THE KEYSTONE NATIONAL POLICY DIALOGUE ON ESTABLISHMENT OF STUDIES TO OPTIMIZE MEDICAL MANAGEMENT OF HIV INFECTION

FINAL REPORT
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EXECUTIVE SUMMARY: Significant government and private sector efforts in basic and applied research have led to an explosion of *new scientific knowledge that could transform the battle against HIV infection.* There are new insights into the pathogenesis of HIV infection, greatly improved monitoring tools, and increasingly effective antiretroviral therapies that more profoundly suppress HIV replication. For the first time in the epidemic the opportunity may exist to fundamentally change HIV infection from a relentlessly progressive disease to a chronic, medically manageable condition, reduce transmissibility of the virus, and to potentially control the epidemic itself. In order to take advantage of this opportunity, there is a critical need to determine how to most effectively use these therapies and tools in clinical practice to optimize the medical management of HIV infection within an increasingly constrained health care delivery and financing environment.

To meet this need, the participants of the Keystone National Policy Dialogue on the Establishment of Studies to Optimize Medical Management of HIV Infection concluded that *innovative HIV antiretroviral trials to evaluate treatment strategies should be conducted* with respect to multiple outcomes, including disease progression, survival, quality of life, and cost-effectiveness. These treatment strategy trials will involve a number of combinations of potent drugs used for prolonged periods in a broad spectrum of HIV-infected individuals. Such treatment strategy trials are likely to require the inclusion of large numbers of patients who will receive one or more drug regimens and whose health status will be followed for many years. The resources to conduct treatment strategy trials successfully do not currently exist in any single research or clinical entity; conduct of these trials will require unprecedented collaboration among members of the pharmaceutical industry, public and private payors, health care delivery systems groups, the patient community, clinicians, researchers, and government.

Many decision leaders are interested in making progress on these issues. Vice President Al Gore held a meeting with pharmaceutical executives and government officials in February, 1996 to discuss drug development of therapeutics, vaccines, and microbicides to combat HIV. The Keystone Dialogue Group was convened *to develop a framework to establish studies to provide information for optimizing the medical management of HIV infection.* The Keystone Dialogue Group consisted of more than forty experts from the pharmaceutical industry, public and private payors, health care delivery system groups, government regulatory, research and policy groups, patient advocacy groups, clinicians, and researchers.

The Keystone Dialogue Group acknowledged and applauded the significant progress that has been, and continues to be made by various HIV researchers from the public and private sectors. The Dialogue Group also realized that accomplishing the range of treatment strategy trials of the size needed in order

to advance important medical management goals will require unprecedented collaboration among the different stakeholders involved and interested in HIV research. The Dialogue Group concluded that *an independent public-private partnership* called the ***Forum for Collaborative HIV Research,*** composed of stakeholders from multiple interests, will be needed to effectively exchange information about medical management of HIV infection and facilitate clinical research of emerging treatment strategies. *The goal of the Forum is to facilitate information exchange and actively catalyze appropriate stakeholders to develop and implement new studies to address critical unanswered questions regarding optimal medical management of HIV disease.* The Dialogue Group believes that the purpose of the Forum is not to supplant the important work now being conducted by existing research entities, but rather to enhance collaboration between interested groups and thereby maximize the breadth, efficiency, and productivity of the clinical research effort. The Dialogue Group proposes that, rather than creating a new structure, the commitment and collaborative spirit of the Keystone dialogue process can be used as a model for shaping the **Forum for Collaborative HIV Research**.

The first project for the Forum will be to continue and complete evaluations of the HIV antiretroviral trials that are underway or planned by the public and/or private sectors, and determine whether such studies have the potential to answer the critical questions related to how best to use antiretroviral therapies to optimize the medical management of HIV infection. The next step will be to identify what, if anything, is impeding the development or implementation of these studies, and for the stakeholders to use the Forum to build collaborative efforts to facilitate the conduct and completion of these studies, particularly strategy trials, that are needed to address critical medical management questions. If existing or planned studies leave gaps in the knowledge base necessary to improve the long-term treatment of HIV disease, then the Forum will facilitate the cooperation among the various participants to design and implement high priority studies which fill these gaps.

To establish the Forum, a commitment from the major participants involved with the Forum for resources, including initial funding, small core staff, a timeline, and a location to house the Forum will be secured. The Forum will begin meeting in the fall of 1996 in order to respond to the rapidly changing treatment environment as well as to demonstrate the commitment of all involved parties to the process.

INTRODUCTION

HIV research and treatment have reached a critical milestone. Government and private efforts have resulted in major improvements in the outlook for HIV-infected individuals. The potential now exists to change HIV infection fundamentally into a chronic, manageable disease and to alter the course of the epidemic by reducing the transmission of the virus.

Although these scientific advances and new therapeutic options are most promising, much work remains to be done if society is to capitalize on these new research advances. We must learn how to optimally use available treatment regimens, including learning when it is most appropriate to start and change treatment; how aggressively to treat; when, if ever, treatment can be stopped; and if optimal treatment can reduce the transmission of HIV and the occurrence of opportunistic conditions. There is a particular need for studies that assess important clinical outcomes such as survival, quality of life, and the long-term consequences of treatment (e.g., toxicity to drugs).

This emerging hope will require a major shift in the paradigm for HIV research. Past clinical research has predominantly focused on establishing the safety and effectiveness of individual agents and a few selected combinations of drugs. We must now evaluate various treatment strategies using different combinations and sequences of potent drugs from several classes over longer periods of time.

This Keystone Dialogue report proposes the development of treatment strategy studies to promote the identification of optimal treatments for HIV infection. Accomplishing the range of treatment strategy studies of the size needed to address this agenda will require an unprecedented collaboration among the pharmaceutical industry, government, researchers, patient advocates, third-party payors, and health care delivery systems groups. Past efforts have been important in laying the foundation for such collaboration, but a more intensive, sustained, and information-rich effort is now necessary. Therefore, the Dialogue Group and this report propose the establishment of a framework to focus and guide such collaboration, the **Forum for Collaborative HIV Research**.

Although ever-expanding therapeutic options present a considerable challenge to optimizing treatment, the Dialogue Group recognized that identification of optimal strategies is not sufficient to solve the problem of HIV/AIDS treatment in the United States. We must also further develop the means to translate these strategies into good clinical practice and to enhance their availability to all affected patient populations. We also need to learn how to educate persons with HIV infection about the benefits of these new treatments so that they are present for and participate in care. We need to educate health care providers about how best to use new treatments to optimize management of their patients. In addition, we need to learn more about how to develop high quality comprehensive health care systems which will assure equitable, early, and ongoing access to skilled providers and effective therapies. In particular, we need to learn how to handle the increased demands for intensive HIV care within an increasingly constrained health care system. A disproportionate share of HIV care is financed by an already strained public sector, especially Medicaid and the AIDS Drug Assistance Program (ADAP) of the Health Resources and Services Administration (HRSA). Earlier treatment intervention and prevention of illness for the estimated 650,000 to 900,000 HIV-infected people in this country will result in additional pressures on payors. Finally, the increasing complexity of managing and treating persons with HIV may require a larger number of qualified providers, or will tax the existing system.

The Dialogue Group members concluded that these important issues were beyond the scope of its immediate charge. However, they recommend further discussions around the financing, access, human resources, quality, and other health services issues that must be addressed if these promising new approaches to medical management are to be available to all in need of HIV treatment.

Keystone National Policy Dialogue on the Establishment of Studies to Optimize Management of HIV Infection

Vice President Al Gore held a meeting with pharmaceutical executives and government officials in February, 1996 to discuss drug development of therapeutics, vaccines, and microbicides to combat HIV. At the conclusion of the meeting, the Vice President announced that the Administration would join with pharmaceutical manufacturers, health insurance companies and other third-party payors, and patient advocacy organizations to develop a collaborative system of clinical trials for HIV drugs that have been approved by the FDA under expedited procedures to determine the best uses and the long-term effectiveness of those drugs. In addition, the need for a multi-stakeholder dialogue was identified by participants in a previous Keystone Center project, the Keystone National Policy Dialogue on Expanded Access to Promising Therapeutic Drugs for HIV Infection and AIDS with Implications for Other Life-Threatening Diseases. As a result, the Keystone National Policy Dialogue on the Establishment of Studies to Optimize

Medical Management of HIV Infection was launched.

The Keystone Dialogue was a three month, intensive process to develop a framework for conducting studies to optimize medical management of HIV infection, in particular, those studies that are not currently underway or are unlikely to be conducted in the near future. The Dialogue Group included more than forty experts from pharmaceutical companies, payors of medical expenses (public and private), government agencies charged with drug approval and HIV research, patient advocacy groups, clinicians, researchers, and others concerned with these issues. A participant list is appended to this report. The Dialogue Group held a series of five meetings. Participants were initially divided into three work groups, focusing on medical management issues, research design and methodologies, and developing a framework to promote collaboration. These work groups were asked to identify the significant issues and propose recommendations for optimizing medical management of HIV infection, using currently available antiretroviral drugs as an example. The conclusions of the three work groups were discussed by the full Dialogue Group and eventually evolved into the recommendations in this final report. All of the deliberations were governed by three ground rules:

1) Participants attended as individuals, not as formal representatives of their respective organization, agency, or company;
2) All comments were off-the-record and not for attribution; and
3) No documents or written materials were made public until the Dialogue Group agreed to their release.

The release of this final report represents the culmination of the Dialogue Group's efforts and reflects the consensus of the Group. "Consensus" means that this report is a fair and accurate description of the discussions, and that the recommendations, taken as a whole package, are supported by the Dialogue Group.

The project was convened and facilitated by The Keystone Center, a non-profit organization that designs and facilitates conflict management and problem-solving processes on complex public policy issues involving health, the environment, and energy.

The project was funded by a diversity of sources, including the Kaiser Family Foundation, the Office of AIDS Research at the National Institutes of Health, and the many private pharmaceutical companies that participated in this process.

ISSUES CRITICAL TO OPTIMIZING MEDICAL MANAGEMENT OF HIV INFECTION

In order to use available therapies for HIV most effectively, several critical issues must be addressed, including accessibility to these therapeutics and more comprehensive information about the long-term effectiveness and consequences of using these therapies in various combinations.

Unprecedented Uncertainty among Providers, Patients, and Third Party Payors

Over the past two years, the number of approved antiretroviral agents has tripled and can be expected to continue to rapidly increase. The rapid development, evaluation, and licensure of growing numbers of HIV therapeutic agents has outpaced the evaluation of their long-term effectiveness resulting in incomplete information to guide clinicians and patients making critical medical management decisions. These new therapeutics are commonly used in combination as well as with an array of other treatments for conditions associated with HIV infection at many stages of disease. Combination antiretroviral therapy is being rapidly adopted in the care of patients with HIV, resulting in high aggregate costs of treatment. Uncertainty exists about the duration of clinical effectiveness, costs, clinical impact such as improved quality of life, and benefits to society. In this climate, physicians and patients may overuse, underuse, or misuse available treatments, limiting their utility in achieving significant public health benefits.

Payors and systems of care are facing explosive demand for treatment and associated expenditures at the same time as resources are becoming increasingly constrained. Public policy strategies to slow HIV therapeutic costs are resulting in reduction in the narrowing of benefits for publicly funded programs supported through the Ryan White CARE Act (CARE Act). The Medicaid Program, the largest single payor of HIV care, presently reimburses for drugs approved by the FDA. Some State Medicaid programs, including Medicaid managed care, as well as commercially-funded managed care systems, are instituting a variety of policies to contain costs, such as requiring prior approval before a therapy is dispensed and placing caps on the number of prescriptions. Proposed federal legislative changes to Medicaid, such as block grants, would put tremendous pressure on all the states to decrease current coverage and payment levels for HIV therapies. Commercial payors, including integrated managed care systems, experience many of the same pressures as the public sector and are implementing a number of cost containment policies. The Medicare program will confront the

same pressure as other payors as patients live longer and become eligible for the program based on their disability or age.

As payment for care increasingly drives clinical decision making, patients will have significantly constrained access to new therapeutics. The potential of new agents may not be fully realized because they may not be affordable for large segments of the population such as publicly-insured individuals; medically indigent patients who are enrolled in CARE Act-funded programs, such as ADAPs; uninsured or underinsured individuals; and participants in commercially or publicly-funded managed care systems.

In order to develop sound HIV-related coverage and reimbursement policies, third party payors and health care delivery systems need clear, scientifically based information about the long-term risks, benefits (including impact on quality and length of life), and associated cost-effectiveness of various HIV treatment regimens and strategies. Such information also would allow development of best practice clinical guidelines targeted at improving outcomes. Given the rapid evolution of new HIV drugs and the dynamic nature of HIV treatment, it is unlikely that clear answers will be available in the near future. Therefore, it is important for payors and health care delivery systems groups to make treatment coverage and reimbursement decisions that are more inclusive and flexible than they might be otherwise. In order to assure that third party payors, health care delivery systems groups, providers and patients join with other stakeholders as active participants in the proposed **Forum for Collaborative HIV Research**, it is imperative that the Forum meet their need as a mechanism to catalyze the development and exchange of scientifically sound information about how best to use available therapies.

Medical Management Goals

Several classes of drugs acting on different steps of the replication cycle of the virus are now available and can be used in combination. Such drug combinations should allow more profound and more prolonged suppression of viral replication. By applying significant pressure to inhibit viral replication, the development of resistance to a specific agent should be delayed or prevented.

We also now know that HIV is actively replicating throughout the course of the infection, causing a gradual loss of immune function. Furthermore, higher levels of the virus in the blood have been linked to more rapid progression of the disease. New methods for monitoring both the state of the immune system and the replication of the virus have significant implications for the clinical management of HIV disease. While maximal suppression of HIV and preservation of immune function could significantly slow the course of the disease, there remain important unanswered questions which must be addressed if we are to provide optimal care. The challenge now is to determine how to best use these therapies and tools in clinical practice to realize their promise for improving the clinical care of patients.

The Keystone Dialogue Group proposes the following goals for optimizing medical management: to initiate antiretroviral therapy and prophylaxis at the most appropriate time in the course of HIV infection; to provide cost-effective and tolerable treatment strategies that will result in maximal long-term suppression of HIV replication; to prevent the development of drug resistance; to enhance compliance/adherence to these optimal regimens; to improve, delay or prevent immunologic dysfunction and opportunistic complications; to decrease virus transmissibility; and to ultimately prolong survival and improve quality of life for HIV-infected individuals. Treatment trials that address strategies aimed at evaluating the feasibility of achieving these goals are essential.

The Need for Strategy Trials

Clinical trial designs that have emphasized shorter term comparisons of fixed drugs and drug combinations will need to be complemented by a series of larger trials that are structured to provide insight into strategies of how to use drugs optimally over a number of years. The Dialogue Group believes that trials addressing the long-term effectiveness of therapies and treatment strategies for HIV infection should be undertaken because the new state of knowledge and recent expansion of therapeutic choices present both a unique opportunity and urgent need to do so. Moreover, in contrast to shorter term trials used for registration, these types of trials present different challenges to design and implement. Strategy trials may require a significantly larger sample size, longer duration, and the need for collaboration of multiple parties in order to marshal the required resources.

Strategy trials are best illustrated in comparison with drug or regimen-based studies.

1. Regimen-based trials

Regimen-based trials are designed to establish the efficacy and safety of a single drug or drug combination. These trials are usually conducted by pharmaceutical companies, sometimes in collaboration with government-funded research or clinical trial networks.

They encompass both the smaller studies common to early drug development and the later, larger trials that often compare specific drugs or drug combinations to a placebo or agent known to be effective. These trials generally provide the following basic information necessary to allow incorporation of the particular agent or agents into a more broad-based treatment strategy: activity information (as measured by surrogate endpoints, including magnitude and duration of effect); optimal dose and schedule; safety and tolerability; drug interaction profile; exploration of synergy with other agents; resistance kinetics and profile; and pharmacokinetics and safety in children.

After regimen-based trials have identified candidate therapies for larger, strategy-based trials, but before the larger trials are implemented, certain critical design elements must be systematically explored. Regimens chosen to be evaluated in the larger trials must have an acceptable balance of activity, tolerability, schedule, and drug interaction profile. In some cases, choosing candidate therapies for these studies will require the generation of supportive data from additional smaller studies. In other cases, the entire strategy premise may require a pilot feasibility study.

2. Treatment strategy trials

In contrast to regimen-based trials, treatment strategy trials evaluate the efficacy of treatment sequences or therapeutic decision points. These questions may be evaluated in a limited way by regimen-based trials. Strategy-based trials should address the critical treatment questions about how best to use available therapies for a broad spectrum of HIV-infected patients and their providers. In addition, they may serve a regulatory purpose, be it contributing to registrational information or to the clinical database required by the accelerated approval regulations, or by post-marketing commitment.

Strategy trials should have the following characteristics:

- The studies will involve the diverse spectrum of persons infected with HIV;
- The designs will be simple and responsive to a rapidly changing standard of care;
- The studies will incorporate therapeutic options available to patients and providers;
- Events that prompt a change in therapy will reflect a judicious approach to current knowledge and practice;
- The studies will be larger and of longer duration than has been common in the past;
- Data collection will be limited to crucial information that can be captured by a diverse spectrum of health care providers;
- The studies will require a high degree of collaboration and cooperation among all stakeholders and will critically assess the issues of primary concern to those stakeholders.

The protocols for the studies should meet the applicable regulatory requirements.

An example of a treatment strategy trial would be to explore when the use of currently available antiretroviral agents should be initiated and how aggressively they should be used in a large, randomized trial comparing four treatment strategies in early HIV infection: immediate therapy combining nucleoside analogues with or without a protease inhibitor versus delayed therapy comparing nucleoside combinations with or without protease inhibitors. Critical design components would include defining when, and on what basis, to initiate therapy in the deferred therapy arm and when, and on what basis, to add a protease inhibitor (or other agent) to the nucleoside arm. Candidate triggers for these decisions include changes in levels of plasma viremia or CD4+ cell counts and clinical status.

The Dialogue Group believes that treatment strategy trials are critical components of the effort to optimize medical management of HIV infection. The Dialogue Group also determined that there currently is no mechanism in place able to facilitate or conduct such important trials without significant collaboration and additional resources.

FORUM FOR COLLABORATIVE HIV RESEARCH TO CATALYZE INFORMATION EXCHANGE AND CRITICAL RESEARCH

Government sponsored clinical trials groups, the pharmaceutical industry, and other research organizations have made significant contributions to our understanding of the treatment and management of HIV infection and disease. However, the autonomy of existing structures can lead to duplication and fragmentation that may not optimally use limited resources. For example, no standing mechanism exists to evaluate studies to identify significant gaps in knowledge, or to prevent unintended redundancies. In addition, no mechanism exists to identify potential shared resources which could be brought to bear on problems that are too large for individual groups to evaluate. Communication and collaboration among multiple stakeholders must be augmented and enhanced to ensure that many critical questions about the medical management of HIV disease are being adequately addressed. At present,

there is no existing forum in which all the major stakeholders can communicate about ongoing clinical research and treatment priorities. Importantly, the concerns of the payors and providers of HIV treatment and care are not routinely addressed.

The Keystone Dialogue Group concluded that an independent ***Forum for Collaborative HIV Research*** (Forum) involving stakeholders from multiple disciplines is needed to effectively exchange information on research and to serve as a mechanism to promote collaboration between various organizations, in order to optimize the medical management of HIV disease.

Why a New Forum is Needed

In determining the proposed structure of this Forum, the Keystone Dialogue Group evaluated a number of options, including the use of an existing group as the coordinating body. Many existing groups and organizations already perform important functions pertinent to the medical management of HIV disease. These include government advisory councils, professional health and medical organizations, HIV/AIDS-specific organizations, and industry groups. However, none of these groups could easily undertake the proposed functions of the Forum, nor do they adequately meet all the desired characteristics of the ideal Forum.

The Keystone Dialogue Group concluded that an ad hoc group representative of the major stakeholders is needed to perform the functions of the proposed Forum and to facilitate effective communication, collaboration, and coordination of these efforts.

Functions of the Forum

The goal of the Forum is to facilitate information exchange and actively catalyze appropriate stakeholders to develop and implement new studies to address critical unanswered questions regarding optimal medical management of HIV disease. The Forum should perform the following functions:

1. Provide a proactive mechanism to survey and synthesize current knowledge, practice patterns, ongoing studies of all sources, and information on medical management of HIV disease;
2. Identify gaps in the current knowledge base or ongoing research which, if filled, would answer critical questions;
3. Make recommendations on how to fill those gaps;
4. Actively catalyze appropriate stakeholders to develop and implement new studies to fill the gaps; and
5. Facilitate the development of a strategy and propose a new mechanism to conduct the needed studies, should existing sources prove inadequate to do so.

These functions serve as the foundation for the Forum. The Keystone Dialogue Group agrees that information exchange and catalyzing collaborations to answer critical questions are the most crucial roles of the Forum. The other functions are primarily to support these fundamental roles.

Characteristics of the Forum

For the Forum to be influential in developing HIV disease management strategies, the Keystone Dialogue Group identified seven characteristics that the Forum must possess to be successful.

1. *Collaboration:* Collaboration is necessary to optimize resource utilization, to avoid unintended duplication of efforts, and to share existing information, as no one participant has all of the information needed.

2. *Ownership:* Each major stakeholder must actively be engaged in and committed to the Forum, and any gaps identified as important by the Forum should be considered important by all major participants.

3. *Independence:* The Forum must be viewed as an independent organization, constituted by, but not a tool of, anyone of the major participants. This characteristic is important in order for activities conducted under the auspices of the Forum to be seen as unbiased. Independence will also increase the credibility of the Forum.

4. *Credibility:* The Forum will consist of leaders from the major participant groups who bring to the table a strong record of leadership and effort in this area, and the resources needed to follow through with their commitments. The key elements of credibility for the Forum are as follows:
    - All participants should be considered equal partners;
    - There must be diversity among the sector representatives;
    - Research designs highlighted by the Forum must adhere to scientifically sound principles; and
    - The Forum's activities and recommendations must be ethically sound.

5. *Productivity and Setting Priorities:* The Forum will catalyze efforts to be effective and productive and will avoid unintended duplication of ongoing activities. The Forum will recommend high-priority studies that are not currently being conducted or considered elsewhere.

6. *Accountability*: The Forum will have accountability to the major stakeholders. Without accountability, it will lack credibility and productivity. (See discussion below concerning accountability.)

7. *Accessibility:* Both the process of the Forum and the product will be accessible to the major participants, to those who gather and those who need the information.

Establishment of the Forum

The participants in the Keystone Dialogue Group witnessed a high level of collaboration, trust, and dedication from many leaders in the HIV research, health care delivery, payor and patient advocacy communities. This enthusiasm for collaboration has occurred, in part, because the potential scientific and medical benefits are much greater at this time, and the elements of this Keystone process – including diverse representation of the major stakeholders, frank and honest discussion, and the credibility and commitment of the participants – are unique and unprecedented in the HIV/AIDS field. Therefore, the Keystone Dialogue Group recommends these elements of diverse and interactive participation as critical for the proposed Forum. The Forum will be an independent collaborative network of major stakeholders, but will not be single-handedly run by government, industry, academia, or other entities. Some of the Forum members will have participated in the Keystone Dialogue project.

The Keystone Dialogue Group proposes that its collaborative efforts continue through the establishment of the Forum for Collaborative HIV Research. It is the intent of the Dialogue Group that this process will build upon the trust and collaborative spirit that has already developed among the participants in the Keystone Dialogue Group. Given the short time period of the Keystone Dialogue project, not all the details of the Forum were determined, such as how membership would be established, the specifics of a decision-making process for the Forum, and other issues. However, it was determined that the primary desired aspect of the Forum is the extensive collaboration and cooperation among a diversity of stakeholders involved and interested in HIV research.

The Forum will not require creating a permanent infrastructure. Successful activation of the
Forum will require real commitment by all the parties to sustain the undertaking and reach the objective of catalyzing new HIV research efforts to answer critical medical management questions. Doing the work necessary to transform the proposed concept of the Forum by Keystone Dialogue Group into a reality will be a test of the willingness and dedication of the major stakeholders to shape and support this collaborative process.

Public/Private Partnership

The Dialogue Group acknowledged that considerable resources, expertise, and commitment are already devoted throughout both the public and private sectors which address aspects of optimal medical management of HIV disease. This cooperation exists in government-sponsored HIV research networks, many pharmaceutical companies, as well as among public and private payors of medical expenses for persons with HIV. These past efforts have been important in laying the foundation for such collaborative efforts, but a more intensive, sustained, and information-rich effort is now necessary to exchange information, assess gaps, and encourage cooperative efforts that will generate the information about how to use our new understanding of HIV most effectively.

Rather than seek to start a new program, the **Forum for Collaborative HIV Research** will work to encourage coordination among the public and private AIDS clinical research efforts. The Forum also will seek to better integrate such research into HIV medical care settings. In this way, studies performed by various research entities, separately or in cooperation, will begin faster, duplication of effort will be reduced, patient enrollment and retention will be facilitated, and costs of getting the answers to the critical questions will be shared.

The Forum could help facilitate and catalyze studies through information exchange or working in various cooperative efforts. Collaboration in these efforts could be demonstrated in many ways, including contribution of time, expertise, financial resources, or provision of other resources. Examples of contributions in a collaborative effort that involves multiple stakeholders could include pharmaceutical companies supplying quantities of drugs for the upcoming studies; government-sponsored clinical trial programs contributing their trial design expertise; community organizations informing and educating patients about the importance of these

studies; and third-party payors covering certain costs of care, such as laboratory testing for those patients participating in the clinical trials. Exactly what is necessary to construct a cooperative effort will be decided collaboratively.

All participants in the Keystone Dialogue Group agreed that without this proposed collaboration, the clinical research that is needed will either take longer to do or will not be accomplished at all. The work of the past decade has brought us to an historic turning point in the battle against HIV/AIDS and we must now work together to complete the task.

Incentives of the Forum

There are many incentives to participate in the Forum, several of which are common to all the stakeholders. For example, all stakeholders would prefer to be part of a collaborative process where scientifically and medically sound clinical studies are planned by many experts in the HIV field. In addition, they all share the desire to translate as quickly as possible new information about emerging trends in HIV treatment strategies into good clinical practices. All stakeholders also want the decisions about the provision of HIV care to be based upon reliable evidence about medical necessity and improved quality of life and health outcomes.

Additional incentives are more specific to individual participants. For example:

The pharmaceutical industry is interested in generating information that will expand the use and indications for its approved antiretrovirals and hence broaden the market for their drug.

The public/private payors and health care delivery systems need scientifically sound information to make informed coverage and reimbursement decisions. These decisions are based on principles of medical necessity, quality of care, and cost-effectiveness. All payors are interested in more adequately forecasting future medical and pharmaceutical costs in the context of continuous improvement of outcomes.

The patient community has a vested interest in incorporating their needs into study design and implementation. They also seek access not only to new HIV therapies, but to high-quality and credible information that can be relied upon for making treatment decisions in conjunction with their health care providers.

Clinicians are interested in providing high-quality care and treatment options to their patients. They want access to timely, high quality information which can be incorporated into personalized treatment decisions for their patients. Evidence-based treatment strategies can also assist health care providers to prioritize and integrate a comprehensive approach to medical management of HIV disease.

Researchers are motivated to contribute to the discovery of new information and progress of medical research. Researchers want to develop and utilize new information to advance science, promote collaboration, and potentially enhance career development.

Government aims to protect and improve public health by support of the discovery of new knowledge and ensuring that public resources are used optimally. Government also has regulatory obligations to fulfill concerning the licensing and use of pharmaceuticals.

Action Plan for the Forum

The first project for the Forum will be to continue and complete the evaluation of the HIV antiretroviral trials that are underway or planned by the public and/or private sector, and determine whether such studies have the potential to answer the critical questions to be addressed in optimizing the medical management of HIV disease. The next step will be to identify what, if anything, is impeding the implementation of these studies, and to use the Forum to help facilitate the conduct of these studies, particularly strategy trials, that are needed to address critical questions. If existing or planned studies still leave gaps in the knowledge base necessary to improve the long-term treatment of HIV disease, then the Forum will facilitate cooperation among the various participants to design and implement those high priority studies to fill the gaps.

Additional strategy-based clinical trials that are beyond those that are currently planned or underway will probably be required to address some of the critical issues outlined in this report. If such trials are needed, the resources required to conduct them cannot be specified with precision until the specific scope of necessary trials has been delineated. It is possible that several trials with

significant numbers of participants (i.e., 1000-2000 patients) of long duration
(i.e., 2 to 3 years), will be required to adequately explore several proposed treatment strategies. Major treatment strategy trials can take significant resources. The Forum will seek to aid the stakeholders in defining innovative and creative approaches to fund these trials.

Location of the Forum

It is proposed that the Forum would be housed at an independent, non-governmental site. Potential locations include one of the several centers for health policy studies that exist at academic institutions or other non-profit health policy or advocacy organizations.

Support of Forum Activities

The annual budget projection for the **Forum for Collaborative HIV Research** is approximately $500,000. This amount is based on the need for core staff, including a Forum Director, project coordinators and support staff. Together, these personnel will handle all administrative, communications, meeting planning, information compilation and coordination of Forum activities. All staff will report to the Forum Director who will work directly with the Project Coordinators for specific Forum projects. This budget also includes funds for six meetings of the Forum per year, and the services of a professional facilitator who will assist with the meetings.

To help assure that all participants claim a real stake in this process, the Forum will be funded by the participating public and private entities--with cash contributions and/or in-kind donations of staff. The level of support will be sufficient to represent a real commitment that will be unlikely to continue without some sign of success. No one participant will contribute so much as to dominate the process and all information concerning sources of funding will be publicly available.

The activities of the Forum would be handled by several integrated levels of staff (both full-time dedicated staff and donated staff):

- Forum Director and Support Staff: 4 FTEs to handle the Forum's administration and communications; donated resources; located at the Forum home office;
- Project Coordinators: Volunteered human resources from major participants to coordinate Forum activities; virtual office; about 25-100% of time;
- Executive Committee: 8-12 people from the Forum will serve as an advisory group to the project coordinators; meet frequently by teleconference; about 5% of time; and
- Forum Members: similar in composition and expertise to the Keystone Dialogue Group, representing government, public and private payors, health care providers, pharmaceutical industry, researchers, clinicians, and patient advocacy organizations; the Forum meetings would be managed by professional facilitators; six, 2-day meetings per year.

Criteria for Success

It is critical to establish the credibility of the **Forum for Collaborative HIV Research** with those who will be most affected by its work--those living with HIV, those conducting and supporting clinical research on HIV, and those who care for and pay for HIV-related care. *Ultimately, the credibility of this Forum will depend on whether it can successfully catalyze new collaborations or studies to answer critical medical management questions.*

The Keystone Dialogue Group firmly believes that the success of this Forum would be evaluated based on whether it catalyzes collaborations, in the short-term, which lead to studies and results in the long term that would not have otherwise happened. More specifically, participants developed the following as criteria for success of the Forum:

- The participants continue to support the Forum. Put more simply, this Forum will depend on the policy and resource contributions (cash or in-kind) from key participants. If they withdraw their support, either the Forum is not addressing unmet needs or has been successful and is no longer needed.
- The existing system of research is working more effectively because of the improved collaborative relationships this Forum has fostered, such as innovating collaborations between pharmaceutical companies and other participants.

- New studies have been launched, or the impediments to the implementation of ongoing studies have been overcome, and resources have been appropriately allocated to support the prioritized work.
- Results from these important studies, catalyzed by the Forum, are translated into improved and more effective medical management information to the benefit of those with HIV infection.

If these criteria are met, establishing a more permanent structure might be considered. However, it might also be decided that the Forum process is more flexible and responsive to the changing challenges posed by the epidemic.

Accountability of the Forum

The Forum must be accountable to the major participants. The major stakeholders will undertake frequent, formal evaluation to determine whether the Forum is responsive to their needs and concerns. At the end of the first 12-18 months of its existence, a decision will be made by the major stakeholders whether to continue or modify the activities of the Forum.

Activating the Forum for Collaborative HIV Research

The following actions will be taken to establish the Forum:

1. Confirm specific commitments from major stakeholders for resources and manpower to support
    - Forum Director and Administrative Staff
    - Project Coordinators
    - Executive Committee

2. Establish link to a health policy center, or alternative location, to house the Forum;
3. Hire Forum Director and administrative staff;
4. Establish timeline and accountable persons for Forum activities; and

Convene first meeting of the Forum in the fall of 1996.

Keystone National Policy Dialogue on Establishment of Studies to Optimize Medical Management of HIV Infection

Participant List

Note: Participants attended as individuals, not as formal representatives of their respective organization, agency, or company, and therefore the opinions expressed in this document do not represent official organization, agency, or company views. Additionally, the positions and organizations of these representatives are reflective of 1996 and may not appropriately reflect current positions or affiliations.

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