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NATIONAL TRANSPORTATION SAFETY BOARD AND FOOD AND DRUG ADMINISTRATION

"TRANSPORTATION SAFETY AND POTENTIALLY SEDATING OR IMPAIRING MEDICATIONS"

Witness Panel I – Measuring Impairment

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I am Dr. Bert Spilker, Senior Vice President of Scientific and Regulatory Affairs for the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. Investing more than $30 billion in 2001 in discovering and developing new medicines, PhRMA companies are leading the way in the search for new cures.

In regard to the subject of this panel's focus, I wish to make seven points.

1. **Every investigational drug is carefully and thoroughly evaluated for adverse reactions it might cause.**

2. **These evaluations are conducted in artificial as well as highly controlled clinical trial settings during the Phase I and II**

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development of a drug, and in close to real-world clinical settings during the Phase III development.

3. Evaluations are made through adverse drug reaction reporting via: spontaneously volunteered verbal communication by patients; in diaries recorded by patients (when kept as part of a trial); and in responses by patients to written questionnaires for quality of life and for other tests. Responses to verbal non-bias questioning, such as, "Have you had any problems or noticed anything different since you were here last?", are the basis for collecting adverse drug reactions during each phase of drug development.

4. Any real-life event such as a traffic accident during a clinical trial is collected as an adverse event, no matter how mild, and every attempt is made to ascertain the cause, whether it be drug-related or non-drug related (i.e., the accident could be due to drowsiness due to a drug or from an event due to the disease under evaluation, or from other non-drug related cause prior to the accident).

5. Adverse drug reactions for an investigational drug are compared against placebo and often versus other approved drugs prescribed for the same disease, either in head-to-head clinical trials, or using data from the respective package inserts. A benefit-risk determination is eventually made by the sponsoring company and by the FDA, and drugs are allowed on the market if their benefits exceed their risks.

6. After market approval, adverse drug events that a company learns about through its post-marketing surveillance program/global safety network, as described in the Code of Federal Regulations are sent to FDA on a periodic basis. The company's network captures reported ADRs occurring anywhere in the world.

7. The relationship between drowsiness as an adverse drug reaction and impairment of performance has not always been demonstrated to be related or correlated. Drowsiness tends to be a subjective feeling, whereas impairment is based on more objective testing. Various methodologies have been utilized to evaluate performance impairment in both real life and clinical trial situations when certain adverse drug reactions (e.g., drowsiness) have been associated with its use in some patients. There are more than a dozen commonly used tests that measure performance impairment. However, there is no accepted universal standard approved by FDA for testing impairment in a clinical trial setting, and a validated reference for what may be a clinically meaningful threshold of impairment is not presently agreed.

In conclusion, well-documented methodologies are currently being utilized during the development phases of a drug for evaluating adverse drug reactions and their potential relationship to performance impairment. Once a drug is approved for marketing, the drug's safety profile continues to be monitored through post-marketing surveillance programs with resultant relevant updating of prescribing information based on the additional information.