contracts, the US Food and Drug Administration (FDA) Center for Drug and Research (CDER) Handbook, the FDA Guidelines on Good Clinical Practice (GCP) in FDA-Regulated Trials, and the International conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use.

(b) Federal Sponsors Agencies, institutes and centers of the federal government are required to operate within the regulatory framework and according to the guidelines and standards described in the preceding paragraph. Patient-oriented cancer clinical trials sponsored by any federal agency with a recognized program in sponsored cancer research are therefore included in this Program. Such federal agencies include, but are not limited to, the following ones that had active protocols in clinical cancer research during the fourth quarter of 2001:

- Department of Health and Human Services
    - Office of the Secretary

1 Definition taken from the OHRP IRB handbook.

- Office on Women's Health
- Office on Minority Health

- Agency for Healthcare Research and Quality
- Centers for Disease Control and Prevention
- Center for Medicare and Medicaid Services
- Food and Drug Administration trials conducted under:
  - an investigational new drug application (IND) as described at 21CFR312 and 21CFR314;
  - a supplemental new drug application (SNDA) as described at 21CFR 314.54 and 21CFR314.70; or
  - an investigational device exemption (IDE) as described at 21CFR812.
- National Institutes of Health; including but not limited to:
  - National Cancer Institute
    - Designated Cancer Centers
    - Cooperative Groups or the Coalition of National Cancer Cooperative Groups
    - Community Clinical Oncology Programs
  - National Center for Complementary and Alternative Medicine
  - National Heart, Lung and Blood Institute
  - National Human Genome Research Institute

- Department of Defense
- Department of Veteran Affairs

(c) Other Trials and Sponsors High-Quality Clinical Trials approved and managed by other Trial Sponsors may be considered for inclusion on a trial-by-trial basis within the context of the Program. Review of such trials shall be undertaken in a timely manner and through an objective and independent review program (see e.g., section 5.2, Eligibility).

3.3 *Approved Investigators.* Approved Investigators are: (a) board certified/board eligible physicians, nurses, and other health care professionals that (i) are capable of participating in organized cancer research through demonstration of training or experience, and (ii) are members of, or on staff, at, a qualified performance site; (b) are certified in the responsible conduct of research involving human subjects as required by federal regulations and OHRP (see more at *Federal Register* 65(11):3716-7); .and (c) have a contractual relationship with a health plan for provision of health care services related to the framework of the High-Quality Clinical Trial or agree to enter into such a relationship for the express purposes of the High-Quality Clinical Trial.

3.4 *Qualified Performance Site* Qualified Performance Sites are those solo or group physician practices, specialty clinics, community hospitals, academic medical centers or other health care facilities that have a formal program in cancer care and management and (a) adhere to all accepted guidelines, procedures and ethical standards pertaining to conflict of interest and protection of human research participants as defined by OHRP, the NIH and FDA; (b) approve all trials through a federally qualified IRB registered with OHRP; (c) have obtained a federal-wide assurance (FWA) or other assurance instrument as might be required under federal and/or state regulations; and (d) have a contractual relationship with a health plan for provision of health services provided in the Clinical Trial or agree to enter into such a relationship for the express purposes of the Clinical Trial.

4.0 Costs

4.1 *Assignment of Cost Components.* (a) General. Costs associated with cancer clinical trials will be apportioned into Routine Care Costs and Protocol-Induced Costs. The health plan

or insurer shall pay Routine Care Costs as described in this report and to the extent that they are covered under the member's certificate of coverage. For example, if a member's plan has a $10 copayment for office visits, that copayment will apply to office visits in the clinical trial. Questions regarding whether a specific item or service is a component of Routine Care Costs or Protocol-Induced Costs will be resolved in accordance with the footnote cited in Section 5.2.

4.2 *Cost Controls.* Program Participants shall be treated at and referred to an Approved Investigator and Qualified Performance Site that are participating providers with the Program Participant's health plan for laboratory work and/or hospitalization whenever possible. Out of network providers will be approved for provision of care in an eligible clinical trial only if an appropriate in network provider is not available and only with prior authorization of the participant's health plan. Health plans and insurers will not provide duplicate payment for those services paid for by Trial Sponsor. Treatment in a Qualified Clinical Trial should not be construed to change existing coverage or negate standard business relationships between the health plans, members and participating providers.

Trial Sponsors and Qualified Performance Sites should (a) identify items and services in each clinical trial for which health plans and insurers are not typically charged, or are provided without charge to Qualified Performance Sites, and (b) the tests and procedures undertaken specifically and solely for the purposes of generating and collecting data and the cost of the investigational item or service. Qualified Performance Sites should have a system for tracking these items and services to ensure that Protocol-Induced Costs are not paid by the health plan or insurer.

4.3 *Aggregate Costs.* No definitive data has been published relative to the marginal costs of cancer management provided in the setting of High-Quality Clinical Trials. The largest published study to date is the 1999 Mayo Clinic Cancer Center study based on data from the Olmstead County reporting project.[2] This was a retrospective comparison of 61 case-control matched pairs with at least five years of follow-up data after treatment on a phase II or phase III trial. No significant difference in cost of care was observed at the end of the first year or in the

[2] Wagner J, Alberts SR, Sloan JA, Cha S, Killian J, O'Connell MJ, et al. (1999) Incremental costs of enrolling cancer patients in clinical trials: a population-based study. J Natl Cancer Inst, 91:847-853.

mean cumulative five-year cost. Similar negative results have been reported by Kaiser-Permanente of Northern California, The Puget Sound Group Health Cooperative, and the American Association of Cancer Institutes[3]. However, it must be noted that the data in these publications is based only on trials of treatment and symptom management; they do not include clinical trials of screening, prevention or diagnosis. It is also important to note that in a recent draft Operational Policy Letter (OPL) on the Coverage of Clinical Trials, CMS stated that the costs of adding trials benefit to Medicare +Choice plans "met the threshold for 'significant cost'." A survey of the thirty voluntary or mandated programs that are currently operational on a state-wide, national or individual private health plan basis was unable to document that any had completed a study of aggregate costs or made such information available.[4]

5.0 Implementation

5.1 *Program Information.* Work group participants believe it important that an easy to access centralized source of information concerning High Quality Clinical Trials be available to all interested persons including consumers, providers, researchers, health plans and governmental officials.

5.2 *Eligibility*[5]. Work group participants also believe it essential to develop a mechanism to review the appropriateness of trials which fall into the category "Other Trials and Sponsors" being included in the Program and to resolve issues related to assignment of costs. Until such time as the federal government completes and publishes its rules and criteria for deeming qualified trials[6], sponsors of trials not specified in section 3.2 part (b) who are seeking

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[3] Summarized in Bennett CL, Adams J, Knox K, Kelahan AM, Silver SM, Bailes JS (2001) Clinical trials: are they a good buy? J Clin Oncol, 19(23):4330-4339.

[4] Kelahan AM, Comis RL, Schilsky RL, O'Connell MJ, et al. (2002). Reimbursement of the costs of routine care and access to clinical trials. *J Natl Cancer Inst* (submitted for publication).

[5] A trial-specific review mechanism is necessary as existing mechanisms to resolve disputes were not designed nor intended to address questions or issues related to clinical trials such as medical rationale, scientific methodology and statistical design or issues related to common acceptance of a trial across purchasers. Using the existing mechanisms to review clinical trials would also mean that the same trial might be reviewed multiple times as new patients are considered for enrollment. Furthermore reviews initiated at the time a patient is being considered for a trial may cause undue delay and result in the patient becoming ineligible.

[6] As part of the 2000 Medicare National Coverage Decision on Clinical Trials, the Agency for Healthcare Research

inclusion of their trials must demonstrate, at a minimum, that these trials meet the definitions of High-Quality Clinical Trial and Therapeutic Intent specified in Section 2.0, are conducted by Approved Investigators at Qualified Performance Sites and meet the standards of federal sponsored trials.

5.3 *Evaluation and Reports.* Regular reports on the status and conduct of the Program shall be generated by participating Health Plans, Approved Investigators and Qualified Performance Sites or their designated agent(s). The frequency, format and information contained in the Report will be mutually decided and agreed to by the parties but shall consist of at least one report at mid-term and one report at the end of each term.

5.4 *Effective Date.* The Effective Date of the Program is _____, 2002.

AGREED AND ACCEPTED, this _____ day of _____ 2002.

_____

and Quality was directed to convene a multi-agency Federal panel to "develop qualifying criteria that will indicate a strong probability that a trial exhibits the desirable characteristics" of a deemed trial.