



Benchmark Evaluations of Tampering with Pharmaceutical Dosage Forms

Opioid Abuse Resistance Conference

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October 2005



Tampering

- To interfere so as to weaken or change for the worse
- Manipulating a pharmaceutical dosage form so as to change its (drug delivery) performance in a way not specified or intended by the manufacturer
 - Tampering is distinguished from abuse in that the latter can occur without manipulation of the dosage form



Scope of Tamper Evaluations

- Simulated IV Tampering
- Simulated Oral/Nasal Tampering
- Simple Extractions
- Advanced Extractions



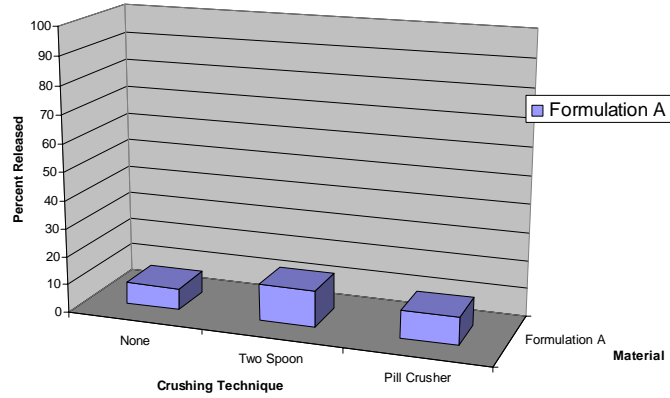
Simulated IV Tampering

- Three analysts (variability in crushing)
 - Run intact or crush material via spoons or pill crusher
 - Transfer to spoon
 - Add 2 ml water - Mix with spatula – heat to boiling - mix
 - Draw into insulin syringe through cotton

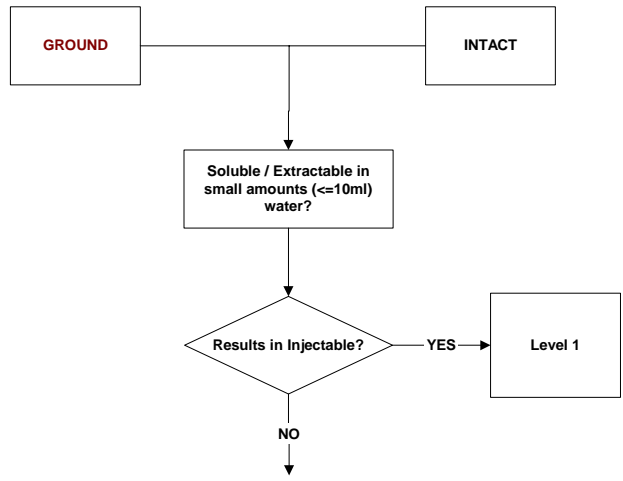


Simulated IV Tampering

EXTRACTION FOR INTRAVENOUS USE



Simulated IV Tampering





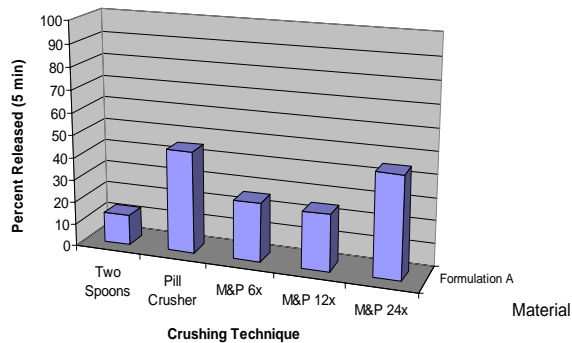
Simulated Oral/Nasal Tampering

- Simulated Oral/Nasal
 - Chewing or crushing for nasal administration.
 - (Mortar & Pestle 6,12,24 strokes)
 - One strike on tablet to fracture, then count strokes
 - Transfer using 50 ml warm media
 - 500 ml of SGF w/pepsin for media
 - Attempting to measure immediate release component
 - Sampled after 5, 25 and 45 minutes

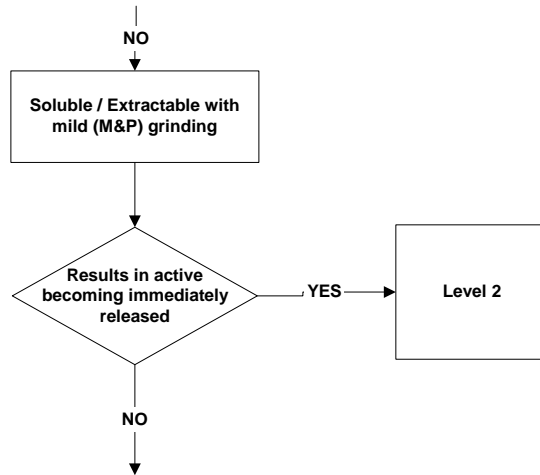


Simulated Oral/Nasal Tampering

CRUSHING FOR ORAL/NASAL USE



Simulated Oral/Nasal Tampering



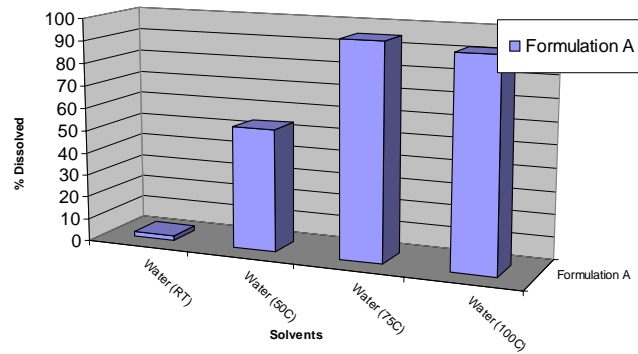
Simple Extractions

- Simple Extraction – 10 ml solvent – 15 and 120 minutes.
 - Water (RT)
 - Water 50C
 - Water 75C
 - Water 100C
 - Acid (0.1N HCl; pH = 1.2)
 - Base (2N NaOH; pH = 13.1)
 - 5% Ethanol (beer)
 - 14% Ethanol (wine)
 - 40% Ethanol (80 proof liquor)



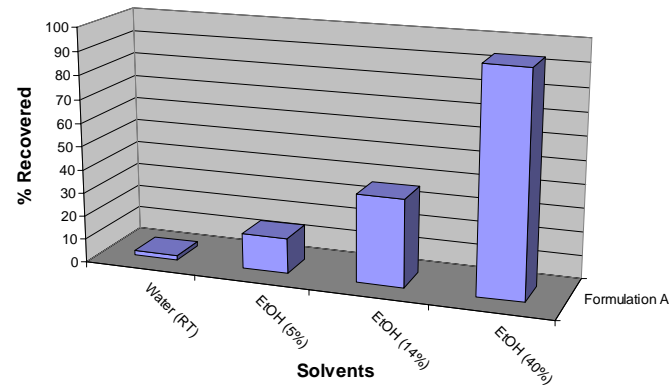
Simple Extractions

Extraction with Water for Oral/Nasal Use

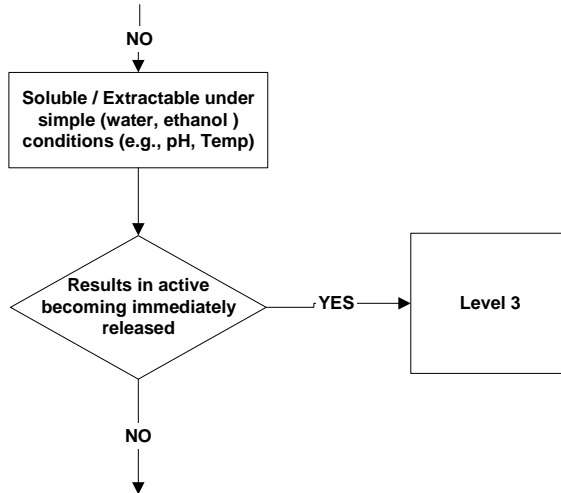


Simple Extractions

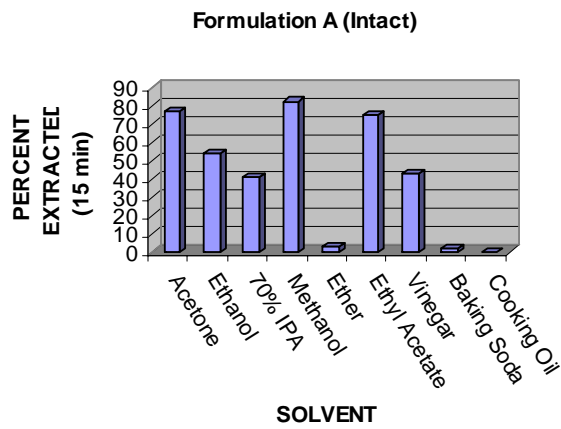
Extraction with Ethanol for Oral/Nasal Use



Simple Extractions



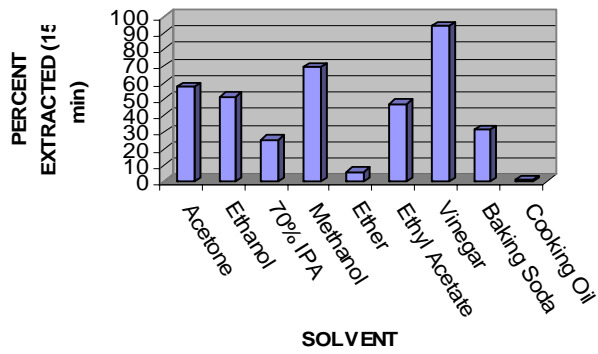
Advanced Extraction (Intact)



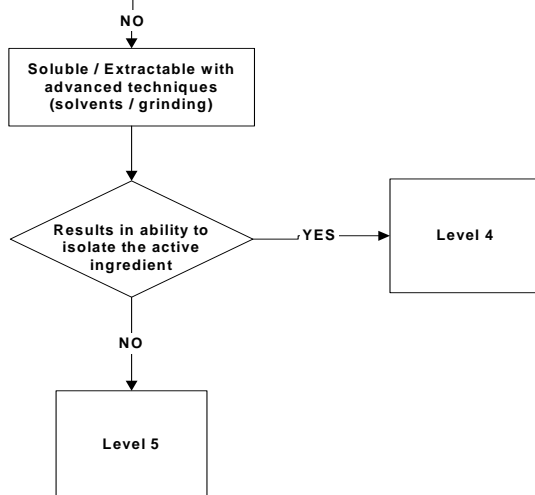


Advanced Extraction (Crushed)

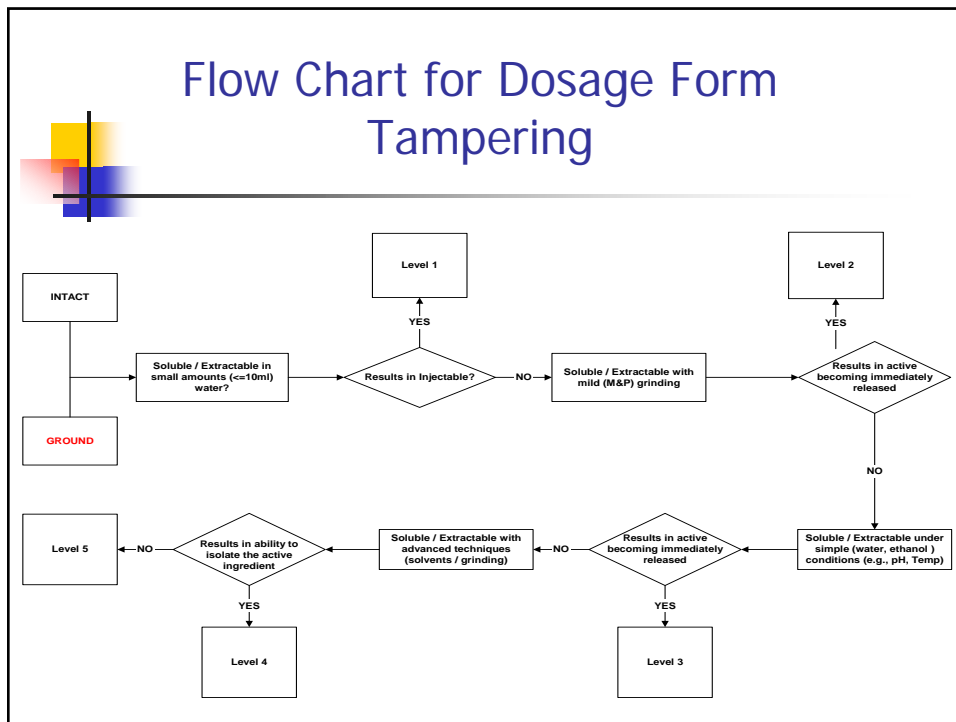
Formulation A (Crushed)



Advanced Extractions



Flow Chart for Dosage Form Tampering



Summary

- A consistent, logical scheme for evaluating the tamper resistance of pharmaceutical formulations
 - Covers tamper methods from simple direct methods intended for IV use to more complex and longer processes
 - Could form the basis for a set of standardized methods for general use