Analog Determination – a Scientific Method

NIST/DEA Emerging Trends in Synthetic Drugs Workshop

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ACECSA

- Advisory Committee for the Evaluation of Controlled Substance Analogs
- www.druganalogs.org
- Core members
- Subject-Matter experts

ACECSA Mission

- The mission of the ACECSA is to recommend minimum scientific standards for the evaluation of non-controlled substances being considered as analogs of controlled substances.

- Science is the key

- Legal decisions/legislation may be discussed, but final considerations are strictly based on science

ACECSA Objectives

- To establish a working definition of “Analog” and related terms within the scope of Forensic Drug Analysis.
- To develop a rigorous scientific method for the evaluation of non-controlled substances for analog consideration that is scientifically valid and peer-reviewed.
- To provide minimum scientific standards for classifying compounds as analogs.

ACECSA Objectives

- To provide a means of information exchange within the forensic science community, law enforcement, legal counsel and government agencies regarding the scientific evaluation and classification of suspected analogs.
- To seek acceptance of ACECSA recommendations.
- To provide training and consultation to the forensic science, criminal justice and other interested stakeholders.
- To create a catalog of evaluated compounds and their scientific analog designations.

ACECSA Sub-Committees

- Structure
- Physicochemical Properties
- Computational Chemistry and Cheminformatics
- Synthetic Pathway
- Pharmacology/Toxicology
- Literature Support
  - *published, unpublished, dissertations, research, meeting abstracts*
  - *Catalog of evaluated compounds*

Structure

- "…the chemical structure of which is substantially similar to the chemical structure…"

- 3 Structural indicators for comparison
  - Core structure class
    - Acyclic, Single Ring, Multi-ring
    - Must be in the same class – no changes
  - Functional groups
  - Presence and location of double bonds
    - Important for 3-D structure

Physicochemical Properties

- Chemical reactivity cannot be separated from structure
- Aspects for comparison
  - Bioavailability
  - Molecular Weight
  - Polar Surface Area
  - Log P
  - Rings
  - Rotatable bonds
- Property estimation software

Synthetic Pathway

- Distinct routes separately patented?
- Distinct routes separately published?
- Must infer the pathway of construction
- Synthetic byproducts/contaminants may indicate pathway
- Commonly available building blocks

Pharmacology/Toxicology

- 3 Discussion Areas:
  - Human *in vivo* data
    - Best and only conclusive data
    - Not determined quantitative value “similar data”
  - Animal *in vivo* and/or *in vitro* data
    - Used after Human data has been evaluated
    - If no human data and animal data is incomplete, QSAR must be considered
  - QSAR
    - Use when no other data (or incomplete data) exists
  - Anecdotal Reports
    - Use as informational only – no scientific controls

Computational Chemistry

- Essential to define a core structure
- Define the Maximum Common Substructures
    - Markush-type representation
- Cheminformatics alert IT platforms
- Molecular Shape
- Med Chem “transformation” rules

- Molecular Similarity
- QSAR

Literature

- Creating a bibliography for anything related
- Organized and searchable
- Citations available
- Catalog of evaluated compounds

Future of the ACECSA

- First pass at a method
  - Still have criteria to develop
- Presentation of a scientific method
- Public comment / Peer review
- General acceptance (perhaps ASTM)

Questions?

Thank You!

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