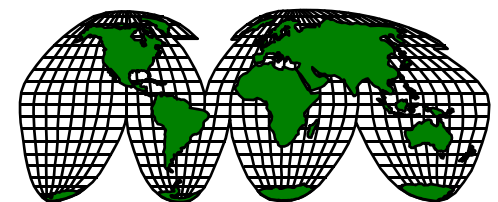
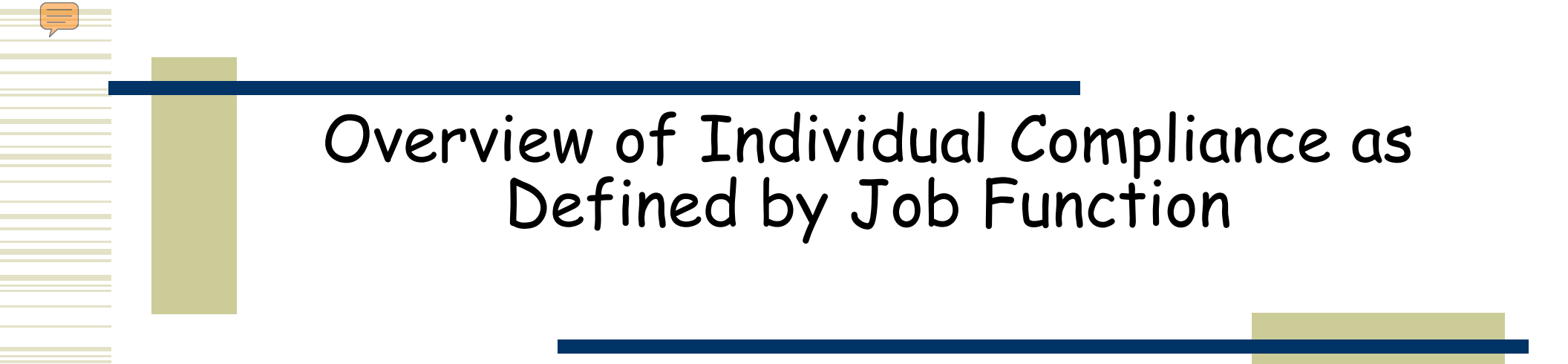


Controlled Substances: Compliance Issues and Practices for the Pharmaceutical Industry

- ◆ Seminar objectives include:
 - providing a detailed review of individual compliance issues as defined by job function;
 - providing a detailed review of corporate compliance issues as defined by recordkeeping;
 - providing examples and hands-on administrative tools for handling controlled substances from purchase through disposal across a variety of registrant types;
 - providing internal auditing tools and techniques for controlled substances programs and preparation for DEA audits;
 - providing an overview of completing forms for DEA 222, ARCOS, inventories, procurement quotas, continuing records, and disposal;
 - providing an overview of List I/ II chemicals inventory and recordkeeping requirements; and
 - providing an in-depth review of import/ export requirements and handling IND materials.





Overview of Individual Compliance as Defined by Job Function

- ◆ Logistics and Accountability are in incremental steps, broken out by job activity:

Initial Registration:	DEA Registrant or Power of Attorney (renewals only)
Ordering:	DEA Registrant or Power of Attorney
Receipt:	Shipping/ Receiving Personnel
Storage & Security:	Security System: Design, Maintenance, and Access
Release Testing:	Standards Room - Analytical Testing
Analysis:	Analyst - Handling and Accountability in the Lab
Distribution for Manufacturing:	Materials Management - Movement into Manufacturing
Manufacturing:	Batch Operator - Manufacturing Processes
Recordkeeping:	QA Accountability Practices
Manufacturing Security:	DEA-Authorized Observer
Waste/ Disposal/ Destruction:	Methods and Accountability



Overview of Corporate Compliance as Defined by Recordkeeping

- ◆ Corporate compliance is often evaluated against both DEA-specified records and adherence to SOPs for internal continuing records.

Routine Recordkeeping:

ARCOS Reporting:

DEA Inspections:

Internal Audits and Investigations

Import/ Export - Shipping

Chain of Custody, Biennial Inventory, & Audits


Annual Inventory

Procedures, Interaction, Relationships




Prologue: *General Regulatory Requirements*

- Movement of CS is via a closed distribution system that regulates and monitors exchanges among registrants. Registration is mandatory to handle CS (with few exceptions - see notes below).




Prologue: General Regulatory Requirements

- ◆ Movement of CS is via a closed distribution system that regulates and monitors exchanges among registrants.
- ◆ Registration is organized by both activity and schedule of CS material being handled.



Prologue: General Regulatory Requirements

- ◆ Movement of CS is via a closed distribution system that regulates and monitors exchanges among registrants.
- ◆ Registration is organized by both activity and schedule of CS material being handled.
- ◆ State law registration must = DEA registration for activity and schedules.



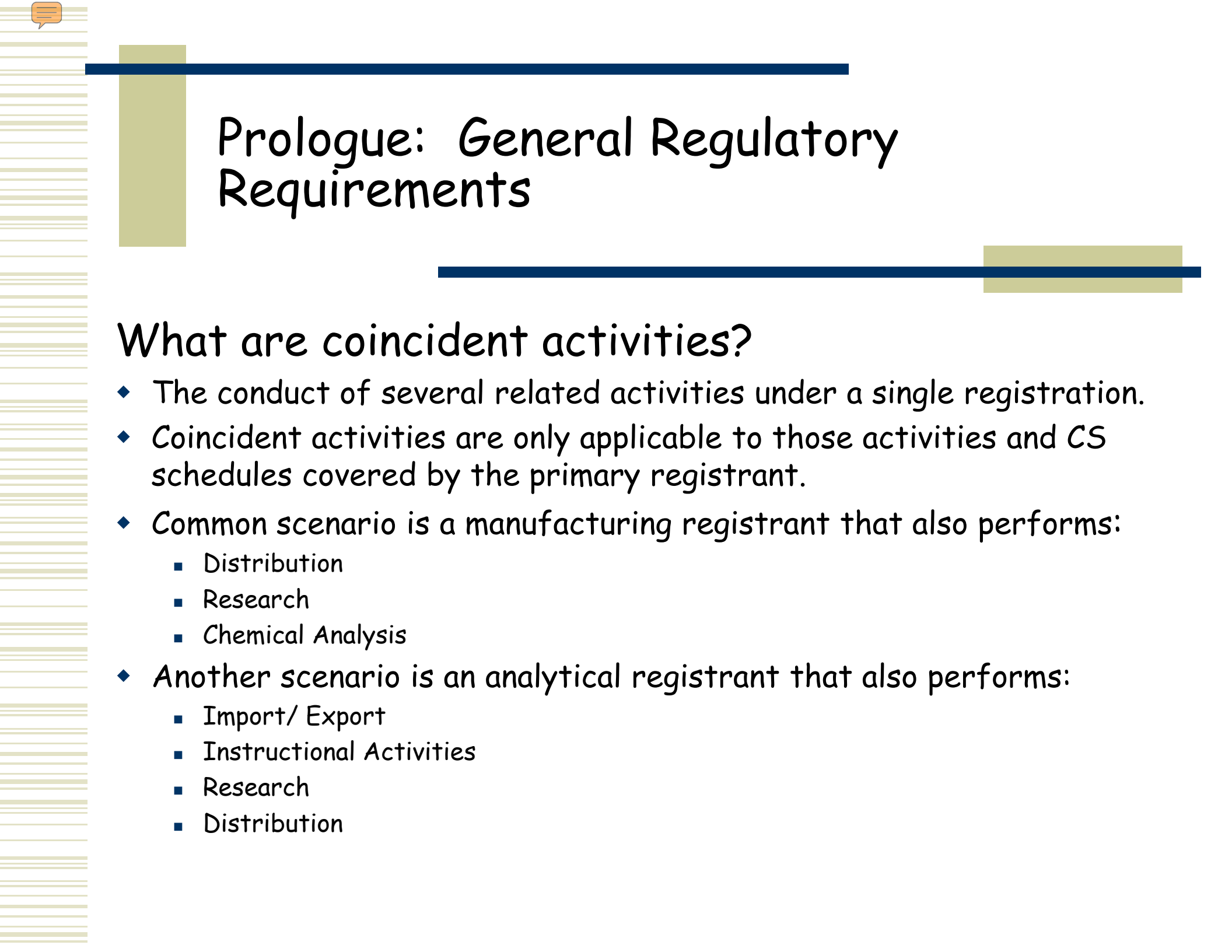
Prologue: General Regulatory Requirements

- ◆ Movement of CS is via a closed distribution system that regulates and monitors exchanges among registrants. Registration is mandatory to handle CS (with few exceptions).
- ◆ Registration is organized by both activity and schedule of CS material being handled.
- ◆ State law registration must = DEA registration for activity and schedules.
- ◆ List I chemical manufacturers, distributors, importers, and exporters must register with DEA. Persons/ firms engaging in 'regulated transactions' with List II chemicals or 'covered machines' are subject to recordkeeping/reporting requirements.



Prologue: General Regulatory Requirements

- Movement of CS is via a **closed distribution system** that regulates and monitors exchanges among registrants.
- Registration is organized by both **activity and schedule** of CS material being handled.
- State law registration must = DEA registration for activity and schedules.
- **List I chemical manufacturers, distributors, importers, and exporters** must register with DEA.
- **Import/ export registration under DEA is in coordination with United Nations treaties.**
 - **US import of C_I, C_{II}, narcotic C_{III} or C_{IV} not allowed** if domestic sources available.
 - **Re-export of C_I, C_{II}, narcotic C_{III} or C_{IV} not allowed.** Complicates international movement of materials.



Prologue: *General Regulatory Requirements*

What are coincident activities?

- ◆ The conduct of several related activities under a single registration.
- ◆ Coincident activities are only applicable to those activities and CS schedules covered by the primary registrant.
- ◆ Common scenario is a manufacturing registrant that also performs:
 - Distribution
 - Research
 - Chemical Analysis
- ◆ Another scenario is an analytical registrant that also performs:
 - Import/ Export
 - Instructional Activities
 - Research
 - Distribution

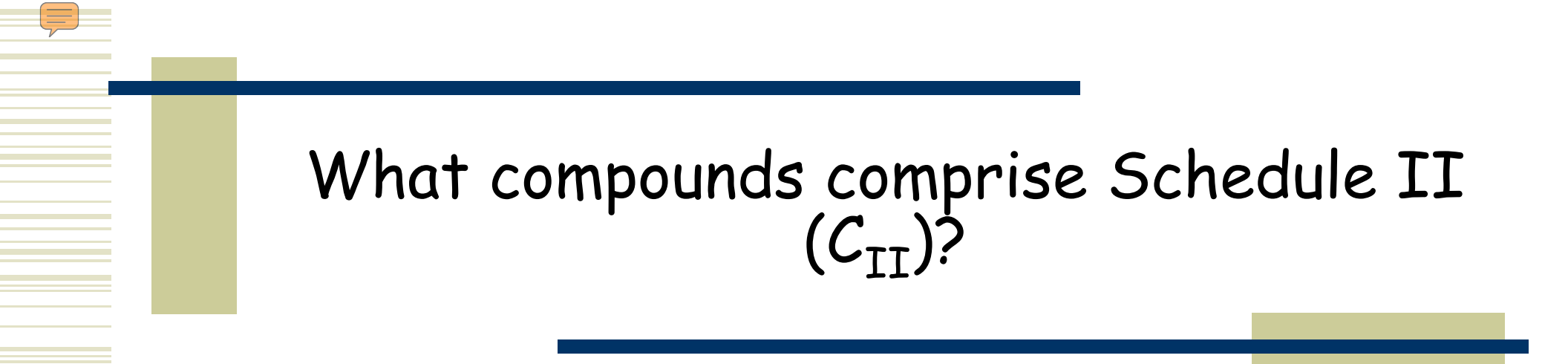
What are the schedule classifications for controlled substances? How are they defined and used?

- Classes of CS compounds are organized into five schedules -- C_I , C_{II} , C_{III} , C_{IV} , or C_V -- based on the potential for physical and psychological abuse/dependence versus medical usefulness.
- Also noted on DEA registration forms as 1, 2N, 2, 3N, 3, 4N, 4, and 5. The "2N" = a non-narcotic C_{II} ; a "2" = a narcotic C_{II} . Same applies for 3N and 4N.
- Schedules used by DEA for:
 - registrations,
 - order forms for CS, and
 - manufacturing and/ or procurement quotas.
- Compounds also assigned 4-digit code numbers (e.g., morphine = 9300) used by DEA for:
 - registrations,
 - order forms for CS, and
 - manufacturing and/ or procurement quotas.
- Office of Diversion Control (202) 307-7297 can clarify status



What compounds comprise Schedule I (C_I)?

- ◆ Schedule I compounds are characterized by:
 - high abuse potential,
 - no currently accepted medical use in US, and
 - a lack of accepted safety for use under medical supervision.
- ◆ There are six categories that include:
 - opiates,
 - opium derivatives,
 - hallucinogens,
 - depressants,
 - stimulants, and
 - CS temporarily listed under the emergency scheduling provisions of 21 CFR 1308.49



What compounds comprise Schedule II (C_{II})?

- ◆ Schedule II compounds are characterized by:
 - high abuse potential,
 - a currently accepted medical use in US or a currently accepted medical use with severe restrictions, and
 - abuse leading to severe psychological or physical dependence.
- ◆ There are six categories that include:
 - opium and opiates, or any salt, compound, derivative, or preparation chemically equivalent, opium poppy, poppy straw, or poppy straw concentrate,
 - coca leaves, including cocaine and ecgonine,
 - certain depressants,
 - certain stimulants,
 - certain hallucinogenic substances, and
 - specifically listed immediate precursors of CS noted in Part 1308.11(g).

What compounds comprise Schedule III (C_{III})?


- ◆ Schedule III compounds are characterized by:
 - less abuse potential than C_I or C_{II} ,
 - currently accepted medical use in US, and
 - abuse may lead to moderate or low physical dependence or high psychological dependence.
- ◆ There are five categories that include:
 - certain stimulants,
 - certain depressants,
 - nalorphine,
 - narcotic drugs in limited quantity, as listed in 1308.13(d), and
 - anabolic steroids.
- ◆ Drug Abuse Control Amendments of 1965 placed previously exempt amphetamines under C_{III} ; most were already under C_{II}
- ◆ Anabolic Steroids Control Act of 1990 added steroids to C_{III} ; no production limits on steroids with low abuse potential or animal use

What compounds comprise Schedule IV (C_{IV})?

- ◆ Schedule IV are characterized by:
 - low abuse potential relative to C_{III} ,
 - currently accepted medical use in US, and
 - abuse may lead to limited physical dependence or psychological dependence, relative to C_{III}
- ◆ There are five categories that include:
 - certain narcotic preparations in limited amounts,
 - certain depressants, including minor tranquilizers,
 - fenfluramine,
 - certain stimulants, and
 - pentazocine.

What compounds comprise Schedule V (C_V)?

- ◆ Schedule V compounds are characterized by:
 - low abuse potential relative to C_{IV} ,
 - currently accepted medical use in US, and
 - abuse may lead to limited physical dependence or psychological dependence, relative to C_{IV} .
- ◆ Three categories include:
 - buprenorphine (narcotic),
 - codeine cough preparations or other narcotic cough preparations in limited amounts, and
 - pyrovalerone (stimulants).



Are there any pharmaceuticals that contain CS compounds but are exempt from the CSA?

- ◆ Exempt Chemical Preparations are exempt from most CSA controls, but only after DEA approval.
- ◆ Intended for laboratory, industrial, educational, or special research purposes and not for general administration to humans or animals.
- ◆ Two sets of criteria apply to exempt chemical preparations:
 - narcotic preparations must contain an adulterating or denaturing agent (e.g., uric acid or radioisotopes), be formulated to reduce abuse, be formulated so the narcotics are not easily extracted
 - non-narcotic preparations must be packaged to minimize abuse and contain an adulterating or denaturing agent (e.g., rubbing alcohol).
- ◆ Federal Register notice is followed by public comment period.
- ◆ Exempt status means only manufacturers required to comply with CSA recordkeeping, reporting, labelling, etc.; these have been modified too:
 - registration and security
 - labelling
 - records and reports

What are the major sections of the Controlled Substances Act?

- ◆ Part 1301: Definitions, Registration, & Security
- ◆ Part 1302: Labelling & Packaging Requirements
- ◆ Part 1303: Quotas
- ◆ Part 1304: Records and Reports of Registrants
- ◆ Part 1305: Order Forms (C_I & C_{II})
- ◆ Part 1306: Prescriptions
- ◆ Part 1307: Miscellaneous (e.g., disposal)
- ◆ Part 1308: Schedules of Controlled Substances
- ◆ Part 1309: Registration of Manufacturers, Distributors, Importers, and Exporters of List I Chemicals
- ◆ Part 1310: Records and Reports of Listed Chemicals and Certain Machines
- ◆ Part 1312: Importation and Exportation of Controlled Substances
- ◆ Part 1313: Importation and Exportation of Listed Chemicals
- ◆ Part 1316: Administrative Functions, Practices, and Procedures