The science and regulatory compliance of the assessment of the abuse potential of new pharmaceuticals

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Recent changes in regulatory policy have mandated that all new pharmaceuticals be evaluated for the potential for abuse. These changes have largely come about in response to increases in overdose deaths noted in the US primarily, but also in other geographic regions. The evaluation of abuse potential can be as simple as a careful assessment of brain penetration of the drug, defining secondary pharmacology, in addition to an understanding if the drug produces behavioral effects in preclinical species as well as in clinical trials. If signals for central nervous system activity are noted, a series of assays, can be employed to better understand whether the new drug produces effects similar to know drugs of abuse, is rewarding when it is administered, and whether repeated administration of the drug will produce physical dependence – characterized by a withdrawal syndrome. The assay for detecting similarity to known drugs of abuse is a Drug Discrimination Assay, in which animals a trained to detect whether they have been administered drugs. For measuring rewarding effects, IV self-administration procedures can be employed, and specific tests for physical dependence are conducted. If indications of abuse potential are noted in the preclinical assays, implementation of human clinical trials to address abuse potential may occur. These assays will be described in detail in the current lecture, enhanced by examples from the scientific literature.