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Presenting on behalf of the Expert Panel

College on Problems of Drug Dependence Conference on
Risk Management and Post-Marketing Surveillance of CNS Drugs

Oct. 27-28, 2008: Implications for REMS

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FDA Public Meeting on Risk Evaluation and Mitigation Strategies
for Certain Opioid Drugs



College on Problems of Drug Dependence

- Since 1929, CPDD has been the leading scientific organization focusing on abuse potential assessment, drug regulation, development and assessment of medication types and forms with reduced abuse potential, and the measurement and control of substance abuse
- CPDD has provided a forum for discussion of the complex issues associated with drug abuse among scientists, public health experts, regulators, and research funders



2008 CPDD RM Conference

Implications for REMS:

1. Decisions about the class wide REMS will have implications for drugs in the pipeline – not just the approved drugs receiving current focus.
2. REMS could either facilitate or discourage new drug and dosage form development, e.g., new molecular sites, prodrugs and novel formulations. *By way of example the tiered drug scheduling system of the Controlled Substances Act is a powerful incentive for developing less abusable medicines. Similarly, REMS should recognize differences in risks even of drugs within a class.*
3. REMS should advance to the greatest extent possible on a scientific foundation while recognizing that the science is at early stages. E.g, the science foundation is very strong in the areas of abuse liability and surveillance. On the other hand we have little scientific evidence that specific REMS strategies will actually reduce drug abuse.
4. REMS could encourage appropriate prescribing OR unintentionally drive prescribing to less optimal drugs, and drive abuse to other drugs.



Major Conclusions & Recommendations

1. CNS drugs pose special challenges for risk management related to possible abuse liability.
2. CSA Scheduling is a form of RM that needs to be harmonized with current RM strategies.
3. Preclinical and human abuse liability testing has good predictive ability for real world abuse of CNS active medications and can thereby serve CSA Scheduling and REMS development.
4. Traditional surveillance surveys do not provide the timely, sensitive and accurate information required to guide the iterative process required.



Major Conclusions & Recommendations

5. Evaluations of the effectiveness of RMPs as well as unintended consequences are needed.
6. Because research on the efficacy of RMPs is in its infancy, it will be important to encourage the funding of research, including controlled trials when possible, to provide the evidence base that is needed, and to investigate issues that may be beyond the requirements or interests of a drug's sponsor.



CPDD Special Meetings Related to Abuse Liability

- 2002: Preclinical and human laboratory methods for the assessment of the abuse potential of new CNS active medications
- 2005: Formulation methods to decrease the abuse potential of CNS active medications
- 2006: Pre-clinical methods for the assessment of abuse potential of new CNS active medications
- 2008: Risk Management and Post-Marketing Surveillance of CNS Drugs



Purpose of the 2008 meeting

State of the art assessment of risk management to develop Expert Report & recommendations

1. The state of the science of risk management
2. Public health implications of risk management
3. The process of developing, implementing and assessing the impact of risk management
4. Key tools used to achieve risk management
5. Surveillance approaches and needs
6. Regulatory approaches
7. Research needs



CPDD Expert Panel

Members:

Charles R. Schuster, Co-chair

Jack Henningfield, Co-chair

Chris-Ellyn Johanson

(Rapporteur)

James Anthony

Andrea Barthwell

Richard Dart

Cynthia McCormick

Edward Sellers

Robert Balster

John Coleman

Charles Gorodetzky

Charles O'Keeffe

Sharon Walsh

Ex-officio liaisons:

Richard Denisco (NIDA)

Shanthi Pal (WHO)

Nick Reuter (SAMHSA)

Frank Vocci (NIDA)



Additional Conclusions 1

1. RM can make drugs with special concerns available to patients under conditions to limit their unintended consequences, including abuse.
2. The regulatory status of RM is in transition, with unclear authority of FDA for requiring RM as a condition for approval for CNS active drugs.
3. Risk management is an iterative process that should be designed to evolve over the life cycle of the drug.
4. While 2005 guidance documents apply to AEs produced by all pharmaceuticals, their application to managing abuse and diversion may require unique strategies.
5. One of the factors driving the development of RM strategies for CNS drugs in the U.S. is that the abuse of prescription opioids and stimulants has increased considerably in the last decade.



Additional Recommendations 1

1. Laboratory based studies for assessing the abuse liability of drugs that target new molecular sites, prodrugs and novel formulations need to be refined.
2. New types of data sources need to be developed to detect emerging problems and complete findings need to be released in a timely fashion.
3. Post marketing surveillance that detects signals of diversion and/or abuse need to be followed up with both quantitative and qualitative field studies to assess the nature and magnitude of the problem to guide interventions changes in RM.



Additional Recommendations 2

4. If it is determined that a signal is valid, the information can be used to develop an intervention.
5. Evaluations of the effectiveness of RMPS as well as unintended consequences are needed.
6. Because research on the efficacy of RMPs is in its infancy, it will be important to encourage the funding of research studies, including controlled trials when possible, to provide the evidence base that is needed.



Additional Recommendations 3

7. The REMs legislation and regulations should be modified to ensure that generic and innovator drugs are held to the same standards for post marketing surveillance and risk management strategies.
8. Collaborative teams to assure the management of risks related to abuse and diversion of pharmaceutical products are essential.
9. CPDD should convene a meeting of appropriate stakeholders to consider an examination of both the curriculum and the educational methods for teaching all health care practitioners.