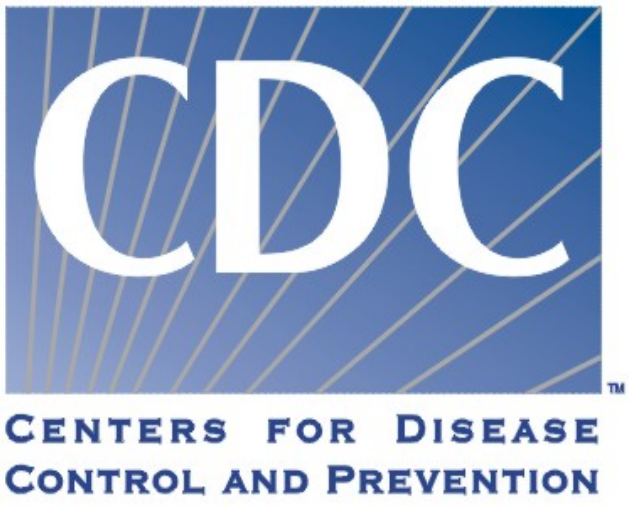
DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION/
Agency for Toxic Substances and Disease Registry



Joint Meeting of the
Ethics Subcommittee of the
Advisory Committee to the Director, CDC
and the
CDC Public Health Ethics Committee
February 27-28, 2007
Atlanta, Georgia

Record of the Proceedings

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Minutes of the Meeting

The Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC) convened a joint meeting of the Ethics Subcommittee of the Advisory Committee to the Director, CDC and the CDC Public Health Ethics Committee (PHEC). The meeting was held on February 27 – 28, 2007 at CDC's 1825 Century Center Building, Atlanta, Georgia, Conference Rooms 1 A/B. Meeting participants are listed in Attachment 1.

Introductory Remarks and Subcommittee Business

Dr. Ruth Macklin, the Ethics Subcommittee Chair, called the joint meeting to order at 1:00 p.m. on February 27, 2007.

Dr. Drue Barrett, Public Health Ethics Coordinator, Office of the Chief Science Officer at CDC, welcomed those present and reviewed housekeeping issues. Before turning the meeting over to Dr. Macklin, she ensured that all Ethics Subcommittee members had submitted their conflict of interest forms.

Dr. Macklin presented an overview of the meeting's agenda and goals, which included 1) providing input to CDC on ethical issues relating to genomics; 2) providing input to CDC on ethical issues relating to public health emergency preparedness and response; 3) providing recommendations for next steps on pandemic influenza ethical guidelines; 4) reviewing policies and procedures for the Ethics Subcommittee; and 5) providing input on ethical considerations for non-research data collections.

Public Health Ethics and Genomics/Genetics

Ethical Issues of Public Health Genomics

Dr. Barbara Koenig, Ethics Subcommittee member, introduced the afternoon's session and provided an overview of ethical issues in public health genomics. A workgroup made up of representatives from both the PHEC and the Ethics Subcommittee has been considering this issue for several months.

Dr. Koenig pointed out that genomics will transform healthcare in the 21st century so that healthcare will be predictive, personalized, and pre-emptive. This vision guides work at the National Institutes of Health (NIH) and other agencies. It affects and permeates efforts in the public health arena, as well as the clinical arena and will do so even more in the near future.

The CDC National Office of Public Health Genomics (NOPHG), addresses genomic issues and their particular application to public health. In the area of genomics, public health presents some overarching issues:

- Is public health different?
- Does the genetic exceptionalism debate play out differently in public health?
- Should bioethicists consider problems in research ethics and the evaluation of evidence in the field of genetics in a different way?

CDC identified several pressing concerns in these areas. To address these concerns, this session focused on gathering input from the Ethics Subcommittee and PHEC regarding ethical issues concerning the return of research results. Four case studies of actual problems that CDC has faced informed this discussion. Ultimately, a guidance document aimed at CDC's internal IRB members and to investigators will be generated.

Emerging technologies in genetics are affecting how disease and research are conceptualized. Fundamental transformations in public health research practice have already begun and will continue. Public health has always collected some biological data, but it is now routine for almost every project to collect biomarker data. A great deal of genetic specimens and data are now available for study, raising issues of what to do with the DNA and how to protect privacy and confidentiality of donors.

This issue intersects with many areas of concern to CDC. Infectious disease and other outbreak investigations are especially affected, particularly planning for pandemic influenza. In an infectious disease outbreak, genomic tools will be used to determine host susceptibility and vaccine response. Large databases of individuals' information will need to be kept and followed for a long time. CDC hosted a Pandemic Flu and Genomics Meeting in January 2006, where the ways in which genomics affects every arena of public health were discussed. For instance, a large number of unexpected deaths occurred in one of the recent influenza seasons. Research ethics challenges emerged regarding conducting genomic analyses with data that were collected in the context of the outbreak investigation. Conventional understandings of human subjects protections may have to be re-thought in cases of serious public health issues.

Further, evidence of clinical utility is important but difficult to ascertain in both medical and preventive applications.

Dr. Koenig discussed a recent article by Russ Altman and colleagues in the *Journal of the American Medical Association* (JAMA) titled "The Incidentalome: A Threat to Personalized Genomic Medicine." This article discusses the implications of genome-scale screening tests. It is now possible to test 500,000 "snip chips" to collect a massive amount of data. Physicians will be overwhelmed by the complexity of unexpected genomics findings. Patients will be subjected to unnecessary follow-up and costs may increase, thereby decreasing the likelihood of overall social benefit. As the number of tests increases, so does the chance of spurious findings. It is difficult for clinicians to ignore abnormal findings, and it will be difficult for researchers to determine which findings are abnormal and which findings they are obligated to reveal. The authors of the article predict that with certain numbers of independent tests, up to 70 percent of the population will have false positive test results. The authors of the JAMA article concluded that genetic education is needed, especially for clinicians and for those who make recommendations about return of research results. Tests should not be ordered "to be on the safe side," which represents a change in typical practice. Finally, it is not prudent to use testing panels comprising a sizable fraction of the genome for clinical care or for screening.

Genomics is extremely important in public health ethics. The genomic "revolution" changes thinking about fundamental cause and etiology, including research paradigms and interactions between the social environment and the biological world. Dr. Koenig offered the example of genomic research on nicotine addiction and smoking behavior. Is smoking caused by genetic susceptibility for a person to be addicted to a chemical, or is smoking a political problem? The answers to these questions affect how smoking research is approached. If a set of interventions is known to be effective, such as increasing taxes or decreasing areas where smoking is permitted, is it wise to study the issues with a set of genomic tools? These issues determine how to set public health priorities.

Also at issue is the proposed United States population biobank, which will examine the intersections of diseases, conditions, genes, and the environment. One of the implications of creating national biobanks, which will be important for public health, is that they will lead to genetic association studies. The Genetic Association Information Network (GAIN), launched last year, has implications for human subjects protections. GAIN is a public/private partnership with access requirements. The initial assumption was that genomic data would be made publicly available through resources at NIH and other places without individual identifying information or connections to individual phenotype data. Researchers with a password would have access to individual coded phenotypes and associated genotypes. These large-scale databases represent a new way of conducting research, and they lead to the important question of whether genetic data can be de-identified.

Participant health information that has been stripped of certain identifiers is called a "limited data set" under the Health Insurance Portability and Accountability Act (HIPAA). These sets may be used or disclosed for research without a participant's authorization or waiver of authorization. The current assumption is that DNA can be de-identified, but the point is arguable. The premise of requiring data sharing is based on the idea that there is no possibility of using DNA as a "fingerprint." The premise also assumes that protections are in place. Dr. Koenig suggested that both assumptions are incorrect.

Removing HIPAA identifiers will not remove all privacy concerns for subjects, since DNA itself is a unique identifier. DNA contributed to biobanks can now be shared without IRB review

because they have been stripped of identifiers and are considered to be exempt. Further, DNA "circulates." That is, there are many intersections with other sources of data, such as criminal justice and through the states. This issue will have differential impact on different populations. Other interactions include large-scale genetic epidemiological databases, newborn screening, military databases, forensic uses, genetic genealogy databases, and others. For instance, a genetic genealogy website can analyze DNA from a blood sample, but the samples are unregulated. The increasing availability of direct-to-consumer genetic testing further complicates the matter.

Dr. Koenig pointed out that a group from Baylor University in Texas suggested dealing with these issues by instituting a rigid consent process. When individuals contribute their DNA to a biobank, then it will be categorized according to "risk." The approach is interesting, but may not be practical. The proposers assert that securing public trust will require recognizing that genetic sequencing studies are human subjects research and should be brought under the protection of existing federal regulations. This recommendation raises the question of whether public trust has been breached. Little is known about the extent of classified work on biological identifiers by the National Security Administration (NSA) or other agencies. Further, revelations about theft of Veterans' Administration (VA) data and insurance databases bring up concerns about how to address the large amounts of DNA that are "floating around." Recently, an official at the National Institute of Mental Health (NIMH) allegedly transferred samples to Pfizer. Questions about ownership of data lead to legal and other disputes.

Another issue for consideration is how an average clinician or public health practitioner can know when a particular test or panel of tests is ready for routine clinical use. As an example, Dr. Koenig pointed to the work of a CDC convened group called the Evaluation of Genomic Applications in Practice and Prevention (EGAPP). A report was issued by this group at the end of 2006 regarding use of a genetic test to determine how participants metabolize powerful drugs in the context of depression. The EGAPP group concluded that even though these types of genetic tests are moving into clinical practice, there is no evidence that they should be used routinely.

The current regulatory environment has serious deficiencies. In making ethical decisions, Dr. Koenig said that they cannot rely on rigorous evaluation by the Food and Drug Administration (FDA) and the Clinical Laboratory Improvement Amendments (CLIA) to help decide which tests are meaningful and which results should be conveyed to participants. This issue becomes more complicated because evaluation of the tests is complicated and includes questions of analytical validity; clinical validity; making strong associations between gene patterns and disease or trait outcomes; and clinical utility. Even if a strong association between a gene and an outcome is proven, does that information improve health for a population or an individual?

Questions remain regarding regulating genetic tests and whether professional standards and practice guidelines are needed. While CDC and others are thinking about evidence, products are moving into the open market. The Federal Trade Commission (FTC) is creating guidance and recommendations in this area and has suggested "a healthy dose of skepticism" in the case of home genetic tests, but movement has been slow. In thinking about biobanks and other issues that will have broad public impact, public engagement to get their views on these complicated ethical choices should be a priority.

The Public Health Ethics and Genomics Workgroup suggested that CDC should first address reporting individual research results to participants in public health investigations. In the past, CDC practice has dictated that results lacking clear clinical implications for participants are not

revealed. Guidance is needed for CDC IRBs and for investigators. These issues are relevant to NIH and other agencies as well, Dr. Koenig concluded.

Discussion Points

- Dr. Macklin reiterated that the Public Health Ethics and Genomics Workgroup had asked the Ethics Subcommittee to focus on the question of the disclosure of results. She asked whether the Subcommittee and PHEC would also be asked to examine the many other issues raised in Dr. Koenig's talk.
- Dr. Koenig replied that the Workgroup elected first to gather input on a concrete topic, but they hope to work on other issues, such as community engagement. They have not set other priorities at this time.
- Dr. Barrett added that the Ethics Subcommittee and the PHEC would be asked to review the general guidance document.
- Dr. Koenig noted that their decision to concentrate on disclosure was based on their perception of the needs in the field.

Introducing the Issue: Returning Genetic Test Results to Participants in Public Health Research

Dr. Cynthia Moore, Associate Director for Science, NOPHG, thanked Dr. Koenig for providing an overview of the issues and "setting the stage" for a focused discussion on returning genetic test results to participants in public health research.

NOPHG's vision is to use genomic knowledge to improve the lives and health of all people, and its mission is to integrate genomics into public health research, policy, and programs. To achieve its mission, the group works across the many organizational units at CDC to identify cross-cutting issues and to build initiatives in genomics that have broad public health implications.

Dr. Moore pointed out that the integration of genetic studies into public health research is increasing as the field learns more about the role of both genes and environment in the genesis of health and disease. CDC has had a role in looking at pathogen genomics for some time, but the agency is moving into studies of the human, or the "host." CDC's research is conducted in many contexts, including investigations of acute disease outbreaks. Most genetic studies are observational and the clinical significance of the findings is often unclear, especially in the study of genetic variants. The trend in research is towards genome-wide studies, which produce large volumes of genetic data with more false positives. This summer, chips that can measure one million single nucleotide polymorphisms (SNPs) will be available for $800.

There are no well-established mechanisms for CDC staff who conduct genetic research to interact on protocol development issues. Some workgroups concentrate on genetic issues, and a NOPHG collaboration is convening researchers to share their experiences two to three times per year. Protocols are reviewed by multiple IRBs at different sites and through different entities. The default position at CDC has been not to report individual genetic research results to research participants. However, because CDC is a federal agency, individual results of participants or their children can be obtained via the Privacy Act.

As studies that incorporate genomics increase, NOPHG is being consulted more frequently for guidance and model protocols. Guidance should be readily accessible and consistently applicable across CDC studies. The issue of reporting individual genetic results to study

participants has generated a great deal of debate in the last few years. There is a lack of consensus regarding this issue in the bioethics community, and there is a dichotomy between autonomy and research focus. There is a perception that genetic research results differ from other research results, including the pervading concept that genetic information is highly predictive and confers risks related to insurability and family relationships. Researchers and IRBs need guidance for situations in which results do not have clear clinical implications for participants.

Dr. Moore asked the Ethics Subcommittee to provide guidance to CDC investigators and IRBs regarding ethical issues concerning the return of individual genetic results to study participants. To help frame the Subcommittee's deliberations, she indicated that CDC representatives would present four case studies as illustrations of genetic work that CDC is currently conducting and to present issues related to return of results. Staff members prepared questions for the Subcommittee's consideration and discussion.

The four case studies included:

- National Birth Defects Prevention Study
- Genetic Studies of a Cluster of Acute Lymphoblastic Leukemia in Churchill County, Nevada
- Genetic Predictors of Developing Hemolytic Uremic Syndrome Among Persons Infected with Shiga Toxin-Producing *Escherichia coli* 0157
- Nicotine Exposure and Metabolism in Alaska Natives

Following the presentations, the Ethics Subcommittee was to address four questions:

- Is there an ethical duty to offer genetic research results to study participants?
- When these results are offered to participants, what ethical considerations should guide the methods and the manner of the reporting?
- What human subjects protections should investigators employ in research protocols in anticipation of evolving clinical significance and future research?
- What are the ethical considerations for reporting genetic research results to participants from special populations and with respect to family relationships?

Dr. Moore indicated that staff would gather the results of the discussion of ethical issues, reframe them, and summarize them. The Public Health Ethics and Genomics Workgroup will use the summary to synthesize recommendations for a CDC best practices guidance document, which they hope to will be available for review at the next joint meeting of the Ethics Subcommittee and PHEC.

Case Study #1: National Birth Defects Prevention Study

Sonja Rasmussen, M.D., Medical Officer
Division of Birth Defects and Developmental Disabilities (DBDDD)
National Center on Birth Defects and Developmental Disabilities (NCBDDD)
Centers for Disease Control and Prevention

Dr. Sonja Rasmussen described the National Birth Defects Prevention Study. Birth defects affect about 120,000 babies in the United States each year, which represents about three percent of all births. Birth defects are one of the leading causes of infant mortality in this country. About 20 percent of infant deaths in 2004 were related to birth defects. About two-thirds of birth defects are of unknown etiology, so it is important to try to understand causes of birth defects in order to develop intervention or prevention strategies. Current evidence suggests a combination of genetic and environmental risk factors for birth defects. The Division of Birth Defects and Developmental Disabilities (DBDDD) looks at genetic factors in the studies that it conducts. Studying gene-environment interaction will lead to a better understanding of etiology and help to identify populations at high risk (persons with a susceptible genotype) and modifiable risk factors.

The National Birth Defects Prevention Study (NBDPS) is a case-control, multi-site study of major birth defects. Nine states participate in the study. The study goal is to evaluate genetic and environmental risk factors. Enrollment in the study began with births on or after October 1, 1997. During the long time frame of this study, ethical thoughts have changed.

The first step of the study is case ascertainment and review. Cases are ascertained through population-based birth defects surveillance systems at the nine sites and are reviewed by clinical geneticists to ensure that they meet the study's case definition criteria. Cases in which the birth defect has a known cause are excluded from the study.

The next component of the study is a maternal interview and DNA collection from the mother, infant, and father. The hour-long interview asks about a wide range of environmental factors. This project was planned to be ongoing, and the investigators knew that they would not be able to provide a list of all of the genes that would ever be studied. Many of the genes proposed for study now were unknown in 1996 and 1997 when the initial IRB protocols were written. The investigators worked with the IRB to create "gene one-pagers" so that the IRB can approve the analysis of additional individual genetic factors. Researchers submit a "one-pager" on each genetic factor for review at DBDDD and by the CDC IRB for expedited review as an amendment to the original protocol. The "one pagers" include:

- Proposed genetic research
- Justification for study of the genetic factor
- Whether the test is of clinical significance
- If the test is of clinical significance, additional efforts that will be made for human subjects protections

The first "one pagers" were for genes that were hypothesized to be connected to birth defects but had no clear-cut clinical significance. The first genetic factor with clinical significance proposed for study was 22q11.2 deletion. A blood test to diagnose 22q11.2 deletion has been clinically available for many years. Infants who have been diagnosed with a 22q11.2 deletion are excluded from the NBDPS because this finding indicates a known cause of a birth defect. Although information on the deletion is clinically useful, some persons might choose not to receive the information. The birth prevalence of the deletion is about 1.8 per 10,000. It can be inherited from a parent in an autosomal dominant pattern, or it can be a *de novo* occurrence. Clinical studies reveal that the effects of the deletion can include congenital heart disease, palatal abnormalities, facial features, learning difficulties, and other problems, including an increased risk for psychiatric problems. In some persons with the deletion, the effects are mild and the person can be unaware of the diagnosis.

There are advantages to identifying this deletion. Identification can explain the cause of birth defects, suggest other studies and tests, allow for early intervention and specialized treatment, provide an opportunity for accurate recurrence risk counseling for the parents, and make prenatal diagnosis available for future pregnancies. At the same time, disadvantages are associated with identifying the deletion. There is no "cure," and it could change a family's perception of the child. Persons with 22q11.2 deletions are at increased risk for other problems such as developmental delay and schizophrenia. Potential impacts on insurance and employment should also be considered.

After many discussions within the DBDDD, with study collaborators at the other sites, and with the IRB, the investigators established the following plan for 22q11.2 deletion testing: Testing will be conducted in a CLIA-certified laboratory so that results can be provided to participants who request them. The participants will be notified of summarized results through an annual newsletter and also informed that they can request individual results of the testing. The informed consent forms reflect these plans. Clinical geneticists or genetic counselors are available at every site to discuss these issues with families, and participants are encouraged to see their health care provider for confirmation of the results. Each year, when new families are included in the study, the newsletter includes an article about the current understanding of 22q11 deletions.

The informed consent forms make it clear that the studies on the samples are not meant to test the medical status of parents or children. In general, the study plan does not include returning results of the tests to the participants and this information is clarified in the consent form. The informed consent form also indicates that summarized results of studies with clinical results will be published in the study newsletter, and participants can request individual results.

Discussion Points

- Dr. Robert Levine recalled that the deletion can be inherited or can occur *de novo*. He asked whether a *de novo* mutation can then be transmitted so that the information could be of importance to the affected baby.
- Dr. Macklin asked how "clinical significance" was defined.
- Dr. Rasmussen replied that coming up with a definition for "clinical significance" has been a challenge. The recommendations from the National Heart, Lung, and Blood Institute (NHLBI) Working Group on Reporting Genetic Results in Research Studies provide guidance for a definition of clinical significance (i.e., a significant risk factor for a condition with important health implications and available therapeutic or preventive interventions).

When making decisions about clinical significance, the study team errs on the side of caution.

- Dr. Vanessa Northington Gamble asked about what the study participants might feel is clinically significant.
- Dr. Macklin suggested that they revisit the issue in a larger discussion, because some test results might have not just clinical, but also psychological importance. Negative consequences could be associated with having information related to genetic testing, but if the child is at risk for developmental delay, then parents may want to seek early intervention that may not be clinical.
- Dr. Rasmussen agreed that the issue was difficult and reiterated that the study investigators recognized that not all study participants may want the study results.
- Dr. Richard Dixon asked about the proportion of people with this deletion who do not have phenotypic consequences.
- Dr. Rasmussen responded that she does not believe a study to answer this question has been performed. Clinical testing for 22q deletion is typically conducted because of a clinical suspicion of the deletion. The study investigators have discussed conducting population-based studies of the prevalence of 22q deletion in the general population. Dr. Dixon clarified that there is uncertainty regarding the "downstream consequences" of the deletion.
- Dr. Rasmussen agreed. The study investigators have discussed what to do if the deletion is discovered in a control case. The family may want information, but they may not suspect that their child had any problems.
- Ms. Kathy Kinlaw asked about the criteria for review of the "gene one-pagers" and the numbers of individuals who have requested information about the deletion.
- Dr. Rasmussen answered that the "one-pagers" undergo the typical CDC clearance process, which includes reviews at several levels and then review at the CDC IRB. The review considers the four criteria and determines whether the justifications are sufficient. The study investigators have not yet conducted studies of 22q11.2 deletions and thus have not released any individual test results related to the deletion.
- Dr. Levine wondered about the assertion that disclosing results of the genetic testing could put a child at increased risk of schizophrenia.
- Dr. Rasmussen clarified that having the deletion is a risk factor for schizophrenia. The investigators' concern, therefore, is that a family might not want that information.

Case Study #2: Genetic Studies of a Cluster of Acute Lymphoblastic Leukemia in Churchill County, Nevada

Carol Rubin, DVM, Chief, Health Sciences Branch
Division of Environmental Hazards and Health Effects (DEHHE)
National Center for Environmental Health (NCEH)

Dr. Rubin emphasized that the study that she would present began not as a genetics study, but as a CDC response activity. Genetics became an important part of the work several years after the fact. An astute clinician noticed that "too many" children were being diagnosed with pediatric leukemia in a small town of 8000 people located in the desert in Nevada. The town is the site of the Top Gun Naval Air Station, but is otherwise relatively remote. The state initiated active surveillance, and at the end of 2001 the surveillance revealed that the number of children in Fallon who had been diagnosed with acute lymphoblasitic leukemia was significantly higher than expected. Cancer cluster investigations are notoriously frustrating, both for investigators and families, because the studies are nearly always inconclusive. CDC has not worked in

cancer cluster investigations regularly for 20 years; however, an expert panel convened and recommended to the State of Nevada that this cluster should be investigated; the panel specifically recommended that the Nevada Commissioner of Health request that NCEH conduct a cross-sectional exposure assessment. The size of the Fallon cluster represented the largest reported unexplained geographic grouping of children with leukemia.

CDC conducted a comprehensive investigation in the field. The work began with a two sets of mailed questionnaires to the families. CDC also set up a clinic to collect samples of blood, urine, and buccal cell swabs. The consent forms were long, as the study examined not only families and children, but also included environmental testing at their current and previous homes. The consent forms addressed collecting genetic data, but from the beginning of their work, the investigators indicated clearly that they would not necessarily conduct any genetic testing. Expert panels reviewed the biologic and environmental samples from the field as they came in. Results were interpreted and returned to the participants immediately if the findings were seen as posing a potential risk; all results were distributed individually and in aggregate when the study was complete. No genetic testing was conducted until the biologic and environmental work was finished.

The environmental work revealed elevations in tungsten, arsenic, and dichlorodiphenyldichloroethylene (DDE). Little is known about the human health effects of tungsten, and it had not previously been considered to be a carcinogen. Tungsten was included in this study because it was part of a standard panel of heavy metals. In Fallon, CDC found the highest levels of tungsten analyzed to date. There was no difference in tungsten levels between the case and comparison parents and children. All persons tested had extremely high levels. Because of these findings, the investigators asked the National Toxicology Program to prioritize testing the carcinogenic potential of tungsten.

The team knew that the area's water had high levels of arsenic. Most of the people who had high levels of arsenic believed they were not exposing themselves to the drinking water because they were drinking bottled water or using water treatment systems. Again, there were no differences in arsenic levels between case and comparison children and families. DDE is a breakdown product of dichlorodiphenyltrichloroethane (DDT) that remains in the body. A comparison of levels found in this study with data from NHANES showed that although there were high levels of DDE in the participants, the levels were higher in the comparison group of parents and were most elevated in parents born in countries where DDT is still used.

Based on these results, the team moved to the "next step" of genetic testing. They knew from the beginning of the process that they were in a difficult situation, so communication was at the core of their efforts. Their communication methods included Town Hall meetings, which were consistently attended by the same CDC staff members to establish relationships with the community. They maintained a website with information about cancer clusters in general, as well as information about the study itself. When high tungsten levels were found, the team immediately reported the findings to the community, advised them not to drink untreated water, and informed them that additional tests had been requested from NIH. The team met individually with families to communicate all results. A large number of CDC staff, including a geneticist, was on-site throughout the process. When all of the results were released, the articles were included in a mini-monograph in *Environmental Health Perspectives* (EHP) so that participants had access to the available peer-reviewed literature. The EHP articles were posted on-line just as the community meeting concluded.

Karen Steinberg, Ph.D., Senior Science Officer
Coordinating Center for Health Promotion
Centers for Disease Control and Prevention

Dr. Steinberg said that even though cluster research is unlikely to reveal a cause for cancer, CDC had to respond to this situation in Nevada. She recalled a particularly tense Town Hall meeting in the community, which was attended by a person with a medical degree and a law degree. He told the people of the town that he could do a genetic test on their children and tell the parents which child would get leukemia and which would not. The families did not accept this person, which is a testament to the good work that CDC did in building communication and trust.

Because exposures to tungsten and arsenic had been documented, the investigators decided to look at candidate genes to determine whether differences might explain why some children got leukemia while others did not. The literature at the time included little about tungsten. Arsenic was known to be a carcinogen but had not been associated as an etiologic agent in leukemia. A book that was published during the cluster investigation reported that tungsten replaced molybdenum and competitively inhibited three enzymes. Arsenic also inhibited these three enzymes which were involved in purine metabolism and detoxification reactions. The investigators looked for variation in the genes that coded for these enzymes and did SNP discovery, focusing on these genes. CDC included experts in the field of childhood leukemia and biochemistry in this investigation.

The team's greatest ethical challenge was in conducting genetic testing on children, especially when participation would not lead to direct benefits. The consent forms stated that individual genetic results would be provided to participants only if the result was medically meaningful. While the researchers advised against obtaining the results, they did not put themselves in an adversarial position by barring the results from participants which could be obtained through the Privacy Act.

Of the 11 cases, 100 percent of them had the same gene variant in the five prime non-coding region of one of the genes that codes for one of the enzymes that is inhibited by tungsten. Fifty-one percent of the control cases had this polymorphism. Fifty-five percent of cases and 25 percent of controls were homozygous for the risk polymorphism. The research team met with the families, shared the results of the testing, provided them with reasoning behind why the team did not recommend getting individual test results, and talked about the significance of the findings, which could have been due to chance. None of the parents demanded any test results. The team studied another leukemia cluster in a similar area, a desert with similar geological features. Some of the children in this area showed high tungsten levels. Testing in this area revealed the same polymorphism in the cases and in a few of the controls. These results could be "an oddity," but findings such as these can also be troubling, said Dr. Rubin.

The public health significance of this work is not necessarily in the genetic testing. Generally, cluster investigations do not reveal causes of disease. In this case, tungsten, arsenic, and DDE were identified as hazards. There is now a new water treatment facility in the area, and recommendations to avoid drinking water other than bottled water until the new treatment plant was on line were made at the time of the study. The National Toxicology Program agreed to study the toxicity and carcinogenicity of tungsten, and the results of genetic testing generated a hypothesis about gene-environment interaction. It is possible that tungsten and arsenic interacted with a genetic predisposition, perhaps *in utero*. In short, the work with regard to genetics revealed little concrete information to share with families.

Documentation does indicate that unless there is direct benefit from participation, children should not be enrolled in genetic studies that could reveal information about their genetic risk. Dr. Rubin noted that in cases like the one in Nevada, with common polymorphisms with low odds ratios that may or may not contribute to risk, but do not determine disease, they may not have the power to discriminate. It is usually not possible to learn exposures across the lifespan.

Discussion Points

- Dr. Gamble asked whether information was shared with parents only orally, or whether the parents received written materials. She expressed interest in knowing what was said to the parents, as well as how it was being said.
- Dr. Steinberg answered that she had printed materials for the parents. Dr. Rubin added that every family was given a dedicated notebook that explained every genetic result, and the CDC website also included information. Dr. Barrett said that they could provide those materials for reference.
- Dr. Steinberg indicated that parents were informed that the results of the test would not predict anything about the children's medical care and would not predict whether the children would develop leukemia.
- Dr. Levine was not sure that the regulations regarding genetic testing on children call for no testing whatsoever if the tests do not lead to direct benefit for the children. He then asked about distributing peer-reviewed literature to the community and whether the information was translated into laymen's terms for them.
- Dr. Steinberg answered that the literature was written in plain language. It was provided on the website and also included in a packet that the participants could show their doctors.
- Dr. Mary des Vignes-Kendrick noted that the consent form refers to learning information that can "significantly affect" a person's health. She said that different people might interpret "significant" impacts differently, and the impacts can include a wide range of mental as well as physical health issues. These issues will be different for parents versus physicians. Dr. Steinberg agreed and said that if the information was predictive in any way, then it would be shared.
- Dr. Macklin assured the group that they would return to the topic of significance.

Case Study #3: Genetic Predictors of Developing Hemolytic Uremic Syndrome Among Persons Infected with Shiga Toxin-Producing *Escherichia coli* 0157

Linda Demma, Ph.D., Senior Epidemiologist
Division of Foodborne, Bacterial, and Mycotic Diseases
National Center for Zoonotic, Vectorborne, and Enteric Diseases
Centers for Disease Control and Prevention

Dr. Linda Demma described a study in its early stages from the National Center for Zoonotic, Vectorborne, and Enteric Diseases (NCZVED) on Hemolytic Uremic Syndrome (HUS), a potentially life-threatening condition. *E. coli* O157 is the leading cause of HUS in children. Ten to twenty percent of *E. coli* O157 infections in children lead to HUS, and the fatality rate in those children is upwards of five percent. The rate of developing HUS in all patients in the recent "spinach outbreak" was 16 to 18 percent, and among children it was 30 percent.

Dr. Demma is a senior epidemiologist for the Foodborne Disease Active Surveillance Network. They have a platform for active surveillance as well as a platform for special studies, given that they are the principal food-borne disease component of the CDC Emerging Infections Program. They collaborate with 10 state health departments to conduct active case ascertainment of culture-confirmed infections in more than 600 clinical diagnostic laboratories in the 10-state catchment area. Dr. Demma is leading a group of researchers who will determine the risk factors for developing HUS among patients with culture-confirmed *E. coli* O157 infection. Some of the leading hypotheses include antibiotic exposure as a risk factor. The team is asking all culture-confirmed *E. coli* O157 patients identified through active surveillance to enroll in the study. The team is conducting an extensive medical chart review focusing on antimicrobial exposures, other treatments, clinical and laboratory characteristics, and the microbiologic characteristics of the infecting strain. The study has enrolled 400 patients as of January 2006.

The team has wondered whether additional risk factors, such as genetic factors, could be examined to determine whether host factors contribute to the development of HUS. Certain genes in immune-mediating pathways are known to cause non-infectious HUS. Therefore, the investigators decided to concentrate on the genes for which variants have been found predictive of non-infectious HUS, which might therefore also be related to development of HUS following *E. coli* O157 infection.

After case ascertainment, chart reviews, patient interviews, and collecting laboratory values and antimicrobial treatment histories, the investigators also characterize the virulence profile of the isolates. Subsequently, upon consent, a specimen kit is sent to patients describing how to give a saliva specimen from mouthwash. Via a prepaid mailer, the patients return their samples to the study collaborator to conduct the single nucleotide polymorphism (SNP) analysis.

None of genes being studied are clinically relevant. They are hypothetically related to HUS, but the connections are not yet significant. In designing the study, the investigators wondered what their course of action should be if the genes become clinically relevant at some point in the future. Would the investigators then be obligated to report to the patients? How long would specimens be stored for future testing? As more is learned about HUS, additional genes could be added to the list, and those additional genes could become clinically relevant. This study is a collaboration with 10 state health departments, and some states have more than one IRB. While the protocols are as similar as possible, they have at least 10 different IRB protocols, and if the state IRB requirements are not in concert with CDC, problems could arise.

Writing the IRB protocol was difficult because of a lack of standard guidelines regarding how to report genetic testing results or for storage of specimens and future testing. The first draft of the protocol stated that if the results become clinically relevant, the researchers will report back to the patients. Storage of specimens was planned to be indefinite, and links will be maintained to the patient to ask for consent to test additional genes. The IRB approved the initial protocol, but the protocol was not ideal and was not feasible for the 10 state health departments. Maintaining a link to patients at the state health departments was not possible. The IRB protocol was revised to state that the researchers would not report results because they are not currently clinically relevant. Specimens will be stored for five years, so if additional genes become identified, then they will be able to be tested. No link to the patient will be maintained.

Currently, there is no effective treatment for HUS other than immediate treatment with fluids. This study emphasizes therapeutic discovery rather than simple diagnostics. If this study can identify some of the immune-mediating genes involved in the pathway leading to HUS pathogenesis, then treatment research can be better targeted. The effect of antimicrobial

treatment on susceptibility to HUS may be influenced by genetic factors, and the combination of epidemiology learned from the cohort study and genetic factors may lead to the identification of ways to prevent HUS therapeutically or through preventive education.

In summary, this team of investigators will not report individual genetic test results to study participants because the results are not currently clinically relevant. Specimens will be stored anonymously for five years so that additional testing will be possible. While there is no treatment for HUS, early intervention with intravenous fluid is crucial for prevention. The team hopes to improve the prognosis for HUS patients. Rapid identification for patients at risk for HUS could be crucial for early therapeutic intervention.

Discussion Points

- Dr. Levine asked about anonymous storage of specimens and whether there could be a one-way link to the identity of the specimen. Commonly, the specimen used by the researchers is stripped of identifiers, but information about the specimen can be fed into the specimen bank for future use. Researchers will still not know the identity of the specimen.
- Dr. Demma replied that identification codes are maintained for each specimen, but CDC researchers never know personal information about the cases in the system.
- Dr. Levine asked whether the maintenance of the ID code means that the specimen could be linked to an identifier in the future.
- Dr. Demma replied that such a link was possible only at the state health department, but each specimen has several layers of codes. The state health department uses a code to link each specimen to the patient, and CDC added several layers of codes to the study so that they could de-identify the specimens from the state laboratory identification number. The can link to their epidemiologic information from the cohort study without maintaining the actual identifier.
- Dr. Thomas Hooyman asked whether the Birth Defect study also had to work with separate IRB protocols in each of its state sites.
- Dr. Rasmussen answered that the Birth Defects study required approval from 27 IRBs. The investigators have encouraged the IRBs to use the same protocols, when possible. Some states have minor differences in their laws, but the informed consent procedures are as close to identical as possible.

Case Study #4: Nicotine Exposure and Metabolism in Alaska Natives

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Dr. England described an upcoming study which will examine nicotine exposure and metabolism in Alaska natives. As a group, American Indians and Alaska Natives have the highest prevalence of tobacco use in the United States and a disproportionate number of tobacco-related deaths. The use of chew tobacco is common among some groups of Alaska Natives, and in western Alaska it is common to mix chew tobacco with ash made from burnt fungus. This combination raises the amount of freebase nicotine to close to 100 percent. The health effects of this product, called iqmik, have never been tested, nor has product testing been conducted.

It has been estimated that about 50 percent of the variance in tobacco use initiation and 70 percent of the variance in maintenance is genetically determined. Variants in the CYP2A6 gene have been associated with different rates of nicotine metabolism. "Fast metablolizers" may clear nicotine more quickly and have cravings sooner, thereby leading to a greater likelihood of becoming addicted. In addition, "fast metabolizers" are likely to chew or smoke tobacco more often than "slow metabolizers." Substantial racial and ethnic differences exist regarding the frequency of slow metabolizers. Different racial and ethnic groups have been studied, but not Alaska Natives. Because of a lack of information about iqmik and about how genetic factors in Alaska Natives contribute to addiction, there is local interest in understanding more about iqmik and how to nicotine addiction among iqmik users. There is also a need for assistance for local tobacco cessation programs, particularly with nicotine replacement therapy.

The Alaska Native Tribal Health Consortium is the grantee group for this study. A local health corporation is the study site. A number of CDC investigators are participating as consultants and to conduct the laboratory analysis and genetic testing. A CDC storage facility in Anchorage will store the specimens. Because the study is participatory research, the investigators have been working with a community advisory committee and the board of the health corporation from the beginning of the process.

The objectives of the study are to examine nicotine and carcinogen exposure in Alaska Natives who use a variety of tobacco products, including commercial chew, iqmik, and cigarettes. These people will be compared to those who use no tobacco. The investigators will characterize nicotine metabolism by looking at the CYP2A6 genotype and by measuring the 3-hydroxycotenine to cotenine ratio, which yields a one-time approximation of nicotine metabolism. The study also incorporates product testing. Information from the study will be used to develop local public health messages and to educate providers. The study results could also help in the development of nicotine replacement guidelines specific for this population.

Initially, the study would only include examination of CYP2A6. The original proposal provided for the addition of other genes in the future, depending on the availability of funding. In the community where this study is being conducted, however, local rules forbid the addition of genes to a protocol that are not explicitly described in the protocol and consent forms without re-consenting all participants. All genes must be named and explored thoroughly in the consent forms. The storage bank requires that the specimens be permanently linked to study participants with their names and dates of birth, so it in not possible to completely de-identify specimens at any time. This permanent linking gives participants the option to withdraw their specimens at any time.

The project investigators did not intend to add genes to the study without returning to the IRB, but they were not aware that patients would have to be re-consented if genes were added. We tried to include in the protocol all genes that we might possibly test in the future and to describe the implications of looking at them. Of these additional genes, the dopamine pathway genes under consideration are not clearly associated with particular diseases, but they are associated with potentially stigmatizing conditions such as alcohol and drug abuse and some psychiatric disorders. The other genes did have clinical relevance. Ultimately, the local collaborators decided not to include any genes with potential clinical relevance, using a broad definition of "clinical relevance," unless the study participants could get the results of their genetic testing. However, the study area is remote, and there is only one genetics counselor in the state of Alaska (I believe), so this prospect was daunting.

To briefly summarize the remaining genes under consideration, there was one of the flavin-containing monooxygenase (FMO) genes associated with "fish-odor syndrome." Its prevalence is not well-described, and it is a benign condition, but it does result in a person having a strong odor and can have severe psychological consequences. The uridine phosphorylase (UDP) glycosyltransferase (UGT) genes are associated with Crigler-Najjar disease, and our study could result in identification of of a carrier; and with Gilbert's Syndrome, which is a benign condition which can cause unexplained jaundice.

Some of the other genes of interest that the investigators tried to add to the study protocol were associated with rare diseases and have potential implications for people who could be carriers. It was difficult for the investigators to decide "how rare is rare enough" to make the decision not to report the results. Further, the team found it difficult to reconcile conditions and disorders that are not life-threatening, but which could have potential clinical relevance. There were some additional concerns about genes associated with conditions that could stigmatize the community.

Discussion Points

- Dr. Macklin asked whether the study protocol could have described the initial genes to be studied and then stated that future studies may include additional genes, thereby giving participants a chance to agree or disagree with that addition. It is generally accepted that if the consent process acknowledges the possibility of future study of genes, most participants will agree to participate.
- Dr. England said that the IRB required that all of the specific genes had to be explicitly described up-front. The IRB would not accept a statement that the study would look at genes of nicotine metabolism and then later add a gene that also had no clinical relevance.
- Dr. Gamble asked whether the investigators knew why the IRB has these specific restrictions, given the histories that some native communities have with genetic research.
- Dr. England understood that the IRBs want to protect study participants from potential exploitation, so their rules are slightly more conservative than rules elsewhere.
- Dr. Gamble reflected on the "lesson learned" regarding how to work with communities and their needs. This community was clear about its needs regarding genetic exploitation.
- Dr. England agreed, adding that the investigators opted to "back off" so that the research team and the community could be in agreement, especially given that they did not know whether the genes would be relevant or not.

Discussion of Ethical Issues Relating to Release of Genetic Test Results

Dr. Macklin reminded the group of the four questions for discussion, so they could provide direct guidance regarding the release of genetic test results. She reminded them that the case studies were presented as examples and were intended to help the subcommittee answer the four questions and considerations submitted to them. She indicated that the group would also consider other issues that might be included in a broader guidance document. She began the discussion by asking the panelists if they believed that the answer to the first question is "No, there is no ethical duty to offer genetic results to study participants."

Discussion Points

- Dr. Levine responded that sometimes there is a duty to provide results, and sometimes there is not.
- Mr. Bruce Jennings thought that the issues expressed by questions 1 and 2 should not be separated or considered in the abstract sense. Instead, he thought that the issue of release or non-release of information should be imbedded in the context of question 2. If the mechanisms to guide the methods and manner of the reporting of test results are poor, then test results should not be disclosed.
- Dr. Macklin asked about the circumstances under which genetic research results should be offered, which was a consideration under question 1.
- Mr. Jennings clarified that perhaps test results should be revealed if appropriate genetic counseling is available so that participants will not misunderstand the information. If proper support is not available, then perhaps test results should not be revealed.
- Dr. Salaam Semann raised the issue of considerations associated with sharing genetic results with affected parties such as spouses, partners, children, and siblings.
- Dr. Macklin directed their attention to question 4, which pertains to family relationships. She suggested that the group consider all four questions together rather than trying to separate them.
- Dr. Levine said that the circumstances depend on whether the researchers are confident in the meaning of the findings. Correlations may emerge in the beginning stages of a genetic or linkage study, but it is not clear whether the correlation has reached a reliable level of sensitivity or specificity. Another consideration is the significance of the findings; that is, do they diagnose an important or "clinically significant" situation, or a more trivial issue? If the finding is "significant," then the researchers are expected, or required, to disclose the information. A third consideration is whether something can be done about the finding. If something can be done about the finding, there is an increased forcefulness in the duty to disclose the information. Researchers still may need to disclose findings if nothing can be done, but the argument in favor of disclosure is weaker in this case.
- Dr. Macklin asked Dr. Levine to clarify whether he referred to the strength of the duty as well as to the considerations. A clinically relevant result may not rise to the level of "significant" or "important," which might require intervention.
- Dr. Levine focused on the strength of the duty to disclose. "Clinical significance" concerns the effect that the findings will have on the life of the study participant. Some findings could be of low importance, while others could make a large difference in a person's life.
- Dr. Koenig agreed with the discussion direction, but she reminded the group to think about the future of genetic research. In the past, investigators studied and measured one gene at a time; however, the future will include 500,000 chip arrays. The paradigm of regulations is built on the old model of measuring one thing.
- Dr. Gamble has been involved in work of this nature with the National Human Genome Research Institute for several years. This group is considering many of these issues as well, and she encouraged collaboration among these groups. The field has changed recently and has incorporated discussions about re-consent, forensics, and other issues. Collaboration is key as the entire field moves forward. She expressed concern regarding a lack of involvement of patients and patients' groups in the discussion. She advocated for talking to groups of people who are affected. She offered the example of the groups in Alaska, who are making their needs known.
- Dr. Macklin wondered whether those issues might fit under question 3, which focuses on human subjects protections. One of the human subjects protections measures could be involvement of the community in some manner.

- Dr. Gamble added that re-consent also falls under this topic area, whether re-consent becomes the default or the exception.
- Mr. Jennings suggested that considerations regarding the duty to disclose information might depend on the research participants. Some participants might want to learn study findings because the findings are about the participant as an individual. These participants might feel that they have a right to the information and that researchers should not judge whether the information is important enough to disclose or not. Another mode of thinking, which is reflected in some of the current literature, is that even if the information does not reveal useful knowledge about the individual, the fact that the person participated in the study gives the participant the right to know the study results. The claims are distinct. A person with the first approach can be informed that the results do not reveal meaningful information, and so the researchers will not share it. That argument does not answer the reasoning behind the second approach. Revelations may not always relate to individuals' desires or rights, but to the meaning of group participation.
- Dr. Macklin asked the Public Health Ethics and Genomics Workgroup whether the questions were limited to individual results, or whether the Ethics Subcommittee should also consider revelation of general study results.
- Dr. Moore replied that they should consider both individual and aggregate results, but she noted that individual results usually cause more ethical consternation. Aggregate results are reported routinely.
- Dr. Georges Benjamin felt that there is always a duty to inform. The information can be represented broadly via a newsletter to a number of people, as the cluster study in Nevada. Individualized and specific information can be shared directly with an individual as well. Community trust depends on sharing information. Genetic research is accelerating at a pace such that relevance of results can eventually be learned. If the information was not already disclosed, then the investigators will have to track the individual study participants. At this point, individuals should be informed of test results and trusted to be a wise and informed observer.
- Dr. Demma revisited her study's experience with state health departments. Her surveillance system could track patients well, since the state health departments maintain patient identifications. Their original protocol stated that if results should become clinically relevant, then the participants' clinicians would be contacted, but this goal is insurmountable, even in a strong surveillance system. What if they lose their funding and the system collapses?
- Dr. Macklin said that this issue relates to the second question, which asks how the benefits of offering genetic results should be balanced with cost and logistical feasibility.
- Dr. Benjamin said that the issue may be a case of resources. He described how a lawyer could find all study participants via a media campaign, public service announcement, or private investigator. Resources and program structure can be problematic and challenging for local health departments, but it is possible.
- Dr. Levine offered a case that could emerge in the "real world." A genomics study in its early stages could yield preliminary evidence that an individual with high blood pressure is more likely to respond favorably to a calcium channel blocker than to an ACE inhibitor. At the early stages of the study, there is no duty to disclose this information to an individual, because no clinical conclusions can be drawn. Other examples from the four case studies shed more light on the question. For instance, if testing was not conducted in a CLIA-certified laboratory, then results could not be shared with patients in most cases. He praised the study that shared an overall correlation with all study subjects and offered to disclose individual results, as this approach required initiative on the part of the individuals. He felt that there were cases in which study information should be withheld. Much of this work is done under conditions of true anonymity, such as a study of seroprevalence of Human Immunodeficiency Virus (HIV) in anonymous blood samples. The value of the

knowledge and epidemiologic information was so important that the consequences of disclosure were not "worth it."

- Dr. John Arras revisited the question of justifying a duty to inform. Some participants may feel that since the information is about them, then they have a right to it. This attitude represents a "market model," especially given that companies in the market offer to analyze assays. The competing framework is a professional, paternalistic value system that determines whether information is significant to the patient.
- Ms. Sharona Hoffman assumed that participants are allowed to choose whether they receive genetic results. If the results could be devastating, then genetic counseling must be made available. It would be irresponsible to provide this information without proper follow-up.
- Dr. Macklin felt that the information will be offered, not mandated. The participants will know that they can refuse the offer.
- Ms. Hoffman suggested that the point would be clearer if it specifically stated that participants would be given a "choice." Timing is also an issue, since participants may initially indicate that they want to receive information, but the test results might not be available for several years. If a significant period of time has elapsed, then their life circumstances may have changed and they should be asked again if they want their results.
- Dr. Hooyman commented on the large numbers of databases collected and maintained by the government, such as the Internal Revenue Service (IRS). A number of interesting questions emerge when these databases begin to interact and potentially share information. He further wondered about the duty to warn, which is a typical clinical question. If a practitioner knows about a potential threat to a person, whether it is pneumonia or a mental health problem, then the practitioner is responsible to warn the person. He wondered about the relationships between clinical ethical findings and the field of genomics. He remarked on the inconsistent requirements of the Alaskan tobacco study, in which subjects' identifiers are maintained, and the *E. coli* study, in which the identifiers are struck.
- Dr. Rubin said that identifiers are preserved in her study, and they have IRB permission to store those samples. Other researchers may request access to the samples.
- Dr. Koenig clarified that some repositories of DNA refuse ever to de-link identifiers, because if the samples are completely de-identified, then people will not be able to withdraw from research. The ability to withdraw and the maintenance of anonymity are in conflict.
- Dr. Gamble said that the release of genetic research should be considered in the context of the Genetic Information Non-Discrimination Act (GINA). She added that information is not just available for release to family members, but also to third parties such as researchers or agencies that collect genetic databases. If another researcher works with a sample, which one reveals information to the participant?
- Dr. Demma said that if her team had followed what they believed were the guidelines, which included maintaining links to specimens for 15 years, then the study would never have been approved and never have begin. A great deal of research may never be conducted if too many restrictions are placed on resources "at the ground level."
- Ms. Kathy Kinlaw raised the concept of "community consent." When there are opportunities for public engagement, researchers could ask the community about what they think is essential. The protocol development stage could incorporate this input, and the consent process could include what is learned. She further stated that the question of duty to offer genetic results cannot be considered separately from whether the information has clear implications. The provision of information is not benign, and so there must be an infrastructure around the provision of information. Feasibility issues should be considered now, not later.

- Dr. James Thomas reflected that the articles provided to the panel as background information offered reasonable answers to some of these questions. He wondered whether the panel should consider "gaps" in the articles.
- Dr. Mary Leinhos responded that she had selected recent articles, commentaries, and debate on this still-contested issue. There are NHLBI guidelines on results notification, but the questions are not at rest.
- Dr. Thomas remarked that the NHLBI article includes some reasonable considerations that the panel has also voiced, such as ensuring that a genetic counselor is available. Those guidelines might apply today, but future studies will do panels of genetic tests, and the stakes will be raised. He was concerned about quality of information and the amount of causality that can be attributed to a genetic marker in a disease, and he was further concerned about "information pollution." People are bombarded with information, and because the information is genetic, it may be perceived as "magic." This "pollution" could cause people to worry about things that are inconsequential and not pay attention to known risks that need attention. Many of these issues may shift attention away from greater public health risks. Somehow, their considerations should include an ethical duty to the researchers to justify the tests that they will include in their studies rather than trying all of the available, affordable tests.
- Dr. Leinhos cautioned against narrowing the first question down to a "duty to warn." Investigators should consider their duties as a matter of respect to study participants, the time that they invest, and their understanding of their relationship with the researchers. These issues have an impact on public trust of scientific enterprise and their willingness to participate in future studies. The issues surrounding reporting of results reach beyond the duty to warn, and they must be weighed with the costs and benefits of the project.
- Dr. England said that talking about "test results" may put more clinical significance on the information than it has. Perhaps they should refer instead to "genetic information," which may or may not be true and may or may not be replicated in future studies. A "test" is offered based on analytic and clinical validity and it has clinical utility, but these preliminary results could have a million pieces of data. Genetic counselors are a limited resource that is part of the old model of genetics rather than forward to the new model of genomics. Needs in the future are not represented in the old model for training genetic counselors. A new type of education, which might involve all types of healthcare professionals as well as genetic counselors, is called for.
- Dr. des Vignes-Kendrick addressed the responsibility of a researcher at the individual and community level. Feedback is required in that loop. Two important issues are the quality of the information and the value of that information to quality of life. Another important consideration is that the results can be based on who is doing the research. For instance, research conducted on a drug by a pharmaceutical company may show different efficacy results than research conducted by a government agency. Information could be questionable both in its accuracy and in its ultimate value to the end-user. While it is important for community members to have information, she did not feel that consumers should receive information that "leaves them up in the air" regarding its relevance and what the consumer should so with the information.
- Dr. Steinberg agreed that "information pollution" is a risk, but she felt that the studies should still be conducted.
- Dr. Thomas concurred that there is certainly a need for genetic research; however, when profit is to be made through tests that amount to fear-mongering, there are dangers associating with spreading a great deal of information that is not important. Some information will be of great genetic importance, of course.
- Dr. Steinberg agreed, adding that while diseases and conditions cannot be predicted based on polymorphisms and their odds ratios, but it might be possible to understand pathways.

As the session came to a close, Dr. Macklin asked members of the Workgroup whether they would be able to draw on the discussion for some answers to their questions. She asked if the Workgroup had any final questions for the assembled group.

- Dr. Koenig was responsible for creating a document to synthesize the discussion. Her main take-home message was that CDC should work on this important issue.
- Dr. Semann noted that the questions posed to the Subcommittee were general, and the answers were, therefore, general. She wondered whether a subset of the questions might be brought to the committee for discussion again. Some of the questions had been answered in the literature.
- Dr. Hooyman asked whether the issue might be framed in a different way, given that the Subcommittee expressed different perspectives to approaching the first question. Looking at the issues from the point of view of "ethical duty" establishes a framework for the discussion. The Subcommittee could write a paper following an outline based on the questions provided for them.
- Dr. Macklin said that some actions are obligatory; some are morally permissible but neither obligatory nor prohibited; and certain other actions must not be done. Some of the discussion offered circumstances in which information might be revealed, but there may be no obligation to do so. Questions of practicality, feasibility, and logistics might feed into these situations, when there might never be sufficient resources, information, or linkages to make the revelations possible. In this case, it would be permissible to reveal study results, but not obligatory. Under some circumstances, results should not be given at all. A possibility for moving forward would be not only to look at the available literature, but to list and synthesize the recommendations that exist in the literature and in the National Bioethics Advisory Committee (NBAC) Human Biological Materials Report. A next step will then be to see where the various recommendations disagree and where there is consensus in the recommendations, remembering that they must keep the future in mind.
- Dr. Arras commented that the subcommittee would not be able to provide an algorithm for considering these questions. He supported Dr. Macklin's suggestion, adding that real progress on these difficult questions will occur in a smaller-group setting after wrestling with the literature and narrowing down the scope of disagreement.
- Dr. Barrett said that they had envisioned this session as the start of a conversation. The National Office of Public Health Genomics wants to move forward in the creation of a guidance document in a timely manner, but the process will take time.
- Mr. Jennings observed that the background articles revealed differences in "center of gravity" or orientation. Some articles advised sharing information with research participants unless a compelling reason exists not to share it, while other authors suggest not sharing information unless there is a very good reason to share it. The subcommittee might be able to choose which approach is more appropriate, in their opinion. He further noted that the articles addressed the question of balancing the economic costs and hassles associated with revealing information properly. It may be true that some research will not be conducted if the ethics requirements are too stringent, but the ethics community will not be swayed by that argument. If revelation of research results is important to society, then why is it a struggle to pay for the infrastructure or resources to do it?
- Dr. Koenig raised the question of collecting genetic data in emergency situations without a waiver of consent. She suggested linking those conversations.

Public Comment Period

Dr. Barrett invited members of the public to make comments. As none were offered, Dr. Macklin introduced the next session.

Development of Guidance Document for Ethics of Genomics in Public Health

Mary Leinhos, Ph.D., Health Scientist
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Dr. Leinhos offered an overview of topics that should be addressed in the proposed guidance. Genetics results notification is one of many ethical issues facing public health genomics. She described the general plan for developing a guidance document to address these questions. There has been a recent dearth of guidance in the area of public health genetics results notification. An HHS IRB Guidebook was last updated in 1993, but it does not encompass all of the genetic work that is conducted today. The NBAC released the Human Biological Materials Report, which addresses genetics and biobanking, in 1999. This report led to a 2001 JAMA article that developed guidance on informed consent for population-based research involving genetics. The evolving technology and science of genomics requires additional thought now.

Investigators and research administrators at CDC have pointed out three specific areas of need:

- Logistics of biobanking or repository protocols
- How to plan for future research that uses banked specimens
- How to deal with issues of significance and participant risk, especially in long-term studies

The logistics of biobanking include questions of how long samples and data can be kept and linked. The data could be permanently linked, unlinked, or even destroyed. In the consent process, there are questions regarding how best to go about enumerating the risks and benefits of keeping data linked.

Planning for future research will include defining and explaining the scope of future studies, even if it is not clear which genes would be studied, or if genome-wide associations are planned. Informed consent is complex and includes the possibility of re-consent, as well as how to explain future studies in the consent process. IRB requirements for future studies could include amendments for each additional study component or additional gene studied.

The third area includes questions regarding how to define “clinical significance” and how to manage it as it may emerge over a long-term study. Challenges are associated with educating participants about the nature of the research and potential risks associated with participating in the research. Further, methods for presenting results to participants that choose to receive

them should be discussed. Cultural and international nuances may arise in presenting results and explaining studies.

The office is in the process of developing a "best practices" document using an evidence base of recent IRB-approved CDC protocols that involve human genetics. They have conducted informal interviews with CDC investigators and research administrators to learn about their concerns and challenges. The document preparation has also included reviewing the bioethics literature and consulting "grey literature" such as reports, recommendations, and consensus statements. Finally, staff have gathered other institutions' IRB guidance related to human genetic research.

In the next month, staff will draft the overall document based on an outline of topics. Various stakeholders at CDC will hold an iterative review and revision. This group will include investigators and the Public Health Ethics and Genomics Workgroup as well as PHEC. After a few rounds of revision, input from the Ethics Subcommittee will be requested at the next meeting in June. The document should be finalized and disseminated agency-wide in July 2007, and a peer-reviewed article based on the guidance document will be written published in the year.

The guidance document will cover a number of topics in two sections: Protocol Elements and Additional Considerations.

Protocol Elements

- ❑ Explaining genetic research to participants
- ❑ Addressing issues that arise with genetic research with children and other vulnerable populations
- ❑ Biobanking studies
- ❑ Planning and writing about future studies that will be conducted with the banked data and specimens
- ❑ Data management
- ❑ Results notification
- ❑ Broad results dissemination to the public via publications
- ❑ Data and specimen sharing with other investigators and researchers
- ❑ Assessing risks and benefits and including them in the consent process
- ❑ Privacy and confidentiality issues

Additional Considerations

- ❑ International research, which will probably refer to other resources
- ❑ Research with families
- ❑ Integrating genomics into acute public health responses, including disease cluster investigations, exposure clusters, and prevention and treatment studies
- ❑ Acute settings

Discussion Points

- Dr. Gamble asked whether the document would address genetics, genomics, or both. She suggested that the document be clear about which topic was being addressed and when.
- Dr. Leinhos said that the document would cover both genetics and genomics, which would be discussed in the introduction with consistent terminology.

- Dr. Marta Gwinn of NOPHG said that this document would abide by the definitions of genetics and genomics established by Allen Guttmacher and Frances Collins in their "Primer on Genomic Medicine," which was published in the *New England Journal of Medicine*. The authors stipulated that genetics is the study of one gene and its association with diseases, where genomics is the study of all the genes in an entire organism and how they interact with each other and the environment.
- Dr. Macklin asked how the Ethics Subcommittee members should direct their comments.
- Dr. Leinhos asked for input in all areas, particularly regarding topics that might be missing from the outline.
- Dr. Macklin noted that none of the documents and discussions address insurability. Some laws governing insurability exist at the state level, but no federal laws oversee this issue. The process of genetic research at her institution includes a disclosure to the effect that insurability could be affected. Periodic anecdotes imply that persons' insurance is cancelled or denied because of genetic conditions. She wondered about what insurance companies are doing in this area, what they look for, whether physicians are expected to provide disclosures to insurance companies, and negative consequences. She felt that this topic should be included in the general guidance and she wondered about research on the topic.
- Ms. Hoffman said that while there is anecdotal evidence available on this issue, no studies have been conducted. The issue is not as serious as one might think with health insurance, because under HIPAA, there can be no discrimination against a member of a group in group insurance. This issue therefore affects the 10 to 15 percent of the population that have individual policies that are not governed by HIPAA. There are questions about life and disability insurance and employment.
- Dr. Macklin noted that they should consider employment as well.
- Scott Campbell of NCBDDD observed that the Europeans operate using a principle of the "right not to know." He was curious about unintended findings that may arise. A specific example is the paternity issue. If families are being tested, when is the researcher obligated not to inform participants about spurious findings.
- Dr. Dixon noted that most of the conversations have focused on the important issue of protection of the individual and how these decisions will affect the individual. However, public health ethics seeks both the interest of the individual and the value for the community. The decisions that they make could affect the ability to develop community understanding of science. As they discuss these issues, they should consider the community. They assume that they know what the community thinks about these issues, but they cannot be sure unless they ask the community what it thinks. He hoped that they would consider the consequences of adopting an "IRB approach" that always puts the interests of the individual first. If there are adverse consequences, then a "middle ground" should protect both the individual and the community.
- Dr. Koenig had also been wondering how the public health context is unique. The enterprise of human subjects protections focuses on the individuals, and it does not do a good job. They do not know how the public balances the benefits and burdens of this kind of research, so there is a need for public engagement. The document should address these issues. She wondered whether instead of dealing with the problematic Human Subjects Protection "superstructure," they should propose not requiring any generic, template language. This measure would help alleviate problems with IRBs imposing language that is irrelevant to a study. IRBs would have to think through the implications of individual studies in specific contexts.
- Dr. Thomas asked whether the "evidence base" to which Dr. Leinhos referred is the list of sources of information that will aid in writing the document. He suggested that they also include focus groups or community interaction, perhaps with people who have been included in studies such as these.

- Dr. Gamble addressed the question of group stigmatization, which is critical in many communities.
- Dr. Macklin noted that international research appears to be treated briefly in the document, perhaps just with a resource list.
- Dr. Leinhos did not intend to give the issue short shrift; rather, she felt that the issue was so large that it would require its own best practices document.
- Dr. Macklin said that the issue is related to group stigmatization and to understanding. She offered the example of conducting genetic studies with tribes in Africa. Informed consent can be a challenge with these groups when individual consent regarding genetic concepts is required from people who may never have given consent for anything in the medical arena. If the issue will be treated in a separate document, then it should be referenced as a separate document. Many researchers have questions about international research, including intellectual property and ownership of samples. Treating the issue briefly could give the impression that it is not a major issue.
- Dr. Hooyman raised the topic of partnering with corporate America, who could then have a potential financial interest in public health research in genetics. There is a separate tax structure for CDC to receive funds from pharmaceutical companies. The organizational relationships and long-term financial investments should be discussed as an "additional consideration."
- Dr. Leinhos wondered whether specific conflict of interest issues pertaining to corporate partnering exist regarding human genetics research, or whether another best practices guidance document is needed to address public health investigations with corporate partners in a more general sense.
- Dr. Hooyman posited that if an insurance company partnered with the CDC on a study such as the tobacco study in Alaska, then the company might not only want to learn about the long-term health effects of tobacco use, but also want the database itself as an insurer or employer. This different ethical consideration should be recognized in this document.
- Dr. Gwinn added that the point is relevant, too, because of a "mad scramble" for intellectual property. A substantial portion of the human genome has been patented. While the point is relevant to genetics and genomics, it is a larger topic than the guidance to be provided to CDC investigators. She suggested that the Ethics Subcommittee take up the question separately in the future. The reliability of test results from different sources, such as a drug company versus a government entity, is a good starting point for the discussion of public / private partnerships and the conduct of research and public health interventions.
- Dr. Macklin said that the issue of partnering would be on the June meeting agenda. They could also expect to see a draft of this guidance document in June.
- Dr. Gamble commented that the outline does not address race and ethnicity. There is a conflation in some people's minds that genetic research is equal to racial research. Investigators should consider defining race and its connections to genetics.
- Dr. Hooyman thanked Dr. Leinhos and all of the investigators who made presentations.

Update of the Public Health Code of Ethics

Dr. James Thomas, Ethics Subcommittee Member, reported that in 2002, the governing board of the American Public Health Association (APHA) adopted the Public Health Code of Ethics. It was acknowledged that the Code was a living document that would be revisited in five years. Since five years have elapsed, there has been discussion in the field about revising the Code.

The National Association City and County Health Officials (NACCHO) adopted the Code after APHA. The Code was developed by the Public Health Leadership Society (PHLS) with funding and help from the CDC. The Code has since been adopted by state and county health departments and it has been influential in the development of certificates in public health. The Association of Schools of Public Health provides schools with guidelines for how individuals can be certified in public health with certain competencies, one of which is ethics.

At a recent meeting at the University of North Carolina, Dr. Thomas discussed revisiting the Code with some of his colleagues. They agreed that revision should be considered, but little financing is available for a revision process that would gather a number of people multiple times. He contacted the PHLS and discovered that they had also had discussions about revising the Code. He spoke with some of the people who were involved in creating the Code, and their feeling and experience was that there has not been an indication from people who use the Code that it needs to be updated. The Code seems to have worked well for those who have used it. For this reason, the next step might not be to revise the Code, but to evaluate it. Their time might be better spent talking with people who use the Code and to learn what has worked and what has not. At the same time, they can examine other organizations and the use of their codes. This work could lead to a later revision.

He asked the Subcommittee for any words of wisdom regarding revising and revisiting a Code. He also asked about the potential role that the Subcommittee and PHEC might have in thinking through the Public Health Code of Ethics.

Discussion Points

- Dr. Macklin noted that people who use the Code find that it works well. The impetus for revising the Code was that a five-year revision was initially planned. She asked whether people who use the Code have made a specific complaint or noted an element of the Code that needs revision. Events in the world can also prompt revisions.
- Dr. Thomas had not heard any feedback to imply that the Code needs to be changed. The Code has been helpful in training people at the health department to think through ethical issues. More work could be done to raise awareness that the Code exists and to encourage more people to use it, but there have been good reviews from the people who have used it. Events in the world have changed since the Code was approved in 2002. The field's awareness of 9/11 has changed, and events such as Hurricane Katrina have brought awareness of public health emergencies to the forefront and may need to be incorporated into the Code.
- Mr. Jennings recalled his own previous research on codes of ethics and change in various professions. Major professional associations usually only alter their codes of ethics when they perceive that broad, structural changes in society threaten the integrity of the profession or create new dilemmas for practitioners that the existing code of ethics or tradition does not address. These fundamental changes are different from Katrina or 9/11. For instance, the American Bar Association (ABA) changed its code of ethics to respond to the advent of large corporate practices, which changed the nature of how law is practiced. The Public Health Code of Ethics may not need to be revamped. He commented that this Code is varied and rich in its content. Therefore, he suggested that while it is too soon for a fundamental change in the Code, but the Code may need a mechanism for developing a discussion around particular applications and interpretations of the Code. By its nature, a code of ethics should be general, but people in the field may need a means for applying it to real-world situations. A web-based repository and ongoing forum of cases in public health

ethics could show how the Code should be interpreted in particular situations. Rather than re-writing the Code, he advised "making it live."

- Dr. Salaam Semann recommended conferring with the organizations who are not using the Code, but who they hoped would use it, to find out why they are not using it. For example, CDC staff are not largely aware of the Code and may not know how to use it. She wondered about how CDC could facilitate increasing use of the Code and filtering it to the public health community.
- Dr. Thomas pointed out that many national public health organizations have adopted the Code, but CDC has not.
- Dr. Stephanie Bailey, Office of the Director, agreed that the Code does not need to be revised, but its uptake needs to be improved. The Code is not translated to the internal practice of CDC. Case studies of the Code's use have been shared through APHA and public health law conferences, but these have not been captured.
- Dr. Barrett said that the PHEC stresses the importance of the Code and provides the Code to its members to provide to their Center-level staff. PHEC developed a framework document to describe its work and refers to the Code as "guiding values" for the committee's activities and for public health. They do need to share more information about the Code, and providing specific examples of the code's use via case studies of its implementation would be useful.
- Dr. Dixon observed that the narrative components of the Code and bases for action include the importance of science. It is important for people in public health to understand what works. They have an obligation to do continuing evaluation of the effects that they are having by the actions that they take in communities.
- Dr. Gamble has used the code for teaching. It is important to show how the Code is used. For example, one of the principles of the Code is advocating for the empowerment of disenfranchised communities. She used the code in a special session of APHA in the context of a health department that wants outcomes; however, programs that address disparities are typically costly and may not show outcomes quickly. Local health departments might choose a program that might not have the biggest outcome just to show effectiveness. These tensions are very real in the world. She felt that describing cases in which the Code was used will increase its uptake and use.
- Dr. Macklin asked the group to reflect on how the Subcommittee and PHEC can assist.
- Dr. Thomas asked the group to share any case studies that could be helpful. A number of case studies from the Code were collected at APHA last year, but more would be welcomed.
- Dr. Roger Bernier recently participated in public engagement discussions regarding priorities for pandemic influenza vaccine and community control measures for pandemic influenza. There did not seem to be awareness of the Public Health Ethics Code in these discussions, and he himself did not feel the need to refer to it and did not have a sense of how the Code could be helpful. He wondered about the practical value of the Code. Codes are expected to be broad, but it is not clear how ethics principles and framework are useful in practical public health. Demonstrations of the practical use of the Code are needed. It is not always clear how ethical theories and frameworks, as well as values and principles, are helpful in dealing with dilemmas. Models in ethical decision-making provide a series of steps in working with ethical issues. None of these measures had entered the discussions of the day as they wrestled with ethical issues. He struggled with how general principles and codes help with the execution of practical public health work.
- Dr. Arras has never used a code to help him think through an issue, but the Public Health Ethics Code is one of the best he has seen and has a better chance of being practically helpful because it links ethical principles with public health functions. It is unrealistic, however, to think that a code of ethics will help people work their way through a problem. Most codes are written too broadly, and even when they are written specifically, competing

codes may make different recommendations. In general, codes of ethics are not useful tools.

- Dr. des Vignes-Kendrick has run a health department and was an active practitioner in public health. Many people worked in population-based health had an implicit understanding of issues such as equity in population-based work. However, it became clear that because employees came to the health department from different background, all employees did not have a firm understanding of what public health and practice is. Having an explicit list of principles that define why public health does what it does, and why it has authority to do what it does, was very helpful. Some of the core courses that she now teaches include explicit class work on ethics and public health, including case examples. She suggested collecting input from those who practice and teach public health, including NACCHO, the Association of State and Territorial Health Officials (ASTHO), and the Association of Schools of Public Health (ASPH). Learning about practical utilization at the local and state health department levels in working with policymakers and community members will have value. Schools of public health are involved in teaching those who will go into local practice as well as those who will transition into academic public health.
- Dr. Thomas said that the Code helps to remind them of the array of issues in public health. He wrote an article on genomics and public health ethics using each principle of the Code, which is an example of how a code helps people examine issues with the breadth of ethical values in mind. Another of his articles will use principles of the Code to look at pandemic influenza. Other codes work at finer levels that allow the examination of particular issues within health education, but the Public Health Code of Ethics is intentionally broad in part because the world of public health is so diverse, to make the Code too particular would render it exclusionary. He recently compared the Code with other codes and found few disagreements between them. Some issues were unaddressed in the finer codes, but were remembered in the broader public health code. He again asked the group to share ideas regarding the application of the code. He summarized that the Code needs more "texture," primarily in its application.
- Dr. Macklin agreed that neither codes nor principles provide answers to dilemmas, because dilemmas arise out of conflicts: conflicting principles, theories, or elements of a code. Further, principles do not exist at a deductive level and cannot resolve a specific problem. Codes and principles are useful for the reasons enumerated by Dr. Thomas and also in justifying a position and providing an ethical analysis. Principles can be used to make an argument or justification for an issue. For instance, the principle of autonomy and the needs of the individual are paramount in the clinical encounter, but public health operates under a utilitarian principle to maximize welfare. Sometimes the utilitarian principle will override the principle of autonomy in a public health intervention.
- Stephanie Bailey did not expect the public to know that there is a Public Health Code of Ethics; however, the public will have ideas regarding how they expect public health to treat them in their interactions. Those ideas are probably reflected in the Code.

With no further business posed, Dr. Macklin adjourned the meeting at 5:39 p.m.

Call to Order

Dr. Macklin called the meeting to order at 8:31 AM on Wednesday, February 28, 2007. After Dr. Barrett addressed transportation issues for members to depart for the airport that afternoon, Dr. Macklin turned the meeting over to Dr. Arras and Mr. Jennings.

Ethical Issues Relating to Emergency Preparedness and Response

Overview, Review of Outline, Topics for Commissioned Papers, Potential Authors

John Arras, Ph.D.
Bruce Jennings, M.A.
Ethics Subcommittee Members

Mr. Jennings explained that he and Dr. Arras had been working with members of PHEC on a workgroup on public health emergency preparedness for several months. The group has held several conference calls and created an outline for a white paper as well as thoughts regarding a group of commissioned papers. He acknowledged the members of the workgroup and thanked them for their advice and for reviewing drafts of the materials that would be put to the Ethics Subcommittee.

Since the Ethics Subcommittee had discussed an overview of the topic of emergency preparedness at a previous meeting, Mr. Jennings focused on the outline for the white paper. The outline represented the topics that were to be covered, the order in which they were to be covered, and a sense of the orientation that the white paper would bring to the topics and types of arguments that the paper would contain.

He asked for the Ethics Subcommittee member's feedback on the outline. He and Dr. Arras believed that there was merit in maintaining some degree of structural continuity between this white paper and the previous white paper on pandemic influenza. Therefore, following the introductory section, the paper will include a framework of general ethical ideas and principles before turning to a discussion of specific topics and issues that arise in the context of emergency preparedness and response. Specific examples will be considered in the light of ethical ideas and principles. The white paper will close with specific guidance for planners and people working in the field. The paper will end not on a directive note, but in a manner that will be concrete and helpful in planning.

The sections of the paper reflect an attempt to identify the aspects of the planning and response process which most saliently raise matters of ethical concern. A great deal has already been said in the literature about emergency planning and public health, so this paper will focus on ethical issues. Section Six, which concerns conducting public health research, emerged out of the interests of the workgroup and from CDC. The white paper should be useful for CDC, but not limited to CDC activities. Many people at many levels, both in public health and non-public health, are involved in the planning process. Section Seven, then, focuses on CDC's role and ethical problems in planning. He hoped that the Ethics Subcommittee would offer guidance on this section.

At this stage in writing, there is no indication of the number of pages of each section or of the length of the entire product. Each section is rich and complex and could require about ten pages of analysis and exposition; however, an 80-page document may be too long. He asked for advice from the group regarding an appropriate and manageable length for the document that will maintain the document's usefulness and substantive content.

Dr. Macklin requested that the group provide general questions and comments before discussing the outline section by section.

Discussion Points: Review of the Outline for the Proposed White Paper

- Dr. Arras noted that six possible topics have been listed for commissioned papers. There should be a relationship between those titles and the content of the white paper. They expect to commission six papers from experts in the field who will address some of the most vexing issues associated with ethics and emergency preparedness. The white paper will then be drafted on the basis of the paper. In considering the outline, he asked the group to think of commissioned papers that might be needed to bolster a section.
- Dr. Barrett added that the commissioned papers will be included as appendices to the white paper.
- Dr. Coughlin suggested that they discuss community values, including the notion of community participation and membership, which are highlighted in the Public Health Code of Ethics. The background paper mentions "hazard-resistant communities" and building resilient communities, but these ideas are only mentioned in passing.
- Dr. Macklin observed that since the white paper will follow the commissioned papers, which have not yet been assigned or written, the time line appears to be long for completing the Paper. Mr. Jennings replied that they had created a detailed timeline that envisioned the final white paper and commissioned papers to be complete by the end of 2007. Dr. Barrett acknowledged that the timeline is ambitious, but some of the work on the white paper and the commissioned papers can be done in parallel..
- Dr. Gamble suggested that one of the commissioned papers be written by a historian who can offer historical perspective on these issues. For example, the pandemic influenza white paper included details about responses to previous influenza epidemics. She has begun to examine "race-place" and "preparedness," studying the response of the Colored Advisory Commission in 1927. Some of the attitudes of the African American community pre-dated Hurricane Katrina. This paper should be written by a historian, not an ethicist who does historical work.
- Dr. Levine thanked Mr. Jennings and Dr. Arras and the workgroup for the impressive outline. He echoed the importance of maintaining consistency throughout the documents that are released by the Ethics Subcommittee. He offered comments on Section Seven, which aims to be particularly relevant to CDC personnel. In developing the pandemic influenza guidelines, he recalled that some of the drafts seemed to be in conflict with CDC policies or practices. The drafters of the paper opted to provide their opinions regarding what the guidelines should look like, regardless of how those recommendations fit with CDC policy. The issue did not occupy a great deal of their time, but it was raised once or twice in the process. Section Seven is an important part of the document, but it should not be an account of current CDC practices and policies, but a reflection of the group's advice regarding what the policies and practices ought to be. The Ethics Subcommittee should not write policy for CDC, but recommend the best policies. He then addressed the length of the document. In the pandemic influenza paper, they refrained from giving detailed analyses because they were also concerned with the length of the document. Although detailed analyses were not included in the paper, the analyses supported each aspect of it. They did include detailed analyses if a recommendation appeared to be a departure from traditional public health enterprise. For example, recommending centralization of decision-making in the setting of a pandemic, the authors explained why they were departing from the usual approach of placing state and local health departments at the center of decision-making.

- Dr. Hooyman addressed the length of the paper and noted that it could be upwards of 160 pages long, including the commissioned papers. He wondered whether it would be read if it were that long.
- Mr. Jennings said that the white paper will stand alone, while the white paper and the commissioned papers will be a "book" and will likely be read by fewer people than the white paper alone. There will also be an executive summary.
- Dr. Arras added that the document will be on the Web.
- Dr. Hooyman said that the vision of the final product will dictate how detailed each section should be. He wondered whether the document should address "issues" or "considerations" rather than "guidance."
- Dr. Richard Besser, of the Coordinating Office for Terrorism Preparedness and Emergency Response (COTPER), advocated for not short-changing the analysis in the document. The paper will be an important contribution to the literature. Analysis from the commissioned papers should not be repeated in the white paper, but listing recommendations without including their basis would be a mistake. Further, historical perspective as well as examples of how ethical issues have arisen in previous responses will make the document relevant for those who are working in emergency preparedness response. Everyone will not read a 200-page document, but many people will read the executive summary and use the full document for reference.
- Dr. Benjamin cautioned the group against "trying to do everything." He suggested that they identify the most important key issues to be addressed from a CDC perspective. This work will be clearer with a specific definition of "public health preparedness." The RAND Corporation is about to publish a consensus piece on definitions of public health preparedness that was commissioned by HHS. The context of "preparedness" will be crucial. Some core issues transcend all events or disasters. CDC also has niche issues such as vaccines, but the document's definition must be useable across a variety of circumstances and disciplines.
- Dr. Macklin wondered whether a common definition for public health emergency preparedness should be used. Dr. Benjamin advised against inventing a new definition and instead advised using one of the definitions that is in common use. Most of the differences between the definitions are wordsmithing, he noted.
- Dr. Thomas viewed the white paper not as an end, but as a means to future steps. The steps or products that will follow the paper should, in part, determine how the white paper is constructed. He wondered what the next steps might be for this paper.
- Dr. Besser said that the "next steps" depend on the white paper. For instance, a discussion of research in a setting of emergency preparedness would lead to an effort to define the processes and procedures that CDC and its grantees will use in those settings.
- Dr. Thomas asked whether the background provided in a white paper might filter into policies or into criteria for RFPs.
- Dr. Besser agreed. For example, they are in the process of reviewing the Strategic National Stockpile, and there are ethical considerations in every product that is, and is not, included in the stockpile. There are also ethical considerations associated with their distribution systems. Every aspect of their work could be affected by the white paper.
- Dr. Thomas asked whether they anticipated questions or issues that the authors of the white paper and commissioned papers could keep in mind as they make recommendations. Dr. Besser replied that the authors should visit COTPER or talk with its staff to help frame the issues. Staff can provide examples of past ethical issues and anticipate future concerns.
- Dr. Thomas reflected that detail is desired, which argues for length rather than brevity in the document.
- Dr. Tanja Popovic said that the document would have a significant impact on practical issues such as training. In the past several years, CDC has focused on workforce capacity

and development. More people will be trained in preparedness, and more CDC staff may go into the field in case of an emergency event. It will be critical to train these people well and to help them learn what to communicate, how to communicate it, and to whom. Other questions include the chain of supervision and how CDC works when staff are deployed and how to collaborate with states. The authors of this document would benefit from learning what happens at the time of an emergency and from seeing the critical issues. The length of the paper will also be determined by its intended use. It could be a spectacular academic paper, but at this point, it should have practical implications in the field. These needs do not necessarily contradict each other. She recognized that creating the paper was a complex process that will take time, and she reassured the group that preparedness itself is a complex process that takes time.

- Dr. Macklin noted that the white paper can move forward before the commissioned papers, especially regarding practical matters that required immediate information and experience from CDC.
- Ms. Kathy Kinlaw raised the important issue of translation and making the document useful on the local public health level. The background papers should be comprehensive and detailed, and the white paper should also be fairly detailed; however, the executive summary may be the most "useful" aspect of the effort. She recalled her work with the pandemic influenza document, which recognized that front-line providers needed guidance in making difficult decisions that were not spelled out in the guidance. This recognition led to their shift from guidance to "considerations." Section Seven of this document should take these local public health responders and their needs into account.
- Dr. Koenig asked for clarification regarding whether the document will be focused on planning. Mr. Jennings replied that they aspire to have things to say that will be pertinent to pre-event planning, event response, and to post-event activity.
- Dr. Koenig supported the idea of the authors of the white paper, as well as the authors of the commissioned papers, spending time in consultation with CDC staff to learn about their "real-world dilemmas." She then addressed the topic of research in the context of public health emergencies, which is a critical issue for CDC across an array of activities as the boundary between research and practice is examined in routine public health work as well as in emergencies. She was not clear whether, and how much of, this work should be reflected in the white paper versus being considered separately. It could be addressed in a commissioned paper.
- Mr. Jennings replied that they have resources for a limited number of commissioned papers. They should not, therefore, duplicate other efforts at CDC. Based on their discussion so far, he did not think that they would have to answer the problem of research versus surveillance. Rather, they would focus on research-like activities and information-gathering activities which seem to take resources away from, or conflict with, more immediate response activities. Certain circumstances may present conflicting demands, but also the opportunity to gather information that would not ordinarily be available in a research or a surveillance context. This document can address the "tradeoffs" associated with situations like these rather than the definition of research and how it should be regulated.
- Dr. des Vignes-Kendrick addressed the usefulness and translation of this paper at the local level. The document should comment on the role of centralized decision-making at the federal level and on the role of state and local officials. A number of ethical issues are associated with decision-making, but if the situation demands a "centralized push," and state and local entities have a limited ability to make meaningful decisions, then the document becomes restricted or meaningless. The legitimacy of the document will then be comprised. The struggle with Hurricane Katrina is only one example of a situation in which state and local officials expressed that decisions made at the centralized federal level had negative impacts on the state and local regions. Public accountability of officials who make these

decisions should extend to questions regarding power and ethical decision-making at the local and state level. This point relates to the issue of CDC employees who work in state and local agencies. If CDC personnel are dispatched to affected areas, but the affected areas themselves see needs elsewhere, then the CDC personnel amount to a "side distraction" that does not address a community's needs.

- Ms. Hoffman said that the document should include discussions of the law as well, especially in areas such as quarantine and seizure. There are contradictory laws that should be considered as well. She noted that the document should carefully emphasize public health emergencies and their differences from other emergencies.
- Dr. Josephine Malilay said that CDC is a member of the Subcommittee for Disaster Reduction, which is an ongoing effort under the auspices of the Office of Science and Technology Policy, Committee for the Environment and Natural Resources. A major effort of this subcommittee has been the production of the "Grand Challenges and Implementation Strategies," a research agenda put forth by more than 20 agencies on disaster reduction for the country. A document on challenges has already been released, but the implementation strategies are under OMB review. This effort includes a section on human health and ecosystem hazards, which includes public health.
- Dr. Semann commented on the importance of including psychologists. People who are deployed to emergency situations may not feel equipped to handle the breakdown of infrastructure, even if they are prepared to deal with infectious diseases or other public health problems. Historically, psychologists and ethicists do not agree about distributive justice. Workers in emergency situations can feel overwhelmed and helpless, and psychologists and ethicists could address this issue practically.
- Dr. Arras said that the paper's section on professionalism could include not only professionals' duties in emergencies, but also what the professionals need to help them do their jobs well.
- Dr. Popovic commented that their work was very exciting and important for CDC. It is important that all documents from the Ethics Subcommittee use consistent terminology to express general ethical principles. They can begin with principles that cut across all issues and then expand to discuss principles that may need to be modified or detailed. She then emphasized the importance of focusing on research in emergency situations. CDC views the debate of research versus practice differently from other agencies, but public health emergencies present unique opportunities to do research. For example, research on mental health in an emergency can only be done in an emergency situation. It might be possible for grants or other proactive mechanisms to fund this research; however, is it ethical? There is a need to balance immediate help with future benefits.
- Dr. Arras indicated that the document will explore the tensions that emerge in trying to conduct research when many frontline issues demand response.
- Dr. Popovic said that CDC has a Public Health Law Office and a Public Health Practice Office, which should be engaged in translation, effects and interactions of public health laws, and putting ideas into practice.
- Mr. Aun Lor pointed out the global implications of the document. He suggested that one of the commissioned papers cover global issues. The United Nations (UN) has a set of guidelines for responding to complex humanitarian emergency situations. The guidelines include human rights and ethical issues.
- Dr. Macklin directed the group's attention to terminology and acronyms.
- Mr. Jennings said that their focus is clearly public health and ethics. They might be able to use the acronym EPR: Emergency Preparedness and Response as opposed to PHEPR: Public Health Emergency Preparedness and Response. Dr. des Vignes-Kendrick said that many who have roles in emergency preparedness have nothing to do with population-based approaches. She suggested leaving "PH" in the acronym because public health has a

different meaning and system approach. Dr. Benjamin agreed that the acronym should be PHEPR.

- Dr. Hooyman noted that "values" are only referenced in the first section of the document. The rest of the narrative discusses "principles." Further, he wondered whether the document should refer to the Public Health Code of Ethics, using the Code as a foundation of principles of the profession. This document could apply the Code in the context of emergency preparedness and response.
- Dr. Macklin asked whether the document should mention values more frequently or whether the distinction between values and principles should be elucidated.
- Dr. Hooyman clarified that the introduction of the document implies that it will identify values and principles, but only identifies and discusses principles.
- Mr. Jennings said that they can address these issues when a draft is generated. He asked the group for their reaction to the difference between parts A and B of Section One. He hoped that Part A would articulate the ethical goals of any planning and response process. Part B would follow those goals to describe ethically-justified ways to make decisions and plans. Aside from the exact terminology that should be used, and whether it is consistent with the Code and the pandemic influenza white paper, he asked the group to discuss whether the strategy of articulating goals and then typing them to procedural topics will work.
- Dr. Macklin replied that a heading can make content clearer for readers. Section A is "Ethical Principles and Goals," which is clear; however, Section B might be clearer if it is headed "Implementation of Ethical Principles and Goals." Using "Guidelines" in the heading could be confusing. The entire document concerns ethics, and with this heading, B flows from A.
- Dr. Barrett said that the role of providing education on ethical aspects that apply to emergency preparedness and response was discussed at a meeting of the Association for Practical and Professional Ethics (APPE). If this document is to be useful, it might include a discussion of practical provision of education. This topic could fall under the section dealing specifically with CDC.
- Dr. Arras said that the document addresses the importance of education and giving people the capability to function properly, which could be included in the section on professionalism. They had not, however, anticipated articulating what the education should look like. Dr. Barrett said that the education piece could either be in the document, or a "next step" after the document. Dr. Arras said that the topic could be an appendix.
- Dr. Thomas said that the Ethics Subcommittee hopes to develop an ethics infrastructure, not to resolve all ethical issues. If they hope to decentralize ethics capacity, then the document should specifically detail how local state and health departments should be prepared. The section on professional obligations is a logical location for this point.
- Mr. Jennings asked Dr. Levine to weigh in on this point. A CDC-funded group at Yale University will likely produce a plan for the education of the public health workforce regarding emergency preparedness. He hoped that they would not duplicate these parallel efforts or "reinvent the wheel."
- Dr. Levine did not know whether the very large Yale project would be complete in 2007. He noted that almost every aspect of what this document is considering is also being considered in the efforts of others. As they make progress on the white paper, should they discover that the Yale project will release information or materials that would allow them to shorten their statement about education and refer to the Yale product, then they can do so. He did not feel that the Yale group would provide material by the time the white paper will be completed.
- Dr. Barrett said that when the document is complete, she will publicize and share it among CDC staff. Her efforts would be aided with guidance from the Ethics Subcommittee

regarding the best way to translate the document so that it is useful for responders and those who are preparing for emergencies.

- Dr. Levine raised a concern about item A3, titled "Equal Liberty and Human Rights." "Equal Liberty" is not a goal or a principle; in fact, the document lists three circumstances in which liberty could be constrained. He did not think that "human rights" gives this document direction. The international covenants and documents concerning human rights are written at a level of abstraction and idealism so that they do not necessarily serve to guide actions. Rather, they are general specifications about an idealized future. Dr. Arras said that the document can still refer to "equal liberty" as long as everyone's liberty is susceptible to similar limitations. Dr. Levine replied that everyone is not susceptible to the same expectations. In these circumstances, people or groups will be singled out, and their liberties will be restricted via quarantine, for instance.
- Mr. Jennings referred to the key distinction between treating people equally, in the sense of treating them the same, versus treating people as equals. This section of the document refers to treating people as equals because emergency planning and response often calls for the differentiation of people and groups to handle the emergency and to meet goals such as reducing harm and injury. The emphasis is that when people are singled out, they will not be singled out arbitrarily or unfairly, and they will be singled out in ways that will not compromise or undermine their sense of being equal or respected members of the moral community.
- Dr. Arras addressed the issue of human rights. He agreed that the covenants on human rights tend to be aspirational, especially in the provision of economic and social rights, but this document is referring to the so-called "negative rights" or rights to liberty and conscience.
- Dr. Levine said that including aspirational standards in a guidance document can take away from its authority and credibility, because the aspirations may seem impossible to meet. Guidance documents should focus on what is expected of people today, where additional papers can describe hopes and expectations for the future.
- Dr. Arras noted that this complex and interesting question cuts both ways. They have been asked to include global perspectives in this white paper, but any document of this kind that was not written in the United States would likely be based on principles of human rights. In order to speak to their colleagues in other countries, the human rights could be acknowledged.
- Dr. Levine agreed that most of the internationally-produced documents include principles of human rights. He postulated that this inclusion could be why the documents do not attract much attention "at the front lines" when people are acting.
- Mr. Lor agreed that most of the human rights language is aspirational, but the UN treaties are international laws. The UN Covenant on Civil and Political Rights, in particular, was signed and ratified, and all signers are bound to it. The human rights covenants were developed to articulate the societal condition for health and well-being. There is no better way to promote trust among public than by respecting and protecting individual and community rights, so human rights should be mentioned even for that point.
- Dr. Dixon felt that Section A (Ethical Principles and Goals of PHEPR) is the most important part of the document, as it establishes the principles from which the rest of the document flows. He wondered whether it was sufficiently strategic; that is, they should ask themselves where they want the document to go, and what they want to happen. All of the principles have co-equal value. Every emergency is different and every response will be different, so one principle may not "trump" others. Ethical behavior is defined by how a person makes decisions about competing goods. This document will be most helpful if it helps people make decisions about competing principles, all of which are valuable. Since this document is targeted toward significant emergencies, it might be easier to sort out some of the

principles. He did not feel that the document should suggest a hierarchy of principles, but rather help people think about a hierarchy in an emergency response so that their decisions are strategic, having outcomes in mind.

- Dr. Besser raised the issue of whether there is an ethical obligation to learn from a current event to reduce harm for future populations. As an emergency responder, he feels that they should not repeat mistakes or miss opportunities presented by current events. That issue should be framed in an ethical context that supports the need for research and information-gathering. Dr. Arras agreed. This issue could be addressed under the general rubric of engendering competence in the public health workforce and giving them an awareness of the past history of interventions. It could also be folded into the section on research itself. In spite of the fact that a pressing public health intervention will face the responders, an emergency also presents the important imbedded value to learn for the future. Dr. Besser agreed that the issue should be addressed in the section on research, but wondered whether an ethical principle should be listed to capture it in the introduction. Dr. Hooyman said that the topic could be incorporated into the principle on public health professionalism. Dr. Arras suggested that it be included under "competency."
- Mr. Jennings suggested that they could add an eighth principle to address the question or build it into one of the other principles. It could also be included in the exposition of Principle Six (Strong, Safe Communities), since learning about past mistakes will be a part of making the community stronger in the future. Plans should always take follow-up and future planning into consideration. The issue is part of building a competent workforce as well as an intrinsic part of the planning process.
- Dr. Popovic added that the clinical world treats the patient, and clinical trials are accepted as part of the research process. These activities advance knowledge while helping people. Elevating this broad acceptance into the context of work during an emergency could be possible and ethically acceptable to the public.
- Dr. des Vignes-Kendrick said that the issue of research during an emergency response points to the need for community involvement in decision-making. All of the people working on these issues are involved in research and publication, so research is high on their list of priorities. The community perspective may view how to utilize limited resources differently. Should they be used in response, or in "lessons learned?" Ethically, the deck could be "stacked" depending on who is involved in the discussion.
- Dr. Besser agreed and felt that listing a separate principle will allow for the clear delineation of these issues. There is an obligation to learn and not to repeat the same mistakes, but that obligation could be at odds with what is going on in the community. In this case, there could be a hierarchy in terms of principles. Research would not be undertaken if it went against a community's values or wishes. These questions do not just apply after the fact of an event, looking back to learn from responses and mistakes, but affect the planning phase and response implementation phase as well.
- Mr. Jennings noted that while there is a danger of not enough institutional memory, there is also danger inherent in too much memory. The document should capture the dynamic aspects of planning so that they look ahead, rather than "fighting the last war." The topic is ethically compelling because it is concerns decision-making in uncertain conditions and is highly contingent. No theory will allow for the prioritization of the goals, and no good algorithm will balance them when they conflict. They do have the capacity, however, to tell professionals to be mindful of all of the goals. Planners should have a broader vision of the range of goals, even though they cannot be prioritized.
- Dr. Levine returned to the topic of human rights documents. The international documents are international law; however, Article Seven of the UN Covenant on Civil and Political Rights classifies medical research as a subset of the larger category of "cruel, inhuman torture or punishment." Documents like this, therefore, do not speak to a modern

understanding of medical or biomedical research. Further, they can speak to human autonomy and dignity without specifying international documents on human rights as their origin.

- Dr. Hooyman referred to Section 4a on distributive justice. The pandemic influenza document includes sexual orientation as a "class" that cannot be discriminated against. For consistency, it should be included in this document as well. Sexual orientation is not a protected legal class, but ethically, people cannot be discriminated against based on it. He continued, noting that all of the principles and goals focus on public health professionals. He wondered if a principle or goal should address how members of the community should behave. Should citizens take on certain preparedness or be willing to give up liberties for the common good?
- Dr. Thomas pointed out that age is mentioned in the section pertaining to distributive justice. In some situations, particularly in pandemics, age is a factor, for instance in terms of immunocompetence. Resources might be given preferentially to the young or the old. He also commented on the particular considerations of an emergency that might bring ethical concerns to the foreground. This white paper, he felt, would benefit from a mention of these ethical challenges. In an emergency, things happen so fast that there is not time to deliberate: deliberations must be done in advance. These ethical issues are not sufficiently addressed in day-to-day public health.
- Jodi Keyserling, of the Division of Global Migration and Quarantine, suggested that section 4a (Distributive Justice) should include people with disabilities. Ethical considerations for these people are often overlooked.
- Dr. Bernier revisited Dr. Dixon's assertion that there is no way to prioritize the principles, but the principles should be listed to help people in the field remember them and to give them tools to make appropriate choices. While this function of the document is helpful, it does not go far enough to help those on the "front lines." More could be done to resolve this problem, in part by taking these questions to the public and soliciting their help in making trade-offs. Their input could be incorporated into the guidance. At this stage, they do not know how these trade-offs would be made in practice. Recent efforts regarding community control measures for pandemic influenza have incorporated public input because CDC decision-makers were worried about the drastic measures that may be needed to slow the spread of pandemic influenza. Schools may be closed, people who are not sick but who are in contact with sick people may have to stay home, and mass gatherings may be cancelled. Through outreach efforts, CDC learned that four out of five people supported these measures. He suggested that they make similar efforts to learn how the public would handle the trade-offs represented by responding to an emergency versus learning from it. Perhaps instead of commissioning papers, they should commission five public dialogues about this issue to incorporate their work into the guidance.
- Dr. Macklin said that when guidance documents are developed in Canada, they conduct public consultations of this sort.
- Dr. Bernier said that the discussion paper being prepared by the CDC Public Health Ethics Committee includes a section that refers to a paper by Childress called "Criteria for Evaluating Conflicting Values and Principles." This paper includes five criteria: effectiveness, proportionality, necessity, least infringement, and public justification. These criteria recognize the conflicts between principles, but tools exist to try to make concrete decisions in these situations.
- Dr. Dixon wondered whether at some point in the practice of clinical medicine, autonomy and paternalism might have been equal in ethical correctness. Over time, the balance has tilted toward patient autonomy. CDC is the world's pre-eminent public health agency, and he suggested that principles rise and fall depending upon the public's values. This document addresses issues that are important, and the document should move public

health forward to make more rapid and better decisions. They could ask questions about research versus response not only to the public, but to the academic, philosophical, and faith-based communities.

- Dr. Jan Devier said that COTPER has partnered with the Coordinating Office for Global Health (COGH) to think strategically about CDC's preparedness planning and response from an international perspective. The white paper could address the international piece as a part of the current piece, or it could focus on domestic issues and refer separately to work that is being done on unique international issues.
- Dr. Besser addressed the topic of individual ethical responsibilities in the community. Individual behavior plays into preparedness and response in several situations. For instance, the issue of hoarding scarce resources carries a significant ethical component. When individuals develop their own stockpiles of, for instance, Tamiflu, it has an impact on public health's ability to respond using ethical guidelines.
- Dr. Coughlin observed that "principle-based approaches" has been highlighted in their discussion. Some aspects of ethical decision-making in the context of preparedness and response might be informed by feminist ethics or the ethics of care. Many of the difficult dilemmas emerge in the private sphere. For instance, an emergency responder could have a child at home that needs care. This person's decision will not just be whether to receive a vaccine or an antiviral, but also how to care for their loved ones. It is important to articulate personal ethical traditions.
- Dr. Arras said that they can provide guidance on how to weigh and balance various principles in the thick of an ethical debate, but they cannot offer guidance in the abstract. He agreed that they should do more to talk about which values or principles take priority in given situations. Merely providing a list of issues for consideration would be insufficient.
- Mr. Jennings added that there will be extensive discussion regarding specific ethical choices and problems in which ethical values and goals may conflict. The document will introduce the range of considerations that are germane to those issues and may even state an opinion on one side of an argument. The document will make some conclusions and judgments. Regarding the general framework of goals, he resisted the notion that their seven goals, and any goals that might be added, were in conflict with each other. Good planning can realize all of the goals. The principal problem is not one of making trade-offs, but of in inclusiveness and moral imagination. Much of the ongoing planning only takes a few of the goals into consideration and does not recognize that planning is also about accountability, transparency, resilience, and community-building. Many planners seem to think that planning is only about harm reduction. A contribution of this document, therefore, is not in teaching people how to adjudicate the trade-offs and conflicts, but in making sure that the list of responsibilities in emergency planning is long enough. Plans will be done differently if all of the goals are taken into consideration. The content of the document has a more participatory community and responsive vision of planning than exists in the real world today. Current planning tends to be closed, elitist, and expert-oriented. This document will see planning as a community-wide problem and a community-wide process. Community-based ethical opinion and ethical analysis by experts may not always coincide. For instance, he posited that after 9/11, the public was too quick to opt for security and against rights. Over time, the public has backed away from that stance. Therefore, in planning, they should be careful of what they ask the public and when and how they ask it.

Discussion Points: Topics for Commissioned Papers and Recommended Authors

- Dr. Macklin suggested that in this time of relative calm, public groups would likely be less "panicky," and the public input groups would be a mechanism to supplement the white paper and possibly to inform it. She then returned to the subject of the commissioned papers,

asking whether the commissioned papers were needed. What would they add to the document? Who will read them? Scholars will read the papers, but she wondered whether they would directly inform the white paper. She noted that differences of opinion will exist among the group that finally approves the paper. She wondered what would happen if the authors of the commissioned papers make statements that are different from the views of the Ethics Subcommittee and/or CDC. The views in the commissioned papers should not be in conflict or tension with the white paper. The original rationale for the commissioned papers was to provide a means for delving more deeply into ethical analysis; however, the document should be as practical as possible. She asked for more details about the rationale behind the commissioned papers and the work that they are expected to do related to the white paper.

- Dr. Arras said that the commissioned papers will educate the writers of the white paper. He felt that it would be valuable to be able to lean on fresh, highly competent work in each of the relevant areas.
- Ms. Kinlaw understood that the commissioned papers are intended to inform the writing of the white paper. She asked Mr. Jennings and Dr. Arras where they needed help in writing the paper and wondered about an alternative method for providing background information to them other than through commissioned papers. She asked whether a team of people could gather papers and write a summary document from literature that already exists, or whether more papers are needed.
- Dr. Leinhos suggested that the professionalism paper address the liability of professionals in the field during an emergency response, especially if there is a shortage of professionals in certain areas. For example, if a person's licensure has expired, the person should be allowed to perform that function in the field, but protections should be in place. This problem applies less to federal employees, but response work is coordinated with non-federal professionals. She also raised the question of jurisdictional issues across federal, local, military, and tribal agencies and groups. The jurisdictions may overlap or be unclear, and ethical issues are associated with those relationships. She then suggested two possible criteria for selecting topics for commissioned papers: 1) technical areas in which advice is needed, and 2) recently-noted ethical issues that have not been covered thoroughly in the literature.
- Ms. Hoffman is working at CDC on a paper about immunity and liability for all public health responders, and she offered to share that work with the authors of the white paper.
- Dr. Koenig agreed that in the commissioned papers, priority should be given to topic areas that have not been thoroughly discussed in the literature. She therefore suggested that topics one (surveillance), four (planning process, coordination, and public communication), five (public health research), and six (professionalism) were most important. A great deal of literature covers distributive justice issues and individual liberties versus public health powers. She endorsed the idea of public engagement, both from an intellectual standpoint and from the standpoint of lending legitimacy to the ultimate product.
- Dr. Macklin asked about possible resources that could be available for public engagement. She agreed that some of the topics listed for commissioned papers have already been addressed in the literature. A great deal has been written about distributive justice in different contexts, she agreed, and the writers of the white paper and those who will act as consultants for it are capable of adapting it for emergency preparedness and response.
- Dr. Arras agreed that some areas have been discussed in the literature, but little or nothing has been written about distributive justice issues as they pertain to stockpiling. One of COTPER's major areas of concern is stockpiling.
- Dr. Macklin said that application of the principles is needed, not general background issues. She wondered about the feasibility of working in a focus group setting or in a setting of public consultation akin to the work done in Canada. The small amount of resources that

would become available if some of the commissioned papers were eliminated would likely not be sufficient to mount the needed public consultation.

- Dr. Popovic said that they would need internal discussions regarding the proposed activities, anticipated costs, and the parties at CDC who could contribute to the effort. She was not sure about the funds and staff resources and infrastructure that would be needed to support the effort.
- Dr. Besser said that the document would probably recognize the importance of public engagement in planning for emergency preparedness and response. Work in, for instance, vaccine distribution and evacuation must be done at the community level. A national-level public engagement will not achieve the necessary granularity for community emergency preparedness and response. An internal discussion would help them get a sense of what a public engagement process would accomplish. He hoped that the development of the ethics white paper would lead to communities' understanding of the importance of engagement and understanding in their own planning.
- Mr. Jennings agreed. He suggested a follow-up activity to the white paper could be a collection of plans and materials to help communities to reach out to their members. A pilot set of meetings or focus groups could provide a model for how to talk about these issues. They do not have to think of the work solely as a national project, but they could think of it as designing a toolkit for local communities to use in their planning.
- Dr. Bernier was unclear regarding the scope of the work. In one sense, the white paper seems to offer guidance about emergency planning and how to do it. He had, however, thought of the paper as an examination of the ethical issues that arise from that kind of work. The focus of the paper appears to be shifting toward best practices for good public health emergency planning. While it is important to help communities directly, the white paper is meant to be national guidance. Getting public input on the content of national guidance will still be valuable, even though public engagement should occur as part of community planning. Decisions about, for instance, pandemic influenza vaccine priorities and community control measures will be made at the local level. The federal government's guidance for pandemic influenza was more informed as a result of the community engagement work. He asked that the community work not be called "focus groups," as focus groups are not highly regarded in the field and tend to be easy to dismiss. These efforts are a deliberative effort rather than "market testing."
- Dr. Koenig concurred with Dr. Bernier's suggestion not to refer to "focus groups." She further noted that communities may eventually need a mechanism for applying these guidelines or for additional local engagement. She wondered how public deliberations can inform the "guts" of national recommendations. The public can provide perspectives and information that are not available in this expert group.
- Ms. Kinlaw commented that by engaging the public at this stage, they will model the claims that they make about public participation. She hoped that they would not just engage the public, but also local public health officials and similar deliberative panels, thereby including the people who will be part of the implementation process.
- Dr. Macklin hoped that the group had provided enough suggestions to move the white paper to its next steps. Mr. Jennings and Dr. Arras said that they had gleaned a great deal of information and thanked the group for their help.

Review of Greenwall Funded Project On Emergency Preparedness

James Thomas, Ph.D.
Ethics Subcommittee Member

Dr. Thomas related his desire to be able to prescribe "best practices" in identifying and addressing ethical issues in the context of a public health emergency. He decided to start the process by describing how public health departments are working. He engaged his health department in North Carolina in an interview process to identify state health department staff members who work with emergencies. North Carolina's principal emergencies are hurricanes and, to a lesser extent, Severe Acute Respiratory Syndrome (SARS), which was a "scare" more than a "reality." He planned to learn about the ethical issues that these professionals identified and how they dealt with them.

The Greenwall Foundation funds ethics-related activities. The process will be relatively brief and includes a group of advisors that will help to identify the questions that should be asked, and at what levels in the health department. Dr. Ellis and Dr. Hooyman are advisors on the project, as are representatives from other health departments and NACCHO. The interviews will be semi-structured in that they will have an agenda, but will be conversational. The project will result in academic articles as well as practice-oriented information to describe North Carolina's ethical procedures. Participants will identify what was missing, what works well, and suggested areas for further pursuit. The project works primarily with the North Carolina State Health Department, but includes connections with strategic county health departments.

National Summit on Public Health Legal Preparedness

Dr. Rick Goodman from the Public Health Law Program at CDC announced that CDC will host a National Summit on Public Health Legal Preparedness from June 18 – 20, 2007. This meeting will examine the four core elements of public health legal preparedness:

- ❑ Essential laws
- ❑ Competencies
- ❑ Coordination across jurisdictions and sectors
- ❑ Requirements for information and best practices

A set of white papers are in development now. The goal of the meeting is to produce a national action agenda on public health legal preparedness. They have sought to incorporate ethicists and ethical expertise into the development of the white papers, so they will echo and build upon many points that had been raised by the Ethics Subcommittee. The output of the Summit will be published as a special issue of the Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports.

Pandemic Influenza Update

HHS Vaccine Priorities Project

Benjamin Schwartz, M.D.,
Senior Science Advisor, National Vaccine Program Office
Department of Health and Human Services

Dr. Schwartz thanked the group for inviting him to the meeting. He presented information pertaining to the prioritization of pandemic influenza vaccine. In 2005, CDC and HHS went through a process to prioritize vaccines with input from the Ethics Subcommittee, and they recently undertook another prioritization activity. While he could not present the results of the prioritization scheme because they are still under review, he was able to present the process that led to the scheme and the ethical considerations that informed it.

Pandemic influenza vaccine must be prioritized. All people are susceptible in a pandemic, and current United States-based vaccine production capacity cannot make enough vaccine to protect the entire population rapidly. In addition, the earliest doses are projected to be available approximately 20 weeks after the identification of the pandemic virus. The mathematical model indicates that the timing of the first pandemic wave in this country will be such that it is possible that no vaccine will be available at the time of the first wave. If vaccine is available, then it will be newly released, and there will not be sufficient amounts to vaccinate a substantial proportion of the United States population.

Efforts are being made to narrow the gap between vaccine that is available for use and the need for it. He recalled a statement by Kathy Kinlaw that, "preparedness now decreases the need for allocation decisions later." With that idea in mind, over $1 billion have been spent to increase vaccine production capacity, to develop and license new vaccine production technologies, and to evaluate adjuvanted vaccine formulations. Adjuvants are substances that can be added to vaccines to improve the immune response to vaccination; therefore, less antigen needs to be included in each dose and the production capacity goes further. Some clinical studies of vaccines against the avian H5N1 virus have supported the use of adjuvants. These advances, combined with increased vaccine production capacity via additional factories, are helping to extend vaccine supplies further. It may be possible in several years to vaccinate as much as half of the United States population with a single month of production. Planning needs to take uncertainty regarding vaccine availability into account.

In the spring and summer of 2005, the Advisory Committee on Immunization Practices (ACIP) and the National Vaccine Advisory Committee (NVAC), two HHS advisory committees, considered prioritization. Many members of the Ethics Subcommittee were included in this activity. The process included many factors, including ethical issues, and the committees' recommendations were adopted unanimously and published in the 2005 HHS Pandemic Plan as guidance for state and local planning and to promote further discussion. These recommendations were not intended to be final national plans for prioritization.

Healthcare workers were at the top of the 2005 prioritization list because of the critical role that they will play in providing care not only for those affected by pandemic illness, but also for all other medical problems. The next population on the list resembles the population that is

annually vaccinated for influenza and includes those who are at high risk because of underlying diseases, people who are at high risk because of their age, and household contacts of those who cannot be directly protected by vaccinations. Not until Tier 2B, after 100 million other people have received the vaccine, do other critical infrastructures and other emergency responders appear in the 2005 scheme.

The HHS advisory committees felt that the most important pandemic response goal was mitigating the adverse health outcomes in the pandemic. There were also certain assumptions about pandemic severity, including a 20 to 30 percent attack rate and a death rate of up to one percent in those who became ill. The advisory committees felt that vaccinating high-risk people will certainly save lives, whereas the impact of vaccinating critical infrastructure was not clear because it is not known whether the critical infrastructure would fall apart in the absence of vaccination. The committee used an assumption of 10 to 15 percent absenteeism at the peak of the pandemic, and the process and outcome met reasonable ethical standards. Dr. Schwartz observed that the more recent process also met ethical standards, but resulted in different recommendations.

As planning and preparedness progressed after the 2005 recommendations were released, it was clear that the recommendations would have to be reconsidered. Public meetings were held in the fall of 2005. The public and stakeholders met in several different sessions, and all of them rated "preserving essential services" as the top goal above "protecting high-risk individuals." Planning assumptions evolved over time as well. Planning was initially based on an assumption of a more severe pandemic with a two percent death rate and with an absenteeism rate of 40 percent. There were also evolving pandemic response strategies, including community mitigation measures. Further, additional analyses of critical infrastructure were conducted.

For all of these reasons, the recommendations needed to be reconsidered. To do this, an inter-agency workgroup was formed. The group itself was comprised of representatives from federal agencies, but the process included input from outside the federal body and included presentations and discussions of ethical issues. The workgroup heard presentations on key issues from stakeholders in public health and Homeland Security. The group considered the 2005 recommendations from ACIP and NVAC as well as a recent analysis by the National Infrastructure Advisory Council (NIAC). They used a formal decision analysis process and posted a Request for Information in the Federal Register and on the website.

Several ethics experts participated in the process. Both the process itself and the recommendations were considered in the context of various ethical precepts. The group concluded that openness and transparency were important. A clearly-shown deliberative process will build trust from the public. There was extensive public participation and engagement before the draft recommendations were created, and there will be many more opportunities for comments. Issues of inclusiveness and reasonableness were considered. "Reasonableness" refers not only to decisions that are rational and well-grounded, but also to decisions that consider public values when there is no scientific "right answer." Accountability is also incorporated into the scheme.

The recommendations recognize the need for fairness. The program goal is to vaccinate everyone who wants to be vaccinated. The workgroup recognized the need to treat all of those who fall within a priority group equally. Minimizing pandemic impacts is an ethical issue, as is the national preparedness goal of protecting health and decreasing societal and economic impacts in a pandemic. The issue of reciprocity affected the group's deliberations as they

sought to protect those who take occupational risks. Further, the recommendations should be flexible and able to be tailored to pandemic severity so as not to use the vaccine unnecessarily to protect infrastructure in a mild event. Recommendations may need to be modified during a pandemic based on the risk groups.

Secretaries Leavitt and Chertoff asked the advisory group to stipulate the critical functions and the critical personnel needed to support those functions in a pandemic. NIAC surveyed critical infrastructure and key resource operators, reviewed existing data and plans, and interviewed subject matter experts. This group generated a pie chart of critical infrastructure and personnel in 15 different sectors. The largest part of the infrastructure was healthcare, and emergency services was prominent as well. About 17 million people are identified as these critical infrastructure. 13.4 million of these persons were identified as "Tier One;" that is, the most critical of the critical. Two-thirds of this group are either in healthcare or emergency services. The total critical infrastructure workforce is 85 million people.

One of most important and interesting parts of the process was the series of public engagement and stakeholder meetings. The meeting considered the goals of pandemic vaccination and assigned values for each. The meetings were structured similarly, with background presentations, small group discussions, and then electronic voting. They took place in Las Cruces, New Mexico, where over 100 participants made up a culturally-diverse group. Four of the 14 tables in the small group discussions were conducted entirely in Spanish. The background presentations were simultaneously translated. About 130 people took part in the meeting in Nassau County, New York. Many of them were older persons. A stakeholders meeting took place in Washington, D.C., with 90 representatives from government critical infrastructure sectors and community organizations.

The meetings were based on assumptions of a severe, 1918-like epidemic, but the leaders of the group made no assumption about increased mortality among young, healthy people. They recognized that the timing and supply of vaccine was uncertain and that vaccination would occur in the context of other pandemic response measures, including strategies at the border, community mitigation, antivirals, and planning by the government and businesses. Participants were asked to rate each of ten potential pandemic vaccine goals on a scale of one to seven, where seven was extremely important and one was unimportant. The goals were related to occupational risk factors and functions as well as to the health risks that might be experienced by different population groups.

The four leading goals identified by the participants in each of the three meetings were the same: The highest-rated goal was protecting people who are working to fight the pandemic and to provide medical care, including public health responders and healthcare workers; The second goal was to protect people who provide essential community services; The third goal was to protect children; and The fourth goal was to protect people who are most vulnerable due to their jobs; that is, those who are asked to go into harm's way. The values expressed as underlying the goals included maintaining essential societal functions, protecting those who will help others during the pandemic, and protecting children as our future.

Dr. Schwartz emphasized the high priority of protecting children, particularly in light of the large elderly population that participated in these meetings. Comments from many people indicated that if they got a dose of the vaccine, they would give it to a grandchild rather than taking it themselves. In each of the meetings, protecting those who are most vulnerable, such as the elderly and those with underlying diseases, was very low among all ten goals.

As a workgroup, it is important to balance the vaccine use in order to achieve multiple pandemic response goals. Also, multiple factors should be considered in defining which groups may have higher priority for vaccination. The workgroup developed their draft prioritization scheme on February 9, 2007. Although it could not be presented yet, Dr. Schwartz indicated that in many ways, it reflects the public input. After the government gives permission for the draft recommendations to be made public, the workgroup will seek comments and suggestions in a number of ways, including: further public and stakeholder meetings, a Web-based public engagement process, written comments to the government pandemic flu website and the Federal Register, and presentation to ACIP and NVAC.

Discussion Points

- Dr. Gamble asked how members of the public were recruited into the public engagement meetings. She also noted that Web-based outreach could limit the people who could be engaged. She asked whether the public meeting attendance was analyzed according to a breakdown of racial and ethnic groups.
- Dr. Schwartz replied that participants were recruited through local organizations, including local health departments and other community organizations. In New York, for example, they worked through a Congressman's office as well as through activities conducted by the Health Department. An important point regarding the New Mexico meeting was that participants were paid a stipend. This approach reached a diverse group that included people who were interested in pandemic influenza as well as wives of local farmers. The meeting included a pre-test and a post-test to measure the participants' knowledge about pandemic influenza, which indicated that all participants gained knowledge in the meeting. They did not break down the scores by race or ethnicity. The scores were collected electronically so the group could see the results immediately after they rated each of the goals. He recognized that Web-based engagement is only one way to get information. People who use their computers and will participate in this method are not necessarily a cross-section of society, but this approach is one good mechanism to get input. The Web-based component will include a collection of demographic information as well as an assessment of people's interest in further participation. He was interested in seeing whether the results of the Web-based efforts will be similar to the results from the meetings.
- Dr. Gamble urged the workgroup to collect information about racial and ethnic diversity in the responses. For certain groups, the radio might be a better way to engage the public than the Web.
- Dr. Arras asked how the latest recommendations differ from the previous recommendations from ACIP and NVAC.
- Dr. Schwartz replied that the latest recommendations incorporate the idea of balance more than the 2005 recommendations. Further, the new recommendations recognize the need to address multiple goals simultaneously. Groups at the top of the list pertain to protecting public health response, maintaining essential services, and protecting national security as well as the general population. This approach is more balanced and recognized the values of the public. The new recommendations also put children higher on the list, which the public values, even with the recognition that this approach might not save as many lives.
- Carolyn Bridges recalled that public engagement occurred during the first effort at prioritization, and she wondered how the findings from the second round of public meetings differed from the first and whether those conclusions might have been influenced by the amount of epidemiology from previous pandemics that was presented. The planning assumptions for these meetings did not include the explicit assumption that there would be increased mortality and morbidity in healthy adults.

- Dr. Schwartz replied that in the first meetings, the first question asked was, "What is the most important goal of vaccination?" The most frequent answer was to protect essential services, and the second-most frequent answer was to protect the most vulnerable people. Few participants in the first meetings chose "to protect children" as their most important goal. The next series of meetings asked the question differently by asking the group to rate ten goals on a scale of one to seven. Phrasing the question this way generated important information that the first public engagement session may have missed. The people at the meetings understood that the elderly and those with underlying disease would be at higher risk. The background presentations also made it clear that these groups are recommended for annual vaccination. The participants therefore understood what they were doing when they rated children above the other populations, and they also understood that they were departing from expert recommendations. He was therefore confident in the conclusions of the meetings.
- Dr. Bernier said that the process of setting priorities for pandemic influenza is a "golden opportunity" to learn about public engagement. There is an obvious difference between the two experiences with the public in their feelings regarding children, but essential services appear to have remained the number-one priority. The role that the public engagement had in the possible reconsideration of the recommendations is interesting.
- Dr. Hooyman asked whether the voting process occurred at the end of the meeting presentations or after the post-test.
- Dr. Schwartz replied that the electronic voting took place after the presentations and small group discussions, but before the post-test.
- Dr. Hooyman was unclear regarding how this work relates to the pandemic influenza guidance document being developed by Dr. Levine and Ms. Kinlaw and others.
- Dr. Schwartz replied that the work was parallel. His experiences working with Ms. Kinlaw and others and working on the first draft of the guidance document helped to inform the process for these recommendations.
- Dr. Coughlin thanked Dr. Schwartz for his presentation. He wondered whether there was an agreed-upon definition of "children" expressed in the meeting. The participants clearly value their children as the future, but there are differing classifications of children, adolescents, and adults, and these distinctions can be meaningful.
- Dr. Schwartz replied that children were considered to be school-age. This definition reflects a relatively standard understanding. It recognizes that over 70 million people are included in this classification. In their final prioritization scheme, they broke the group into several subgroups based on age and underlying illnesses that may increase risk.
- Dr. Macklin thanked Dr. Schwartz and looked forward to seeing the document when it was made public. She indicated that she went through a similar prioritization with small groups of first-year medical students. At least one of those groups put children at the bottom of the list. When asked why, the students replied that children do not contribute to society and that there are "enough children in the world."

Update on Ethical Guidance Document and Discussion of Next Steps

Kathy Kinlaw, M.Div.
Robert Levine, M.D.
Ethics Subcommittee Members

Ms. Kinlaw reminded the group that their ethical guidelines document came at the original request of Dr. James LeDuc and answers a few particular questions. The final draft of the document was presented to the Advisory Committee to the Director in December, was approved, and was sent to the Director of CDC. The Director of CDC has approved the

document and has sent it to the Secretary of HHS. Mention was made in the Pandemic Influenza Update in December that the document would be available in early 2007. There have already been a number of requests for the document.

Several publication and translation efforts are underway. Dr. LeDuc invited Ms. Kinlaw and Dr. Levine to co-author a paper on ethical and legal considerations in pandemic influenza. That document has been vetted and will be part of an Institute of Medicine (IOM) publication. A document that will only consider the ethical considerations is in development as well.

She noted that the morning's conversation had been helpful because it addressed the question of what Ethics Subcommittee members are asked to do in attending to a particular topic. The white paper was their first product in the area of pandemic influenza. Pending questions concerning their "next steps" concern how the document will be interpreted and how useful it will be. Subcommittee members have opportunities to identify relevant case applications for the influenza guidance. She asked the group to consider whether they should develop "case law." That is, take the document into particular settings for interpretation and application. Important questions also exist regarding education about the document, both internally at CDC and more broadly. She further asked the group for their input on how to engage people further, including dialogues with the community, healthcare professionals, and others.

Dr. Levine then addressed "next steps," priorities, and lessons learned. His first priority was a recommendation that in a pandemic, there will be a need for people who are not ordinarily licensed to perform certain healthcare interventions and procedures to carry out these procedures. Plans must be in place in the areas of legal questions, liability, and training. Many procedures are classified as sub-specialty procedures, which they should keep in mind.

He indicated a need to clarify why central authority is essential in many aspects of pandemic preparedness and response, especially since this idea is not in harmony with traditional public health tenets. He recommended specifying what is meant by "community engagement." This concept appeared one time in a regulation, when the FDA specified a requirement for community consultation in order to do research in emergency situations when informed consent might not be possible. There is a vast spectrum of ways to interpret "community engagement," from brief meetings to survey instruments to more sophisticated approaches. Additional discussion is needed regarding how to construct community engagement and the purpose that it is supposed to serve. For instance, if the community expresses a desire that is contrary to expert opinion or knowledge, then what will be the deciding factor?

Dr. Levine also felt that the discussion of "evidence-informed interventions" should be improved. This topic initially focused on the need to validate interventions, particularly "non-pharmaceutical" interventions or "liberty-limiting" interventions. This validation may not be possible outside the fields of pharmaceuticals, biologicals, devices, and the like. A recommendation later was to use the standard of "evidence-informed." Essentially, proposed interventions should rely on the best evidence available, even if little evidence is available, to see that they will accomplish the desired effect.

He called for a more nuanced discussion of assigning priority to "critical infrastructure personnel." Some people should be assigned high priority because they are likely to contribute to the preservation of a well-ordered, well-functioning society. Additional specification is needed regarding who these people are and the criteria that will define them as "critical" and give them high priority.

Dr. Levine expressed his hope that Dr. Schwartz and his colleagues planned to publish their experiences with the public engagement process and deliberative democracy. In particular, the issue of providing a stipend is important and should be shared.

Discussion Points

- Dr. Macklin wondered whether, since Dr. Levine had listed "things he should have done or would have done," an appendix or update should be prepared to augment the ethical guidelines, which have been finalized and approved.
- Dr. Levine responded that none of these documents are "the final word." The document being developed by Dr. Arras and Mr. Jennings will further expand and build on elements of the ethical guidance for pandemic influenza, and Dr. Koenig's document will develop them even further. No policy recommendation, report, or guidance document is ever final. The items that he identified could be done better or could be elaborated in whatever form is appropriate.
- Dr. Macklin said that the documents under development will be read and used by people other than those who will consult the ethical guidelines. The ethical guidelines are final in the sense of the process that the document goes through in order to be approved and released. She added that his suggestions were well-taken and would be useful, and she hoped for another mechanism to use them in the guidance.
- Dr. Levine replied that in the field of regulations for protection human subjects, changes in regulations can take ten or 15 years. He hoped that commentary on the already-published document could be shared, but he did not want to suspend the utility of the document by submitting it to a formal revision process.
- Dr. Koenig wondered whether the Institute of Medicine (IOM) report and other developing papers could incorporate these ideas.
- Ms. Kinlaw said that the IOM paper is complete, but the white paper can examine the content of the guidelines and steps for the future. The idea of publishing a commentary is a good means for dealing with these additional issues. Dr. Arras and Mr. Jennings will be dealing with these issues in their document as well. She suggested that if they move into the realm of case studies and case law, then the process issues can be dealt with more thoroughly.
- Dr. Popovic noted that as it is important to engage the public and hear what they think about certain issues, in this case, it will be important to hear from the people for whom the document was intended. There are a number of requests for the document already, and she suggested gathering feedback on it both internally and externally. Internally, the PHEC can help to gather information from the people who work in influenza in every part of CDC. Mechanisms for gathering external feedback exist as well.
- Dr. Barrett said that they have developed a two-page fact sheet that summarizes the major points in the document. They also developed a checklist to be used by planners or responders. Collecting feedback on these specific, concrete products will be useful as well. Her contact information is listed on the document, and comments are welcomed, but a more formal process for gathering feedback is also possible.
- Dr. Popovic said that they could ask some simple questions regarding the usefulness of the document and any elements that it might be missing. Different professionals will find different applications for the document in what they do.
- Dr. Hooyman said that the Ethics Subcommittee membership is beginning to evolve and rotate, and so they should make an effort to capture a "historical memory" of this work to help the Subcommittee best serve CDC. He asked whether "guidelines" are required to be published in the Federal Register for public comments, and if not, whether they could be published for 30 days of public comment.

- Dr. Popovic said that the guidelines could be published in the *MMWR* or through other venues such as their website.
- Dr. Devier said she was thrilled to see the product. The most important part of the work is when the product is in action. The engagement of this group needs to be mirrored at the state and local levels, where decisions are being made. She suggested that the group think about how the document can be publicized so that public health professionals understand public health ethics in the context of pandemic influenza. People have been thinking carefully about the legal aspects of these issues, and there is space for substantive engagement regarding ethical aspects now when they have time to plan. Further, she encouraged the group to think about how to share the document with ethicists at the state and local level who might be interested in taking up some of the thorny public health ethics questions. Teams of ethicists could be formed at the state and local level to foster these discussions. We know that we will not have enough vaccines and antivirals immediately, and communities will be faced with non-pharmaceutical questions. Discussions about these complicated ethical issues must go on at the local and state levels with a range of disciplines as well as with communities.
- Dr. Barrett said that some of this process has begun. The Pandemic Flu Exercise conducted by CDC had an "ethics desk," and the ethicists used their document as a framework for providing input as part of that response. She has done training for Epidemic Intelligence Service (EIS) officers about the document, and she is scheduled to train other CDC responders. They have presented at the APPE meeting and have created a submission for the American Society of Bioethics and Humanities (ASBE) on the pandemic flu document.
- Dr. Gamble said that she sits on the editorial board of the *American Journal of Public Health*, which sometimes publishes special editions. She offered to see whether a special edition about these topics might be possible at her editorial board meeting next week.
- Dr. Popovic reminded the group that NACCHO, ASTHO, the Council of State and Territorial Epidemiologists (CSTE), and other partners who will be interested in the document and who have ways of distributing it.
- Dr. Barrett indicated that they have plans to distribute the document through CDC's partners.

Ethics Subcommittee Procedural Issues

Review of Ethics Subcommittee Policies and Procedures

Ruth Macklin, Ph.D.
Ethics Subcommittee Chair

Dr. Macklin pointed out that the Ethics Subcommittee is a Federal Advisory Committee and therefore falls under the requirements of the Federal Advisory Committee Act (FACA). Previously, the Subcommittee did not have a set of "Policies and Procedures," and questions had been raised about the appointment of the chair, terms of office of the members, the specific relationship between the Subcommittee and its parent committee. At their last meeting, the Ethics Subcommittee requested clarity regarding how to deal with questions that may be posed to Subcommittee members by the press. After several conversations with Dr. Barrett and Dr. Dixon, a first draft of "Ethics Subcommittee Policies and Procedures" was created.

The document includes:

- ❑ The Ethics Subcommittee purpose and history of when it was established
- ❑ Membership on the Subcommittee, including who appoints members, term lengths, and the status of appointed Subcommittee members; designation of the chair; meeting frequency, realizing that meetings must be announced in the Federal Register
- ❑ How topics are included on the agenda
- ❑ Products of the Ethics Subcommittee
- ❑ Voting, when and if it becomes necessary
- ❑ The Ethics Subcommittee's relationship the Advisory Committee to the Director
- ❑ Conflicts of interest
- ❑ Compensation
- ❑ Member responsibilities
- ❑ Media interaction

Discussion Points

- Dr. Levine commented that some Ethics Subcommittee members have never received compensation. He recently received his first check after many years of involvement.
- Dr. Macklin said that in their discussions, they should distinguish between compensation and reimbursement. She asked whether any Ethics Subcommittee had never received reimbursement or compensation. Two members raised their hands.
- Dr. Barrett commented on the compensation, noting that a representative from the office that handles compensation issues was not present at the meeting. She has been in touch with the office regarding who has received their $250 honorarium as well as regarding the status of any outstanding travel vouchers. She asked any members with concerns in this area to inform her, and she would contact the office in question. She noted that some people had actually received their reimbursements, but thought they had not.
- Dr. Macklin cautioned the group that some accounting transactions can "slip through the cracks," especially with automatic electronic transfers, which sometimes have little information. If members get compensation from other federal agencies, then the process can be confusing.
- Dr. Barrett said that there was a problem in distributing honoraria for earlier meetings. Some lingering problems may remain, even though the office has worked hard to fix the problems.
- Dr. Levine noted that the payments can be even more confusing because the Department of Defense handles some payments.
- Dr. Hooyman asked about compensation for telephone consultation and time spent on conference calls.
- Dr. Barrett said that any activities that took place outside the activities of the Ethics Subcommittee were taken out of this document. A consultation that does not reflect specific Ethics Subcommittee business will be handled separately. She explained that the $31.25 hourly rate is based on a $250 per day honorarium divided into an eight-hour day.
- Dr. Thomas asked about how compensation applies to people working on white papers.
- Dr. Barrett said that they have been keeping a tally of the time that they spend on the telephone with Ethics Subcommittee members specifically talking about the document. Compensation is not provided for independent time devoted to the papers.
- Dr. Macklin noted the distinction between the commissioned papers and the white papers that are prepared by Ethics Subcommittee members. The commissioned papers are at the general "going rate" of $1000 per paper. This distinction raises a question of fairness. She wondered whether it is assumed that members of the Ethics Subcommittee are expected to

give up their time for all of the Subcommittee activities. She guessed that the time devoted by the preparers of these documents will be at least as great, if not greater, than the authors of the commissioned papers. She wondered about the justice of paying people outside the Ethics Subcommittee to do this work.

- Dr. Barrett said that she thought that the FACA rules state that work that takes place outside a meeting is not compensated.
- Dr. Kathy Ramadai did not think that compensation was prohibited, but rather dependent upon the discretion of the group and availability of funds.
- Dr. Macklin pointed out a sentence that read, "support for preparation of Ethics Subcommittee reports to the ACD will be provided by the DFO."
- Dr. Barrett clarified that the sentence referred to administrative, not financial, support. She continued that the $31.25 hourly rate comes from a different budget. It is difficult to pay by the hour for consultations because Ethics Subcommittee members are special government employees. They are trying to operate under a system in which another honorarium is awarded when eight hours of work have been amassed.
- Dr. Gamble reflected that the document's purpose implies that no other committees have addressed ethical issues in the past. She recommended referring to this particular iteration of this Ethics Subcommittee to make this distinction.
- Mr. Jennings said that the guidance regarding interactions with the media was written clearly, but offered a question about a specific example. When speaking with a journalist under normal circumstances, he does not identify himself as a member of this Ethics Subcommittee. However, if a journalist consults him about a public health issue, knows that he is a member of this Subcommittee, and wants to refer to this membership in the article, Mr. Jennings would specify that he speaks only for himself and not as a CDC representative or as a representative of the Ethics Subcommittee. It is possible, however, that the journalist might identify him as a member of the Subcommittee without any disclaimer. He wondered if he should ever allow a reporter to mention his Subcommittee membership unless he has authorization from CDC to do so in a specific case.
- Dr. Levine said that it is not possible to stop journalists from referring to a member's inclusion in the Ethics Subcommittee. Mr. Jennings said that he could not inform the journalist about his membership. Dr. Barrett indicated that the Subcommittee membership is public information.
- Dr. Koenig recalled discussions in which they had agreed that if Ethics Subcommittee members are called about specific issues related to the Subcommittee, then they would inform the chair and CDC staff know about the contact. Other federal committees on which she has served have used these informal arrangements, which were useful in helping them be in agreement about how to present topics. This communication could take place before or after the interview.
- Dr. Hooyman said that they cannot control how journalists report. Mr. Jennings agreed. He had not thought about a reporter asking him about Ethics Subcommittee affairs, but about general public health questions. If he receives a call about the workings of the Subcommittee, he will refer the caller to Dr. Macklin or Dr. Barrett.
- Dr. Dixon asked whether the ACD has guidance for its full members on this issue. If so, then they should follow that guidance.
- Dr. Benjamin said that the only person who speaks for the Ethics Subcommittee is the chair of the Subcommittee, under the guidance of the administrative agent. If a member receives a call about the Ethics Subcommittee, then the call should be referred to Dr. Barrett. They may delegate authority for speaking for the Subcommittee to another member. Journalists can capture thoughts in a variety of ways and based on a variety of the organizations with which they are associated. The Subcommittee members cannot control how they are represented in the media. They can only specify that they are speaking as an individual.

They may want to temper their comments based on their positions and many affiliations. He advised that if a reporter calls, Ethics Subcommittee members should not respond immediately, but take time to think about what to say and how to represent themselves. Dr. des Vignes-Kendrick concurred with the procedure to refer calls to the Chair.

- Dr. Benjamin said that Dr. Barrett's referral number should be readily available to give to journalists. He reminded them that they do not have an obligation to talk to the media.
- Dr. Macklin noted that these meetings are open to the public. She asked whether the complete proceedings are publicly available. Dr. Barrett replied that the minutes of the meeting will be posted on the CDC Website. .
- Dr. Macklin said that these postings take place a long time after the meeting itself. If a journalist calls, a potential response could be to refer the journalist to the minutes, which are a complete record. The journalist may call before the minutes are available, however, which could pose a problem. She asked whether a sentence in the Ethics Subcommittee policy document should refer to notifying CDC about interviews when they take place.
- Dr. Koenig replied that as a courtesy, disclosure should be recommended. She was called by a newspaper after the last meeting, and she notified Dr. Barrett about the call.
- Dr. Benjamin remarked that some media outlets, particularly the *Atlanta Journal and Constitution*, have agendas. As they enter the political season, more agendas will emerge. He believes that even though some people like publicity, it is never good to get damaging news in the press. He felt that they should all be careful in this election cycle as journalists will be looking for a new angle for a story. They should not lie to or mislead reporters, but reporters could play their statements off of each other. A single spokesperson should therefore speak for the Ethics Subcommittee.
- Dr. Hooyman suggested that the policy document also specify that any time a member is interviewed or responds to a media request and CDC is mentioned, the Designated Federal Official (DFO) will be notified. When the pandemic influenza guidelines are made public, Ms. Kinlaw and Dr. Levine will receive calls. If they are being asked about the document, he felt that they should answer those questions and not have to refer to Dr. Barrett.
- Dr. Benjamin agreed and suggested that they should then inform Dr. Barrett about the call. He advised, however, if time permits, to return the reporter's call after speaking with Dr. Barrett to ensure that the reporter has not already gotten a CDC comment.
- Dr. Macklin summarized that they will keep a record of media interviews related to the Ethics Subcommittee. If problems arise in the future, then they can determine whether this policy is adequate or whether it needs revision.
- Dr. Hooyman said that since this document deals with procedural issues, he wondered whether the document should include evaluation of the Ethics Subcommittee activities.
- Dr. Macklin felt that a mechanism for evaluation could be included in the document. It should not be so specific, though, that it would hold the Subcommittee accountable for having a formal evaluation for every meeting and every activity that they have.
- Dr. Dixon felt that evaluation was important, but he did not feel that it needed to be included in the foundational documents for a committee.

Process for Evaluating Ethics Subcommittee Actions

Tom Hooyman, Ph.D.
Ethics Subcommittee Member

Dr. Hooyman shared his thoughts about how to frame the question for evaluating "ethics capacity." He recalled that one of the Ethics Subcommittee's first charges was to help CDC build its ethics capacity. He considered two areas within an organization that deal with capacity:

- ❑ The people within the organization,
- ❑ The infrastructure present in that organization that allows those people to do the best that they can in the work in which they are engaged

He thinks of ethics capacity as having "mind-body-spirit" components. The "mind" refers to knowledge, or "Ethics 101." "Body" refers to ethical skills such as decision-making and critical analysis. The third component, which is "spirit," "soul," or "character," refers to an understanding of public health ethics. In short, "they get it." Those three components come together in CDC employees. He hoped that evaluation efforts of the Ethics Subcommittee would assess how the Subcommittee is having an impact on these aspects of CDC.

The internal ethics committee is now a part of CDC's infrastructure, and it did not exist before the external Subcommittee came into being. The evaluation effort that Dr. Hooyman suggested was not unlike work that some hospitals do in evaluating advances and influences that the group has on its infrastructure. There are a number of ways to conduct evaluation. The group could evaluate itself or could employ a feedback mechanism for their "customers," which could be CDC or even the population as a whole. These questions will determine how they might craft a Human Resources 360 agenda. He felt that they had been evaluating their effectiveness and conducting quality-improvement-type activities all along, but asked for the group to consider how to operationalize their work in that area.

Discussion Points

- Dr. Macklin recalled that this topic arose in the context of a series of telephone consultations on specific topics requested by CDC. At the time, Dr. Hooyman wondered whether the consultations were helpful to CDC, how the Ethics Subcommittee would know that they were effective, and how to evaluate them. These questions can apply to any of the Subcommittee's work. She asked whether the process should be formal, and if so, when it should occur. At present, they rely on informal feedback regarding whether their presentations, papers, and discussions are helpful.
- Dr. Hooyman suggested five criteria to address skills set and knowledge gained. These criteria could be developed further to assess, for instance, a baseline of how the internal committee perceives its capability and knowledge base. If the Ethics Subcommittee hopes to build capacity for CDC, the internal committee would seem to be a critical group. Pre/post assessments and gap analysis could be conducted, and then re-administered some time later and examined to find the causes of increases in confidence and knowledge. The process could be formal or take the form of a less formal "debriefing."
- Dr. Macklin said that these criteria address evaluating ethics capacity. Other items might need to be evaluated later.
- Ms. Kinlaw felt that some ability to assess whether the Ethics Subcommittee is making an impact, and whether they are making the impact that they thought they would make, is worthwhile. She wondered how to make these assessments so that they yield significant information. They are not only "debriefing" and looking back on the process of creating the pandemic influenza document, but also inserting opportunities to determine perceptions of the document as it is being rolled out. Telephone consultations present an opportunity for immediate feedback from the people who have asked for the consultation. The feedback could be brief, and a mechanism for follow-up could be built into the approach. It could also be possible to do a written follow-up, but it would also be helpful to have a mechanism within the organization for a neutral party to have conversations with key individuals at different levels for an honest assessment of the Ethics Subcommittee's work.

- Dr. Dixon thought that the internal committee should think about evaluation not only from the standpoint of their education, but also in how well they serve CDC. He suggested that a small subcommittee with members of the internal and external committees work on developing a standardized approach for evaluation to share at the next meeting.
- Dr. Macklin asked for volunteers for this exercise. The volunteers were: Dr. Dixon, Mr. Lor, Dr. Thomas, Ms. Kinlaw, and Dr. Devier.
- Dr. Thomas asked for clarification regarding what should be evaluated. They could evaluate the Ethics Subcommittee and its value, the CDC ethics infrastructure; how the CDC infrastructure changes over time and the Subcommittee's effect on the change; the ethics skills of CDC staff apart from the infrastructure; and the level of ethics in CDC actions and products. All of these items are worthy of evaluation, but they should be specific regarding what they are willing to take on.
- Dr. Macklin reminded the group that an evaluation was included in their meeting packets, and she asked them to turn in their forms.
- Dr. Bernier noted that the internal PHEC has been working on a discussion paper that describes elements of public health work at CDC. They will circulate the document to the Ethics Subcommittee for comment. It includes a list of what the CDC internal committee believes to be the benefits of public health ethics at CDC. This list of benefits might be a logical place to begin when deciding what to evaluate.

Demonstration of CDC Public Health Ethics Intranet Site

Roberto Garza, M.P.A., M.S., ORISE Fellow
Office of the Chief Science Officer
Centers for Disease Control and Prevention

Mr. Garza officially unveiled the CDC Public Health Ethics (PHEC) Intranet site. He thanked Dr. Barrett for her help throughout the process of creating this site as well as the Internet site. He also thanked a number of other consultants and contributors.

In creating the Intranet site, his goal was to build a site that consumers would return to, that was uncluttered, and was simple and intuitive. The site is accessible through a link to the Office of the Chief Science Officer on CDC's Intranet. A movie on the front page of the site contains phrases from the PHEC's mission statement. The front page of the site also has a "spotlight" section with new or pertinent information. A one-sentence description of PHEC and what it does is part of the first page, and it includes examples of ethical dilemmas that CDC staff might confront.

The website includes links to information on what is public health ethics, how public health ethics can enhance CDC activities, and the vision, mission, and goals of PHEC. Their mission is to "ensure health and improve trust."

A full record of all PHEC meetings is on the site, including agendas, minutes, PowerPoint presentations, and handouts. The site also describes the Ethics Subcommittee, its membership roster, and its meeting agendas and minutes. A list of resources is provided for visitors to conduct their own research. Mr. Garza noted that the list of resources was provided by Fred Grinnell at UT Southwestern. The site includes a full record of all public health ethics trainings at CDC.

The website describes how CDC staff can request an ethics consultation. First, the staff member contacts his or her Division's Public Health Ethics Lead. Next, the staff member downloads a discussion document which outlines the guidelines and procedures for doing a consultation. They hope to develop "interactive ethics" in the coming months. This feature will function like a "blog" in which an ethical dilemma is posted to generate discussion. CDC capacity will increase as staff become familiar with public health ethics dilemmas. After a few weeks of discussion, the commentary could be summarized for a "teaching moment."

Discussion Points

- Dr. Arras asked whether the external Ethics Subcommittee could have access to this site.
- Mr. Garza explained that only CDC staff have access to the Intranet site. He described the Internet site, which is housed on www.cdc.gov. This page includes a simple description of the public health ethics initiative. It will become more interactive and offer products in the future.
- Dr. Barrett said that the pandemic influenza document would be posted on the Internet site. The Intranet site has more information than the Internet site now.
- Dr. Koenig said that members of the Ethics Subcommittee might want to see the Intranet site and have access to previous PHEC meeting minutes. She wondered whether they could have a way to log onto the site.
- Dr. Barrett suggested that some of the information posted on the Intranet could be posted on the Internet, since it was doubtful that Ethics Subcommittee members could have access to the Intranet.
- Ms. Kinlaw wondered whether a password on the Internet site could allow Ethics Subcommittee members to access some of the information on the Intranet site. Mr. Garza said that he would find out whether access would be possible.
- Dr. Gamble said that they hoped to encourage people at the local and state levels to begin to do ethics consultations. The step-by-step process on the Intranet site could be helpful, therefore, to people outside CDC. She further noted that a Google search on "public health ethics" returns the CDC site high on the list.
- Dr. Hooyman commented that any information on the Intranet site that is not proprietary could be put on the external site. Information to prepare for Ethics Subcommittee meetings could be for download as well. He further suggested that they employ text messaging technology during meetings. Dr. Barrett stressed that their meetings were open to the public, and all specific comments would become part of the record.
- Dr. Arras supported the idea of making as much of the Intranet information public as possible. He asked about the criteria that govern which information is included on which site. Dr. Barrett replied that level of clearance determines where information is posted, and PHEC tries to follow what most of the CDC advisory committees post, which tends to consist of agendas and meeting minutes. If they attain proper clearance and if the Ethics Subcommittee members are comfortable, then more information can be posted on the Internet.
- Dr. Mary Neumann suggested the alternative of an Extranet site, which is used by the Division of HIV/AIDS Prevention with some of their multi-site research projects. The Extranet site is password-accessible by project officers and external Principal Investigators. The contents of the Intranet could be duplicated on such a site. Draft materials could be included on this site as well, where they are not likely to be permitted on the Internet site.
- Dr. Barrett said that they have been exploring Site Scape, a document-sharing approach that involves outside persons logging into a central site with passwords. Documents could also be shared before meetings in this manner.

- Dr. Arras stressed the potential educational value of this kind of website. For instance, the President's Council on Bioethics maintains a powerful website with summaries of their meetings and lists of resources. An Internet site is an opportunity to educate the public on these issues.
- Ms. Kinlaw complimented Mr. Garza and PHEC on the impressive site.
- Dr. Koenig hoped that the Extranet "mirror" site would be possible.

Public Comment Period

Dr. Barrett asked whether anyone wished to make public comment. No comments were offered.

Ethical Considerations for Non-Research Data Collection

Lisa M. Lee, Ph.D, Assistant Science Officer
Office of the Chief Science Officer
Centers for Disease Control and Prevention

Dr. Lee offered an update on the current status of the Office of Human Research Protections (OHRP) guidance for defining research vis a vis public health practice. There are two types of public health information and data collection: research and practice. Fundamentally, practice includes all things that are not research, including public health surveillance, program evaluation, outbreak investigation, and, at the local level, service information. CDC is committed to protecting individuals and communities who participate in all public health activities.

Protections are associated with each type of information collection. The federal human subjects regulations or "Common Law" to protect research participants, 45 CFR Part 46, are familiar to most people. A variety of protections exist for participants in practice activities as well. Most of them exist at the state and local level through legislation or policy at the state level; therefore there are inconsistencies across states. Ideally, comprehensive and consistent legislation would exist in every state or at the federal level.

In 1999, CDC wrote a document called "Guidelines for Defining Public Health Research and Public Health Non-Research." The document was a collaborative effort with a number of partners, including the Council of State and Territorial Epidemiologists (CSTE) and Office for Protection of Research Risks (OPRR), which evolved into OHRP now housed in the Department of Health and Human Services. Most surveillance systems and program evaluation activities conducted in public health was determined not to be research. These guidelines still govern public health's work. Last year, OHRP drafted a guidance document which reflects that office's interpretation on research versus non-research. This document redefines information collection done as part of public health practice as research All public health activities, then, will be subject to the common law. All HHS agencies that are affected by this redefinition have read and are commenting on the draft guidance. When HHS comes to an internal consensus, a document will be posted for public comment.

Dr. Lee said that much of CDC's activity in promoting health by preventing and controlling disease, injury, and disability would be impeded if the agency were forced to consider all of its public health activities as research. Further, CDC is not convinced that review under 45 CFR Part 46 would improve the protections that already exist for public health data that are not research. The common rule was based on an individual biomedical and behavioral research model. This model does not work for certain types of research, and it is not certain that it will add to protection for non-research activities. Given its potential extraordinary administrative burden and its potential to incapacitate many of the tasks directly related to CDC's mission, the draft guidance from OHPR has caused consternation at CDC.

All HHS agencies affected by the redefinition were invited to respond and comment on the draft guidance. CDC's response defined the roles and responsibilities of CDC and public health and how those roles and responsibilities differed from individual, biomedical and behavioral research. The response outlined the potential, significant negative impact that the redefinition would have on CDC's ability to carry out its mission and discussed some of the core concepts of the regulatory definition of research. The CDC response further proposed that the draft guidance does not align with the original intent of the definition of research in the common rule. CDC's response asserted that public health's patient not the individual, but the community. 45 CFR Part 46 does not oversee individual interactions with providers and patients and is not appropriate to oversee non-research activities with public health and its patient, the community. Public health is guided by principles of equity, social justice, efficiency, and fiscal responsibility. Public health uses evidence-based activities to intervene with populations.

Internally, CDC staff have discussed whether "research" is defined by a standardized method, involves sampling, or including a statistical test. Public health practice, especially surveillance, may use some of the same robust, standardized methods as research. This criterion alone does not differentiate practice from research. Staff have also called for an examination of the assumption that an IRB review is the best way to protect participants in non-research activities. Generally, public health activities pose minimal risk and protections already exist. CDC is not sure that the gain is worth the cost.

CDC has also discussed the major impact that changing these definitions would have on their local public health partners. If local health departments require physicians to report a disease event that becomes research, then the physician is in a healthcare dilemma: does the physician follow the law stating that every case must be reported, even if the patient does not consent? Localities will be placed in untenable situations.

The CDC-wide and HHS-wide discussions are ongoing. The hope is to continue to use the thoughtful and thoroughly vetted guidances that were created in 1999 which define research based on its primary purpose or fundamental objective. The guidelines refer to this purpose as "intent" or "primary intent." It has become clear that the word "intent" is troublesome for some. The word refers to the primary purpose or fundamental objective of the activity. Research's intent is to generate or contribute to generalizable knowledge and could include activities that offer no direct benefit to participants. The intent of non-research is to prevent or control disease, disability, or injury and to improve health in a specific population. Although knowledge, even generalizable knowledge, may result from public health activities, the primary intent is to prevent or control disease; therefore the activities are designated as public health practice.

OHRP released the guidance in mid-2006. All affected agencies had an opportunity to respond, and they have met in person and by phone. The comments are being compiled and the revised

guidance will be distributed to agencies in March 2007. [Note: This target date has been deloyed to Summer 2007 per OHRP]. Next, HHS will convene the agencies for a final "walk-through" for unresolved issues and to come to a consensus on the document or state areas of further disagreement. The guidance will be submitted to the Assistant Secretary for Health for comments and changes, and there is a plan for public comment. Until HHS releases an official guidance, CDC continues to base its work on the 1999 guidance and interprets the definition of research or non-research to be based on the primary intent of the activity.

CDC hopes to describe a framework for protecting the rights and welfare of individuals and communities involved in any public health activity. A large literature exists on this issue. Dr. Lee hoped not to create a new framework, but synthesize existing recommendations and to help CDC operationalize and validate them.

While this issue includes many questions, we are not attempting to develop the ethics of public health. This activity will focus on the small piece of protection. Nor or we seeking to define the boundaries of research versus non-research. The question here is, given that an activity is determined to be non-research, how can CDC be ethical and responsible in protecting people and communities involved?

Discussion Points

- Dr. Macklin commented that some of their background material describes the difference between CDC's distinction between research and non-research and the states' view of the distinction. The distinctions are made differently at the different entities: where CDC bases its definition on intent or purpose, state departments of health approach the question from a stance of, "if we do it, it is not research; if an academic does it, then it is research." Their distinction is based on the actor, even if the methods, techniques, and questions are the same. She wondered if these differences create conflict between CDC and state health departments.
- Dr. Lee replied that 45 CFR Part 46 refers to research that is funded through federal dollars. Most state health departments are well-funded through federal dollars. If the CDC is involved in a project at any level, either via funding or through expertise that is provided, then the work is subject to these rules and the federal definition.
- Dr. Koenig felt that this movement toward a redefinition was troubling. She wondered whether all of the comments have already been provided to OHRP and whether CDC knows how the final guidance will be worded.
- Dr. Lee explained that CDC received the draft guidance in June 2006 without an invitation to participate in its creation. It was clear that several meetings would give the affected agencies an opportunity to comment. CDC's response was the crux of Dr. Lee's presentation. Many of the other affected agencies such as the Centers for Medicare and Medicaid Services (CMS) provided responses were in line with CDC's perspective. Even though the implications for NIH are limited, that agency was also aligned with CDC. This feedback has now been provided and they are in the process of clarifying the feedback through conference calls. OHRP hopes to complete and distribute the revision by March 2007.
- Dr. Koenig suggested that independent of CDC, the Ethics Subcommittee draft a letter including assessments of the redefinition and send the letter to the Advisory Committee of the OHRP. This letter could come from the perspective of two ethics groups trying to intersect with each other and make the point of how problematic these changes could be. This activity is within the Subcommittee's purview and authority. She volunteered to draft this letter.

- Dr. Lee commented that the actual guidance has not been distributed outside of HHS because it is still under revision. CSTE learned of the new guidance and expressed a letter of concern which was submitted with CDC's response. Ultimately, there will be a public comment period.
- Dr. Koenig said that future responses should address the issue of emergency. She added that hinging the response on the distinction between research and non-research might not be the most effective approach.
- Dr. Lee replied that the document itself focuses on that boundary.
- Ms. Kinlaw asked about the impetus behind this "sea change" to redefine collection of information to be researched.
- Dr. Lee felt that the guidance would probably not be described as a "sea change." It could be asserted that no guidance ever existed on the differences between research and non-research. The individual biomedical research model does not suite public health, so CDC has done its best to fit into the model because CDC is an HHS agency and therefore bound by its policies. The 1999 guidance was intended to help researchers understand how their work fit into the model. OHRP's decision to create a guidance was partly based on program announcements that had been sent to the Department for clearance. The Department felt that some of these programs resembled research, even though CDC felt that they were surveillance or program evaluation and clearly not research. CDC replied that according to its definition of research versus non-research, the development of which included OHRP's predecessor, the proposed work was not research. OHRP reviewed CDC's guidance, which led to the development of this new guidance.
- Chad Heilig noted that OHRP has been in discussion with other agencies about the interpretation or definition of research. Their efforts have included the entire Department, including NIH, CMS, and FDA.
- Dr. Lee said that CMS, SAMHSA, and CDC are probably most affected by this change, but NIH's concerns have been voiced as well.
- Mr. Jennings suggested that a recent report from the Hastings Center might be helpful. This report refers to this topic in relationship to quality improvement. Its authors addressed the question of the managerial oversight and protection that should be in place for non-research activities other than those covered by IRB systems. The report addresses the inadequacies of the regular IRB system by asserting that if some risk is associated with the activity, then a special kind of review mechanism that is knowledgeable about and appropriate to the activity. Normal IRBs that consider a different kind of research might not evaluate quality improvement appropriately. This observation may not apply to the public health surveillance context, but it could help CDC add details to their response and to craft their managerial structure for oversight of non-research activities beyond the federal regulations.
- Dr. Lee said that they are not looking to PHEC to define research and non-research, but rather to protect the 1999 definition as much as possible. She then addressed the idea of an alternative to an IRB such as a practice review. Systems, laws, and policies in every state protect sensitive public health data. These protections are not consistent across states, though, so they aspire to create an overarching model for equal protections so that public health research does not operate under 50 different systems, but one system.
- Dr. Arras was unclear regarding the rationale for OHRP's suggested rule change. Further, he asked for a discussion regarding how to tackle this problem without relying on the distinction between research and non-research.
- Dr. Lee did not know the motivation behind the rule change. OHRP's proposed definition does not change the common rule, but reinterprets it. Legislation will not be changed.
- Dr. Arras asked about the argument and reasoning behind the change. Dr. Levine clarified the original intent of the definitions of research and non-research, from which the proposed changes depart. He was among the authors of the original definitions. A number of

physicians informed the Senate in 1973 that distinguishing between research and the practice of medicine would be difficult. At the time, investigational work was called "research" based on the FDA's definition of investigational drugs and on the idea that every surgical procedure is an "experiment" in the strictest sense. Legislation created a Commission to consider the boundaries between biomedical or behavioral research and the "routine and accepted practice of medicine." Dr. Levine considered the boundaries and drafted definitions. He concluded that research and practice are far apart and that boundary disputes concerned the validation of drugs. The Commission considered the boundaries between clinical practice and research, not the boundaries between public health practice, quality improvement work, evaluation of health benefit programs, and other activities.

- As the chair of the External Review Group to CDC in the early 1990's, Dr. Levine recommended that rather than redefining categories, researchers pursue exemptions. There is ample precedent for special case exemptions, which began for research in the field of policy and benefits programs. Groups seem to seek to redefine "research" so that it does not include their interests, but each group's separate definition includes elements that other groups want to exclude. Dr. Levine felt that OHRP has taken this issue on because of complaints from different sectors, including quality improvement, program evaluation, and others. The Secretary's Advisory Committee on Human Research Protection recommended that OHRP revise the policies. OHRP's revision does not appear to respond to any of the groups' needs, but reinterpret the original definitions so that they embrace the categories that were never considered when the definitions were created.
- Dr. Levine commented on the idea that research definitions are based on the intent of the research. He had been engaged in debates regarding how to define intent and whether intent should be based on the project or on the investigators. Behaviorists feel that only actions can be monitored, not intent. However, IRBs must approve projects before they are completed. By way of compromise, the guidance include the word "design" to include a description of behavior as well as the intent of the research.
- Dr. Koenig posited that other motivations might underlie this move toward change, including debates regarding the very definition of a "human" in human subjects. The reflected that these guidelines seem not to benefit any of the parties and agencies involved. The change in interpretation will affect every hospital and organization. No group will be able to engaged in quality control.
- Dr. Mark White commented that front page of that day's *New York Times* had an article about IRB "mission creep" and how it applies to anthropologists and historians.

Development of Ethical Guidance for Non-Research Data Collections

Drue Barrett, Ph.D., Public Health Ethics Coordinator
Office of the Chief Science Officer
Centers for Disease Control and Prevention

Dr. Barrett spoke about how to proceed on this issue. After a number of internal discussions, the PHEC concluded not to try to define research versus non-research; rather, they hope to develop ethical guidance for CDC staff and external partners for efforts that are considered to be non-research. They hope that the guidance will be useful for people who are involved in research and IRBs as well.

PHEC has talked with CDC's Human Research Protection Office (HRPO) and the Office of Public Health Practice, and both groups feel that this guidance will be useful. Therefore, they suggest forming a workgroup of members of PHEC, interested CDC staff, and members of the Ethics Subcommittee. They are in early stages of discussion regarding the products of the

workgroup. She asked which Ethics Subcommittee members would be interested in working on this issue.

Discussion Points

- Dr. Macklin noted that Ethics Subcommittee members are involved in many workgroups. She therefore volunteered to help with the effort. Dr. Gamble also volunteered.
- Dr. Koenig repeated her offer to create a letter for OHRP and asked for Dr. Levine's historical input. She said that if the Subcommittee did not feel that a letter would be a useful strategy, then she could write the letter as a citizen during the public comment period.
- Dr. Lee addressed the issue that Dr. Levine raised of vocabulary, including research intention, research design, purpose, and fundamental approach. They have struggled to find a common vocabulary. If they can establish a comprehensive protection plan for public health services, a common vocabulary is needed. Regarding the issue of seeking exemptions for projects based on the current definition of research, many issues need thought and clarification. For example, CDC works with hundreds of community-based organizations that do not have IRBs and would not know how to create one. Asking these groups to apply for exemptions would put a great burden on public health practitioners, not all of whom work in a public health department.
- Dr. Levine responded that by its nature, the IRB cannot always convene quickly or to answer exemption requests. The field of quality improvement revises its protocols frequently, and the rules from OHRP state that every change in protocol must be reviewed and approved at a meeting. Since the IRB is not an appropriate mechanism, the quality improvement field has drafted the idea of creating a body responsible for ethical conduct in their field. This body would devise its own rules and procedures in response to the needs of the field and would not necessarily have to review every project in the field, but it would set standards. He then addressed the question of how much risk is tolerable when using research-type procedures in public health. Public health cannot conceive of the risks and impacts that go on in the public benefits program, such as research designed to evaluate changes in aid for dependent children programs. Applying for exemptions removes arguments regarding which projects are research and which are practice.
- Dr. Macklin asked Dr. Lee whether she needed further assistance from the Ethics Subcommittee. Dr. Lee answered that she would appreciate gathering a group to think additionally about how to protect participants in non-research projects and perhaps to create a framework or model to operationalize those suggestions. Dr. Macklin clarified that this endeavor could lead to a document or a letter to OHRP. .
- Dr. Koenig pointed out that suggesting protections for non-research participants depends on the CDC's ability to call its work "practice."

Meeting Wrap-Up and Next Steps

Dr. Macklin led the members in a review of action items and potential future agenda items that were raised over the course of the meeting.

Action Items

- The workgroup on genomics and the release of test results will take the Ethics Subcommittee's feedback and generate a new draft for the Subcommittee's review at the next meeting. Discussion of the more general ethics guidance regarding genomics and public health investigations will lead to additional considerations and more substantive guidance. Dr. Koenig and Dr. Hooyman need additional assistance from Subcommittee members to participate in this effort. Dr. Gamble agreed to join this workgroup.
- Dr. Arras and Mr. Jennings heard a great deal of feedback regarding the draft of the white paper on ethical issues relating to emergency preparedness and response. They will produce a draft based on their outline and the Subcommittee's feedback.
- The Ethics Subcommittee will follow up on the possibility of community consultations or engagement regarding ethical issues associated with emergency preparedness and response. Dr. Macklin commented that "engagement" is part of an implementation process and occurs when an activity is in process. Their hope for this activity is to consult communities about these issues. The possibility of conducting these activities and acquiring outside funds will be discussed internally at CDC.
- The Ethics Subcommittee did not completely resolve the question of commissioned papers for the white paper on emergency preparedness and response. One proposal was to omit the papers on distributive justice and civil liberties, as these topics have been discussed extensively in the literature. History and psychology were suggested as additional commissioned paper topics. Still unresolved, however, is the need for the commissioned papers in serving the writing of the white paper, and who the authors of the commissioned papers might be. The original timeline for this work was likely unrealistic. Other suggestions for this work included scheduling meetings with CDC staff responsible for emergency preparedness and including the authors of the commissioned papers, if the papers are written.
- The pandemic influenza guidance document will be complete in May. The ethical guidance is complete. The Ethics Subcommittee will hear an update and follow-up on the guidelines in June.
- A new workgroup for non-research data collections will include representatives from the internal and external committees.

Next Meeting

Dr. Macklin indicated that the next meeting date would be June 14-15, 2007. The Subcommittee clearly needs to meet for a day and a half, if not for two full days.

Discussion Points

- Dr. Barrett asked whether attendees preferred starting the meeting on the afternoon of the first day, thereby only requiring a one-night stay. Another option was to conduct the meeting over a full first day.
- Dr. Macklin said that they could discuss timing questions on e-mail.
- Dr. Arras expressed concern about the issue of commissioned papers for the emergency preparedness and response white paper. He did not feel that they should wait until June to resolve the question. Funds are available for up to six commissioned papers.
- Dr. Koenig suggested that Mr. Jennings and Dr. Arras serve as the final arbiters of the paper topics and authors, with input as needed from the Ethics Subcommittee, particularly regarding the authors.
- Dr. Macklin hoped to learn the topics and authors as well as the instructions that the authors will be given. This effort should follow an outline in order to maintain a relationship with the white paper and to address its issues, rather than the projects and interests of the authors.

- Ms. Kinlaw noted that some of the proposed categories for commissioned papers do not require a new position paper, but a review of the state of the literature.
- Dr. Gamble said that in her work with commissioned papers, she provided the authors with a list of questions to answer.
- Dr. Koenig said that even though a great deal of literature has been produced regarding distributive justice, literature on the issue of stockpiling is not prominent.
- Dr. Barrett clarified that the workgroup would create a list and collect input on it, but the final decision rests with the workgroup. She also noted that a new item on the June meeting agenda is the issue of partnering with industry. People who work in partnership within CDC will present overviews of their activities, and then the Ethics Subcommittee will discuss where to focus its activities.
- Dr. Dixon expressed his hope that their discussion regarding partnerships would be broad and include more than just partnerships with industry.
- Dr. Barrett reminded the attendees to complete their evaluation forms and leave them with her or e-mail them to her.

Closing Session

Dr. Macklin thanked the Ethics Subcommittee and the PHEC members for their excellent input, and for contributing their valuable time to the joint meeting.

With no further business brought before the Ethics Subcommittee or PHEC, Dr. Macklin adjourned the meeting at 3:30 PM on February 28, 2007.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

7.03.07
Date

Ruth Macklin, Ph.D.
Chair, Public Health Ethics Subcommittee

ATTACHMENT 1
List of Participants

February 27, 2007

Ethics Subcommittee Members
Dr. Ruth Macklin, Chair
Dr. John Arras
Dr. Georges Benjamin
Dr. Mary des Vignes-Kendrick
Dr. Vanessa Northington Gamble
Dr. Thomas Hooyman
Mr. Bruce Jennings
Ms. Kathy Kinlaw
Dr. Barbara Koenig
Dr. Robert Levine
Dr. James Thomas

Designated Federal Official for Ethics Subcommittee
Drue Barrett

PHEC Members
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Roger Bernier
Scott Campbell
Steve Coughlin
Jan Devier
Richard Dixon
Barbara Ellis
Roberto Garza
Michael Grays
Gail Horlick
Mary Leinhos
Brian Lindsey
Aun Lor
Mary Neumann
Salaam Semaan
Tom Simon
Anne Sowell
Mark White

Other CDC Staff
Stephanie Bailey
Michele Beckman
Diane Broadalski
Linda Demma
Nicole Dowling
Betsey Dunaway
Lucinda England
Jill Ferdinands
Marta Gwinn
Chad Heilig
Sharona Hoffman
Mary Jenkins
Jodi Keyserling
Shin Kim
Katherine Kolor
Kay Lawton
Kathleen McDuffie
Cynthia Moore
Mary Patrick
Joan Redmond-Leonard
Marilyn Radke
Sonja Rasmussen
Julie Robitaille
Carol Rubin
Karen Steinerg
Venkatachalam Udhayakumar
Diane Smelser
Lyna Zhang

February 28, 2007

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Dr. Vanessa Northington Gamble
Dr. Thomas Hooyman
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Roger Bernier
Scott Campbell
Steve Coughlin
Jan Devier
Richard Dixon
Shahul Ebrahim
Barbara Ellis
Debraelee Esbitt
Roberto Garza
Gail Horlick
Mary Leinhos
Aun Lor
Josephine Malilay
Mary Neumann
George Ryan
Scott Santibanez
Salaam Semaan
Anne Sowell
Rachel Weiss

Other CDC Staff
Richard Besser
Carolyn Bridges
Richard Goodman
Sudevi Gluosh
Chad Heilig
Margaret Haering
Sharona Hoffman
Heather Horton
Jodi Keyserling
Lisa M. Lee
Sherline Lee
Deborah Levy
Kathleen McDuffie
Daphane Moffett
Nicki Pesik
Harold Pietz
Joe Posid
Joan Redmond-Leonard
Marilyn Radke
Von Roebuck
Toscha Stanley
James Stephens
Nicole Smith

ATTACHMENT 2
Acronyms Used in This Report

ACD	Advisory Committee to the Director
ACIP	Advisory Committee on Immunization Practices
APHA	American Public Health Association
APPE	Association for Practical and Professional Ethics
ASBH	American Society of Bioethics and Humanities
ASPH	Association of Schools of Public Health
ASTHO	Association of State and Territorial Health Officials
CDC	Centers for Disease Control and Prevention
CLIA	Clinical Laboratory Improvement Amendments
CMS	Centers for Medicare and Medicaid Services
COGH	Coordinating Office for Global Health
COTPER	Coordinating Office for Terrorism Preparedness and Emergency Response
CSTE	Council of State and Territorial Epidemiologists
DBDDD	Division of Birth Defects and Developmental Disabilities
DDE	Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
DFO	Designated Federal Official
DNA	Deoxyribonucleic acid
FACA	Federal Advisory Committee Act
FDA	Food and Drug Administration
FMO	Flavin-containing monooxygenase
GAIN	Genetic Association Information Network
EGAPP	Evaluation of Genomic Applications in Practice and Prevention
EIS	Epidemic Intelligence Service
FTC	Federal Trade Commission
GINA	Genetic Information Non-Discrimination Act
HHS	Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HUS	Hemolytic Uremic Syndrome
IOM	Institute of Medicine
IRB	Institutional Review Board
JAMA	Journal of the American Medical Association
MMWR	Morbidity and Mortality Weekly Report
NACCHO	National Association of City and County Health Officials
NBAC	National Bioethics Advisory Committee
NCBDDD	National Center on Birth Defects and Developmental Disabilities
NCEH	National Center for Environmental Health
NCZVED	National Center for Zoonotic, Vectorborne, and Enteric Diseases
NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
NIAC	National Infrastructure Advisory Council

NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NOAA	National Oceanic and Atmospheric Administration
NOPHG	National Office of Public Health Genomics
NSA	National Security Administration
NVAC	National Vaccine Advisory Committee
OHRP	Office of Human Research Protections
ORISE	Oak Ridge Institute for Science and Education
PHEC	Public Health Ethics Committee
PHEPR	Public Health Emergency Planning and Response
PHLS	Public Health Leadership Society
PHPPO	Public Health Practice Programs Office
SARS	Severe Acute Respiratory Syndrome
SNP	Single nucleotide polymorphism
UGT	Uridine phosphorylase (UDP) glycosyltransferase
UN	United Nations
VA	Veterans' Administration
WHO	World Health Organization