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Drug and Chemical Evaluation Section (ODE)

U.S. Drug Enforcement Administration

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Drug and Chemical Evaluation Section (ODE) Chemical Role includes:

- Determination of chemicals used in the manufacture of controlled substances.
- Use of existing regulatory mechanisms to control compounds used in this manufacture.

Current Activities

- Iodine Regulations (NPRM)
- Sodium Permanganate
- Elimination of Ephedrine/Pseudoephedrine Chemical Mixture Exemptions
- Control of Precursors to Fentanyl
- Positional Isomers Definition

Methamphetamine Production

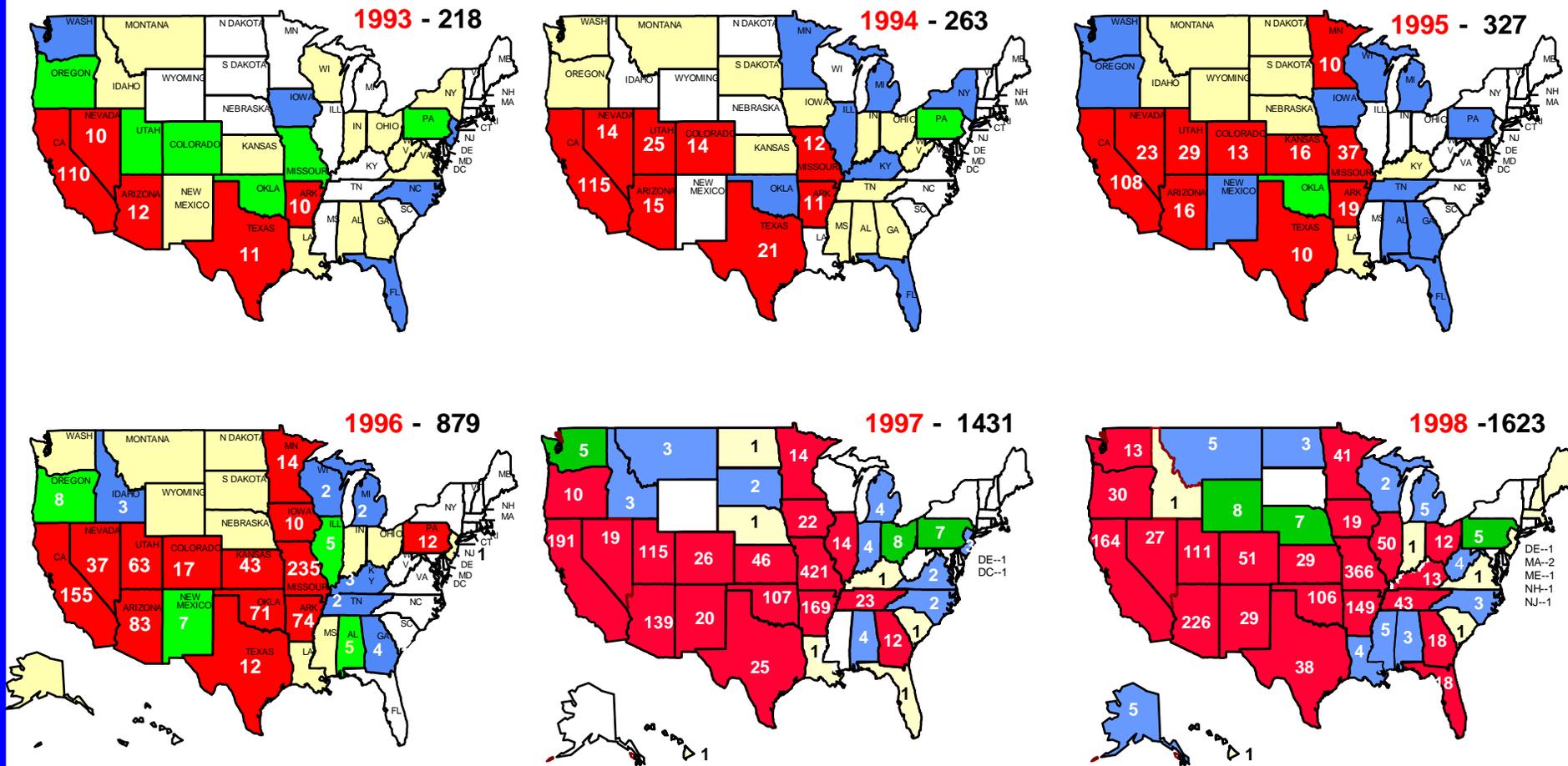
Iodine Control

- Iodine used as reagent in Methamphetamine production
- Number one U.S. clandestinely produced drug

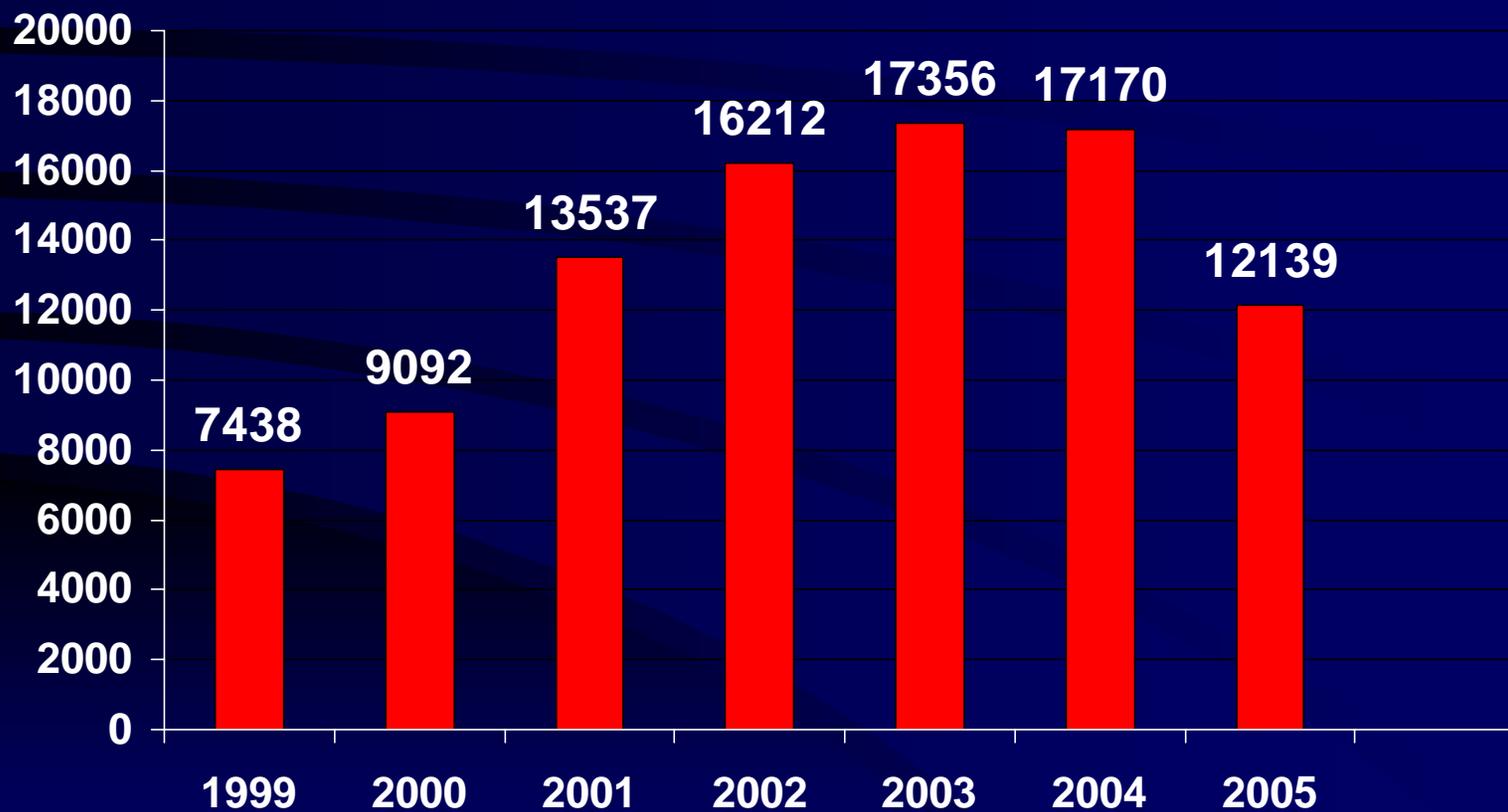


Methamphetamine Clandestine Laboratory Seizures

With DEA participation



**DEA and State and Local Law Enforcement Methamphetamine Seizures
(Includes Labs, dump sites, glassware and equipment seizures)
Calendar Years 1999 – 2005 (Reported through June 2006)**



Methamphetamine Production

- P2P + Methylamine \longrightarrow d,l-methamphetamine
- Ephedrine + Hydriodic Acid + Red-P \longrightarrow d-methamphetamine

Methamphetamine Production

- Ephedrine + Hydriodic Acid + Red-P → d-methamphetamine
-
- Pseudoephedrine + Iodine + Red-P → d-methamphetamine
- or Ephedrine Crystals
-
- Pseudoephedrine + Iodine + Red-P → d-methamphetamine
- or Ephedrine Tincture*

- * Hydrogen Peroxide used to precipitate out crystals





“Mexican Crime Group Methamphetamine ‘SUPER LAB’ Seizure in California.”



“Two Large Capacity Methamphetamine Clan Labs.”



Office of Diversion Control, ODE

Existing Iodine Controls

- List II Chemical
- Threshold 0.4 kilograms
- Only domestic transactions regulated
- Import/Export transactions exempted
- Iodine tinctures (considered chemical mixtures) are exempt

Iodine Problem

- Widely used in clandestine laboratories
- Since tinctures are exempt, lab operators have discovered they can acquire unregulated 7% tincture, add hydrogen peroxide and precipitate out iodine crystals for clan lab use
- Scope of diversion is an international problem

Proposed Changes to Iodine Regulations

- NPRM Published August 11, 2006 with 60-day comment period
- Move from List II to List I
 - Impose registration requirement
- Add Import/Export Controls
- Remove threshold so that all transactions regulated regardless of size
- Control chemical mixtures at concentration level which will regulate 7% iodine tincture
 - Used primarily in livestock/horse industry
 - No household use

Iodine Control

- Will not adversely impact any of the iodine products sold in retail drug store setting
- Will exempt iodine-povidone complexes (all concentrations)
- Will not regulate iodine 2% tincture
- Will not control any of the iodide compounds sold via prescription or radiolabeled for diagnostic purposes.
- Currently reviewing comments and considering further exemptions where appropriate

Sodium Permanganate

Sodium Permanganate

- Direct Substitute for Potassium Permanganate in cocaine processing
- NPRM to control as a List II chemical published March 1, 2005
- Final Rule published October 17, 2006

Cocaine Production



Cocaine is extracted from the coca leaf after the leaves are picked and dried.

TYPES OF CHEMICALS HISTORICALLY USED IN THE PRODUCTION OF COCAINE

SOLVENTS - Methyl Ethyl Ketone (MEK), Methyl isobutyl Ketone (MIBK), Acetone, Ethyl ether, Toluene, Kerosene

**ACIDS - Sulfuric Acid
Hydrochloric Acid**

**BASES - Calcium, Sodium or Potassium Carbonate,
Calcium Oxide
Ammonia Water**

OXIDANTS - Potassium Permanganate



PRODUCTION OF ILLICIT COCAINE FOUR STEPS

**COLLECTION OF COCA
LEAVES**

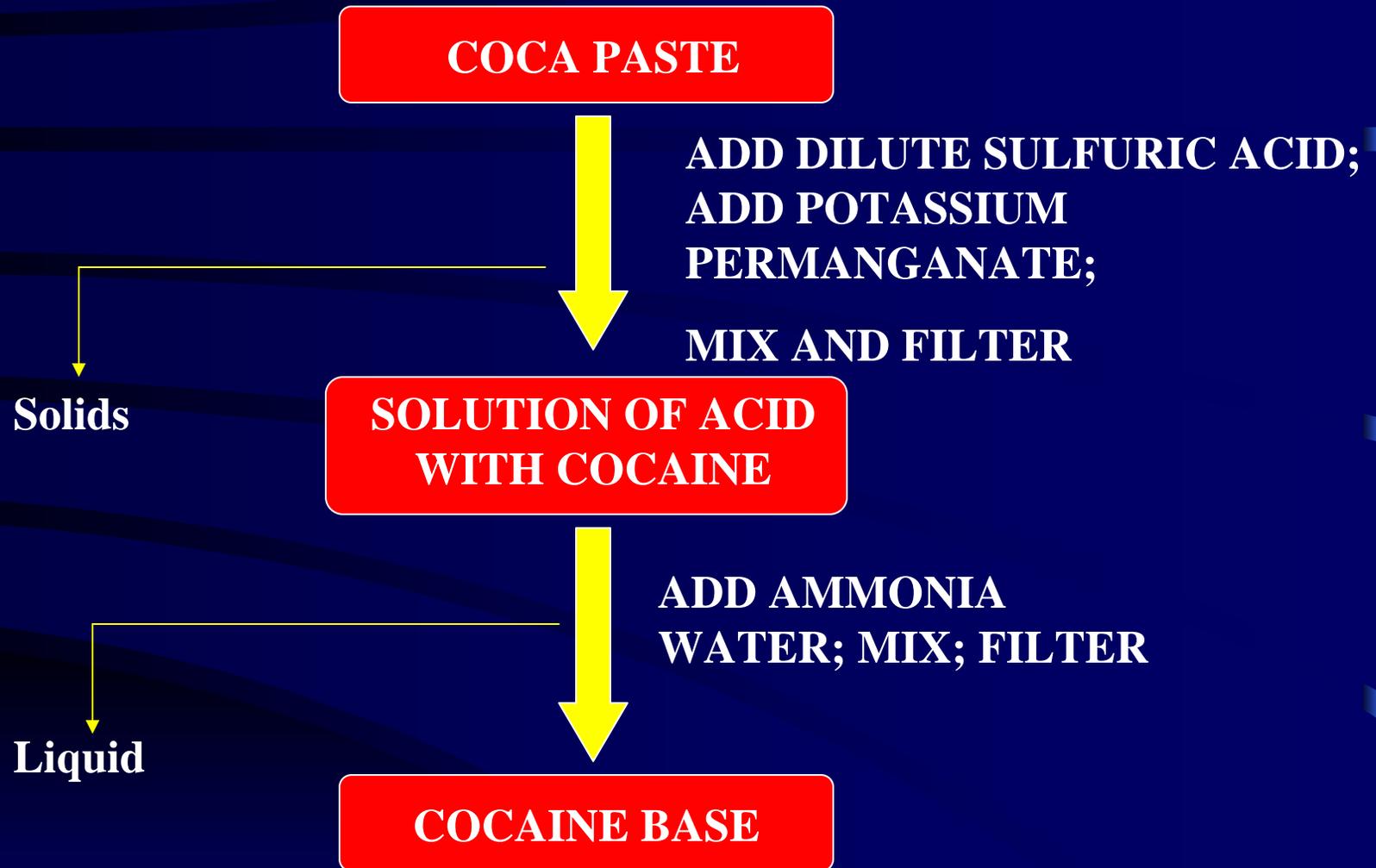
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graph TD; A[COLLECTION OF COCA LEAVES] --> B[PRODUCTION OF COCA PASTE BY SOLVENT PROCESS OR ACID PROCESS]; B --> C[PRODUCTION OF COCAINE BASE]; C --> D[PRODUCTION OF COCAINE HYDROCHLORIDE];
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**PRODUCTION OF COCA PASTE BY
SOLVENT PROCESS OR
ACID PROCESS**

**PRODUCTION OF COCAINE
BASE**

**PRODUCTION OF COCAINE
HYDROCHLORIDE**

Production of Coca Base





Sodium Permanganate

- Direct Substitute for Potassium Permanganate
- Potassium permanganate one of the most important chemicals for cocaine production
- U.S. producers changing production toward increase production of Sodium Permanganate
- Sodium Permanganate available as a 40% solution has advantage of being miscible with water in all proportions (Potassium Permanganate has only 6.38% solubility in water)

Proposed Controls for Sodium Permanganate

- Since directly substitutable for Potassium Permanganate
- Propose Same level of Control
- List II – No Registration
- Thresholds: 55 kgs domestic, 500 kgs import/export
- Chemical Mixtures \leq 15 percent exempt

Ephedrine/ Pseudoephedrine Exemptions

Ephedrine/ Pseudoephedrine Exemptions

This Interim Rule announces the removal of the CSA exemptions for chemical mixtures containing ephedrine and/or pseudoephedrine.

- In a Final Rulemaking [68 FR 23195] published on May 1, 2003, DEA initially created an exemption from CSA chemical regulations for all chemical mixtures containing five percent or less total ephedrine/pseudoephedrine.
- Additionally, that rulemaking created an exemption for chemical mixtures consisting of unaltered harvested plant material containing ephedrine alkaloids (e.g. ephedra).
- This Interim Rule, however, removes these two exemptions. Therefore, these materials shall now be subject to all CSA provisions.

- The Combat Methamphetamine Epidemic Act of 2005 (CMEA) added additional controls on ephedrine and pseudoephedrine and mandated that DEA limit the domestic production and importation of materials containing ephedrine and pseudoephedrine to quantities necessary for medical, scientific and other legitimate purposes.
- DEA has growing concerns regarding ephedra and dietary supplements containing ephedra, and their use as the source of the precursor material for use in the illicit production of methamphetamine.
- While the FDA has taken action to eliminate ephedra dietary supplements from the U.S. market, DEA has seen increases in number of import requests for ephedra, leading to a concern that these products are being diverted for use in illicit manufacture of methamphetamine.

- Given these concerns, and Congressional direction to limit the importation of materials containing ephedrine/pseudoephedrine, DEA is eliminating the exemptions for this material.

Clandestine Fentanyl



Pharmacology

- Synthetic opioid
- Schedule II narcotic
- Low therapeutic index
 - Euphoria vs respiratory depression
- Effects are similar to morphine and heroin, but with two principle differences:
 - 1) Duration of action (rapid onset, shorter acting)
 - 2) Potency (much greater potency)
 - 50 -100x more potent analgesic than Morphine
 - 30 - 50 x more potent analgesic than Heroin
 - Potency depends on route of administration and the effect being measured



History of Fentanyl Abuse

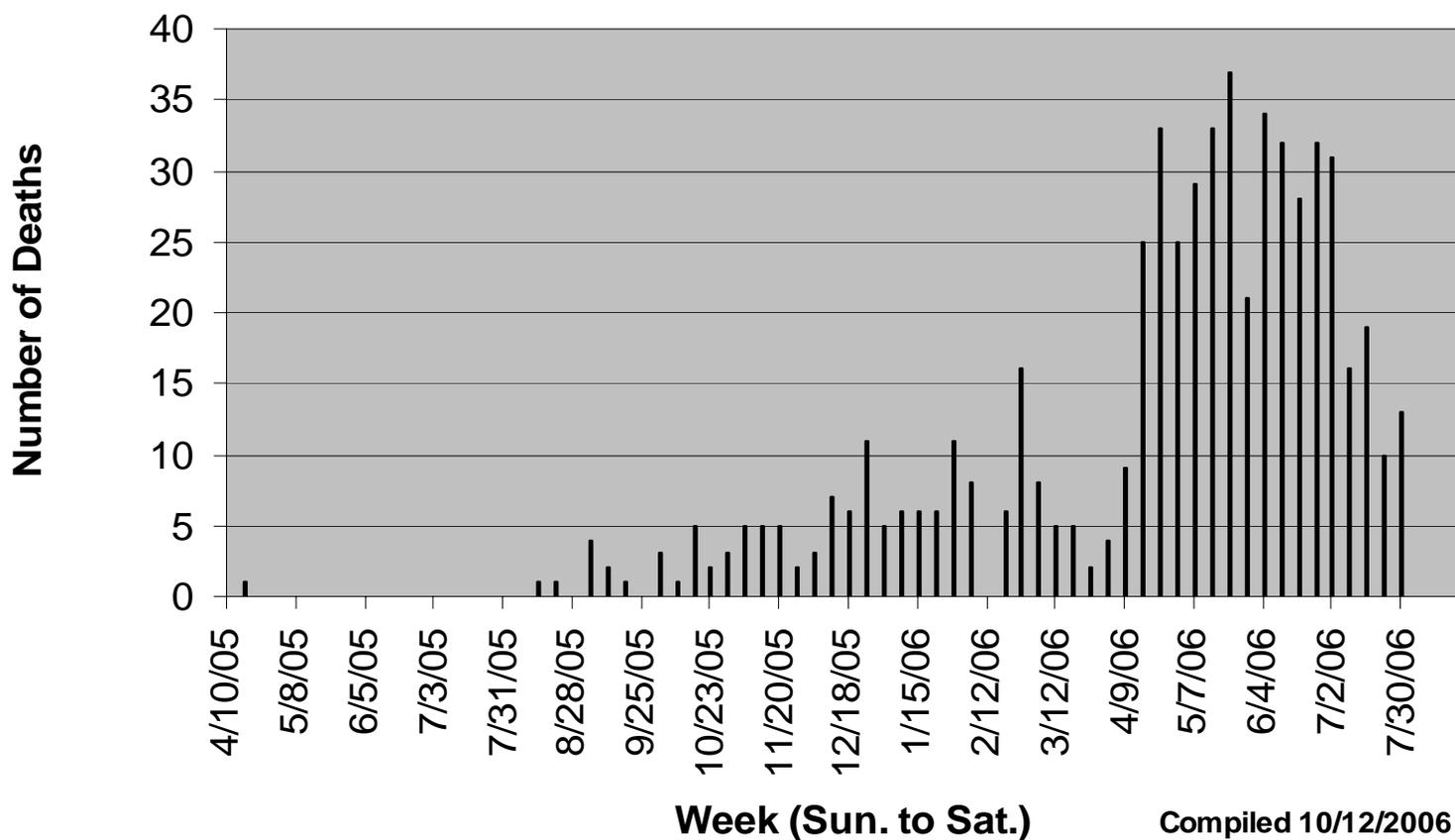
- 1970's to present – Abuse of injectables
 - Medical professionals (doctors/nurses/pharmacists) often in a hospital setting
- 1990's to present– Abuse of transdermal patch & Troche
- 2000's – Clan labs making fentanyl
 - 6 Fentanyl clan labs since 2000
 - 5 of which are known or suspect to have used Siegfried Method
 - DEA preparing regulations to control precursor chemicals
 - 499 Confirmed Death + 288 Suspected deaths in U.S.



**Illicitly Manufactured Fentanyl-Related Deaths
by Location Since 3/4/2005
(DEA Compiled: 10/12/06)**

Location (City/area and surrounding counties)	Confirmed Deaths	Suspected Deaths
Chicago, Illinois	214	2
Detroit, Michigan	150	62
Philadelphia, PA/Camden, NJ/Wilmington, DE	215	14
Rest of PA		57
New York State		45
St. Louis, Missouri	27	14
Other areas		13
Total Deaths =>	606	207

Illicitly Manufactured Fentanyl-Related Deaths/Week in U.S. From March 4, 2005 – August 5, 2006 (Total DEA Confirmed Deaths Graphed: 606)



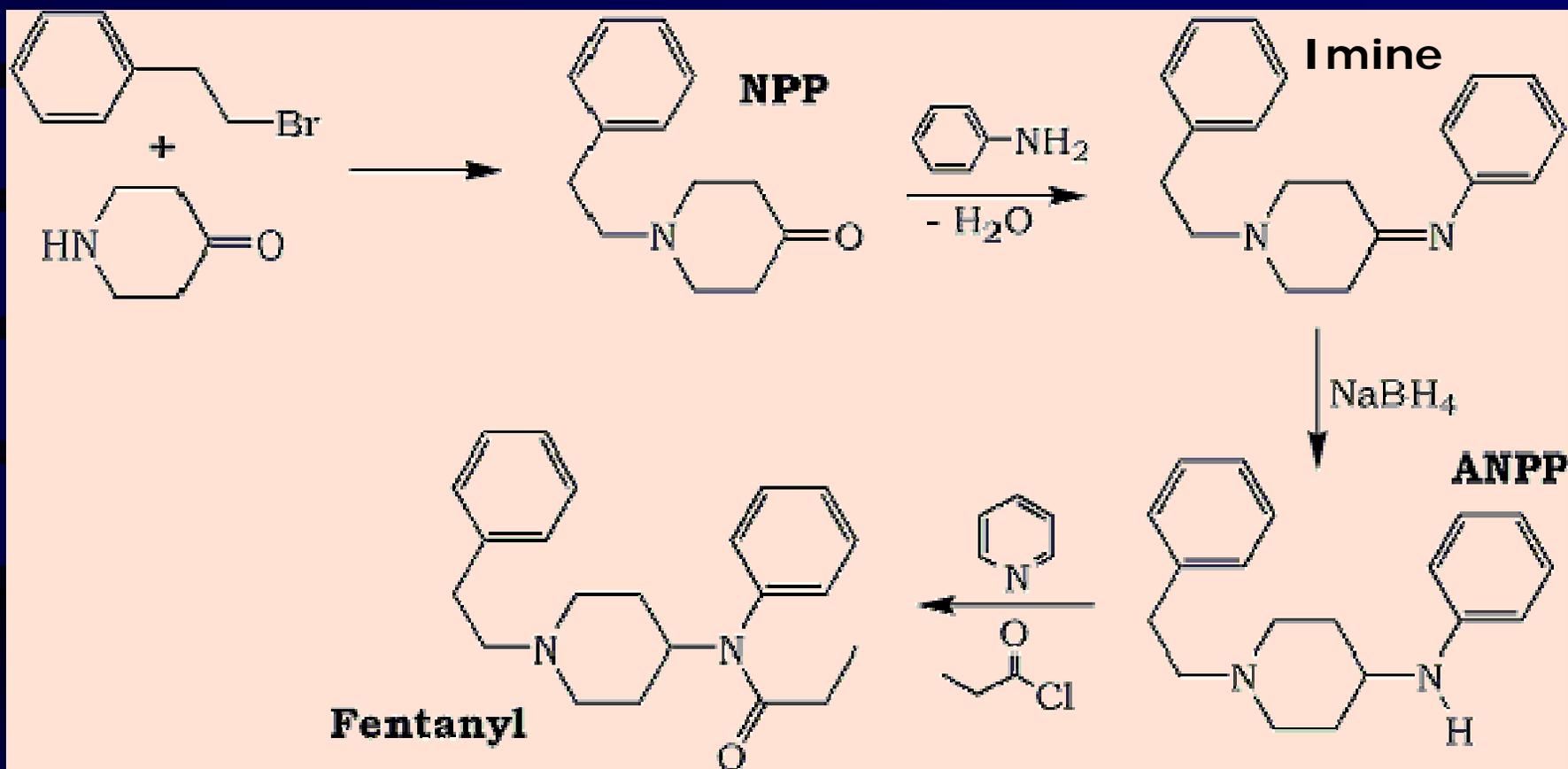
Clandestine Lab in Toluca, Mexico

Sunday, May 21, 2006 PGR/SIEDO and AFI



Control, O
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Siegfried Method



Control of Precursors

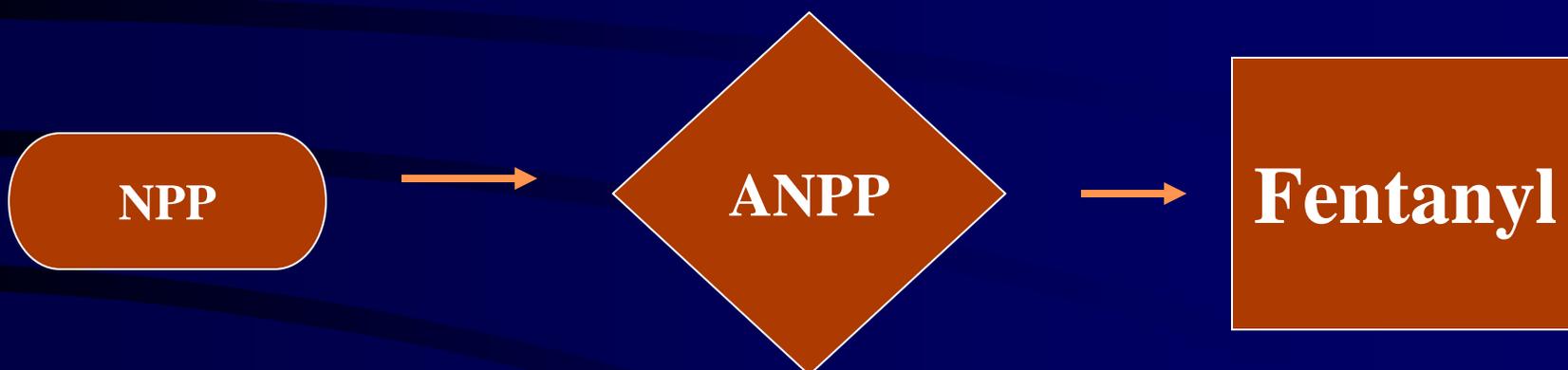
- DEA is moving to control precursors:
 - NPP (N-phenethyl-4-piperidone) as a listed chemical in List I
 - ANPP (4-anilino-N-phenethyl-4-piperidine) as an immediate precursor in Schedule II

Legitimate Uses Of NPP

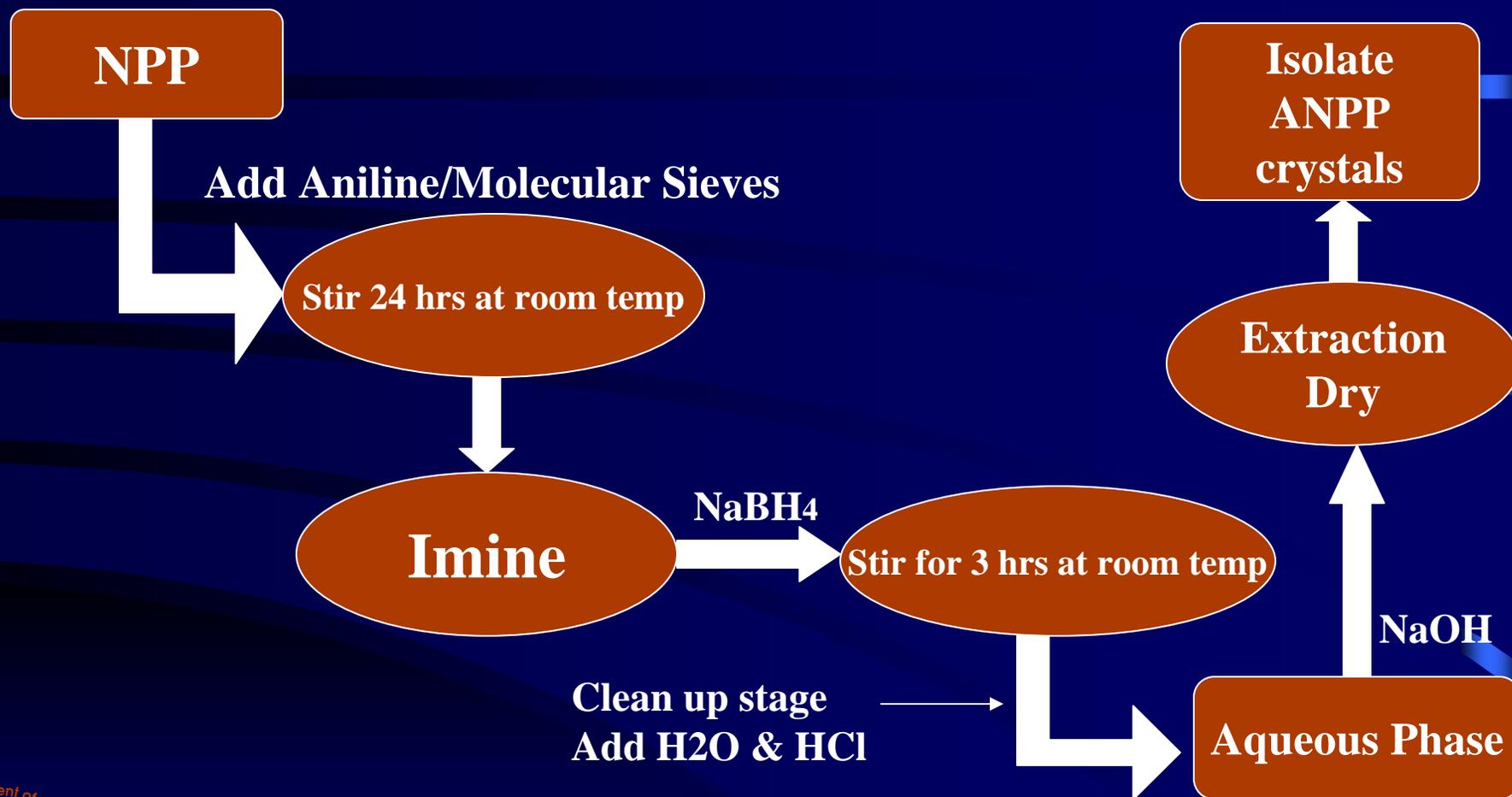
- Legitimate uses of NPP:
 - Pharmaceutical Industry
 - Pharmaceutical R&D to synthesis experimental compounds
 - Analytical Reference Standards
- Drugs prepared from NPP:
 - Fentanyl
 - Carfentanyl
 - Cinitapride – gastrointestinal motility agent
 - Fenspiride – nonsteroidal anti-inflammatory agent
- Specialty Chemical
 - Low volume
 - Only 6 domestic chemical suppliers of NPP
 - Only 24 domestic purchases since January 1, 2004



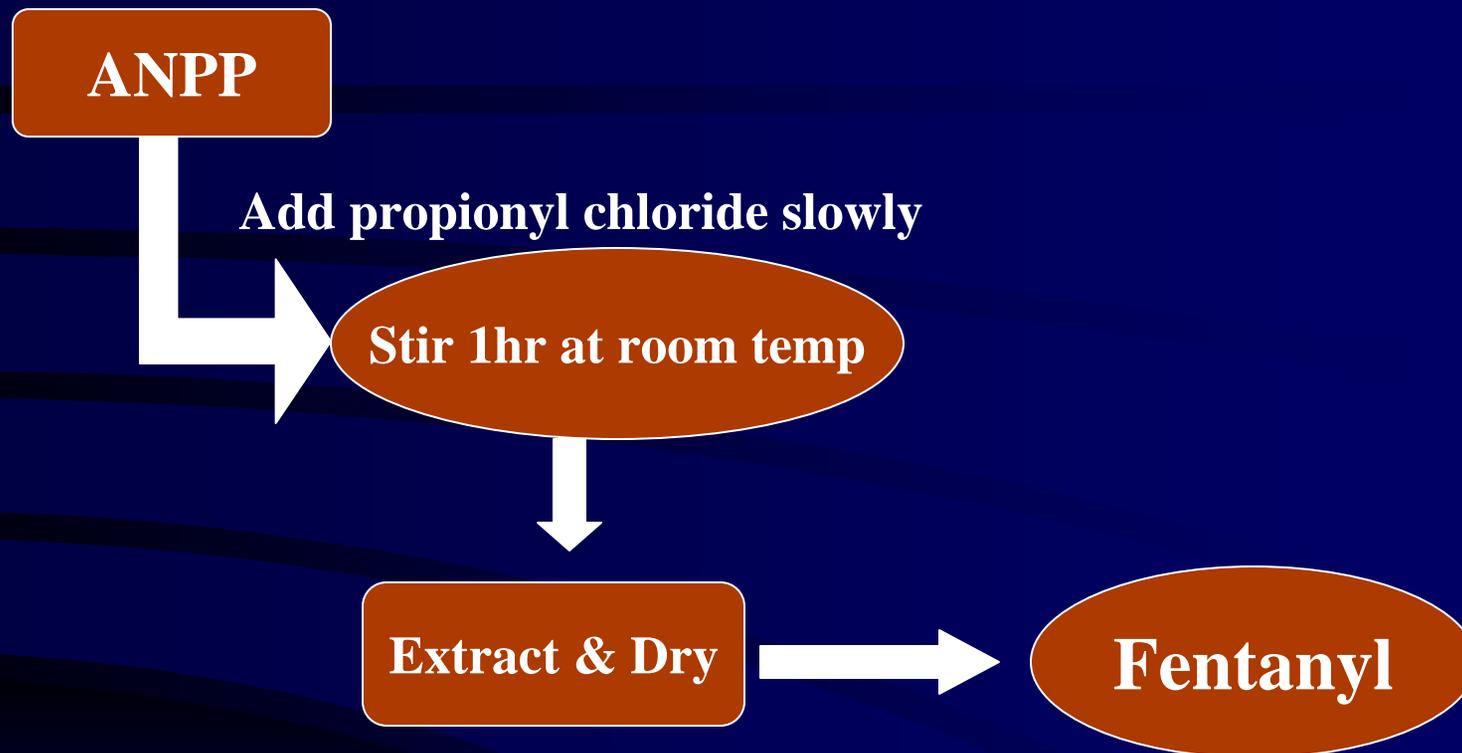
Fentanyl Synthesis: Siegfried Method



Siegfried Method: Making ANPP



Siegfried Method: Making Fentanyl



LA Area Fentanyl / MDA Lab

- November 2005, law enforcement seized a lab in the LA area suspected to be Fentanyl lab.
- Chemists analyzed the samples submitted and confirmed fentanyl and MDA present.
- A 5 kilogram bag of “NPP” (1-phenethyl-4 piperidone) precursor was seized.



Definition of Positional Isomers

- This Rulemaking establishes a specific, technical definition for the term “positional isomer” as it relates to Schedule I hallucinogens.

Background: Positional Isomers

- The CSA (21 U.S.C. 802(14) and 21 U.S.C. 812(c)(I)(c)) specify which hallucinogenic compounds are considered Schedule I Controlled Substances. The CSA states that all salts, isomers and salts of isomers of these compounds are also Schedule I Controlled Substances.
- Under 21 CFR 1308.11(d), the CSA states that the term isomers shall include “optical, positional and geometric isomers”.
- Optical and geometric isomerism easily determined.
- The definition will include precise language that will allow for an unambiguous determination of which isomers of Schedule I hallucinogenic substances are considered to be “positional”, and therefore subject to Schedule I control.

- The addition of a definition for the term “positional isomer” will assist legitimate research and industry in determining the control status of materials that are isomers of Schedule I hallucinogens.
- While DEA will remain the authority on ultimately determining the control status of a given material, providing a specific definition for “positional isomer” will ensure consistent criteria are utilized in making these determinations.
- The addition of a definition for the term “positional isomer” will not result in the control of additional substances or have a negative impact on legitimate researchers or industry working with isomers of Schedule I hallucinogenic substances.

Status: Positional Isomers

- A Notice of Proposed Rulemaking (NPRM) was Published in Federal Register on May 25, 2006
- A final rule is being circulated for signature.

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