New Regulations are Necessary

- **Consumers are well aware that the current system has failed them**
- **The failure has been attributed to “faster” drug approvals**
  - **partially undeserved attribution: more complex pathogenetic and drug mechanisms**
  - **PDUFA did not ‘accelerate’ review and approval as much as it ‘corrected’ undue delays**
- **Malfeasance by sponsors and within FDA has been alleged – sometimes true and sometimes false**
- **Deficiencies in current safety surveillance system and its associated enforcement capabilities are well documented**
- **New regulations will benefit public health if wisely implemented [APPLE PIE]**

The Primary Benefit of Enhancing the Science of Drug Safety and the Regulations that Govern It Is EQUIPOISE

- **"The FDA must strengthen its post-marketing safety surveillance and its oversight of the advertising and promotion of drugs" *(Slater.NEJM 2005;352:294)***
- **The FDA has been chronically under-resourced and devoid of buck-stopping leadership for extended time periods**
- **For the most part, the categories targeted in the IOM report for regulatory reform are appropriate**

“…[T]he Committee cautions against assuming that altering the statue alone will solve all difficulties related to FDAs regulatory authorities”

The Future of Drug Safety, Chapter 5, pg. 151

FROM THE PATIENT PERSPECTIVE: Equipoise may be diminished by several considerations

- **New legislation takes time**
- **Most of the benefits of enhanced enforcement are realized post-hoc [Enforcement as litigation takes time]**
- **Even as budgetary goals are reached, execution requires a well-tooled infrastructure [Mathews, WSJ, 3/3/07, pg.A1]**
- **Many of the proposed enhancements, e.g., extensive Risk Management Plans cost money and time, which will likely translate into higher drug prices which we can ill-afford**
- **Practitioner and patient information about new drugs may suffer**

Patient Perspective (cont.)

- **Enhanced enforcement may drain critical resources from areas of more urgent need, e.g., study of the Science of Drug Safety**
- **Restricted use in name of safety may limit access to the detriment of health [Gottlieb.WSJ, 3/6/07, pg.A19]**

Recommendations for New Regulations

- **5.1 RiskMAPs can include a variety of limits on distribution**
- **5.2 Increased enforcement authority to include fines, injunctions, withdrawals**
- **5.3 Black triangle warnings associated with restrictions on direct-to-consumer advertising**
- **5.4 Safety evaluation at or before 5 years**

New Regulations vs. Historical Events

- 1. RiskMAPs/Limits on Distribution
- 2. Enhanced Enforcement Authority
- 3. Black Triangle Label with Restriction on DTC
- 4. Periodic Safety Reviews

- Fen-phen-failure to report post-marketing AEs (Avorn,*Powerful Medicines*, 2004)
- BayCol-alleged failure to properly evaluate post-market AEs (JAMA 2004; 292:2622-2631)
- Ketek-alleged fraudulent clinical trial and issue of disclosure (Mathews.WSJ,2/13/07, pg.D4)

New Regulations vs. Historical Events

- 1. RiskMAPs/Limits on Distribution
- 2. Enhanced Enforcement Authority
- 3. Black Triangle Label with restriction on DTC
- 4. Periodic Safety Reviews

- Vioxx-post-market clinical trials resulted in recognition of common event occurring more frequently in drug-treated population
- Tysabri-withdrawal reversed by patient demand with enhanced labeling (USFDA website:infopage/natalizumab, 2006)

Direct-to-Consumer(DTC) Advertising

A revised concept of DTC advertising **could provide a valuable tool for prescriber and patient information exchange and eventually replace drug detailing**

- **Consider that current mechanisms to learn about new drugs and safety problems as they develop are poor**
- **Consider that patient information cannot be impeded**
- **Consider that FDA-approved communication should dominate learning about new drugs**
- **Consider that DTC ads could be linked to the passive adverse event reporting system**
- **Consider that DTC ads contain black-box warnings and could contain information regarding ongoing studies, warnings, and safety alerts**

SUMMARY

- **It is important to consider wise implementation of many of the regulations recommended in the IOM report, *however, it must be recognized that until the Science of Safety is strengthened; practitioner and patient education are enhanced greatly; a cohort of drug safety professionals are trained; and engagement of the public is accomplished, public health will not have been advanced.***