

Investigators

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Goals:

- To develop an Extractability Rating System to generate, document, and summarize laboratory data on extractability of prescription opioids
 - Definitions of extractability and its key dimensions
 - Categorization system for “ease of extractability”
 - Standard Extractability Battery
 - Scoring systems for SEB
- Develop an approach to implementing ERS to produce extractability ratings of existing products, in the absence of laboratory data
- To provide ratings of selected products



Extractability Techniques: Examples

111 statements generated; reduced to 32 unique and plausible techniques

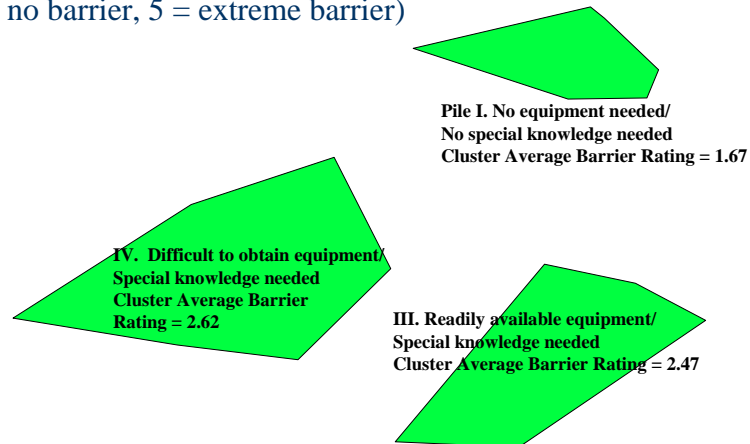
- Bite and chew pill
- Crush pill and smoke or snort it
- Dissolve the drugs in solvents such as freon, methylene chloride, or acetone
- Boil patch and prep for IV
- Slowly add drops of NaOH until the water reaches pH9... crystals will fall off in water... freeze water for 10 minutes... filter crystals... dissolve crystals in anhydrous alcohol... add HCL and shake ... let alcohol evaporate



Concept Map: Three cluster solution

Average ratings of barrier to use:

(1 = no barrier, 5 = extreme barrier)

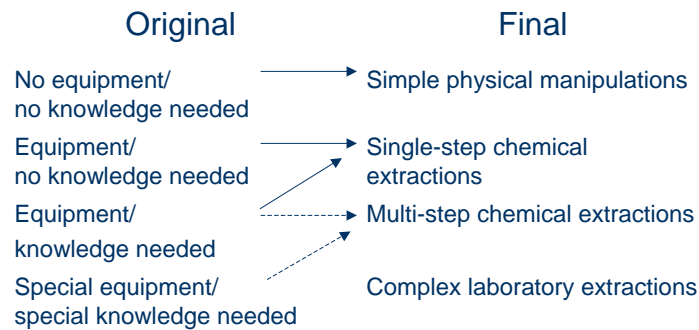


Expert Meeting Conclusions: Extractability Definition

- Ease of extractability
 - The difficulty of an extraction procedure carried out to modify, purify, or prepare an active ingredient for an alternative route of administration
- Purity
 - The weight of active in an extract divided by the total weight of the extract
- Efficiency
 - The weight of active in an extract divided by the starting weight of an extract
- Potency
 - The number of active doses in an extract



Expert Meeting Conclusions: Category System



STANDARDIZED EXTRACTABILITY BATTERY: _____

Technique	Category of Difficulty	Purity	Percent extracted	Routes of Administration					Total Number of Routes of Administration
				IV	PO	SL/Buccal	Smoking	Nasal	
Simple Physical Methods:									
Crushing	I								
Cutting	I								
Peeling	I								
Simple chemical manipulations									
Cold Water	II A								
Hot Water	II A								
Ethanol	II B								
Olive Oil	II B								
IPA	II C								
Acetic acid	II C								
Acetone	II C								
Gasoline	II C								
Methanol	II C								
Mineral Spirits	II C								
Ether	II C								
Ethyl acetate	II C								
Coleman Fuel	II C								
Methylene chloride	II C								
Chloroform	II C								
Multi-step extractions									
Acid dissolution followed by: Methylene Cl, then separate methylene Cl, discard, add methylene Cl to aqueous, adjust pH, let separate, reduce to dryness	III								
Complex procedures requiring laboratory setup and specialized	IV								

Scoring System 1: Scoring Table

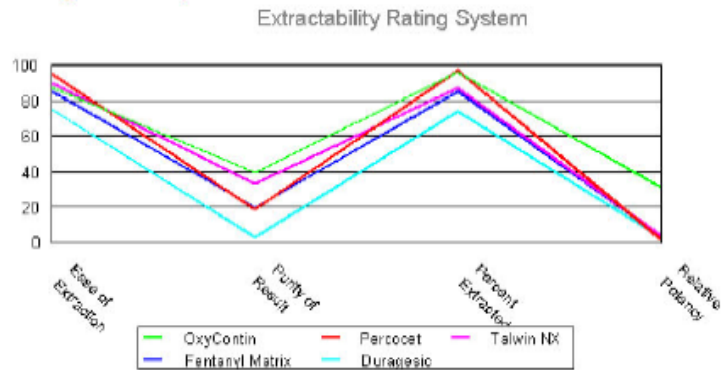
- Purpose: To reduce data from SEB to that relevant to abuse liability in real world
- Generates “extractability profile” of each drug

	Ease	Purity	Efficiency	Potency
IV				
PO				
SL				
Smoking				
Nasal				



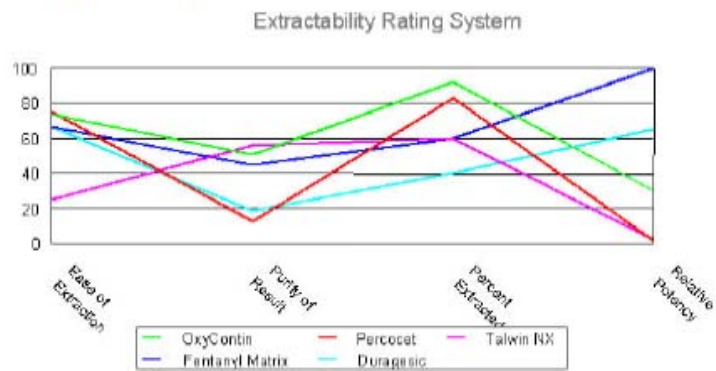
Summary of Oral Extractability

Figure 3: All Drugs Summary Profile for PO Route of Administration



Summary of IV Extractability

Figure 4: All Drugs Summary Profile for IV Route of Administration



Composite Measure

- Efforts were made to reduce Scoring Tables into a single composite score
- These were not successful:
 - Dimensions of extractability do not correlate, suggesting that in raw form they cannot be combined into a single composite
 - Various mathematical approaches to generating a composite did not result in reliable values



Overall Results of Extractability Study

- By expert consensus process, definitions of extractability, its key dimensions, and definitions of these dimensions were produced
- The “traditional” classification system for ease of extractability was empirically examined, found wanting, and revised
- A Standard Extractability Battery was developed, which can serve as an initial industry standard on minimum data required for testing and documenting extractability
- Scoring Tables developed which generate an “extractability profile” of a drug product

