K72 Scientific Method for Controlled Substance Analog Determination

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After attending this presentation, attendees will understand relevant scientific concepts needed to comprehensively evaluate non-controlled substances as potential analogs of controlled substances, acceptance criteria associated with those concepts, the ability to establish laboratory practices to present scientific data regarding analog determination in court, and assist in the scientific prosecution or defense of analog drug cases.

This presentation will impact the forensic science community by providing laboratories with objective, science-based criteria to evaluate compounds and a means to establish consistency in analog determinations made in laboratories across the country. This presentation will introduce toxicological, chemical, and synthetic concepts surrounding the evaluation of potential controlled substance analogs and offer a scientific method for this evaluation.

The Advisory Committee for the Evaluation of Controlled Substance Analogs (ACECSA) was established by scientists from federal, state and private forensic laboratories, academia, and law to develop a scientifically valid and peer-reviewed means of evaluating the analog status of non-controlled substances and serve as a resource to law enforcement, legal counsel, laboratories, and government agencies in the scientific categorization of non-controlled substances. The Committee was gathered intentionally to maintain an independent, un-biased, and un-weighted stance in the scientific and legal communities. The main goal of constructing this group was to address a lack within the forensic chemistry field regarding the evaluation of analogs. To date, there are no guidelines, recommendations, or methods that exist in our field and no consensus or consistency in the determination of these compounds. Scientifically-sound guidelines or recommendations for analog determination are needed in the forensic arena in response to the overwhelming “designer drug” explosion and the difficult task of legislating potentially harmful new drugs.

The members of the ACECSA, in collaboration with national and international subject-matter experts, developed five aspects of a compound that should be included in evaluating analog status: Chemical Structure; Physicochemical Properties; QSAR/Computational Chemistry; Synthetic Pathway; and, Toxicology/Pharmacology will present applicable concepts and associated acceptance criteria to demonstrate the comprehensive approach to analog determination.

The Chemical Structure subcommittee aims to develop a process by which potential controlled substance analogs are evaluated and compared on the basis of their structural similarity. This structure evaluation process focuses on both 2D and 3D aspects of a chemical’s structure. Initial investigations look at core structures and functional groups.

The use of physicochemical properties in proposing potential new drug candidates has its basis primarily in the bioavailability of the compound *in vivo*. For example, solubility, partition coefficient, and pKa/pKb provide preliminary *in vitro* guidance as to the potential bioavailability.

Solubility primarily affects the dosage form and route of administration. Partition coefficient is used to predict membrane permeability. The compound’s acidity or basicity determines where an orally-administered drug might be absorbed in the body. These properties will be retrieved from scientific literature (if available) or may be calculated by modern computer programs designed and used for this purpose.

The Quantitative Structure-Activity Relationship/Computational Chemistry subcommittee will utilize available predicted activities for new chemicals. It will also evaluate the utility of similarity co-efficient models such as Tanimoto.

The goal of the Synthetic Pathway subcommittee is to analyze the structure of potential controlled substance analogs by the pathway in which they were created, i.e., deducing their chemical construction. The pathway of chemical synthesis of any organic compound can be modified by employing different building blocks; this serves as a rapid means to generate analogs of beneficial, or controlled, chemical compounds.

The Toxicology subcommittee will evaluate available pharmacological and toxicological data regarding novel compounds and compare their properties to existing controlled or scheduled drugs. This will include receptor binding and functional assay data, human and animal dosing studies, case reports, behavioral studies, adverse event reporting, and epidemiological data with clinical indicators, provided in the latter two cases that they are accompanied by analytical confirmation of the substance identity.

Analog, Controlled Substance, Method of Evaluation

 ** Presenting Author*