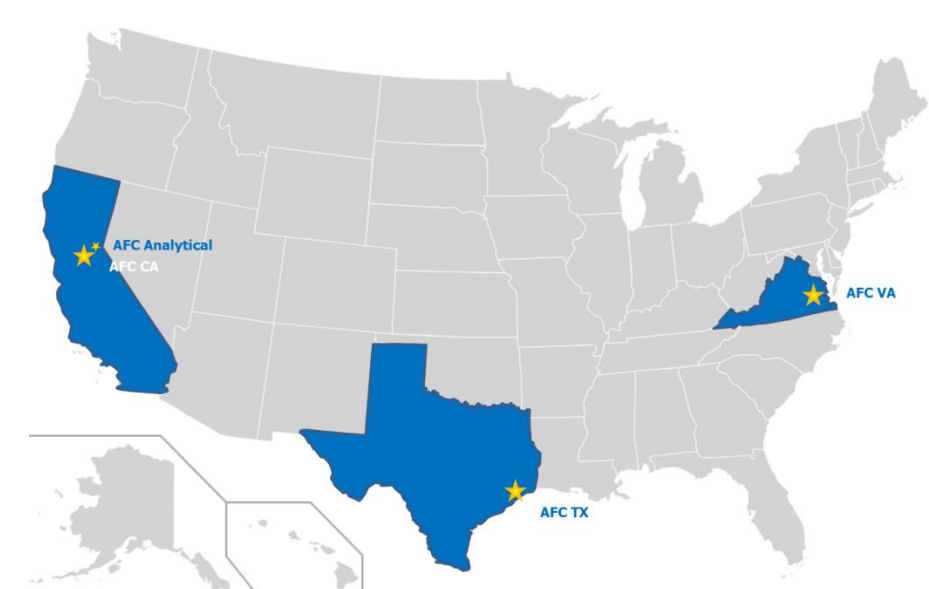


Strong Process R&D to Support API Manufacturing

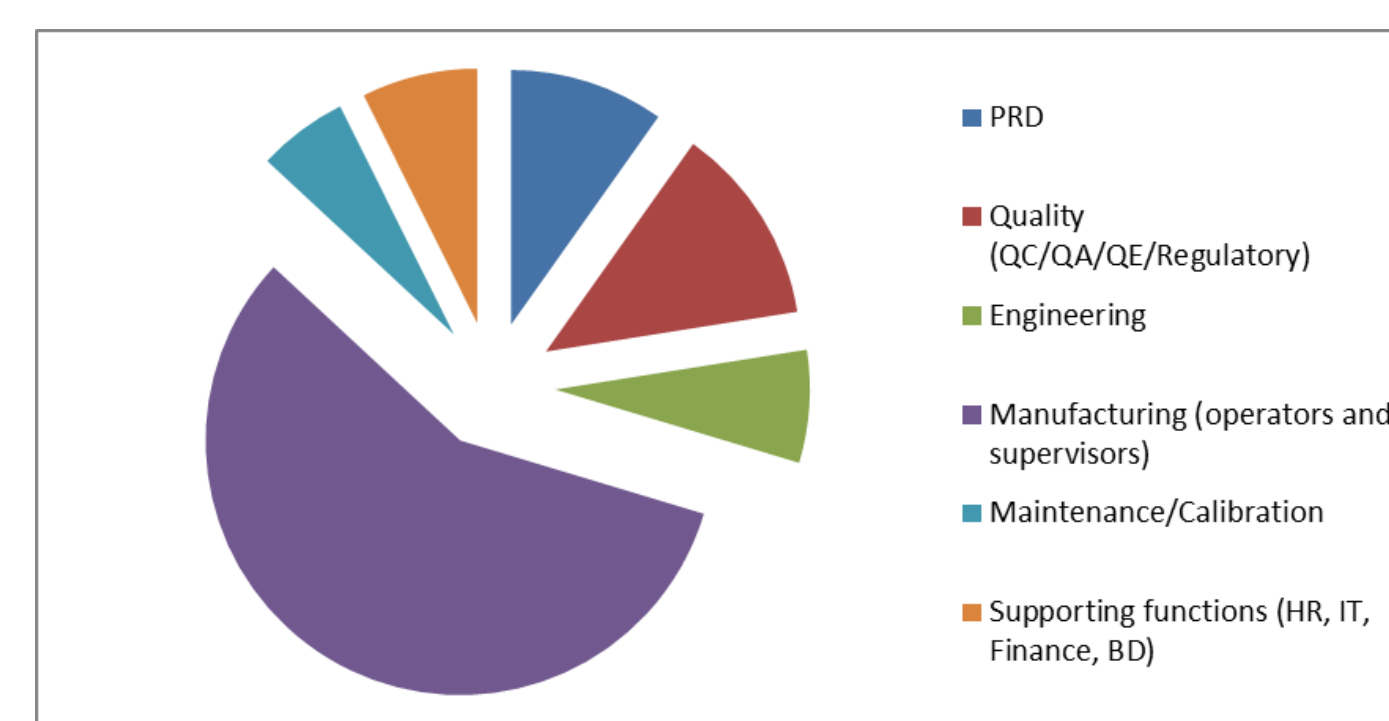
From Paper Chemistry to Process Validation, AFC's PR&D Group is Leading the Way

The PR&D group supports AFC at all sites



- Core Process R&D is located at the California site
- Additional research groups are located at Texas and Virginia to provide Technical Transfer, Optimization, Continuous Improvement and Production Support
- The PR&D group is 48 scientists strong
 - 32 PhD organic chemists and chemical engineers
 - 16 BS chemists

AFC PR&D is a Driving Force for Growth and Efficiency



- Process R&D supports products at all Phases of Development
 - Technical Transfer of existing routes
 - Development of new routes
 - Continued optimization of commercial processes
 - Working with procurement to find the most cost effective and reliable raw material suppliers
- Analytical Method Development group supports all development and scale-up activities

RFPs are Thoroughly Assessed by Technical Staff at AFC to Prepare Enabling Proposals

The Chemistry is evaluated and the Process is laid out in the plant

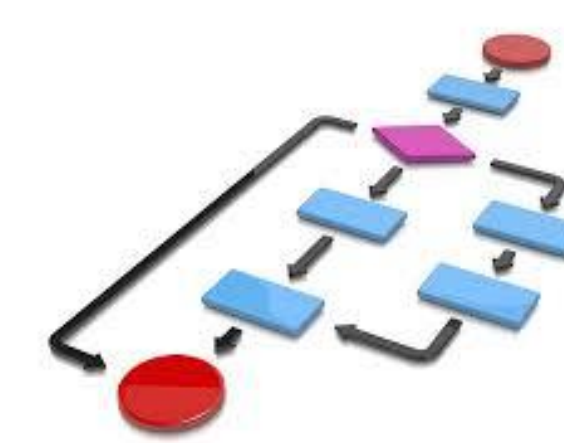
RFP/Process evaluation

- RFPs are evaluated through business development
- The technical packages are reviewed by technical staff
- Any technical questions or clarification are resolved through a teleconference with the customer
- A Project Manager is then assigned to assemble a proposal



Process lay out

- The technical staff then evaluates the best set of equipment to run the scope requested
- The process is then laid out in the equipment and scaled to maximize efficiency
- Based on this layout, the Project Manager assembles all of the costs for the process and reviews it with other technical staff to look for efficiencies



Proposal

- The final process is then written up as a proposal which is presented to the customer by the business development lead
- Once the proposal is accepted, the Project Manager assembles an Integrated Product Team (IPT) to start working on the Project



AFC's Experienced Process R&D Scientists Scale-up Processes from the Lab to the Plant

From gram to multi kilo, your process is effectively scaled-up

Process familiarization

- The work is started in the R&D labs; this could be a technical transfer, new development, or optimization project.
- This work is done using jacketed reactors, overhead agitators, and programmable temperature control and addition pumps to mimic plant conditions as close as possible



- Based on the Process that was demonstrated, it is either scaled to the kilo-lab or taken directly to one of our pilot facilities
- This activity is all done within the IPT to ensure that all parts of the process are ready to be run under cGMP

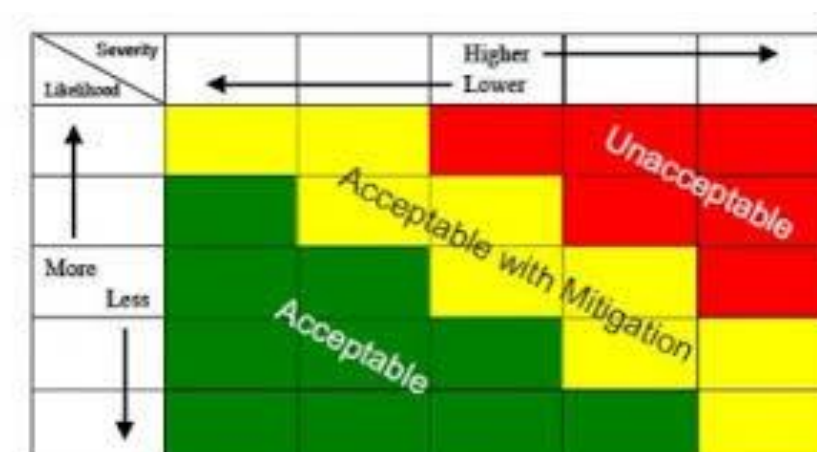


AFC's Process R&D Performs DOE for Parameter Ranging in Support of Validation

From gram to multi kilo, your process is carefully scaled-up

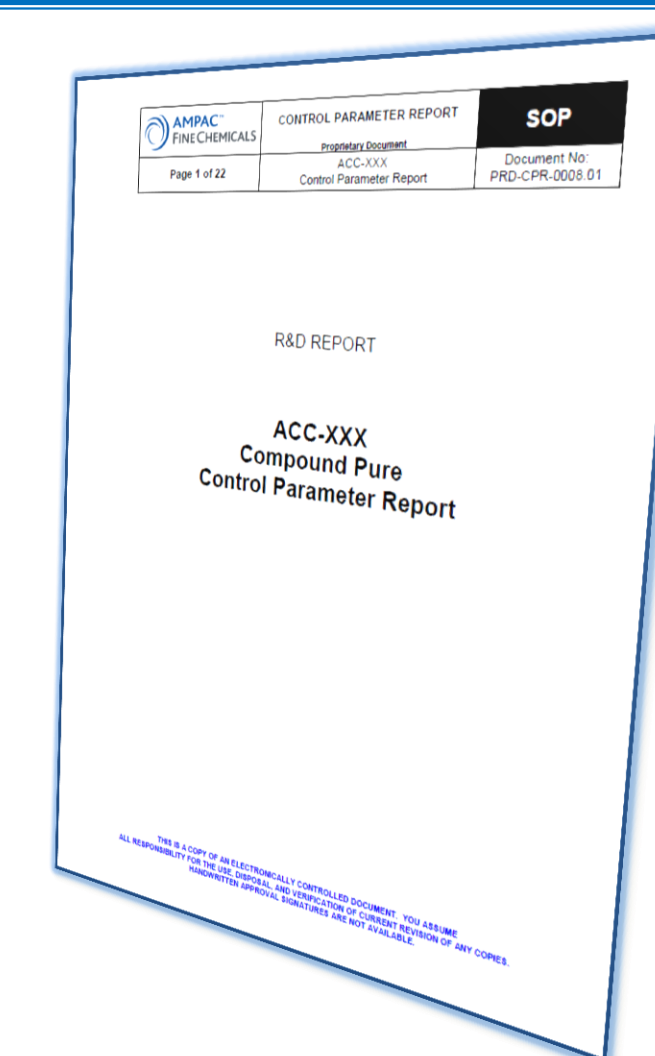
Process knowledge is captured

- As AFC develops a process in preparation for Validation, we start with the existing on-site knowledge and development reports as a basis
- This is supplemented with DOE studies to define process ranges and abuse studies to determine limits



Validation

- Prior to Validation, AFC performs a risk based parameter assessment to identify non-critical, controlled, and critical parameters through a matrix approach
- The process also defines risk mitigation and the entire process is captured in a Critical Parameter Report (CPR)



Critical Parameter Report

- The CPR is the repository for all known proven technical knowledge of the process including the Critical Parameter Table with Proven Acceptable Ranges (PAR) and safe hold points for the process
- This report is the basis for the Validation Master Plan, Protocols, and Reports and will be used to write the Master Batch Records for the Validation

AFC Technologies are Successfully Performed at all Scales

Reactions are evaluated and carefully scaled-up

AFC's PR&D evaluates and scales a wide variety of reactions by batch and continuous processing

- Hydrogenations
- Azide chemistries
- Nitrations
- Diazomethane
- Ozone
- Hydrazine
- Pyrophoric Reactions



PR&D can perform HPAPI Process Development

AFC operates multiple dedicated labs for HPAPI process development

- Lab is on a separate HVAC system
- HEPA filters and Positive Pressure Differential to ensure complete isolation
- Glove box for product handling
- Gowning/de-gowning room

- Dedicated kilo/small scale facility
- Two matching commercial facilities



Chromatography (SMB) is Supported at ALL SCALES

SMB group performs

- Separation screening
- Productivity Estimates
- Demonstration at bench scale (100 g)
- Kilo manufacturing under cGMP

SMB group supports Manufacturing

- DOE and Critical Parameters evaluation for filling
- Modelling in support of filling
- Troubleshooting
- Use test in support of supplier qualification

