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The Role of Forensic Analysis in the Biotechnological Manufacturing Industry

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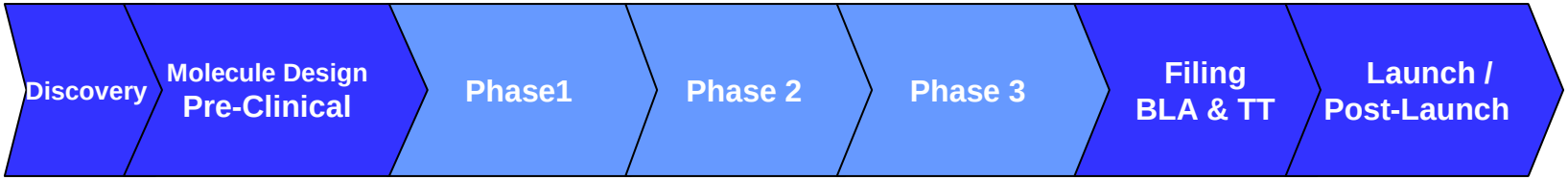
What is Forensic Analysis?

- “Forensic”
  - relating to or dealing with the application of scientific knowledge to legal problems. (Merriam-Webster Dictionary)

- “Forensic Analysis”
  - Generation of scientific data to establish the nature of extraneous matter as part of an investigation through sound science. (Practical definition)

Forensic Analysis is Present at all Product Commercialization Stages



Manufacturability Assessment	Process Characterization	Determination of Typical Particle Profile	Deviations/OOS Investigations
Selecting candidate with minimum self-association/aggregation	Tools to measure protein oligomers, subvisible and visible particles, effect of process conditions on aggregation and particle formation.	Focus visual inspection, and on particle ID and characterization. Also determination of Leachables/ extractables & device impact.	Particle ID and characterization. Subvisible particle characterization for more involved investigations.

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Scenarios that Lead to Forensic Analysis in Manufacturing Operations

- Commercial Product Incidents
  - Biological Product Deviations
    - Product Recalls
  - Customer Complaints
  - Manufacturing Incidents
    - Commercial Product Disposition Holds

- Commercial Facilities and Equipment Incidents
  - Real-time on-site support to prevent production Delays

- Raw Material Screening
  - Adulteration, tampering, counterfeiting, patent infringements.

Key Elements for a Successful Forensic Support Operation

- Adequate Facilities 
- State-Of-The-Art Instrumentation
- Qualified Personnel 
- Business Processes and Procedures

Challenges in Forensic Analysis

- Aggressive timelines
- High business impact ($ billions at stake)
- Wide range of unknown materials
  - Polymeric, organic, inorganic, metallic, proteinaceous, insects, and others.
- Multiple departments and sites

Commercial Product Investigation Team

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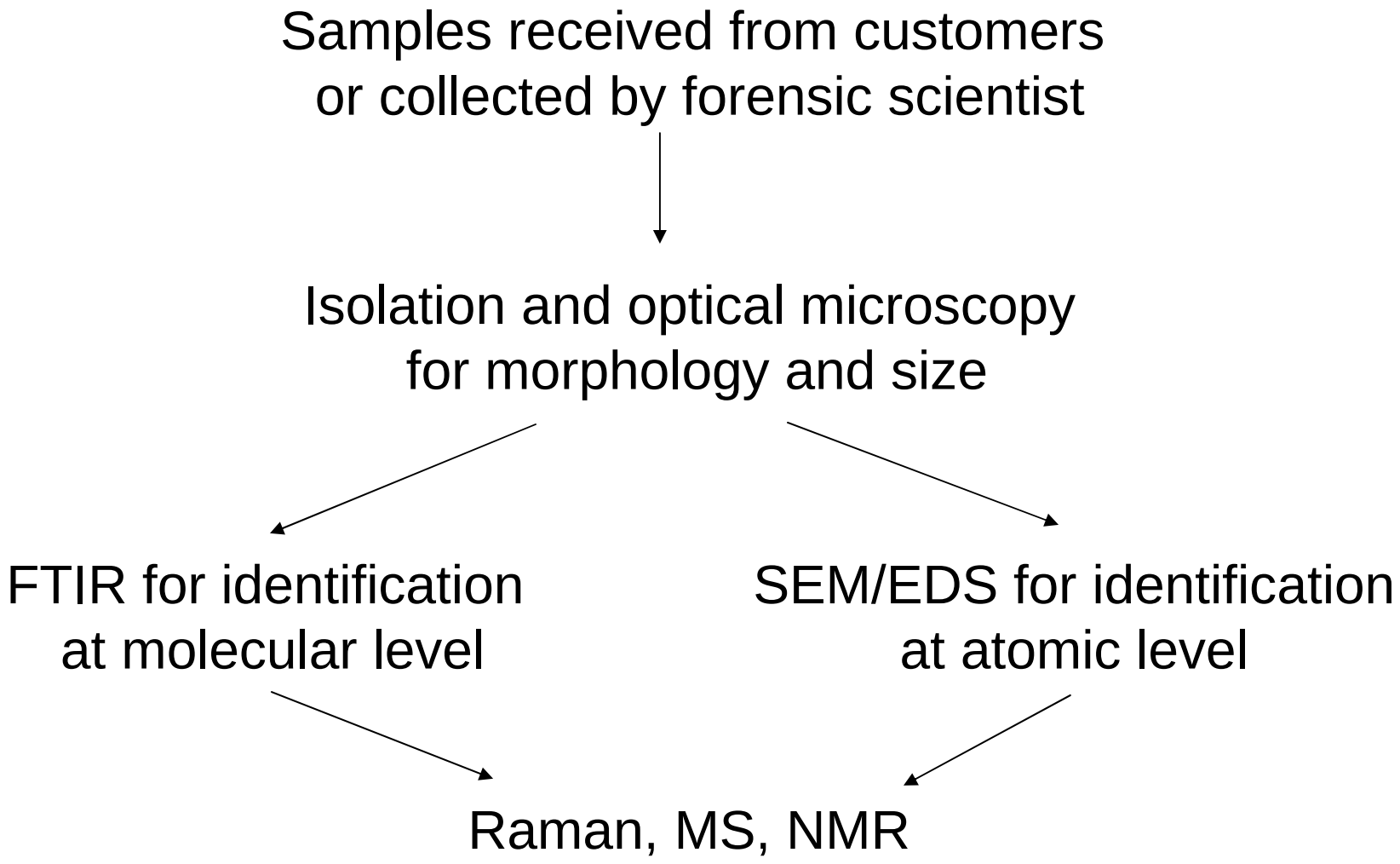
Support Priorities

- Commercial Products
- Clinical Manufacturing
- Manufacturing Equipment
- Process Development

Forensic Analysis Process Flow



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Conclusions

- Forensic Analysis plays a key role during commercialization and long-term production of biopharmaceutical products.
- Data generated in the forensic laboratory is often the basis for complex investigations that may have significant regulatory and quality implications.
- Successful forensic analysis operations require optimal combination of technical expertise, instrumental capabilities, and business processes.

Acknowledgments

- RJ Lee Group
- AML FAST Lab
- YOU!!!

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Facilities

- Particle-free hood for specimen isolation and preparation
- Positive-pressure conditions
- Mechanical room for vacuum pumps
- Dry air/nitrogen, liquid nitrogen supply

Personnel

- Most important requirement
  - Expertise in:
    - Microscopy
    - Spectroscopy
    - Out-of-the-box thinkers
- Experience in biopharmaceutical industry
- Specific knowledge of manufacturing processes