

AHRQ's Centers for Education & Research on Therapeutics (CERTs): Contributions to Drug Safety Surveillance

Hugh H. Tilson, MD, DrPH

Chair, CERTs Steering Committee

July 20, 2005



CERTs Program

- ◆ **US Congress authorized in 1997**
- ◆ **Administered by AHRQ, in consultation with FDA, as cooperative agreements**
- ◆ **Funded through public and private sources**
- ◆ **First four centers: 1999; next three centers: 2000**
- ◆ **Four additional centers: pending**
- ◆ **291 Projects**
- ◆ **138 Partners**
- ◆ **> 200 Peer-Reviewed Publications**

Congressional Authorization

- ◆ **SEC. 912. PRIVATE-PUBLIC PARTNERSHIPS TO IMPROVE ORGANIZATION AND DELIVERY....**
- ◆ **(b) CENTERS FOR EDUCATION AND RESEARCH ON THERAPEUTICS-**
- ◆ **(1) IN GENERAL- The Secretary, acting through the Director and in consultation with the Commissioner of Food and Drugs, shall establish a program for the purpose of making one or more grants for the establishment and operation of one or more centers to carry out the activities specified in paragraph (2).**

Congressional Authorization

(2) REQUIRED ACTIVITIES:

(A) The conduct of state-of-the-art **research** ...

(i) To increase awareness of—

- (I) **new uses of drugs**, biological products, and devices;
- (II) **ways to improve the effective use of drugs**, biological products, and devices; and
- (III) **risks of new uses and risks of combinations of drugs** and biological products.

(ii) To **provide objective clinical information** to the following individuals and entities:

- (I) **Health care practitioners** and other providers of health care...
- (II) **Pharmacists, pharmacy benefit managers** and **purchasers**.
- (III) **Health maintenance organizations** and other managed care...
- (IV) **Health care insurers** and **governmental agencies**.
- (V) **Patients** and **consumers**.

Congressional Authorization

(2) REQUIRED ACTIVITIES- Continued

(A) The conduct of state-of-the-art **research ...**

(iii) To improve the quality of health care while reducing the cost of health care through—

(II) an increase in the appropriate use of drugs, biological products, or devices; and

(II) the prevention of adverse effects of drugs, biological products, and devices and the consequences of such effects, such as unnecessary hospitalizations.

(B) The conduct of **research on the comparative effectiveness, cost-effectiveness, and safety of drugs, biological products, and devices.**

A core value of the CERTs program is the belief that collaboration of groups with different perspectives and resources is critical if the results are to be applicable in the "real world."



CERTs Model for Public-Private Partnerships

- ◆ **Authorized by Congress as a public-private partnership program**
- ◆ **Investigators work closely with FDA, industry and other public and private organizations, BUT remain independent**
- ◆ **CERTs focus on research and education activities that are in the public interest and would not otherwise be done, e.g.**
 - **safety concerns associated with older, off-patent therapies**
 - **rare effects of newly marketed drugs**
 - **appropriate use of drugs**
- ◆ **Sometimes these activities are aligned with the concerns of FDA, industry and other organizations**
- ◆ **As research program, CERTs can focus on drug safety issues outside of FDA's purview as a regulatory body, e.g. physician training**

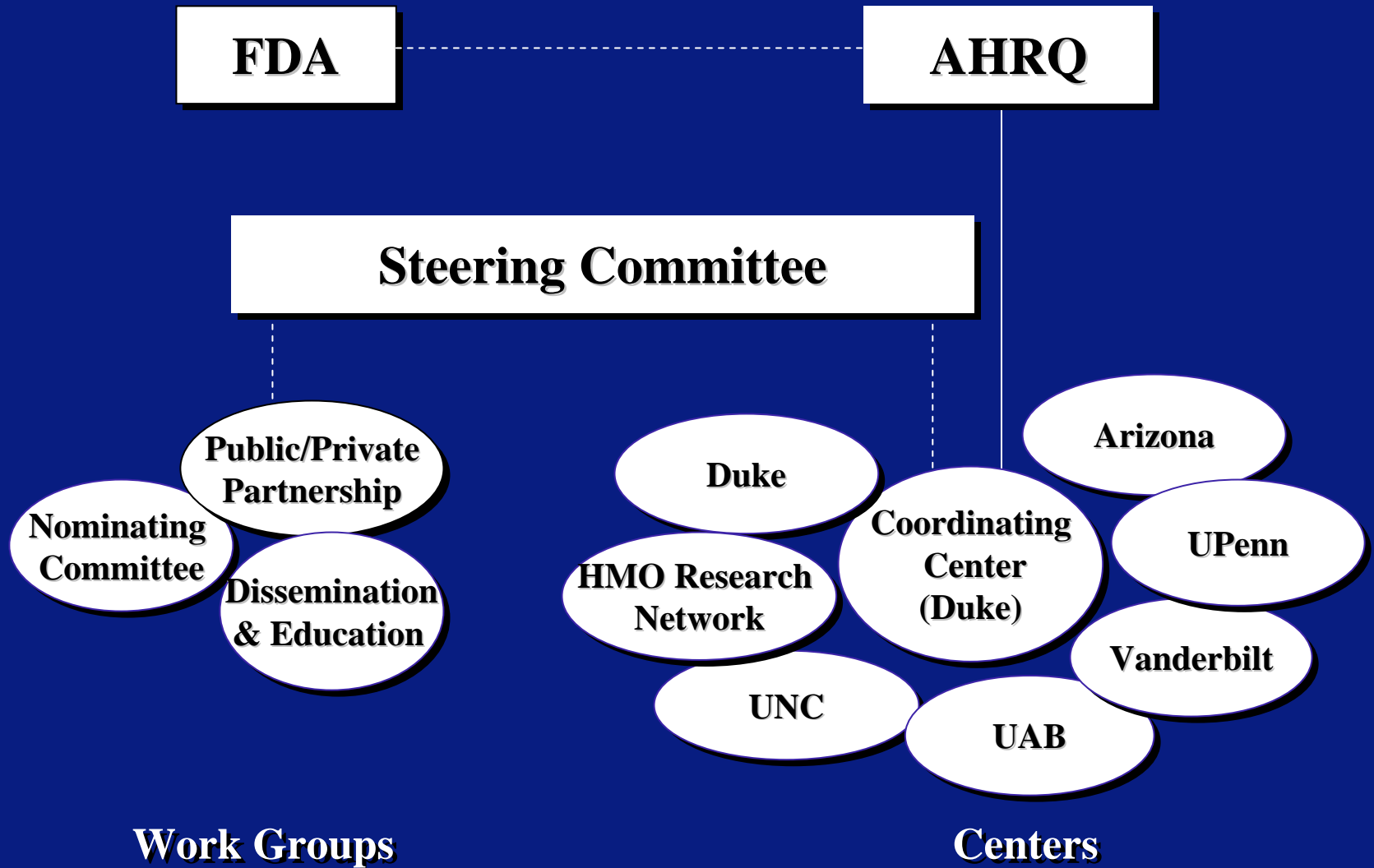
CERTs Model for Public-Private Partnerships – Continued

- ◆ **Charge of public-private and public-public partnerships to expand scope of work**
- ◆ **Core AHRQ support (\$800,000/year for each research center)**
- ◆ **Public-private partnership principles**
- ◆ **Steering Committee with members from the public and private sector; advisory to the CERTs**
- ◆ **Subcommittee to conduct conflicts review**

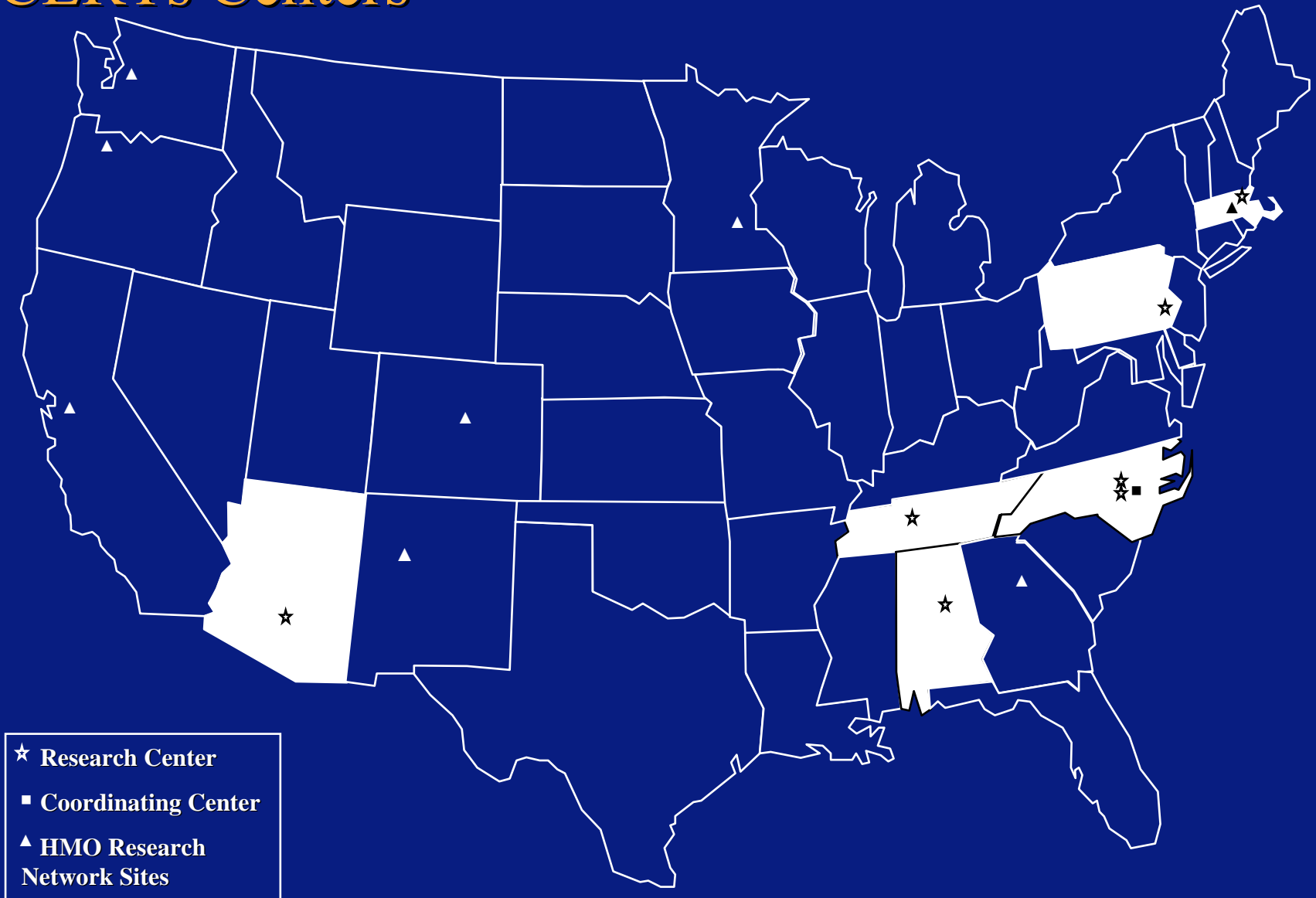
CERTs Vision and Mission

- ◆ **Vision:** To serve as a trusted national resource for people seeking to improve health through the best use of medical therapies.
- ◆ **Mission:** To conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products.

CERTs Structure



CERTs Centers



CERTs Centers

Center	Emphasis
Duke University Medical Center	Therapies for disorders of the heart and blood vessels
HMO Research Network	Drug use, safety, and effectiveness in delivery systems serving defined populations
University of Alabama at Birmingham	Therapies for musculoskeletal disorders
University of Arizona Health Sciences Center	Drug interactions that result in harm
University of North Carolina at Chapel Hill	Therapies for children
University of Pennsylvania School of Medicine	Therapies for infection; antibiotic drug resistance
Vanderbilt University Medical Center	Prescription drug use in a Medicaid population

New CERTs Centers

- ◆ **Mental Health**
- ◆ **Elderly**
- ◆ **Therapeutic Devices**
- ◆ **Consumers and Patients**

CERTs Steering Committee

- ◆ **Private sector expertise**
- ◆ **Research centers**
- ◆ **Government**
- ◆ **End-user perspective**
- ◆ **Advisory to the CERTs**

CERTs Contributions to Drug Safety: RESEARCH

- ◆ **Risks and benefits of individual drugs, drug classes, or combinations**
- ◆ **Actual use**
 - **Patterns of use**
 - **Quantifying inappropriate and unsafe use**
- ◆ **Tools and strategies to increase appropriate use**
- ◆ **Safety surveillance methods**

Identification of Drug Risks

- ◆ **Example**: Using TennCare data, the CERTs found an association between the oral use of erythromycin and the risk of sudden death from cardiac arrest.
- ◆ **Potential**: Epidemiologic studies to elucidate specific drug risks and benefits.

Actual Use

- ◆ **Example**: The CERTs, in collaboration with CDRH/FDA and the Society for Thoracic Surgeons, evaluated the trends in use and outcomes of transmyocardial revascularization (TMR) in community practice. The study found a widespread use of TMR in combination with CABG (an off-label indication) and some estimations of patient-specific risks associated with TMR, though additional studies are needed.
- ◆ **Potential**: Monitor patterns of use of a wide array of therapeutic agents, addressing inappropriate use and identifying predictors of inappropriate use.

Interventions to Improve Use

- ◆ **Example**: The CERTs are evaluating computer-based clinical decision support systems to support appropriate prescribing in the ambulatory setting.
- ◆ **Potential**: The CERTs can develop and test a wide array of interventions to improve prescribing in the general population and in high risk groups. These interventions can be tested in CERTs-affiliated inpatient and ambulatory settings, and through available data resources.

Safety Surveillance Methodology

- ◆ **Example**: FDA is co-sponsoring a pilot study with the CERTs -- using data extracts created via AHRQ funded safety studies -- to assess when adverse drug reactions discovered after marketing could have been identified through routine screening of administrative datasets.
- ◆ **Example**: The CERTs have developed an Internet-based international registry for drug-induced arrhythmias (QTdrugs.org). The registry was used to detect that IV Methadone induced torsades de pointes (after 45 years of monitored administration in MMT centers). The CERTs subsequently determined the mechanism.

CERTs Contributions to Drug Safety: EDUCATION

- ◆ **Clinician and patient educational materials**
- ◆ **Web site resources**
- ◆ **Publications, e.g. CERTs annual report**
- ◆ **Training and mentoring future generations of clinicians, researchers and pharmacovigilance professionals**

Education

- ◆ **Example**: The CERTs, in collaboration with FDA, developed an educational module focused on preventing adverse drug reactions. It was sent to medical & pharmacy schools and is available via the Internet.
- ◆ **Example**: The CERTs developed an interactive web-based “virtual medicine cabinet” as a colorful educational tool for health care consumers. The medicine cabinet opens and displays familiar-looking bottles and packages showing generic examples of multiple classes of over-the-counter medications typically found in people’s medicine cabinets. Visitors can click on the medicines to find out how safe they are in combination with other drugs and find links to additional information.

Convening Experts

- ◆ **The CERTs held a series of expert “think tank” workshops to**
 - **(1) review how therapeutics risk information is assessed, communicated and managed**
 - **(2) identify research questions that improve health outcomes.**
- ◆ **Collaboration with AHRQ, FDA and PhRMA**

*“Postmarketing Assessments
of Pharmaceutical Risk”*

“Think Tank” Workshop

May 29 – 31, 2002

Chapel Hill, NC

Selected Key Research Questions-1

- **What system is needed to assure that we:**
 - **Routinely address long term adverse effects**
 - **Routinely address adverse events throughout drug development**
- **What level of risk associated with a drug is acceptable to the public? What level of risk is acceptable to a prescriber? What factors influence risk acceptability?**

Selected Key Research Questions-2

- **What do conflicts between results from analysis of structured studies, spontaneous reports and large, structured databases mean?**
- **What are the “core competencies” needed by a pharmacovigilance professional?**
- **What will it take to improve the quality and adequately staff the effort?**

Risk Assessment: The Bottom Line

- ◆ **The system of risk assessment requires a major overhaul**
- ◆ **The major overhaul should be evidence based**
- ◆ **There is much we need to know to improve our approach to Risk Assessment**
- ◆ **We MUST get on with it!**

CERTs Contributions to Address Drug Safety Issues

- ◆ **Clinical expertise**
- ◆ **Methodological expertise**
 - **Drug risks, benefits & use**
 - **Interventions to improve appropriate use**
 - **Safety surveillance approaches**
 - **Resources: population databases, delivery system research laboratories**
- ◆ **Dissemination & education**
 - **Clinicians, patients and policymakers**
 - **Future clinicians and researchers**
- ◆ **Convener of stakeholders**

THE WAY FORWARD

- ◆ **Improving drug safety will take getting ALL of us on the same map (and heading the same direction!)**

