

## Section IV. Laboratory Manipulations and Extraction Studies (Category 1): Day 2 Summary & Conclusion

*3:30 – 3:45*

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# Key Messages

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- What are the appropriate comparators?
  - Other ADFs---equivalent or better
  - IR---better
- Multiple conditions for injection
  - Limited to water/saline
  - Shaking, intact/cut/crushed tablets
  - Minutes to hours, customized to product attributes
- Extraction
  - Common solvents with different characteristics
- Test to plateau or failure
- Third party testing: agency and sponsor discussion

# Key Messages

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- Standardization of core elements
- Tailor experiments
  - API & formulation
  - Routes of abuse
  - Identify vulnerabilities
- Laboratory resources are not unlimited
  - Wise choices
  - Flexible, adaptive, approach
  - Iteration when necessary

# Implications for Industry: FDA Guidance (Source: Ed Cone)

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- Adherence to guidance provides orderly R&D pathway and decision framework
- Laboratory assessments must be tailored to API & formulation
- Experimental designs should be dynamic in nature and explore boundaries
- Minor ADF weaknesses can be present in effective formulations
- Pathway to tiered labeling
- Methods to assess pro-drugs & NCEs
- Extends to generic assessments
- Applies to other CNS-actives

# Key Messages

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- New evolving science
- Improvements in methodology needed
  - Hardness measures
  - Chewing model
  - Viscosity measures
  - Measures of work (effort X time X resources)
- Generic guidance
- Generic equivalence in Category 1 tests



# IN-VITRO EXPERIMENTS

## (Source: Bob Bianchi)

- Develop written protocols that produce statistically valid, reproducible results.
  - Include related comparator product
  - Include controls
  - Include quality assurance procedures
  - All experiments must be conducted at least in triplicate
  - Use graphs and charts to illustrate data
  - Experiments should be conducted by an independent laboratory that is blinded to the fullest extent possible in addition to in house laboratory experiments

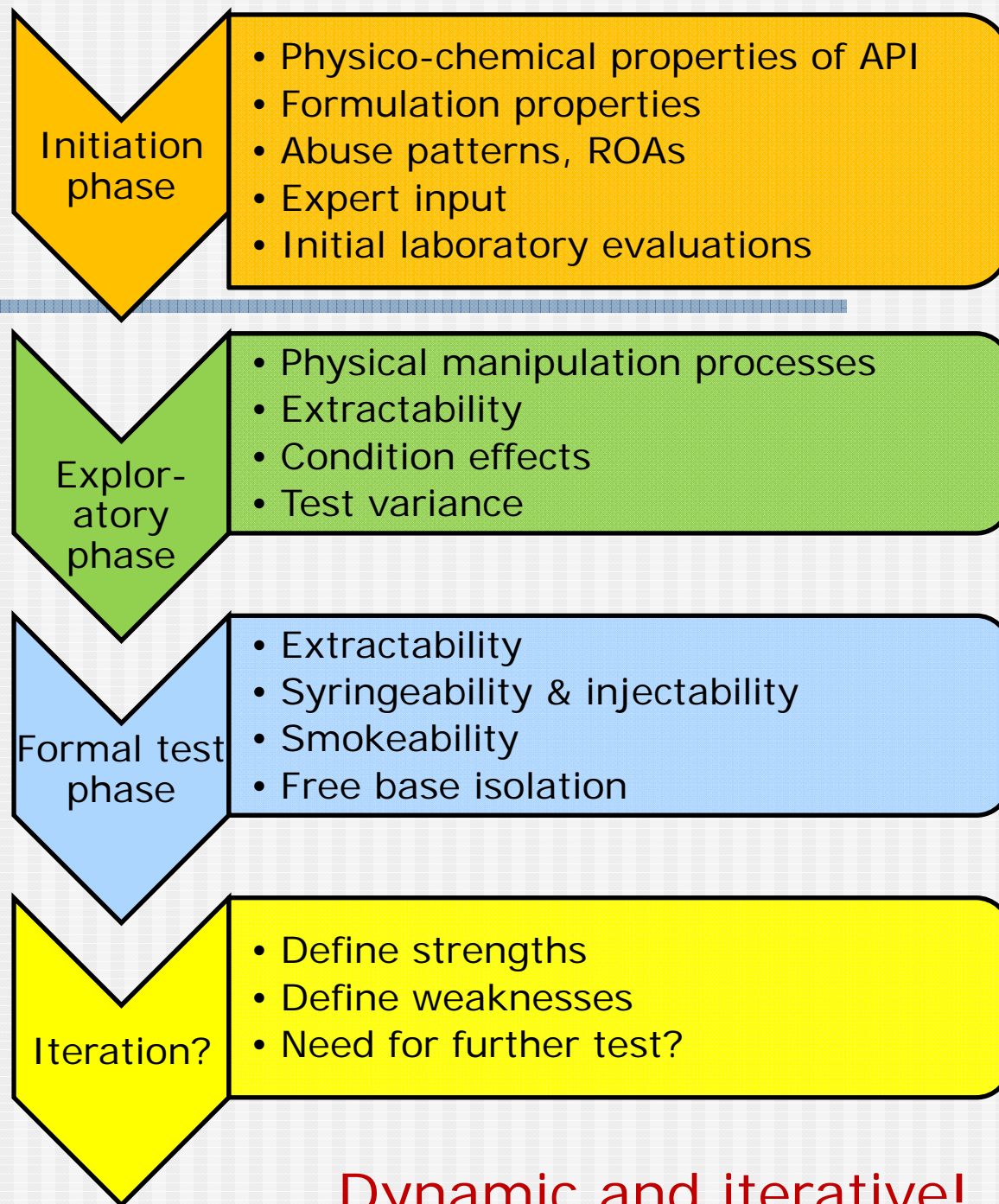


# Summary

## (Source: Bob Bianchi)

- No objective measure exists to measure tamperability/extractability
- Each product/system requires unique experiments designed to address vulnerabilities
- Use independent laboratory & abuse experts
- Consider all modes of abuse & all strengths
- Include photographs, graphs & charts where appropriate
- **No product has been proven to be tamper proof**

# Systematic *In Vitro* Lab Studies



Dynamic and iterative!



# Implications for Real World Abusers

(Source: Ed Cone)

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- Tampering practices will become more innovative
- Internet pseudoscience will continue to evolve
  - Focus on means to overcome polymeric matrices
  - Separate/deactivate antagonists
  - Separate aversives
  - Use of extensive informational resources
- Potential increase in abuse by intended ROA
- Enhance focus on immediate release products
- Increase in purchases on Internet for softer-target RXs