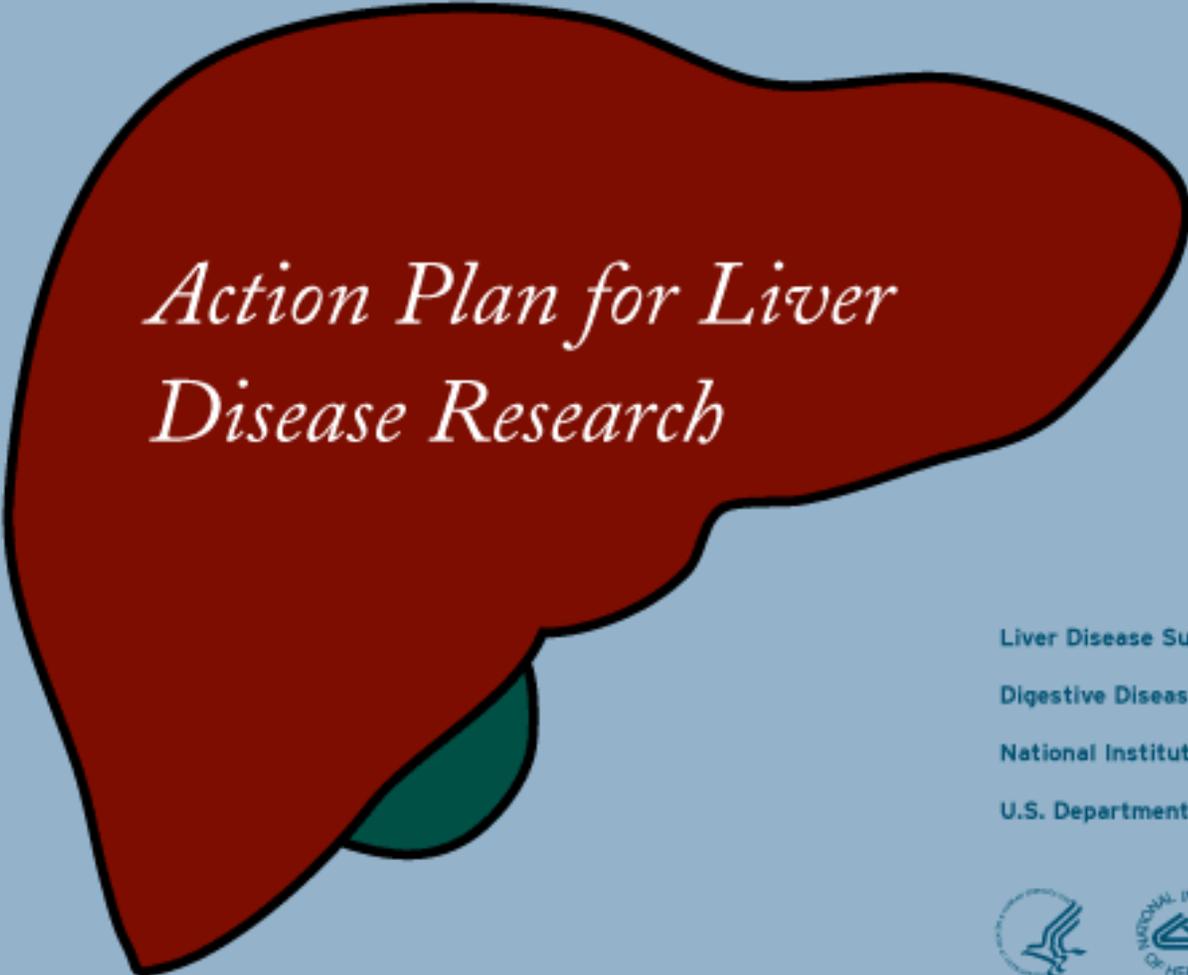


# NATIONAL INSTITUTES OF HEALTH



*Action Plan for Liver  
Disease Research*

Liver Disease Subcommittee

Digestive Diseases Interagency Coordinating Committee

National Institutes of Health

U.S. Department of Health and Human Services



# Meeting Agenda: Afternoon

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- **Overview of Action Plan**
    - Structure
    - Chapters
    - Axiomatic principals
  - **Reaching the entire community**
    - Web site
    - Other outreach
  - **Twelve areas**
    - Definition
    - Membership
    - Charge to groups
  - **Standards for assessment**
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# Liver Disease Action Plan

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- **Final Report: concise, accurate, factual (~50 pgs)**
  - **Introduction: Purpose & Background**
  - **Burden of Liver Disease in the U.S.**
  - **Current status of liver disease research, overview**
  - **12-15 Chapters on separate focus areas**
    - **Introduction, including overview of area, summary of pathogenesis, epidemiology, current understanding, impact**
    - **Current research & recent advances**
    - **Major needs**
    - **Opportunities for future research (recommendations)**
  - **Major goals**
  - **Means of assessment**
  - **Executive summary and recommendations**
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# Five Principles-1

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## 1. Stress basic research

- Important advances in management & prevention of liver disease will come primarily from fundamental advances in knowledge of liver & liver disease.

## 2. Strive to translate rapidly findings from basic research to practical means of prevention, control and cure of liver disease

- Findings from basic research should be applied to clinical issues (bench-to bedside) in a timely, reasoned manner.

## 3. Ensure that clinical advances made in research are disseminated to the medical community and patients with liver disease

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# Five Principles-2

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**4. Use all mechanisms and sources of support of research and promote cooperation & coordination**

- No single mechanism of support of research is adequate or ideal for all situations or types of research. Coordination of support between funding agencies will help ensure efficient use of resources

**5. Emphasize training and career development in research on liver diseases**

- The future of liver disease research depends upon continued recruitment of excellent new investigators into the field.
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# Liver Disease Action Plan

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- **This Action Plan is directed at the NIH and its mechanisms used to support its mission**
  - **Flexible enough to be useful regardless of funding levels during the next 5 years**
  - **Compatible with other NIH initiatives, particularly the NIH Roadmap. Three themes...**
    - **New pathways to discovery**
    - **Research teams for the future**
    - **Reengineering the clinical research enterprise**
  - **Common theme: translation of basic research into practical means of management & prevention of disease**
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# **Liver Disease Action Plan**

## ***Broad Participation & Input***

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- **Action Plan should be the result of wide consensus and input from all groups involved in liver disease research as well as concerned and committed lay organizations and persons with liver disease**
  - **Outreach will use internet and e-mail contacts.**
  - **Editorial in Hepatology “Action Plan for Liver Disease Research” January 2004**
  - **Web site (handout provided)**
  - **Public Comment**
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*Nov 25, 2003*

# **Liver Disease Action Plan Web Site**

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- **Propose to develop a web site that describes the process for development of the Action Plan**
  - **Summarizes information & data accrued on burden of liver disease and status of research funding**
  - **Invites input from community of liver disease investigators and lay persons with interests in promoting liver disease research**
  - **Communications will be monitored & summarized by NIDDK information office and distributed to appropriate groups.**
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# Public Comment

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- Multiple academic and lay organizations asked to participate in this meeting and the process of developing an Action Plan

- AASLD

- ALF

- AGA

- ASTS

- ASGE

- IDSA

- ILTS

- NASPGHAN

- Hepatitis Foundation International

- Hepatitis C Action Coalition

- Hepatitis B Foundation

- Natl AIDS Treatment Advocacy Project

- Treatment Action Group

- Harm Reduction Coalition

# Twelve Topic Areas Working Groups

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- Each working group would ideally include
  - A member from Liver Disease Subcommittee
  - A member from LDRB
  - An intramural researcher in the area
  - Three-five extramural researchers representing all involved ICs
- Each working group would be asked to prepare a 3-5 page report giving overview of research area, major recent advances, most critical future needs, and recommendations for future initiatives.

# Cell and Molecular Biology - 1

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- Hepatocyte biology
- Cholangiocyte biology
- Cell injury, necrosis, apoptosis
- Regeneration
- Developmental biology and stem cells
- Bile, bile acids, bilirubin and cholestasis
- Fibrosis
- Immunology & cytokines
- Cell-signaling, receptors, transport & trafficking
- Nutrition: lipids, carbohydrates & proteins
- Gene regulation
- Proteomics

# Viral Hepatitis - 2

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- Hepatitis A and E
- Hepatitis B and D
- Hepatitis C
- Other infectious diseases of liver
- HIV and liver disease

# Fatty Liver Disease - 3

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- Alcohol metabolism
- Alcohol injury and pathogenesis
- Alcoholic liver disease (clinical)
- Mechanisms of steatosis and injury
- NASH (clinical)

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*Nov 25, 2003*

# **Drug & Toxicant Induced Liver Injury - 4**

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- **Drug & toxicant metabolism & the liver**
  - **Mechanisms of drug & toxicant-induced liver injury**
  - **Drug-induced liver disease (clinical)**
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*Nov 25, 2003*

# Autoimmune Liver Disease - 5

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- **Primary biliary cirrhosis**
  - **Primary sclerosing cholangitis**
  - **Autoimmune hepatitis**
  - **Other autoimmune conditions**
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*Nov 25, 2003*

# Pediatric Liver Disease - 6

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- **Biliary atresia**
  - **Neonatal cholestatic syndromes**
  - **Alagille's syndrome**
  - **Alpha-1-antitrypsin deficiency**
  - **Glycogen or lysosomal storage diseases**
  - **Other pediatric liver diseases**
  - **Liver disease of pregnancy**
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*Nov 25, 2003*

# Genetic Liver Disease - 7

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- **Copper metabolism and Wilson's disease**
  - **Iron metabolism and hemochromatosis**
  - **Porphyrin metabolism and porphyria**
  - **Cystic fibrosis**
  - **Polycystic liver disease**
  - **Other genetic liver diseases**
  - **Gene therapy**
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# Liver Transplantation - 8

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- **Outcomes and complications**
- **Transplant immunology & tolerance**
- **Cryopreservation**
- **Xenotransplantation**
- **Hepatocyte transplantation**
- **Living donor liver transplantation**
- **Acute liver failure**

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*Nov 25, 2003*

# Complications of Liver Disease - 9

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- Symptoms (fatigue, itching)
- Cirrhosis
- Portal hypertension
- Ascites & fluid balance
- Varices & variceal hemorrhage
- Portosystemic encephalopathy
- Hepatorenal syndrome
- Hepatopulmonary syndrome

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*Nov 25, 2003*

# Liver Cancer - 10

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- HCC, pathogenesis
  - HCC, epidemiology, screening & diagnosis
  - HCC, management & therapy
  - Cholangiocarcinoma
  - Angiosarcoma
  - Hepatoblastoma
  - Other hepatic malignancies
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*Nov 25, 2003*

# Gallstones - 11

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- **Gallbladder function**
  - **Gallstones**
  - **Other diseases of the gallbladder**
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*Nov 25, 2003*

# Bioengineering & Biotechnology - 12

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- **Diagnostics**
  - **Imaging**
  - **Artificial liver support**
  - **Liver biopsy methods**
  - **Artificial liver**
  - **Other biotechnology**
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*Nov 25, 2003*

# Action Plan Evaluation

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- How can we assess progress? The success or lack of success of this Action Plan?
- Requires prospective means of measurement
- What should be the basis of the assessment?
  - Number of grants funded
  - Number of investigators funded (particularly new)
  - Number and quality of publications
  - \$ spent on liver disease research
  - Decrease in incidence of liver disease
  - Decline in morbidity or mortality from liver disease
  - Specific goals or guideposts

# Action Plan Goals

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- **Propose “Top Ten” goals for liver disease research to accomplish in the next 5 years.**
- **Examples**
  - **Safe & effective therapies that can control disease activity in >90% of patients with chronic hepatitis B**
  - **Safe & effective therapy that can eradicate HCV in >90% of patients with chronic hepatitis C**
  - **A hepatitis C vaccine that shows efficacy in experimental animal models & is immunogenic in man**
  - **Reliable means of assessing stage of liver disease without biopsy or other invasive method**
  - **Reliable serum marker for HCC that will identify >90% of patients with small HCC**
  - **Effective therapy that improves survival in acute alcoholic hepatitis**
  - **Define the molecular pathogenesis of NASH**

# Action Plan Timeline

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- **Nov 2003: Meeting of Liver Subcommittee to finalize design and initiate process of developing Action Plan**
- **Dec 1, 2003: Selection and instructions to members of working groups**
- **Dec 1, 2003: Web site initiated**
- **Feb 1, 2004: First draft of working groups**
- **Feb 2004: 3rd meeting of Liver Subcommittee**
- **Mar 2004: Second draft of working groups**
- **\*Apr 2004: Final draft submitted**

**\*Subsequent to this meeting, the completion date was revised to late Spring, 2004.**