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**CONTACTS:** Melissa Wagoner (Kennedy)

202.224.2633

Craig Orfield (Enzi) 202.224.6770

**\*\*SUMMARY INCLUDED, LONGER SUMMARY AVAILABLE UPON REQUEST\*\***

**KENNEDY, ENZI RE-INTRODUCE VITAL DRUG SAFETY LEGISLATION**

Washington, D.C. – Today, Senator Edward M. Kennedy, Chairman of the Health, Education, Labor, and Pensions (HELP) Committee along with Senator Mike Enzi, HELP Committee Ranking Member, re-introduced the Enhancing Drug Safety and Innovation Act. First introduced August 3, 2006, the Enhancing Drug Safety and Innovation Act would require drug makers and FDA to engage in better safety planning before a drug is approved for release to the public while improving the FDA's response to risks identified after a drug is on the market. The issue of drug safety will be taken up by the HELP Committee in early Spring, when the committee considers the reauthorization of the Prescription Drug User Fee Act.

Senator Kennedy and Senator Enzi hope to report out a bill addressing the drug user fee reauthorization, drug safety, and three other FDA reauthorizations shortly after Easter, for consideration on the Senate floor by late spring, and a conference with the House with final passage before the August recess.

Senator Kennedy said, "We need a more effective system to identify and assess the serious risks of drugs, inform health care providers and patients about such risks, and manage or mitigate these risks as soon as they are detected, and our bill will make that happen."

"Our bill, the 'Enhancing Drug Safety and Innovation Act,' will raise the bar to ensure that drug safety is not an afterthought, but an integral part of the process throughout the life of a drug," Enzi said. "It requires drug makers and FDA to engage in better safety planning from the very beginning, before a drug is approved for release to the public, in order to improve both the understanding of and response to risks that arise after a drug is on the market."

The Drug Safety legislation, which reflects the comments and input of dozens of stakeholders, including the FDA, patient and consumer groups, industry trade associations, individual companies, and scientific experts, will:

- \* Integrate safety issues and the approval process by requiring earlier and more focused consideration of safety issues;
- \* Establish a flexible planning mechanism to obtain the necessary safety information about each new drug or indication;
- \* Permit adaptation of the safety plan in response to new information; and,
- \* Bring fairness, timeliness and finality to the dispute resolution process.

Other key provisions of the bill:

- \* Establishing a collaboration among the FDA, academic research institutions, and the biomedical research industry to improve the process of drug development and evaluation, and advance

the FDA's Critical Path Initiative;

\* Establishing a publicly available database of clinical trials to help enhance patient enrollment in clinical trials of drugs, provide a mechanism to track subsequent progress of trials, and ensure that the results of trials are made public, and that patients, doctors, and pharmacists have the most up-to-date information;

\* Making improvements to the FDA's process of screening advisory committee members for financial conflicts of interest to ensure that these committees provide independent expert advice, and to bolster the credibility of the product review process.

## **The Enhancing Drug Safety and Innovation Act of 2007 – Short Summary**

### **Title I: Risk Evaluation and Mitigation Strategy (REMS)**

Drugs and biologics will be approved with risk evaluation and mitigation strategies (REMS). The REMS will be reviewed at least annually for three years, as well as in labeling supplements and when FDA requests a review. Sponsors would propose a REMS and FDA would approve it after structured negotiations, if necessary.

#### **Minimal Elements of a REMS —**

- FDA-approved professional labeling (a current requirement);
- 15-day, quarterly, and annual reports of adverse events (a current requirement);
- A pharmaco-vigilance statement about how to assess known serious risks and to identify unexpected serious risks (new);
- A timetable for periodic assessment of the REMS (new).

**Additional Elements —** Based on the nature and magnitude of safety issues, additional elements of a REMS may include —

- Patient materials, such as a Medication Guide, for distribution when drug is dispensed;
- A communication plan to physicians about serious risks or safety protocols with the drug;
- Post-approval epidemiological studies to assess signals of serious adverse events or to screen for serious adverse events in expanded populations;
- Post approval clinical trials to assess signals of serious adverse events;
- Pre-clearance of, specific disclosures in, and/or restrictions on DTC advertisements;
- Restrictions on product use or distribution to address a specific expected serious risk (what is currently known as a RiskMAP).

**Timeframes —** Assessments, FDA review, and discussion of a REMS —

- In the context of an application or supplemental application, FDA must begin to discuss the proposed REMS with the sponsor at least 60 days before the PDUFA action deadline;
- If there is new safety information after approval, FDA may order sponsor to submit assessment of a REMS and must begin discussions within a set time period;
- A sponsor may submit an assessment of, and propose modifications to, a REMS at any time. Modifications can be adding, changing, or eliminating an element of the REMS.

**Dispute Resolution —** When there is disagreement between FDA and the sponsor about the REMS, the sponsor may initiate a structured dispute resolution process —

- This process begins by the sponsor proposing a REMS or assessing whether changes to an

existing REMS are needed, and can be terminated by FDA and the sponsor reaching agreement at any point before issuance of an order;

- Once discussions of the sponsor's proposed REMS begin (day 1), the sponsor may request review from day 15 until day 35;
- Review takes place at one of the next two monthly meetings of the Drug Safety Oversight Board (made up of FDA, NIH, VA and other HHS);
- Drug Safety Oversight Board reviews both proposals and issues a recommendation to the Secretary within 5 days;
- The Secretary must respond within 7 days after that, by issuing an order that resolves the dispute (can also be done w/in the PDUFA action letter, if that is the context);
- Once FDA/sponsor discussions begin, the dispute resolution process takes from 36 days to 89 days, depending on circumstances. Agreement terminates dispute resolution process.

#### **Compliance —**

- Non-compliance with an element of a REMS would be a prohibited act;
- Civil money penalties for violation of a component of an approved REMS.

**Application to generic drugs —** A generic drug would be required to meet each element of a REMS except communication plans (carried out by FDA), and post-approval study and clinical trial requirements (generally not applicable by the time a drug goes generic). There are provisions to ensure that the patenting of components of a system for restrictions on distribution and use are not used as tools to thwart generic competition.

**Resources —** Increased drug user fees would be used to review REMS and for FDA's general drug safety surveillance.

**Title II: Reagan – Udall Institute for Applied Biomedical Research —** Establishes a non-profit institute to lead collaborations amongst the FDA, academic research institutions, and industry directed to improving the process of drug, device, and biologic development and evaluation. Collaborative research projects will be selected that are designed to bolster R & D productivity, provide new tools for improving safety in drug, device, and biologic evaluation, and in the long term make product development more predictable and manageable. Like the NIH Foundation, this institute will be financially supported by both industry and the government.

#### **Title III: Clinical Trials Databases**

**Registry Database —** To enhance patient enrollment and provide a mechanism to track subsequent progress of trials, clinical trials of late Phase II, Phase III and Phase IV would be required to register in a publicly available database. The required data elements would be based on the World Health Organization international consensus data set.

**Results Database —** To ensure that results of trials are made public, and that patients and providers have the most current information, all Phase III and Phase IV trials would be required to deposit their results in a publicly available database. There would be a process to determine whether and when to add those Phase II trials that had to register. Several pieces of information would be placed in fields in the database entry, while the bulk of the information describing the results would be in two summary documents (lay and technical). Results could be submitted to the database but not made publicly available pending regulatory action and/or publication.

**Title IV: Conflicts of Interest —**The bill requires public disclosure of waivers of conflicts of interest of advisory committee members before advisory committee meetings, and greater efforts by FDA to identify qualified advisory committee members with minimal conflicts.

