International Regulatory Environment for the Abuse Liability Evaluation

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Willem Scholten PharmD, MPA

Quality Assurance and Safety: Medicines, Department of Medicines Policy and Standards
Drug Control

- Single Convention on Narcotic Drugs (1961)
- Convention on Psychotropic Substances (1971)

Substances liable for abuse
Drug Control

- Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988)

Precursors (starting materials) for producing drugs in the other two conventions
The UN system and drugs

- Commission on Narcotic Drugs (CND)
  Meets annually in March in Vienna
- International Narcotics Control Board (INCB) Vienna
- United Nations Office on Drugs and Crime (UNODC) Vienna
- World Health Organization (WHO) Geneva
The WHO and drugs

- Substance evaluation
- Access to Controlled Medications
- Mental health and substance abuse
- Nomination of 3 INCB members
The WHO and substance evaluation

- For 1961 Convention:
  - WHO assesses
    - abuse liability
    - capability to produce ill effects

- For 1971 Convention:
  - WHO is determinative as to medical and scientific matters
The CND and substance evaluation

- For 1961 Convention:
  - CND can accept or reject WHO recommendation

- For 1971 Convention:
  - CND can take into regard economic, social, legal, administrative and other factors it may consider relevant
  - CND can choose for other schedule than recommended
<table>
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<td>• Expert Advisory Panel on Drug Dependence (Dependence Liability Evaluation)</td>
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<td><strong>Expert Committees</strong></td>
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<td>• eligible experts: members from all panels</td>
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<td><strong>Expert Committee on Drug Dependence (ECDD)</strong></td>
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<td>• In practice from:</td>
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Expert Committee on Drug Dependence (ECDD)

Recently members from Expert Advisory Panels on

• Drug Dependence (Dependence Liability Evaluation)
• Drug Evaluation
• Drug Policies and Management
• International Pharmacopoeia and Pharmaceutical Preparations
Expert Committee on Drug Dependence (ECDD)

Expert Committee on Habit-Forming Drugs (1949)
Expert Committee on Drugs Liable to Produce Addiction (1950 – 1956)
Expert Committee on Addiction-Producing Drugs (1957 – 1964)
Expert Committee on Dependence-Producing Drugs (1965 – 1966)
Expert Committee on Drug Dependence (ECDD) (1969 – present)
Expert Committee on Drug Dependence (ECDD)

Links to all ECDD reports 1949 – 2006 are available at

www.who.int/medicines

Report of 34th ECDD (March 28-31, 2006):
in preparation
Evaluation procedure

Guidelines for the WHO review of dependence-producing psychoactive substances for international control (WHO/EDM/QSM/2000.5)

See:
www.who.int/medicinedocs/collect/edmweb/pdf/whozip40e/whozip40e.pdf

or www.who.int/medicines
Evaluation procedure

**Step one:**

Pre-review

Screening: critical review yes/no?

Proposed by:
- WHO Secretariat
- ECDD Member
- Participating NGO
### Pre-reviews

**Examples:**
- amfepramone (2000)
- amineptine (2000)
- buprenorphine (2000)
- butorphanol (INN) (2002)
- carisoprodol (2000)
- dronabinol (2000)
- GHB (2006)
- ketamine (INN) (2002)
- khat (2002)
- oripavine (2002)
- pentazocine (2000)
- poppy straw (2000)
- zaleplon (INN) (2002)
- zopiclone (INN) (2002)

*Red: critical review was recommended*
Evaluation procedure

**Step two:**

Critical review if

- notification from a country
- on request of CND
- 'positive' pre-review
- clandestinely manufacturing (no therapeutic use)*

* If therapeutic use: pre-review first
Critical reviews

Examples:
2C-B (2000)
4-MTA (2000)
amfepramone (INN) (2002)
amineptine (INN) (2002)
buprenorphine (INN) (2002 - 2006)
butorphanol (INN) (2006)
diazepam (2000)
dronabinol (INN) (2002 - 2006)
GHB (2000)
ketamine (INN) (2006 - )
khat (*Catha edulis* Forsk.) (2006)
MBDB (2000)
oripavine (2002- 2006)
tramadol (INN) (2002)
zolpidem (2000)
zopiclone (INN) (2006)

Red: scheduling or change of the schedule was recommended
Evaluation procedure

Critical review document: summary of available data

WHO Secretariat

- collects and assembles data
- requests information through questionnaire
  - to Member States
  - to other relevant sources
Critical review document

- substance identification
- chemistry
- general pharmacology
- toxicology, including adverse reactions in humans
- pharmacokinetics
- dependence potential
- epidemiology of use and abuse; estimate of abuse potential
- nature and magnitude of public health problems
- national control
- therapeutic and industrial use
- production, consumption and international trade
- illicit manufacture and illicit traffic
- international control
Critical review document

- substance identification
- chemistry
- *general pharmacology*
- *toxicology*, including adverse reactions in humans
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- nature and magnitude of public health problems
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- illicit manufacture and illicit traffic
- international control
Future review

Substances for evaluation in the 35th ECDD (2008) (as far as identified by 34th ECDD)

- gamma-hydroxybutyrate (GHB) *Critical*
- gamma-butyrolactone (GLB) *Pre-review*
- 1,4-butanediol (1,4-BD) *Pre-review*

Need for animal data in cooperation with CPDD (a WHO Collaborating Centre)
Conclusion

In WHO Substance evaluation

Many aspects are considered

Pre-clinical data: a smaller but important aspect in this process
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Willem Scholten PharmD, MPA
Quality Assurance and Safety: Medicines
Department of Medicines Policy and Standards

scholtenw@who.int
+41 22 79 15540