Testimony
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Statement for hearing entitled, "Viral Hepatitis: The Secret Epidemic"

Statement of

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Good morning, Chairman Towns, Ranking Member Issa, and other distinguished Members of the Committee. I am Dr. Howard Koh, the Assistant Secretary for Health in the Department of Health and Human Services (HHS or the Department). I am honored to be here today to discuss the silent epidemic of viral hepatitis in this country, and the coordinated steps the Department is taking to effectively address this significant public health problem through better prevention, care and monitoring efforts.

Viral hepatitis is a collective term describing liver inflammation or hepatitis caused by a group of several different viruses. Three viruses, Hepatitis A virus (HAV), Hepatitis B virus (HBV) and Hepatitis C virus (HCV) cause most viral hepatitis in the United States. Spread in unsanitary conditions, hepatitis A cases have declined significantly in the U.S. in recent years as a result of vaccination programs and food safety efforts. Today, I will focus my remarks on the prevention of HBV and HCV transmission and associated morbidity and mortality. Unlike HAV, HBV and HCV infections are blood-borne and often persist for years, resulting in ongoing (chronic) but usually asymptomatic liver inflammation, and in some cases scarring (cirrhosis) that leads to liver failure and/or and liver cancer. Chronic hepatitis is a major cause of liver cancer and chronic liver disease globally and in the United States.

HBV and HCV Disease Burden

Worldwide, 480 million to 540 million persons are living with chronic viral hepatitis, with 350 million[1,2] to 370[3] million infected with HBV and 130 million to 170 million infected with HCV.[4]

[1] Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. Int J Epidemiol 2005;34:1329--39

All told, chronic viral hepatitis afflicts about 1 in every 12 persons worldwide. About 54,000 persons with chronic hepatitis B infections immigrate to the U.S. annually. Chronic hepatitis causes considerable morbidity. Globally, an estimated 78% of primary liver cancer and 57% of liver cirrhosis are caused by chronic viral hepatitis and about one million deaths from viral hepatitis occur each year.[4] Liver cancer is the fourth -leading cause of death from cancer worldwide, the third -leading cause among men.[5] The most recent liver cancer surveillance data indicate that long-term liver cancer incidence is increasing in the U.S., with an average annual percentage change in incidence between 2001 and 2006 of 3.5% per year.[6]

In the United States, viral hepatitis remains no less of a problem; 3.5 million to 5.3 million Americans have chronic viral hepatitis.[7,8,9] The vast majority, an estimated 65 % and 75% are not aware they are infected with HBV and HCV, respectively.[7] In the absence of appropriate treatment, 15-40% of infected persons will develop liver cirrhosis.[10,11,12] Viral hepatitis is the leading cause of liver transplantation in the United States.[13] Co-factors, including HIV, excessive alcohol use, and fatty liver disease associated with obesity and diabetes, amplify the

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[2] World Health Organization. Hepatitis B. Geneva, Switzerland: World Health Organization; 2000. Available at http://www.who.int/mediacentre/factsheets/fs204/en/print.html

[3] W.M. Lee, Hepatitis B virus infection, *N Engl J Med* **337** (1997) (24), pp. 1733–1745.
[4] Perz, J.F., The contribution of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *Journal of Hepatology* 2006; 45 (4):529-538.
[5] WHO Cancer Fact Sheet No 297 Feb 2009. http://www.who.int/mediacentre/factsheets/fs297/en/print.html
[6] CDC. Hepatocellular carcinoma – United States, 2001-2006. MMWR 2010;59 (17:517-20).
[7] IOM (Institute of Medicine). *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C.* Washington, DC: The National Academies Press. At 21 (2010)
[8] Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med 2006;144:705--14
[9] CDC. Surveillance for Acute Viral Hepatitis – United States, 2007. 2009;58 (No. SS-3)
[10] CDC. Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. 2008;57 (No. RR-8)
[11] Lok AS, McMahon BJ. Chronic Hepatitis B. *Hepatology*2007; 45:507-539
[12] Seeff LB. Natural History of Chronic Hepatitis C. *Hepatology* 2002; 36:S35-S46.
[13] Brown RS Jr. Hepatitis C and liver transplantation. *Nature* 2005;436:973-978.

effects of viral hepatitis, hastening development of liver disease. Fifteen to thirty percent of all persons infected with HIV have chronic viral hepatitis,[14] and liver disease is now the main non-AIDS cause of death in HIV-infected persons.[15] In contrast to almost all other types of cancer, liver cancer rates have tripled over the last several decades,[16] fueled in large part by the progression of viral hepatitis to end-stage disease among persons infected years ago. In the United States, viral hepatitis causes 12,000 to 15,000 deaths annually,[17,18] and viral hepatitis-related illness, deaths, and costs are all expected to rise substantially in the coming years.

Viral hepatitis poses a major health threat for certain populations. Among persons aged 46 to 64 years (i.e., baby boomers), about 1 in 33 have chronic viral hepatitis.[9] One out of every 7 African American men in their 40s is living with chronic hepatitis C,[9] and approximately 1 in 12 Asian Americans is living with chronic hepatitis B.[19] Similarly, the profiles of persons with liver cancer mirror the demographic characteristics of persons with chronic viral hepatitis; liver cancer incidence is highest among Asians/Pacific Islanders, and is increasing among Hispanics, African Americans, baby boomers, and males.[20]

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[14] Sherman KE, Rouster SD, Chung RT, Rajicic N. Hepatitis C virus prevalence among patients coinfected with human immunodeficiency virus: a cross-sectional analysis of the U.S. Adult AIDS Clinical Trials Group. *Clin Infect Dis* 2002;34:831-7.
[15] D:A:D Study Group. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D study. *AIDS* 2010 [epublication May 6, 2010 ahead of print]
[16] Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. J Clin Oncol 2009;27:1485--91.
[17] Vogt T, Wise ME, Shih H, Williams IT. Hepatitis B Mortality in the United States, 1990-2004 [Abstract]. 45th Annual Meeting of Infectious Diseases Society of America, San Diego, CA; October 4-7, 2007
[18] Wise M et al. Changing trends in hepatitis C-related mortality in the United States, 1995–2004. *Hepatology* 2008;47:1–8.
[19] CDC. Screening for Chronic Hepatitis B Among Asian/Pacific Islander Populations – New York City, 2005. MMWR 2006; 55(18):505-509.
[20] CDC. Hepatocellular carcinoma – United States, 2001-2006. MMWR 2010;59(17;517-20.

New HBV and HCV infections add to the burden of chronic viral hepatitis and liver disease. In 2007, there were an estimated 43,000 new cases of HBV infection.[10] HBV is spread from mother to child at the time of birth, among household contacts through incidental blood exposures in the home, through injection drug use, and through sexual contact. Viral hepatitis transmission should never occur as a result of health care delivery, but transmission has been documented in a variety of health care settings when providers have failed to follow basic infection control practices. Rates of HBV infection are highest among adults, reflecting low hepatitis B vaccination coverage among persons with risks such as injection drug use and multiple sexual partners. Prevention of mother-to-child transmission is critical, as 90% of HBV -infected newborns remain infected[21,22,23], and about 1 in 4 die from complications of chronic viral hepatitis in later life.[11] Outbreaks of hepatitis B occur in persons not currently recommended to receive the vaccine, such as persons with diabetes, patients in outpatient settings, and residents of long term care facilities; they also occur in health care settings when providers fail to follow basic infection control.

Surveillance data suggest nearly 20,000[10] persons are newly infected with HCV annually in the United States. HCV is primarily a blood-borne virus spread through injection drug use. Transmission also occurs in health care settings as a result of unacceptable lapses in infection control, primarily related to the misuse of syringes and medication vials. Non-injecting drug users who snort cocaine and other drugs also have elevated risks for HCV, possibly from blood exposure associated with intranasal use. Perhaps typically thought of as an urban disease, HCV

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[21] Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. Proc R Soc Lond B Biol Sci 1993;253:197--201

[22] McMahon BJ, Alward WL, Hall DB, et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. J Infect Dis 1985;151:599--603.

[23] Hyams KC. Risks of chronicity following acute hepatitis B virus infection: a review. Clin Infect Dis 1995;20:992--1000

transmission has been detected among young drug users in suburban and rural communities. In addition, after reports from Europe for several years, sexual transmission of HCV has been detected among U.S. cohorts of HIV-infected men who have sex with men (MSM). In certain circumstances, HCV can be transmitted sexually and at the time of birth.

Public Health Prevention Measures to Address Viral Hepatitis

Public health measures can prevent transmission. These measures have helped our nation achieve remarkable declines in the number of new infections with both viruses. Safe and effective vaccines are available to provide long term protection from hepatitis B. In 1991, the Centers for Disease Control and Prevention (CDC) and the national Advisory Committee on Immunization Practices (ACIP) set forth an ambitious vaccine-based strategy to eliminate HBV transmission in the United States.[24] This strategy involves vaccinating newborns and older children, as well as vaccinating at-risk adults.

Routine vaccination of infants and catch-up vaccination of older children under federally - supported vaccination programs has successfully driven down rates of HBV transmission and acute cases of disease, with rates falling 82% from 8.5 cases per 100,000 population in 1990 to 1.5 cases per 100,000 population in 2007, the most recent year for which data are available.[10]

[24] CDC. Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States Through Universal Childhood Vaccination: Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991;40 (RR-13): 1-19. http://www.cdc.gov/mmwr/preview/mmwrhtml/00033405.htm

Rates have declined most dramatically—98%—among children aged 15 years and younger. Vaccine coverage among children aged 19 months to 35 months is 93%.[25,26]

In the United States, approximately 24,000 HBV-infected women give birth each year[27], most of whom are identified by prenatal screening. Their infants are recommended to receive protective hepatitis B vaccination and other prevention services. State and local prevention programs currently do not have the capacity to manage all of the estimated newborns who are exposed. To assure newborns exposed to HBV are protected, CDC recommends that all infants receive a birth dose of hepatitis B vaccine. In 2008, 55% of newborns received a birth dose in the first three days of life.[30] As not all newborns receive protective interventions, each year hundreds of infants are infected with HBV in the United States.[28]

Hepatitis B vaccine is also recommended for adults with sexual and blood exposure risks. As the result of improvements in infection control and ongoing hepatitis B vaccination, relatively few cases now occur in certain populations such as dialysis patients and healthcare workers that previously were considered to be at high risk. However, while the number of new cases has declined among adults, 95 % of all new cases are among adults. A high proportion of those cases occur among persons with risk behaviors such as injecting drug users, MSM, and persons with multiple sex partners. Rates are particularly high among males aged 25 to 44 years old.[10]

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[25] Estimated Vaccination Coverage* with Individual Vaccines and Selected Vaccination Series Among Children 19-35 Months of Age by State and Local Area US, National Immunization Survey, Q1/2008-Q4/2008† http://www2a.cdc.gov/nip/coverage/nis/nis_iap2.asp?fmt=v&rpt=tab02_antigen_iap&qtr=Q1/2008-Q4/2008

[26] CDC. National, State, and Local Area Vaccination Coverage Among Children Aged 19--35 Months --- United States, 2008. MMWR 2009;58: 921-926.

[27] CDC. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. MMWR 2005;54 (RR-16):1–31.

[28] CDC Unpublished Data

Unlike HBV, there is no vaccine yet developed for HCV. However, since HCV was discovered in the 1980s, the development of prevention interventions has caused a significant decline in new cases. Screening of donated blood and other tissues and organs now protects recipients of these donations. Screening, together with behavioral education, and access to clean syringes and drug treatment have had a role in reducing the number of new cases of HCV related to injection drug use[8]. In addition, the adoption of standard precautions in health care settings has reduced transmission risks for all blood -borne viruses, including HBV and HCV.

The onset of liver cancer and other liver disease can be prevented through screening and care for persons chronically infected with HBV or HCV. Current treatments can halt or even reverse the liver damage caused by viral hepatitis. New treatments on the immediate horizon hold even greater promise for a definitive cure. CDC recommends screening to identify persons with viral hepatitis and prevention and care services to reduce transmission and morbidity.

Prevention and care for viral hepatitis makes economic sense. Published studies estimate that medical costs for viral hepatitis run in the billions of dollars per year.[29,30] Numerous studies reveal the cost-effective benefits of screening and care for populations at risk for viral hepatitis.[31],[32],[33],[34] Hepatitis screening linked to vaccination and care is a cost -effective

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[29] JB Wong, GM McQuillan, JG McHutchison and T Poynard. *Estimating future hepatitis C morbidity, mortality, and costs in the United States*, American Journal of Public Health, Vol 90, Issue 10 1562-1569.
[30] Milliman Study for Vertex Pharmaceuticals. Consequences of Hepatitis C Virus – Costs of a Baby Boomer Epidemic of Liver Disease. 2009
[31] A Rajendra, JB Wong Economics of chronic hepatitis B and hepatitis C Journal of Hepatology, 2007 Oct: 47 (4):608-17. Epub 2007 Jul 30
[32] Kanwal F, et al., Treatment alternatives for hepatitis B cirrhosis: a cost-effectiveness analysis. The American Journal of *Gastroenterology*, 2006;101(9):2067-2089.
[33] Spackman DE, Veenstra D. A cost-effectiveness analysis of currently approved treatments for HBeAg-positive chronic hepatitis B. *PharmacoEconomics*, 2008;26(11):937-949.

prevention approach to eliminating health disparities for Asian and Pacific Island Americans.[35] Preliminary data from a CDC model show that by identifying and referring for appropriate care all HCV-infected persons in primary care, approximately 87,000 cases of end stage liver disease and 11,000 liver transplants can be prevented, and 840,000 undiscounted life years would be gained, with an estimated cost per discounted quality adjusted life year, or QALY, of $43,000. Similarly, preliminary estimates reveal that expanded HBV screening and care could avert approximately 140,000 cases of end stage liver disease and gain 3.3 million QALYs.

The Institute of Medicine Report

In January 2010, The Institute of Medicine (IOM) issued a report titled, *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C.* The report identified multiple barriers that have combined to create a situation in which inadequate public resources are available to support the prevention, care and monitoring needed to fully and effectively address this important public health problem.

The IOM report described deficiencies that have created adverse consequences for the health of our nation:

- Inadequate disease surveillance systems underreport acute and chronic infections, so the full extent of the problem is unknown;
- At-risk people do not know that they are at risk or how to prevent becoming infected;
- At-risk people may not have access to prevention services;

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[34] Wong JB, et al., Cost-effectiveness of interferon-alpha 2b treatment for hepatitis B e antigen-positive chronic hepatitis B. *Ann Intern Med*, 1995;122(9):664-675

[35] Hutton DW, Tan D, So SK, et al. Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B. *Ann Intern Med*, 2007;147(7):460-469.

- Chronically infected people do not know they are infected;
- Many healthcare providers do not screen people for risk factors or do not know how to manage infected people; and
- Infected people often have inadequate access to testing, social support, and medical management services.

The IOM called for an intensified, coordinated national effort to improve the prevention of viral hepatitis and better protect the health of Americans.

The HHS Response to the IOM Report

HHS and its agencies are fully committed to accelerating progress towards the prevention of viral hepatitis and associated disease in the U.S., and advancing this strategy. In January, HHS established an interagency work group on viral hepatitis, which I chair, that has diverse representation from HHS operating divisions. A work group subcommittee is currently drafting a comprehensive strategic action plan for HHS to improve the coordination of viral hepatitis prevention, care and monitoring activities within the Department. The action plan is grouped by focus areas: Increasing community awareness and provider education; strengthening surveillance for viral hepatitis; preventing viral hepatitis transmission through vaccination; preventing blood-borne transmission; and improving clinical preventive care and treatment services. The current timeline is to complete this action plan by October 1, fall 2010.

There are millions of persons who are unaware they have a potentially life -threatening disease. Major goals of viral hepatitis prevention programs are to screen high-risk persons and to increase the number of infected persons who know their status and are linked to preventive and care services. For communities experiencing health disparities, culturally appropriate education programs can increase awareness of this silent epidemic, and of the health benefits and vaccination and screening, while addressing issues of stigma. Provider education can increase understanding of screening and vaccination policies, interpretation of laboratory tests, and management of viral hepatitis care and treatment. Viral hepatitis services can be integrated with other appropriate prevention services for HIV, STD, and cancer. Public health surveillance and case management can link communities with viral hepatitis prevention and care services. .

HHS also recognizes the important health benefits of eliminating HBV transmission. State and local perinatal prevention have a proven track record of success and can provide the necessary services to eliminate HBV among newborns in this country. Studies have shown that cost is a major barrier to successful implementation of adult immunization strategies. Health reform provides new opportunities to increase uptake of immunizations recommended by the HHS Advisory Committee on Immunization Practices (ACIP).

More interventions are needed to prevent hepatitis C. Efforts to find an effective vaccine for HCV should be a continued priority. In the meantime, other new hepatitis C prevention tools must be developed, tested and translated into action. One avenue to explore is to refine and adapt HIV prevention strategies for hepatitis C prevention. Hepatitis C testing and counseling to increase awareness of infection status will promote safe behavioral practices. Together, these

approaches can substantially reduce transmission among injection drug users. HHS is working to ensure adherence to proper infection control practices are needed to reduce transmission risks in health care settings, including improved oversight and regulatory approaches, development of new technologies, and training for health care professionals. Rapid tests can improve access to screening, and new assays may improve detection of recent hepatitis C infection. Studies of HCV transmission will help form the evidence base for new interventions. Also, studies suggest that, if detected early, many hepatitis C infections can be cleared (i.e., cured)[36]. As new and improved therapies are introduced, research should be conducted to guide how best to use them to preserve the health of those infected and prevent transmission.

The HHS interagency working group will also examine ways to improve viral hepatitis surveillance. Effective prevention requires state and local systems that provide consistent and reliable reporting of new infections, rapid detection of disease outbreaks, and identification and referral of persons with chronic infection for appropriate care and treatment. Currently, CDC estimates that about only 10 percent of new cases of viral hepatitis are reported each year. Two-thirds of states report cases of HCV infection, but those that do have large backlogs of uninvestigated cases.[8] As a result, a clear picture of the nature and scope of chronic HCV infections across every State is not available at this time. HHS is working to improve monitoring of viral hepatitis.

[36] Licata A, DiBona D, Schepis F, Shahied L, Craxi A, Camma C. When and How to Treat Acute Hepatitis C? J Hepatol 2003;39:1056-1062

Viral Hepatitis Prevention Activities within HHS

Multiple agencies within HHS are working hard to maximize the impact of available resources in responding to the viral hepatitis epidemic and respond to the recommendations of the IOM report.

Centers for Disease Control and Prevention (CDC)

At CDC, the primary responsibility for prevention and control activities rests with the Division of Viral Hepatitis. Those activities are broadly grouped under four programmatic priorities:

1) Reduce illness and death by identifying persons with viral hepatitis early and referring them to care;
2) Eliminate hepatitis B transmission;
3) Develop, test and translate into action tools to decrease the incidence of HCV; and
4) Guide and evaluate prevention efforts by improving the monitoring of viral hepatitis.

To address those priorities, CDC currently supports viral hepatitis coordinators in 49 states and the District of Columbia. These coordinators are tasked with integrating viral hepatitis services with other public health efforts to reach populations at risk. While funding does not support direct service provision, the coordinators seek whenever possible to leverage available resources and integrate viral hepatitis education, vaccination, and screening with services provided by federally-supported STD and HIV testing and treatment sites, federally qualified health centers supported by the Health Resources and Services Administration, and other programs.

In addition to supporting coordinators, CDC assists states in responding to disease outbreaks by deploying field investigators and by conducting rapid laboratory serologic and genetic testing to identify sources of infection and direct control strategies. CDC also provides technical support to all states for monitoring acute and chronic infections, including assisting states in adopting surveillance for chronic HBV and HCV infections and investigating cases suggestive of the emergence of rare or new causes of viral hepatitis. Funding for enhanced surveillance activities is provided to 9 state and local health departments.

CDC's surveillance activities also include monitoring liver cancer incidence and prevalence through the National Program of Cancer Registries, in collaboration with the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Data indicate that liver cancer incidence rates vary widely across states, and persistent racial and ethnic disparities exist[21]. These surveillance efforts articulate the burden of liver cancer and can assist states in targeting prevention and control efforts, including primary prevention efforts targeted to the populations most at risk of contracting HBV and HCV.

To identify and address health disparities, CDC surveys populations at increased risk for viral hepatitis, including racial and ethnic minority communities, MSM, and injection drug users. CDC follows approximately 12,000 patients in care for viral hepatitis to study the implementation of recommended preventive and care services.

CDC also supports state and local perinatal prevention coordinators to prevent mother-to-child transmission of hepatitis B. This effort includes ensuring the screening of pregnant women,

vaccination of infants at birth, follow-up with infants to ensure completion of the vaccine series, and testing of infants to ensure the development of antibodies. Similarly, through immunization funding for its Adult Hepatitis B Vaccination Initiative, CDC has begun to close the gap in vaccination of at risk adults. Since the beginning of the Initiative in FY 2007, CDC has made approximately $42 million in Section 317 funds available for the purchase of hepatitis B vaccine for use in over 2,600 venues.

Healthcare-associated transmission of viral hepatitis is entirely preventable through adherence to basic infection control. In the area of healthcare-associated transmission of hepatitis, CDC monitors the size and scope of the problem and assists state and local health departments with healthcare-associated outbreak investigations. Perhaps most importantly, CDC identifies best practices regarding infection control and educates providers, patients and industry about these practices through evidence-based infection control guidelines, peer-reviewed publications, and educational campaigns.

In addition to CDC's work with the states, CDC conducts prevention research to guide policy and program development. CDC fosters development of new approaches to health education, investigation of new screening tests and strategies, studies of licensed and experimental vaccines, and the emergence and implications of viral mutations for diagnosis, prevention, and therapy.

Finally, CDC works with the World Health Organization and other partners to prevent viral hepatitis globally. As of 2008, a total of 177 countries had incorporated hepatitis B vaccine in their national infant immunization programs, and an estimated 69% of the 2008 birth cohort received hepatitis B vaccine. Worldwide, only about 27% of newborns received the birth dose of

hepatitis B vaccine.[37] The FY 2011 Budget includes an increase of 10 percent over the FY 2010 Omnibus to support these activities.

National Institutes of Health (NIH)

At NIH, the primary responsibility for hepatitis research and prevention activities rests with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Allergy and Infectious Diseases (NIAID). NIDDK and NIAID support many activities in hepatitis B and C research and education including the following:

Hepatitis B Research: NIAID supports basic and translational research on hepatitis B. Efforts include drug discovery and development and vaccine improvements, as well as many efforts related to HBV pathogenesis and the varying human responses to infection. In addition, the Institute supports many resources for outside investigators to screen and develop new HBV-specific therapeutic candidates at no cost. NIAID resources include tissue culture and animal model screens and preclinical drug development services. In addition, NIAID is currently soliciting applications for research on new classes of HBV therapies.

Hepatitis B Research Network: This multi-center research Network, established in 2008, aims to advance understanding of disease processes and natural history, as well as to develop effective approaches to treating and controlling hepatitis B. The Network currently includes 21 clinical sites across the United States, including Hawaii, and a central data coordinating center. The Network's centers are in the final stages of planning multiple clinical trials in both adults and

[37] CDC. Implementation of Newborn Hepatitis B Vaccination – Worldwide, 2006. MMWR 2008;57(46):1249-1252.

children that are responsive to the recommendations of the IOM report regarding pregnant women and at-risk populations.

Clinical Research on Hepatitis C: NIH conducts many clinical trials of available antiviral therapies against hepatitis C, such as the drug interferon. Research to develop a vaccine against hepatitis C is also a major priority for the NIH. Basic and applied studies on hepatitis C virus vaccine development are being funded by NIAID, NIDDK, the National Cancer Institute, and the National Institute on Drug Abuse, including those being conducted by the NIDDK intramural NIDDK Liver Diseases Branch and NIAID's Laboratory of Infectious Diseases.

Basic Research on Hepatitis C Virus Infection: NIAID and the NIDDK Liver Diseases Branch conduct basic research and fund research on how the hepatitis C virus infects human cells. New animal models and cell culture systems developed by NIAID and NIDDK-funded investigators are instrumental to advancing hepatitis C prevention and therapy. For example, high-impact research projects are developing a mouse model of hepatitis C virus infection and pioneering advanced tissue culture systems that mimic human liver biology for studying the viral life cycle testing new antiviral agents, and identifying viral and human host factors that may serve as targets for future therapies.

The NIAID-supported Hepatitis C Cooperative Research Centers seek to improve basic understanding of HCV pathology. This program, renewed in Fiscal Year (FY) 2010, sponsors five centers which will advance understanding of the host immune response to infection and the factors that determine whether HCV infections are cleared or persist chronically. The underlying mission of the Centers is to help define successful immune response to HCV and

identify new targets for drugs, vaccines, and other therapeutic strategies for the prevention or treatment of HCV infection.

NIAID intramural scientists and grantees pursue basic and translational studies on the pathogenesis and molecular biology of HCV, investigate the basic immunology of HCV infection, and partner with industry to further the development of HCV vaccines. NIAID scientists also are collaborating with international researchers to understand why cirrhosis is a fairly stable disease for decades in some patients, while in others it may lead to liver-related death or liver cancer. Investigators are performing genetic analyses and searching for biomarkers for the early detection of liver cancer.

NIAID currently is developing and evaluating new agents to treat HCV/HIV co-infected individuals and is supporting clinical research to define the most effective, long-term treatment strategies for HIV/HCV co-infecton. Currently, NIAID researchers are conducting several clinical studies of patients with chronic viral hepatitis at the NIH Clinical Center. These studies are focused on developing better therapeutics for the management of HCV infection in HIV co-infected individuals.

Trans-NIH and Trans-Agency Viral Hepatitis Research Planning: Strategic research plans, such as the trans-NIH *Action Plan for Liver Disease Research*, and the National Commission on Digestive Diseases' research plan, both developed with trans-NIH and trans-HHS input, highlight important research goals relevant to controlling hepatitis B and C. These plans (available at http://liverplan.niddk.nih.gov and http://NCDD.niddk.nih.gov) are currently being implemented by the NIH and partners in the larger research community.

NIH Consensus Development Conferences and Meetings: The NIDDK has provided leadership, along with other NIH Institutes, Centers, and Offices, and other professional organizations, for convening several consensus development conferences on hepatitis B and C, including Management of Hepatitis C (2002), and Management of Hepatitis B (2008). The NIDDK also helped to organize a meeting on Management of Chronic Hepatitis B in 2006, as well as the International Symposium on Viral Hepatitis and Liver Disease in 2009. Recommendations from these conferences and meetings helped to inform the IOM's report.

Health Resources and Services Administration (HRSA)

Within HRSA, many of the activities related to Hepatitis B and C are overseen by the HIV/AIDS Bureau (HAB) and the Bureau of Primary Health Care (BPHC). HAB and BPHC are collaborating on ways to increase screening and referral to treatment for Federally Qualified Health Center (FQHC) patients who are mono-infected with hepatitis C and those who are dually infected with HIV and hepatitis. Examples of HAB and BPHC hepatitis B and C activities include the following":

- HRSA/BPHC is working with the Association of Asian Pacific Community Health Organizations (AAPCHO) and the White House Initiative on Asian American and Pacific Islanders to develop strategies for improving prevention and treatment of viral hepatitis among Asian and Pacific Islander Americans.
- Hepatitis C Treatment Expansion Initiative - Evaluation and Technical Assistance Center (CFDA: 93.928): Under the Special Projects of National Significance Program of the Ryan White HIV/AIDS program, administered by HRSA's HIV/AIDS Bureau, this initiative will provide funds for up to 2 years to build capacity among Ryan White-funded

organizations through the implementation of demonstration models for enhancing HCV treatment protocols in integrated HIV medical treatment settings in the context of providing HIV primary medical care and treatment to individuals co-infected with HCV. In addition to treatment implementation, awarded organizations will also assist the Evaluation and Technical Assistance Center in assessing the effectiveness, feasibility and costs of these service delivery models.

- HRSA supports FQHC services for viral hepatitis treatment and prevention in the following ways:
    - Requiring that, as a condition of health center funding and the FQHC "Look-Alike" designation, all federally-funded health centers and FQHC Look-Alikes provide diagnostic lab services, screenings for communicable diseases, and immunizations against vaccine-preventable diseases, including HBV.
    - Requiring that federally-funded health centers and FQHC Look-Alikes provide health education to patients and the general community. This includes patient education on diseases that may be prevalent in the community or for which the population may be vulnerable, such as viral hepatitis.
    - HRSA promotes screening and treatment of viral hepatitis through a national cooperative agreement. Activities resulting from this agreement include raising awareness of viral hepatitis among health center providers and patients, and providing technical assistance on strategies to treat and prevent viral hepatitis. For example, HRSA recently met with the National Alliance of State and Territorial AIDS Directors and the Northeast Hepatitis Coordinators' Alliance to strategize on hepatitis prevention and treatment in FQHCs.

- In order to better monitor hepatitis incidence in health center patients, HRSA revised its health center grantee reporting mechanism to track patient hepatitis rates.
- The only successful treatment available for endstage liver disease due to HCV is liver transplantation. HRSA provides oversight for the Organ Procurement and Transplantation Network (OPTN) operated under contract by United Network for Organ Sharing (UNOS). Currently there are 16,072 patients on the nationwide liver transplant waiting list, and 6.320 liver transplants were performed in 2009. Because of the critical shortage of donor organs, 1,461 patients died in 2009 waiting for a liver transplant. About 40% of liver transplants performed in the U.S. have HCV, and experts expect this number to rise significantly during the next decade. Although liver transplantation can successfully treat chronic liver failure due to HCV, a major challenge facing these recipients is recurrence of HCV in the new liver that eventually leads to reduced graft survival.[38]

Food and Drug Administration (FDA)

The FDA has multiple centers working on hepatitis B and C prevention activities:

CDER Activities Relating to Hepatitis B and C: FDA's Center for Drug Evaluation and Research (CDER) has the responsibility of reviewing drug products and certain biological products including therapeutic proteins and monoclonal antibodies for the treatment and/or prevention of viral hepatitis including hepatitis B and C.

[38] TD Schiano and P Martin, Review: Management of HCV infection and liver transplantation, International Journal of Medical Sciences (2006) 3(2):79-83.

Currently, there is a great deal of interest within industry in developing treatments for both hepatitis B and C. FDA has approved five drugs and two interferon products to treat hepatitis B. FDA has approved three distinct types of interferon products from three different sponsors for the treatment of hepatitis C. FDA has also approved multiple versions of ribavirin, a drug approved to increase the effectiveness of intereferons in the treatment of hepatits C.

CDER also regularly meets with numerous issue groups and pharmaceutical companies to discuss drug development plans, protocols and proposals. CDER is currently collaborating with the Forum for HIV Research to plan a workshop on hepatitis C drug development. FDA also held a public meeting in April 2010 to discuss expanded access to direct-acting antiviral agents for the treatment of chronic hepatitis C infection in patients with unmet medical need. CDER is in the process of drafting a guidance to industry on the development of direct-acting antivirals for the treatment of hepatitis C. And lastly, FDA issued a Citizen Petition response which recognized the crisis of hepatitis C among people with bleeding disorders and the need to take definite steps to allow people with bleeding disorders and hepatitis C and other patients with hepatitis C with no treatment options to have access to promising investigational drugs beyond current clinical trials.

CBER Activities Relating to Hepatitis B and C: The FDA's Center for Biologics Evaluation and Research (CBER) regulates biological products for human use under applicable federal laws, including the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act. CBER protects and promotes the public health by ensuring that biological products are safe and effective and available to those who need them. CBER also provides the public with information

to promote the safe and appropriate use of biological products. CBER regulates an array of diverse and complex biological products, both investigational and licensed, including vaccines, blood and blood products, and human tissues and cellular products. In carrying out its mission to ensure the safety, purity, and potency (effectiveness) of biological products, CBER engages in a number of activities pertinent to HBV and HCV.

Scientists in CBER laboratories are currently working on several research projects pertaining to HCV. One research program, *Hepatitis C Vaccines: Development of in vitro and in vivo Systems for HCV Replication and Evaluation of Vaccine Efficacy*, seeks to evaluate new methods and models for evaluating the immune responses to HCV in systems that may be predictive of outcomes in people. Evaluating immune correlates of protection will be invaluable in the assessment of candidate HCV vaccines and to support development of new HCV vaccines.

Another research program – *Studies of Efficacy, Safety and Potency Assay Development for Prophylactic and Therapeutic Vaccines against Hepatitis Viruses* – is focused on developing scientific tools to understand the immunobiology and pathogenesis of HCV. Studies include the development of a small animal model for HCV infection, identification of efficacy biomarkers (*i.e.*, immunologic correlates of protection), development of neutralization tests for the virus, use of nanotechnology for induction of protective immune responses, and studies on the safety of therapeutic vaccines for this virus. These studies will provide the ability to evaluate new technologies being applied to vaccine development, and will be pivotal in guiding and assessing the safety, efficacy and manufacturing issues associated with HCV vaccines.

CBER also engages in research activities pertaining to the safety and efficacy of plasma-derived products in the context of HBV and HCV. CBER research studies have impacted: (1) the safety of blood and blood products with respect to viral pathogens in transfusion recipients; (2) the establishment of national, international, or global standards that would ensure the safety of blood and potency of plasma-derived products; and (3) the development of cell culture based-assays to test for pathogen inactivation.

CDRH Activities Relating to Hepatitis B and C: FDA's Center for Devices and Radiological Health (CDRH), which is responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the United States, has a dedicated Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD) charged with regulating all aspects of in-home and laboratory diagnostic tests (*in vitro* diagnostic devices, or IVDs). OIVD's multidisciplinary group of scientists, medical technologists, policy analysts, engineers, pathologists, and clinicians has a dual charge to foster the rapid transfer of new IVDs into the marketplace while preventing marketing of unsafe or ineffective devices, and is engaged in a number of activities related to hepatitis B and hepatitis C.

In addition, OIVD scientific reviewers and managers participate in several interagency groups associated with viral liver disease. The Hepatitis "Think C" Personalized Medicine Group works to improve the dosage of anti-viral medication at the individual patient level through a combination of appropriate diagnostic test and drug regimes. The Liver Fibrosis Interagency Group meets to discuss the ongoing search for new diagnostic biomarkers for liver fibrosis, which could replace the current practice of diagnosis by liver biopsy.

Indian Health Service (IHS)

IHS works to prevent viral hepatitis in its beneficiary population. IHS has a vaccination program to prevent hepatitis B in the Indian communities it serves. Routine vaccination of all newborns occurs at IHS birthing hospitals, with the first dose of hepatitis B vaccine administered as soon as possible after birth. The hepatitis B vaccine series started at birth is completed as part of normal pediatric vaccine schedule. Catch-up hepatitis B vaccination is offered to children and adolescents who need it. Vaccination of at-risk adults varies by site. Screening for the hepatitis B surface antigen in pregnant IHS patients is generally done as part of the regular health care treatment protocol. Treatment of chronic hepatitis B is provided, most notably in Alaska.

Treatment of hepatitis C occurs at some service units, with four IHS areas providing hepatitis C treatment in at least one service unit. Again, the Alaska Area offers the most developed program. The Seattle Indian Health Board Viral Hepatitis Education and Training (VHET) Project offers education and training of providers in screening of at-risk adults for hepatitis B and hepatitis C, and in hepatitis A and B vaccination. The IHS is also developing electronic health record-based surveillance methods to describe the epidemiology of hepatitis C in the HIS beneficiary population.

HHS Office of Minority Health (OMH)

OMH helped sponsor the IOM report, and is ingworking to elevate viral hepatitis as a priority public health issue. AActivities led by OMH include the following:

Hepatitis B Video, titled "B"/PSA: The OMH was asked by the Association of Asian Pacific Community Health Organizations and the Hepatitis B Foundation to collaborate on the national release of the Hepatitis "B" video/PSA. The PSA was awarded the Grand Prize of the B Real Short Film Competition at the Los Angeles Asian Pacific Film Festival in 2009 and, prior to the partnership with OMH, was played in every major feature at the Asian American International Film Festival in New York. As part of the partnership, the PSA was recently aired on ABC during the Oprah Winfrey Show, CNN's Anderson Cooper, Good Morning America, Today Show, the evening news and various Asian media networks. The PSA will be translated into six different Asian languages.

World Hepatitis Day: The OMH, Association of Asian Pacific Community Health Organizations, National Alliance of State and Territorial AIDS Directors, and National Viral Hepatitis Roundtable recently hosted a World Hepatitis Day event to highlight the importance of global action to eliminate viral hepatitis in Asian American, Native Hawaiian, Pacific Islander, African American, American Indian, Alaska Native, and Hispanic/Latino communities.

Compendium Distribution: Compendium on Local Hepatitis B Activities: The Association of Asian Pacific Community Health Organizations (AAPCHO) received an OMH National Umbrella Cooperative Agreement to enhance hepatitis B activities in communities across the nation. As part of this award, AAPCHO will work with the Hepatitis B Foundation and Asian Pacific Islander American Health Forum to develop and implement a comprehensive strategy to promote and distribute a hepatitis B compendium to catalyze partnerships for local and national action.

The compendium includes case studies on the successes and lessons learned from local coalitions that are part of AAPCHO's hepatitis "B Activated" network. The case studies provide examples and recommendations for enhancing coalition efforts for increasing local awareness, and enhancing screening and vaccination activities. The compendium is intended for communities who are interested in developing or strengthening local hepatitis B awareness and prevention efforts.

Bilingual Bicultural Demonstration Program: Funded by OMH under the Bilingual Bicultural Demonstration Program, the Asian Liver Center at Stanford University's "Building the Community Partnership for San Francisco: Hep B Free Campaign" works to screen, vaccinate and treat all San Francisco Asian and Pacific Islander residents against hepatitis B by providing convenient, free or low-cost testing opportunities at partnering health facilities.

Community Partnership: The Immigrant and Refugee Community Organization (IRCO), an OMH Community Partnership grantee, seeks to decrease the prevalence of hepatitis B and HIV in the Asian and Pacific Islander, African Refugee, and Immigrant communities in Portland, Oregon. Since September 2009, IRCO has reached 210 members of the Asian and African refugee and immigrant community and trained 43 healthcare interpreters on hepatitis B transmission, symptoms, and the importance of early detection.

Closing

Given the substantial and increasing disease and economic burden from viral hepatitis, HHS is taking immediate and coordinated steps to reverse these trends, which represent a health priority for our nation. HHS greatly appreciates the committee's interest in these important issues.

Thank you for the opportunity to share this information with you. I recognize that the problems I have identified are significant ones, but I am confident that working together we can succeed in protecting this nation against the needless disease, pain, suffering, and death caused by viral hepatitis. Thank you. I will be happy to answer any questions.