Useful Applications of Smart, Fast Gas Chromatography with the NeSSI Platform

Mike Cost, Parker Hannifin
George Schreiner, Justice Laboratory Software
John Crandall, Falcon Analytical
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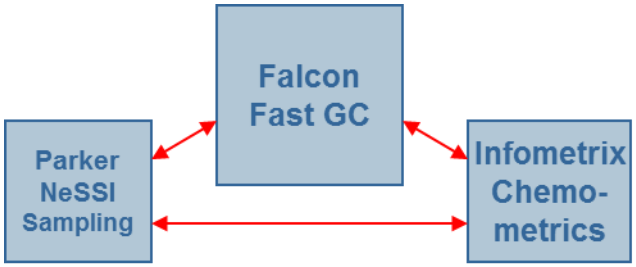
Outline of Presentation

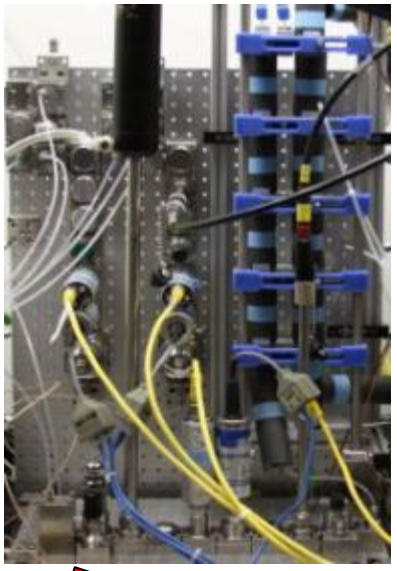


- NeSSI, Fast Gas Chromatography and Chemometrics are still (after all these years) considered new technology.
- Thought leaders and early adopters alike are excited, make lots of positive noise about these new technologies and have implemented to an extent……..a limited extent.
- However, to reach genuine commercial viability for the technologies, some dragons must be slain.
  - Reliability and robustness of NeSSI must be PROVEN in the eyes of large scale users.
  - Depth and breadth of Fast GC applications must be PROVEN to meet or beat requirements of the old traditional GCs.
  - Chemometric applications must be PROVEN to be useful in the hands of the average user.
- Here are real world and very useful applications of the triangular relationship of the technologies.
  - A batch approach to automated process analytical chemistry
  - A micro scale bioreactor continuous monitoring system

Parker

A View of the Current State

- Density
- Refractive Index
- Viscosity
- Optical Absorbance
- Dielectric
- Conductivity
- pH/ISE/ORP
- Turbidity
- Thermal Conductivity
- Ultrasonic
- Moisture
- Gas Specific



Gen III:
Microanalytical
Systems

Platform for microAnalytical, remote wireless, advanced gas & liquid sensors

Gen II: Electrically Networked Systems

IS Serial Bus, miniTransducers, local wireless

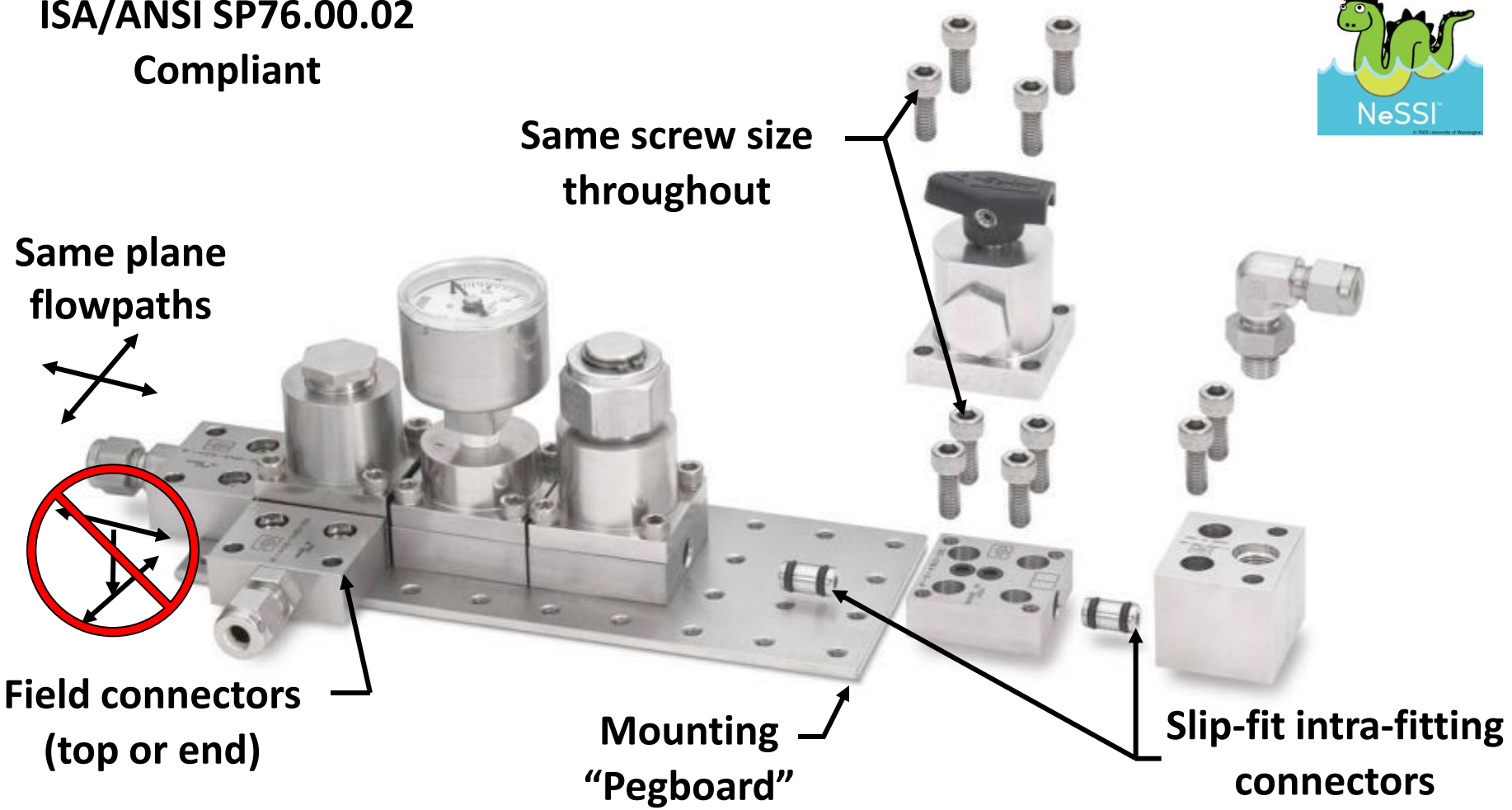
Gen I: Fluid Handling Systems

Mostly Mechanical Components

Intraflow™ Parker Modular (NeSSI™) Systems: Gen I

(Foundation of Modular Approach)

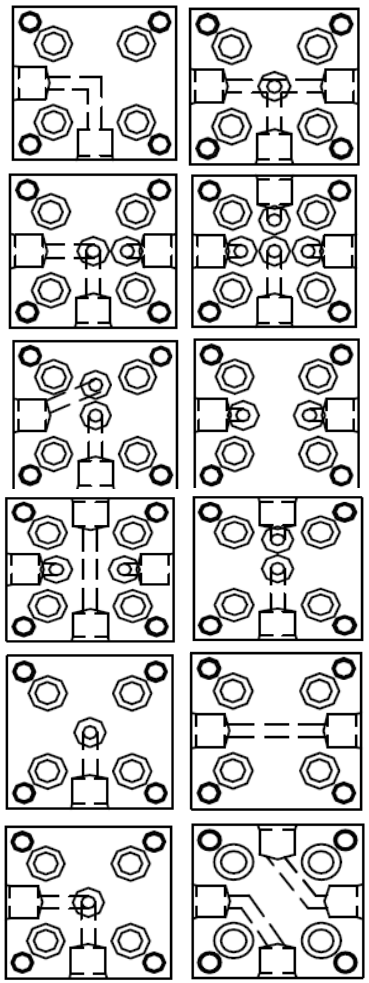
ISA/ANSI SP76.00.02 Compliant

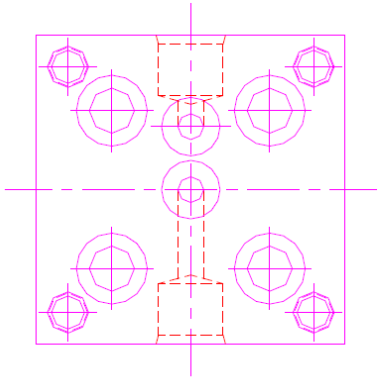


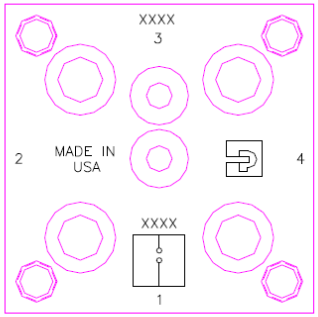
Intraflow™ Substrates/Flowpath Options:

The Library is Has Become Much Larger to Accommodate Laboratory and Process Applications (over 100 flow options)

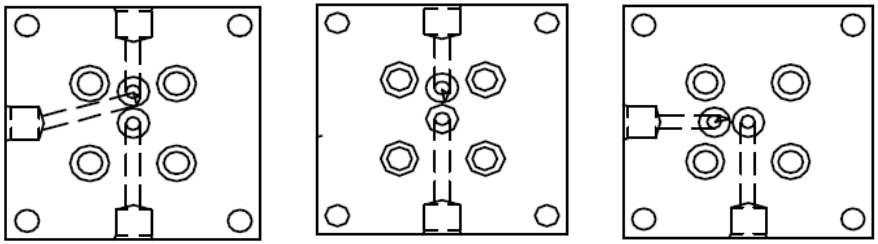
Part Number Configurator/Generator

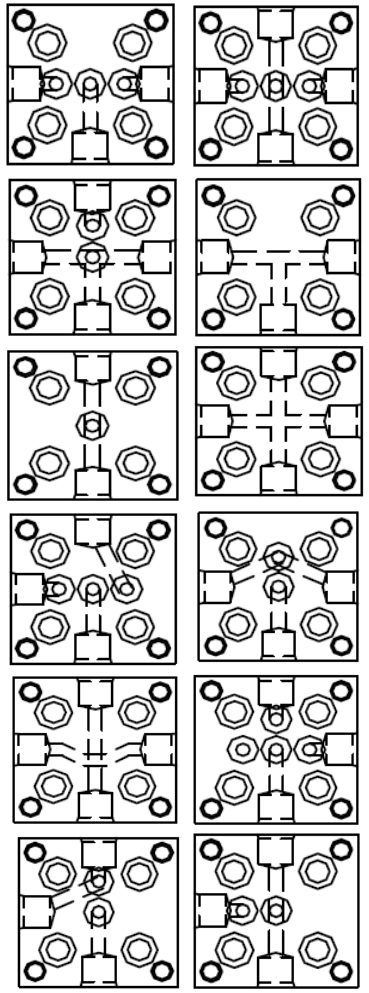




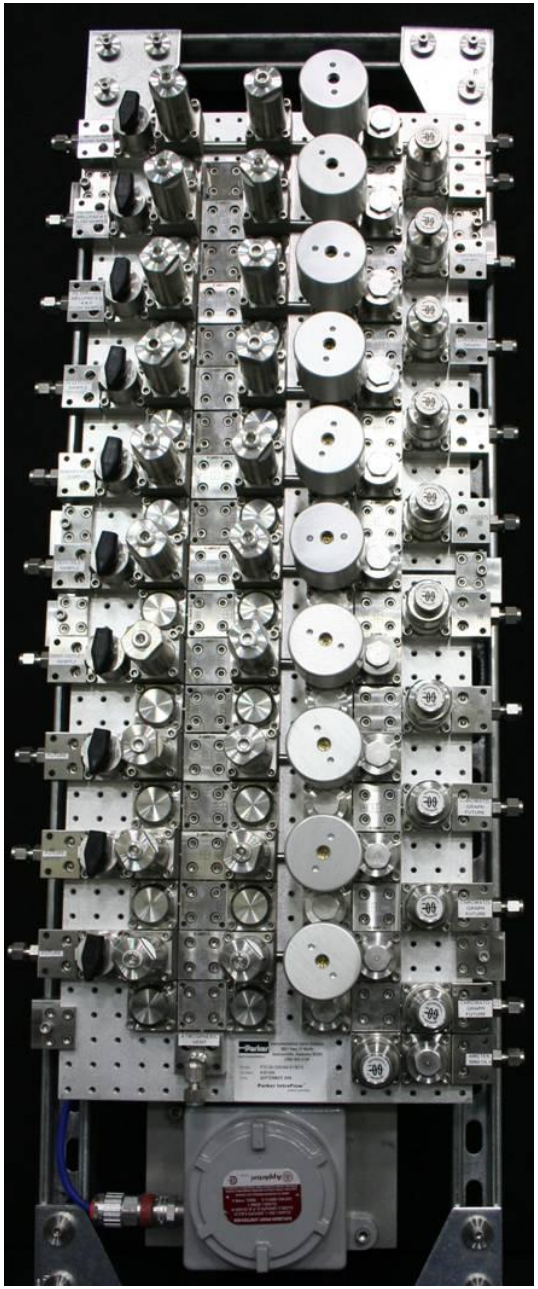


IntraFlow™ Fitting





High Pressure Process Application

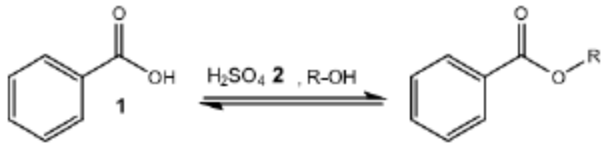


10-Stream Natural Gas BTU Analysis System

- Coalescing & Membrane Separator Drain Header
- Restricted Orifice Header Pressure Control
- Freeze Protection Heating
- Sample pressure 1,500 – 3,000psig

Micro Reactor Fluid Control with Intraflow™

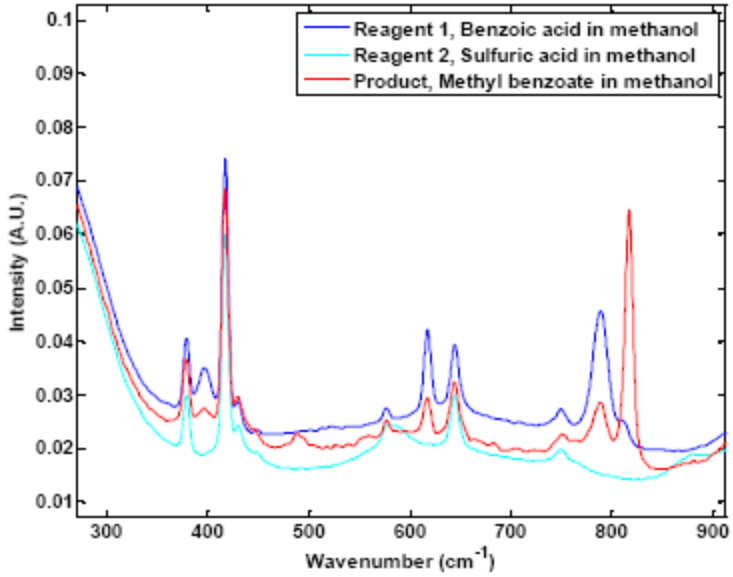
Esterification of Benzoic Acid



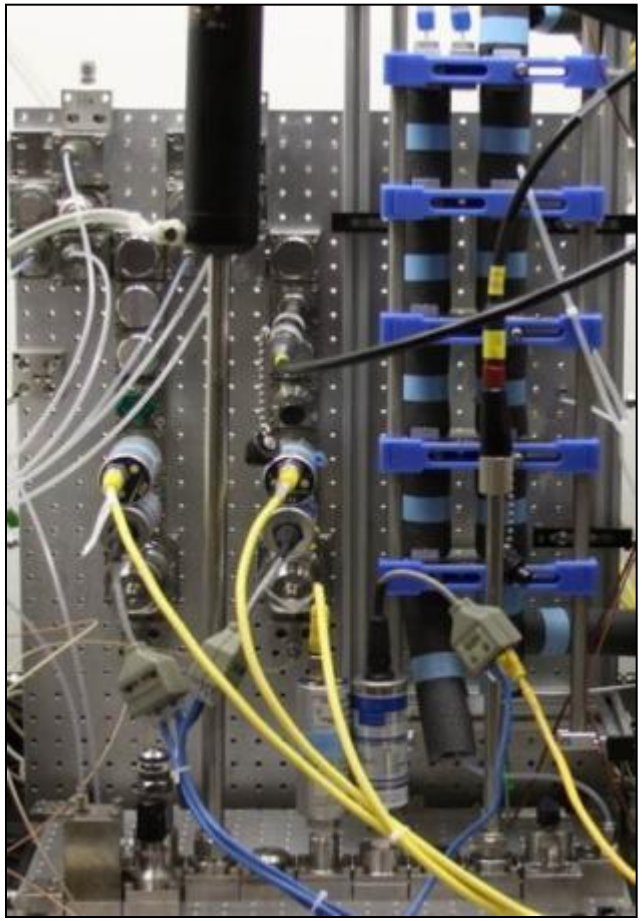
This esterification reaction is ideal for Phase 2 as the product yield heavily relies on control of:

- Temperature
- Flow rates
- Chemical Stoichiometries.

The reaction was performed in a continuous flow reactor, with positive results:

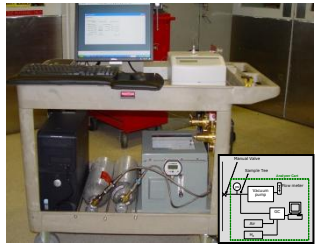


Raman spectra of the 2 reagents prior to mixing, and product collected on the sampling system after the reaction. The appearance of a methyl benzoate peak at 815 cm^{-1} indicates the reaction proceeded successfully.



Coolant Leak Detection into Blood Product Freeze Dryers (batch process)

- Previous State
  - Human olfactory sensory panels “sniffed” out the leaks
  - The “measurement” was subjective. What if the nose has a cold?
- Current State
  - A micro GC and Chemometrics measure the freeze dryer compartment after cleaning and after freeze drying. Reference: “Lyophilizer Heat Transfer Fluid Monitoring via Gas Chromatographic Methods” by John Kutney, Talecris, IFPAC, 2008 Baltimore. Can be viewed at falconfast.net.
  - Quantitative analysis at the ppb level results.
  - However…
    - The level of automation implemented is minimal
    - Personnel turnover makes system operations difficult
    - The instrumentation is at the end of product life cycle

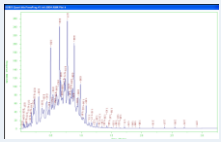


Solution (aka future state): NeSSI, Fast GC and Chemometics with Full Automation

- Automation Strategy
  - Use smart software
  - Evaluate step by step results as a human would
  - On alarm, stop and notify a human
  - On success proceed to the next step
- Automation Suite of Elements
  - IntraFlow^{tm} NeSSI
    - Switches streams
    - Monitors critical parameters: T, P, F
  - Calidus & ChromPerfect (CP)
    - Performs chromatographic analyses
    - CP operating Calidus, NeSSI & directing data flow is the master
    - Receives permissions from & reports (alarms) results to SCADA
  - LineUp & InStep
    - Aligns chromatograms to target chromatogram
    - Assesses results as "consistent with expectations" or "outlier, sound the alarm"

1) ChromPerfect watches for stream ID and permission from the SCADA system
   i) Stream ID is defined as Freeze Drier E, F or G
   ii) Permission indicates the sequence of operation for that freeze drier may begin
   iii) ChromPerfect starts the appropriate stream vacuum pump

2) On permission, ChromPerfect downloads the appropriate method and sequence to Calidus
   i) Methods include operating conditions and data processing parameters
   ii) Sequences include sample identification and number of runs as follows
      (1) Run 5 blanks (analytical cycle without actuating the sample valve)
      Assess results as clean (pass, continue) or dirty (fail, stop and alarm)
      (2) Run 1 zero air
      Assess results as system suitable (pass, continue) or not suitable (fail, stop and alarm)
      (3) Run 1 validation sample
      Assess results as system suitable (pass, continue) or not suitable (fail, stop and alarm)

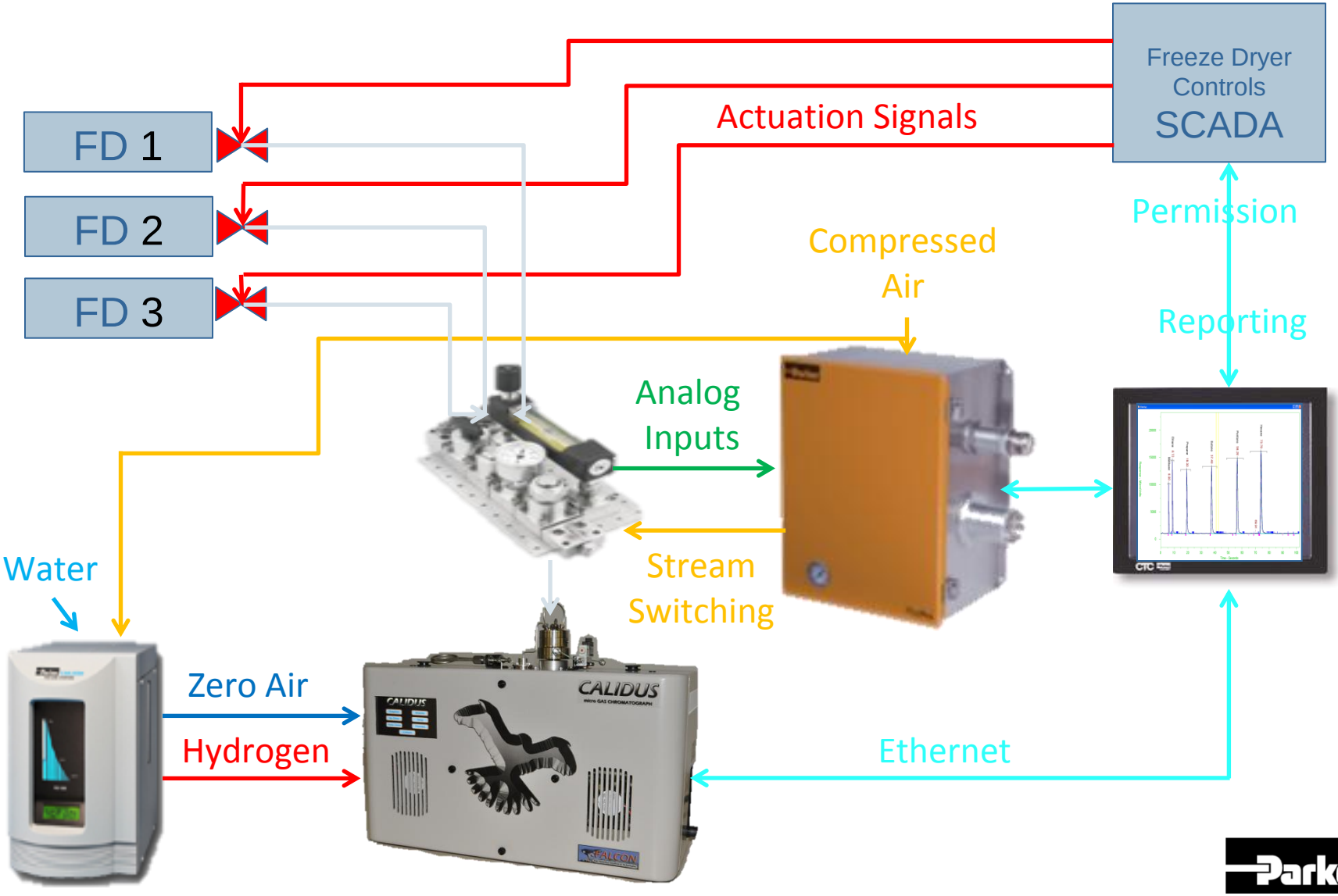


      (4) Run 5 freeze drier samples and report
      (a) Each chromatogram to be displayed
      (b) Sample data, P, T and other assessment parameters
      (c) Component name
      (d) Retention time (if Syltherm)
      (e) Total area
      (f) Calculated Concentration
      (g) Assess results as valid measurement (pass, continue or not valid (fail, stop and alarm)

3) Report results
   i) Average last three of the 5 runs
   ii) Report average concentration

Assessment of the Freeze Dryer condition (clean or alarm)

System Overview for the 3 Stream Batch NeSSI/Fast GC/Chemometric System (not to scale)

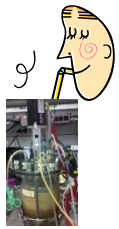


8 Stream micro-Scale Bioreactor System

- Continuous monitoring was required
  - Production monitoring for a specialty chemical
  - Nutrient monitoring & feed rate for microbes
  - Oxygen monitoring & feed rate for microbes
- There are multiple small systems
  - In this case there are 8 reactors
  - Process flow rates are small < 1 liter/minute
  - Calibration for the semivolatile organic is problematic
  - Manual sampling & monitoring is virtually impossible
- Fermentor off gas analysis was required
  - Sampling the broth is complicated
  - The broth will plug virtually any automatic sampling mechanism
  - The off gas concentration indicates production yield

Automation Strategy

- Automation Strategy
  - Use smart software
  - Control critical parameters: T, P, and especially flow rate (don't suck the reactors dry)



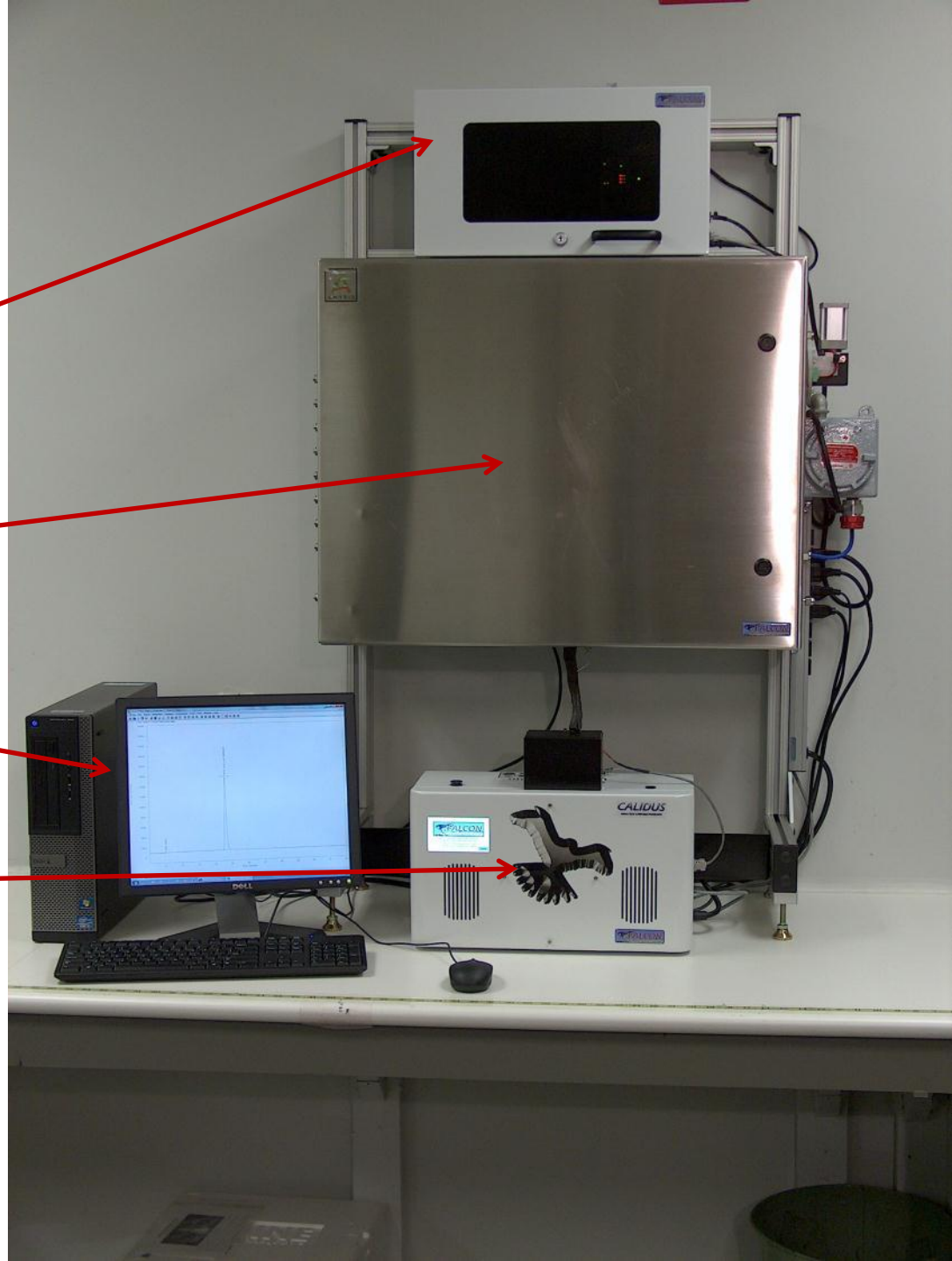
- Automation Suite of Elements
  - IntraFlow^{tm} NeSSI
    - Switches streams & controls flow rates
    - Performs periodic autocalibration sample via the permeation calibration system
    - Monitors critical parameters: T, P, F
  - Calidus & ChromPerfect (CP)
    - Performs chromatographic analyses
    - CP operating Calidus, NeSSI & directing data flow is the master
    - Receives permissions & reports (alarms) results from/to LIMS
  - LineUp & InStep
    - Aligns chromatograms to target chromatogram
    - Assesses results as "consistent with expectations" or "outlier, sound the alarm"

System Conceptual Overview for the 8 Stream Continuous

NeSSI/ Fast GC/Chemometric System (not to scale)

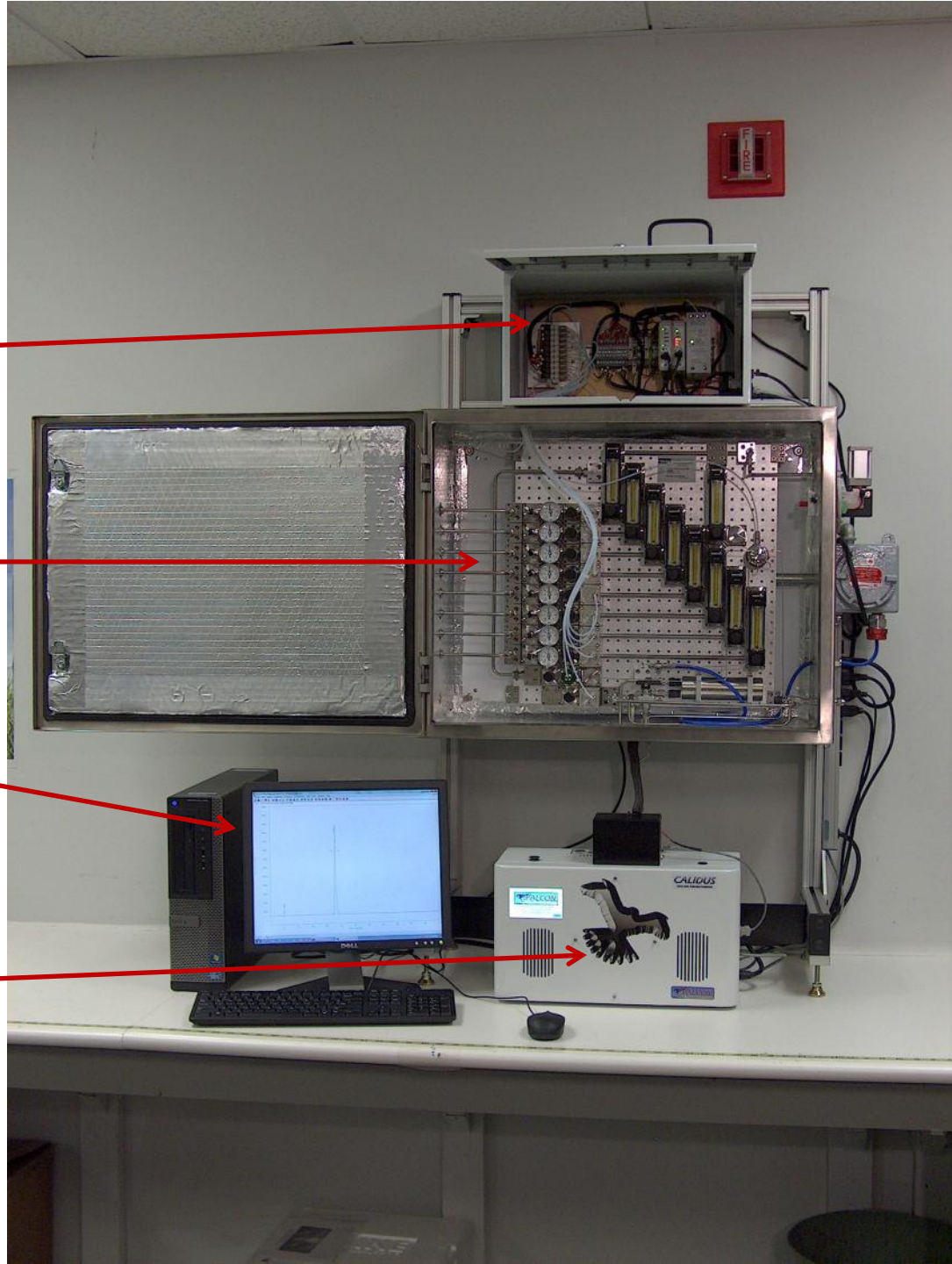
8 Stream Gas Analysis System

- Electronics, I/O
- 8 Stream Sample System
- System Computer
- Calidus Fast Gas Chromatograph



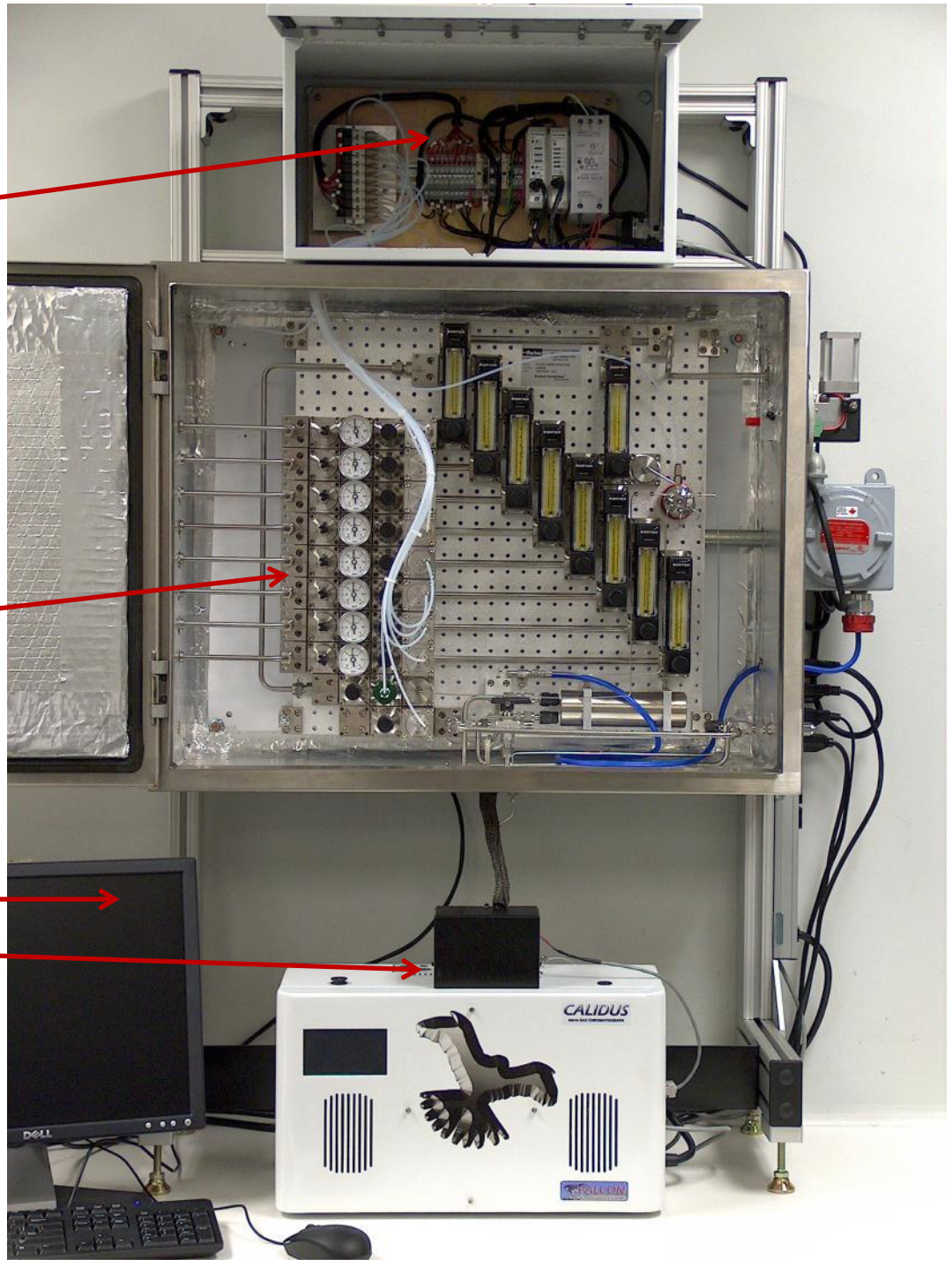
Enclosures View

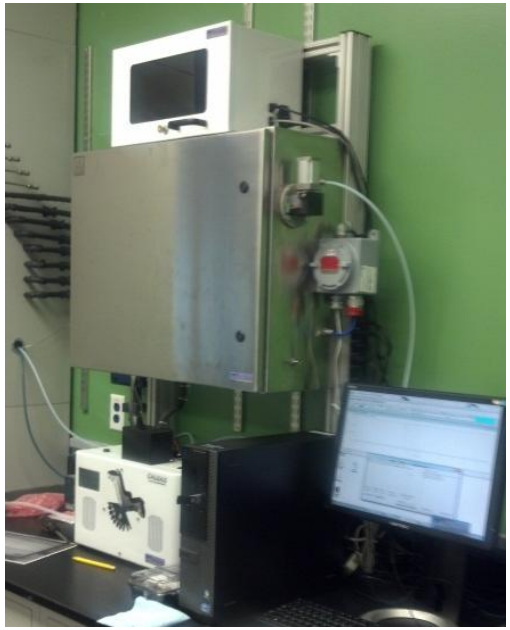
- Electronics, I/O
- 8 Stream Sample System
- System Computer
- Calidus Fast Gas Chromatograph



Component Description

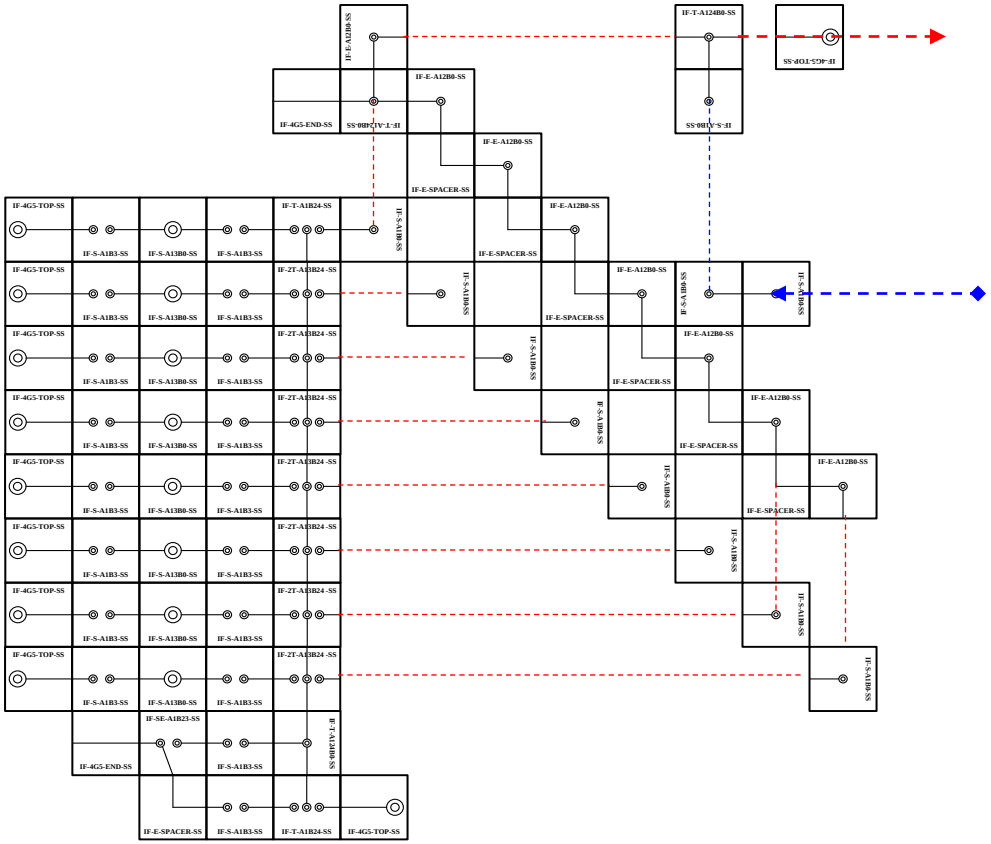
- Electronics, I/O
  - Power supply
  - Ethernet switch
  - 24 VDC outputs
  - Electronic to pneumatic switching
  - MODBUS modules are available to fit here
- 8 Stream Sample System
  - Block valves
  - Pressure gauge
  - Flow rotameters
  - Permeation tube calibrator
- System Computer
- Calidus Fast Gas Chromatograph
  - Gas sample valve oven & transfer line



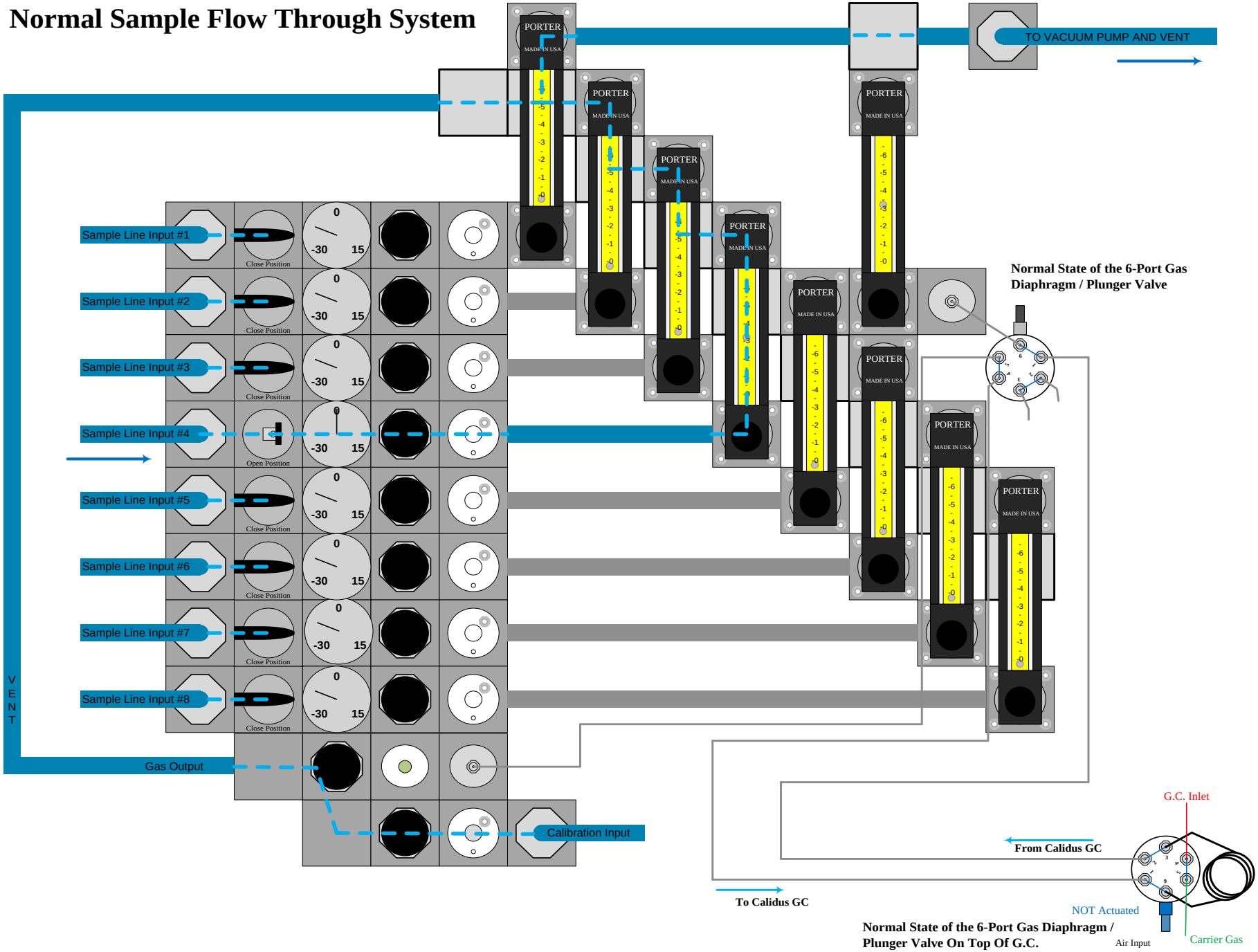


Sample Flow Design

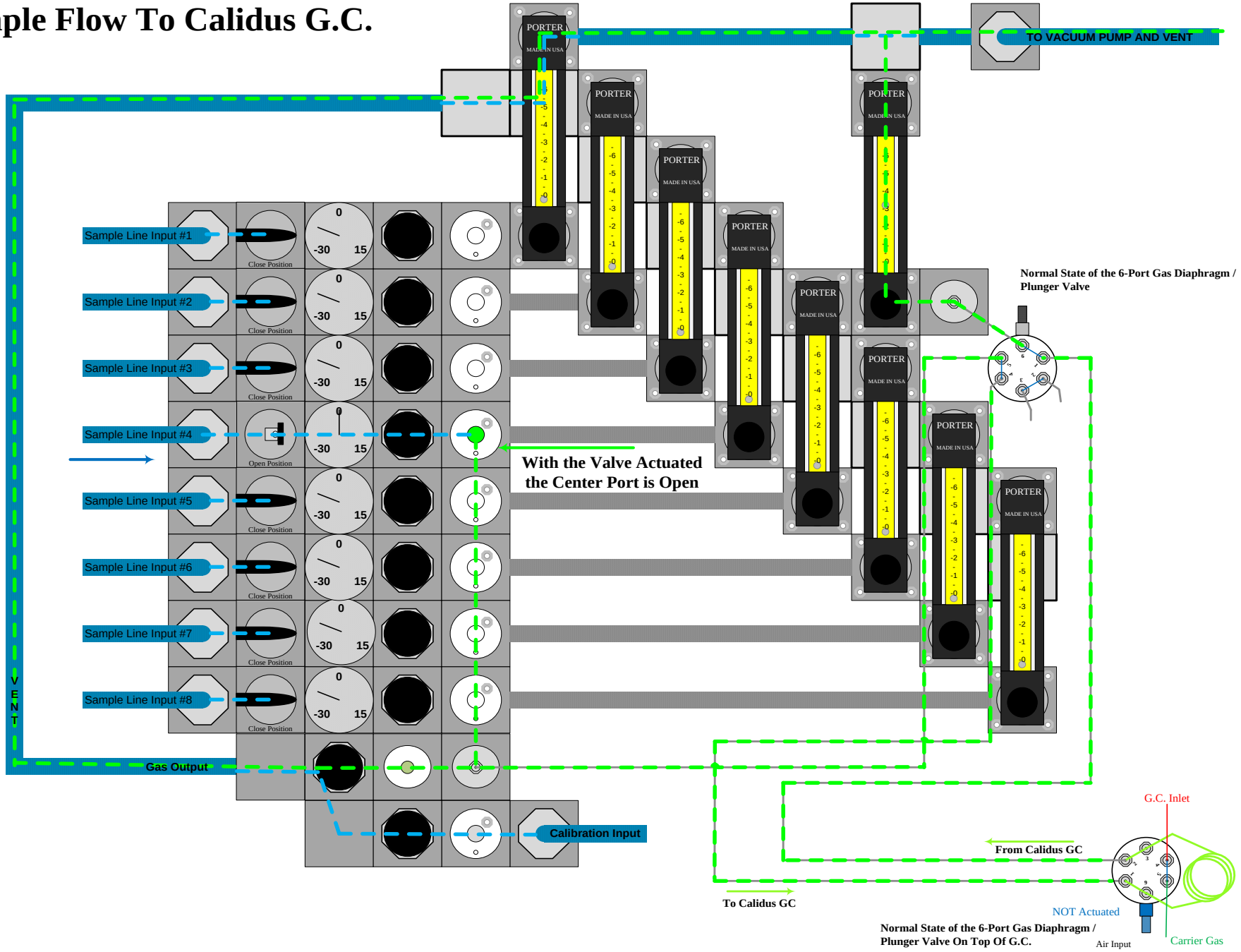
Block Diagram of Parker Interflow System



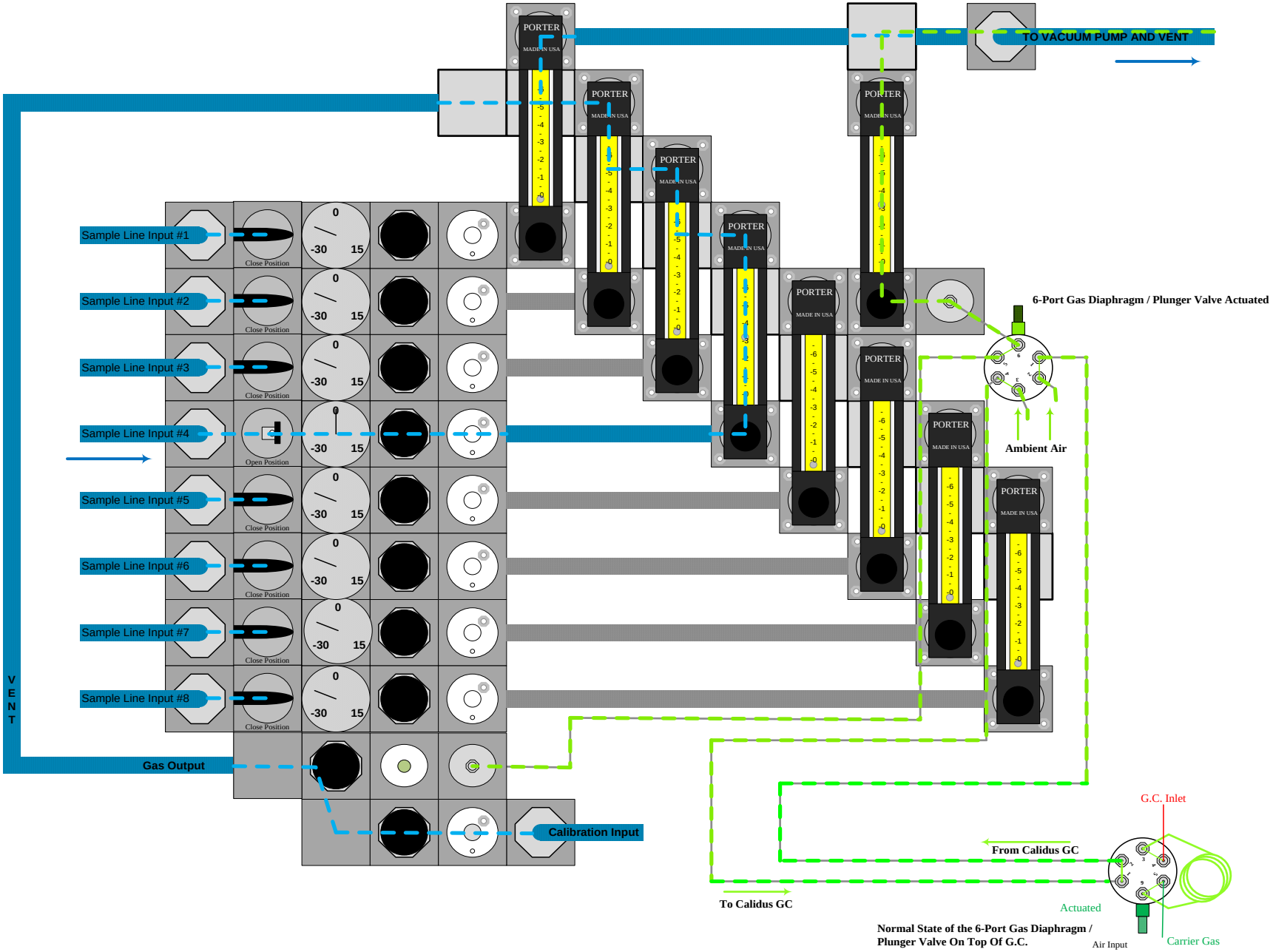
Normal Sample Flow Through System



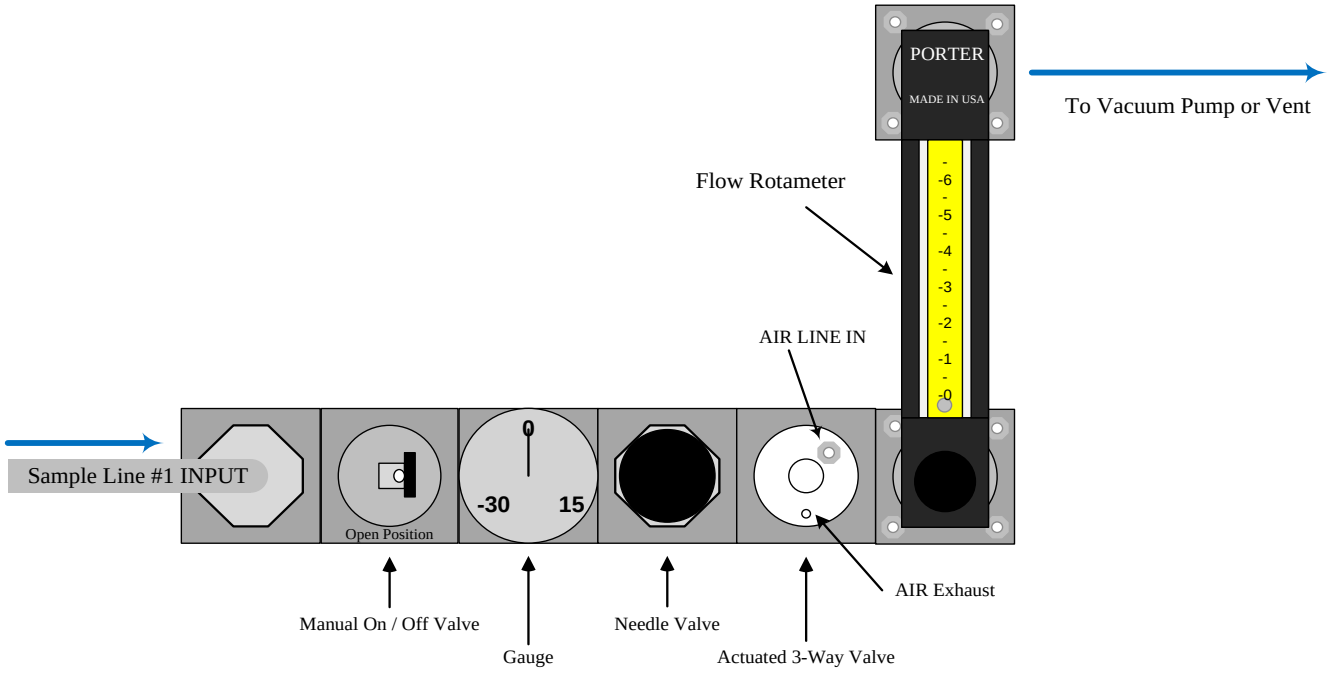
Sample Flow To Calidus G.C.

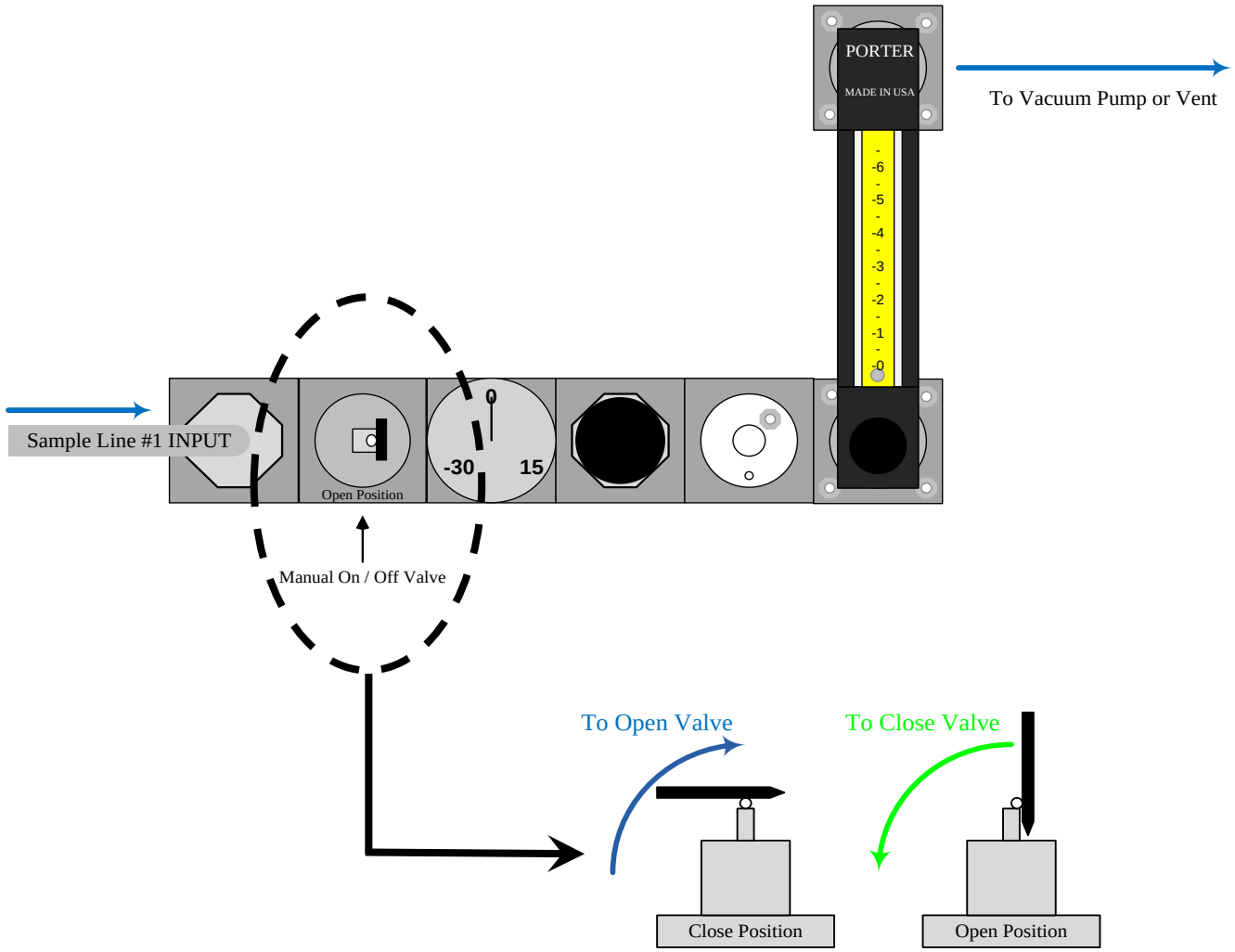


Normal Sample Flow Through System With The 6-Port Gas Diaphragm / Plunger Valve Actuated



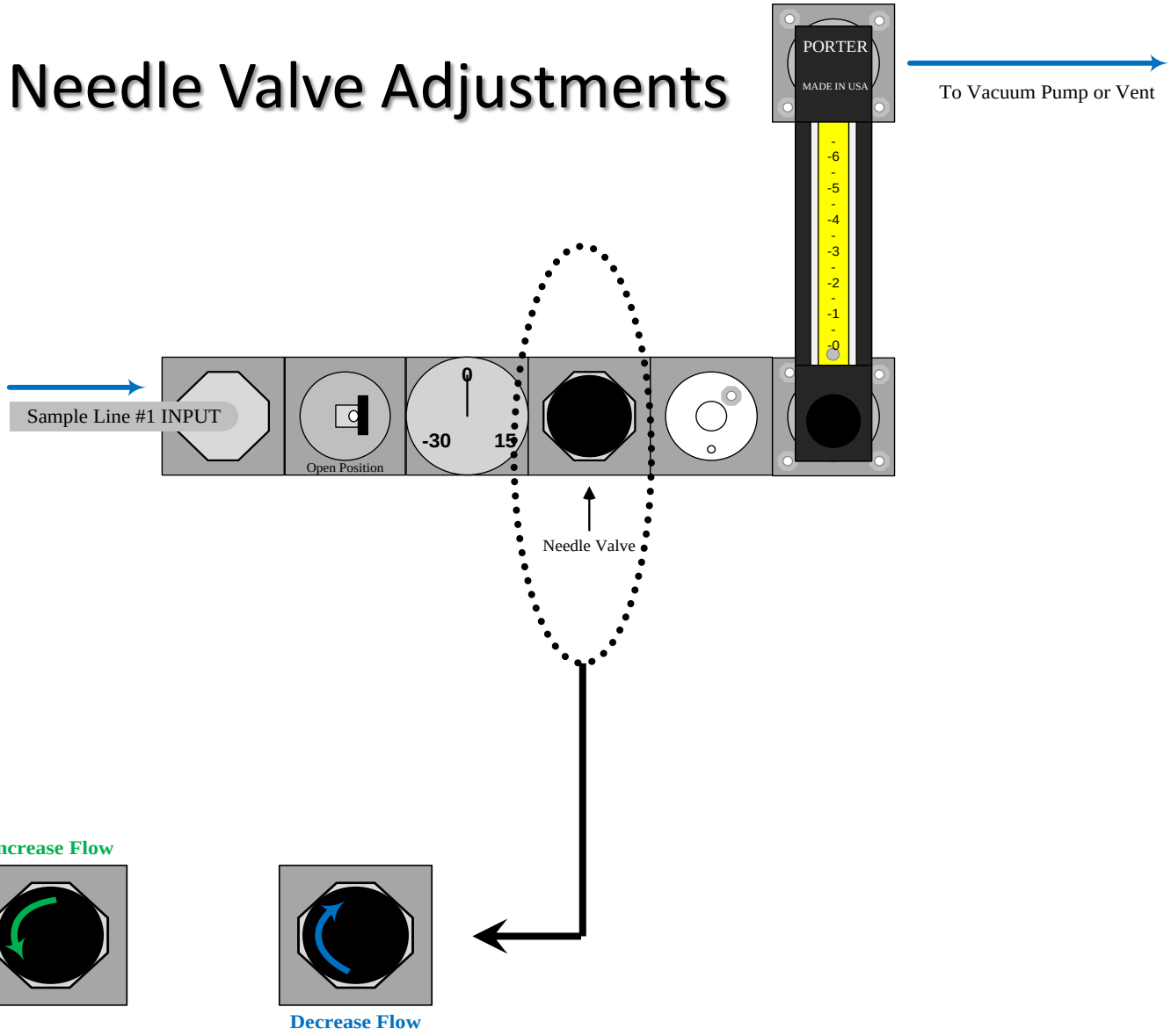
Location and Identification of Parts on Sample Line #1

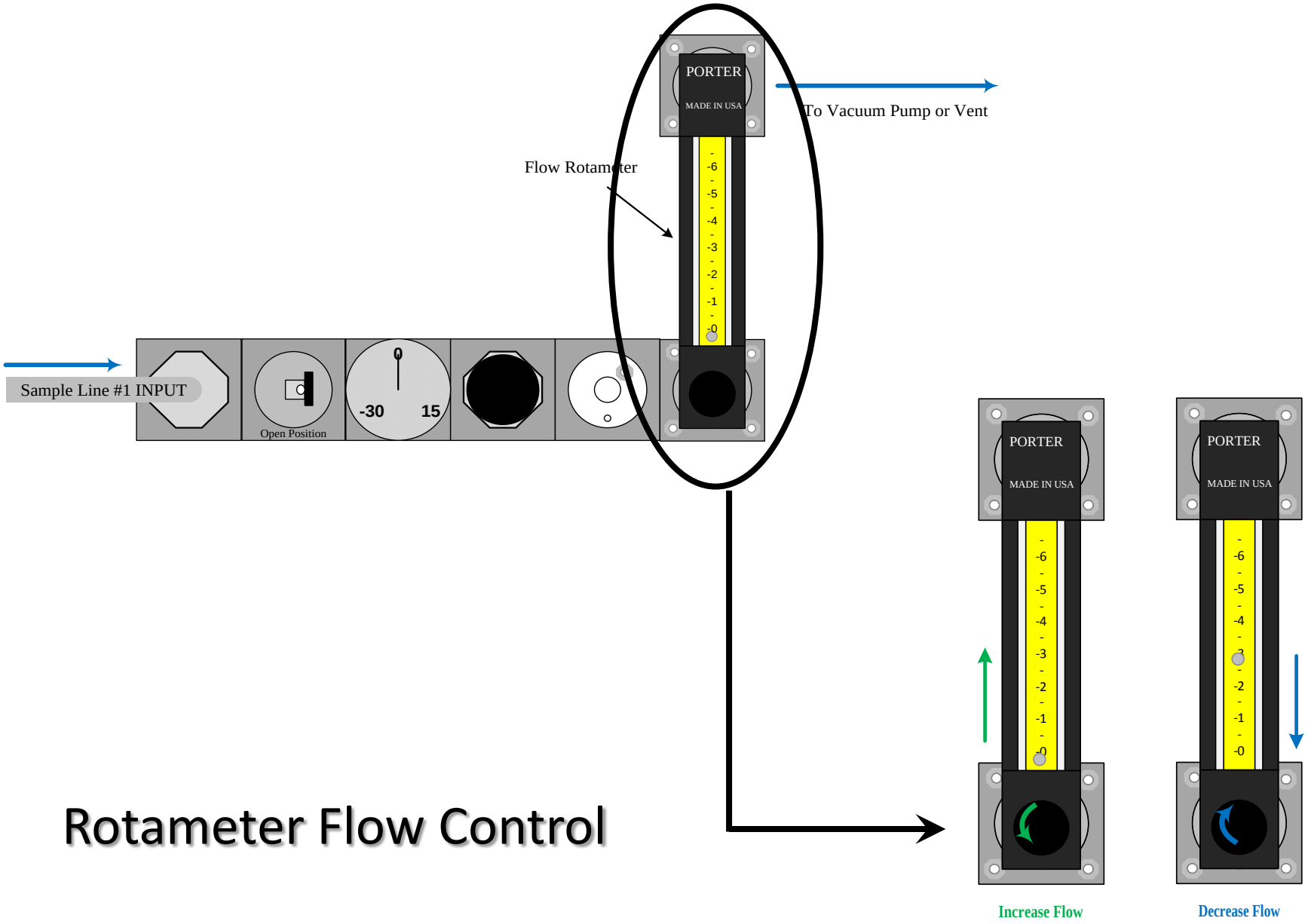




Manual Valve Operation

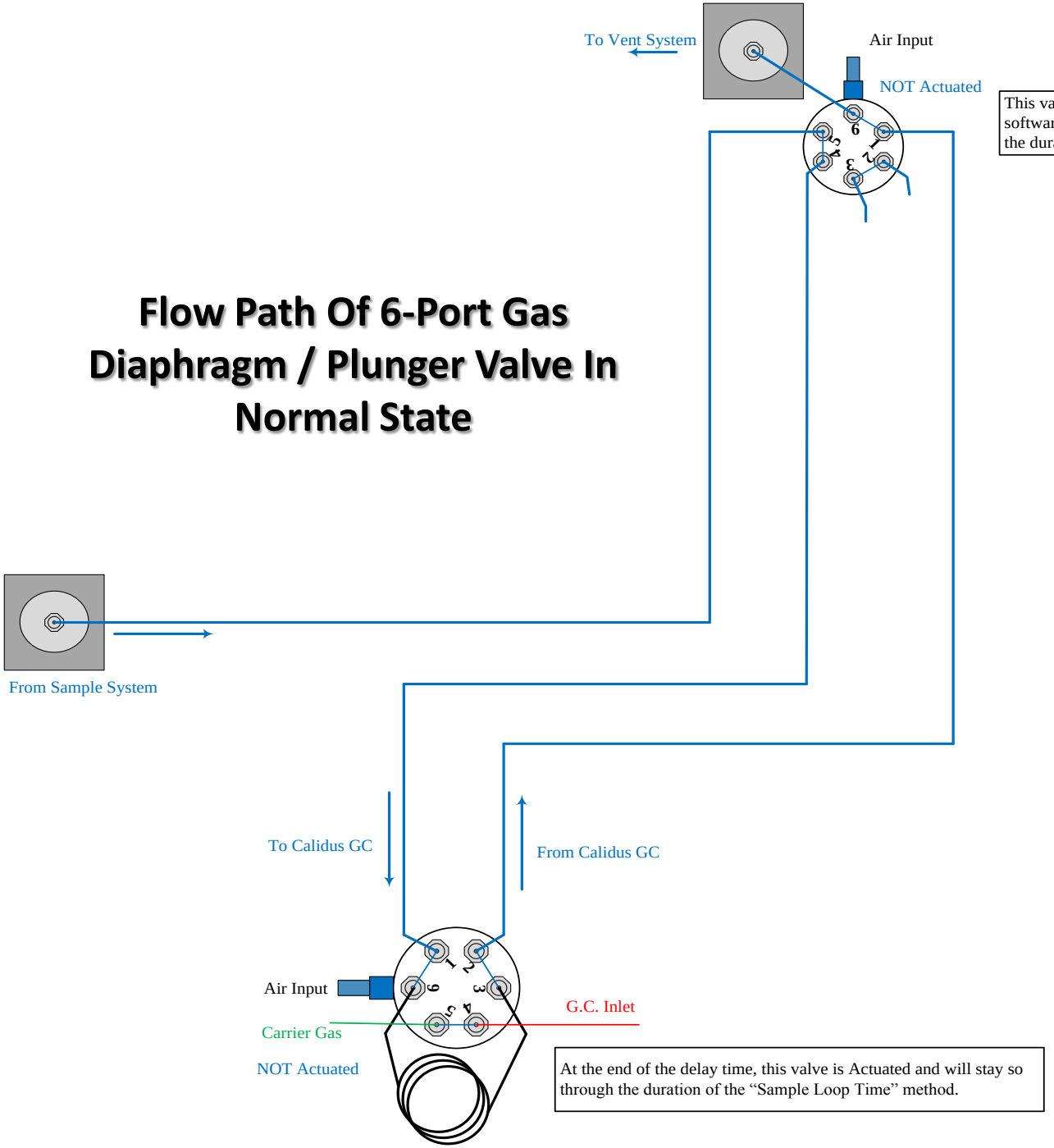
Needle Valve Adjustments



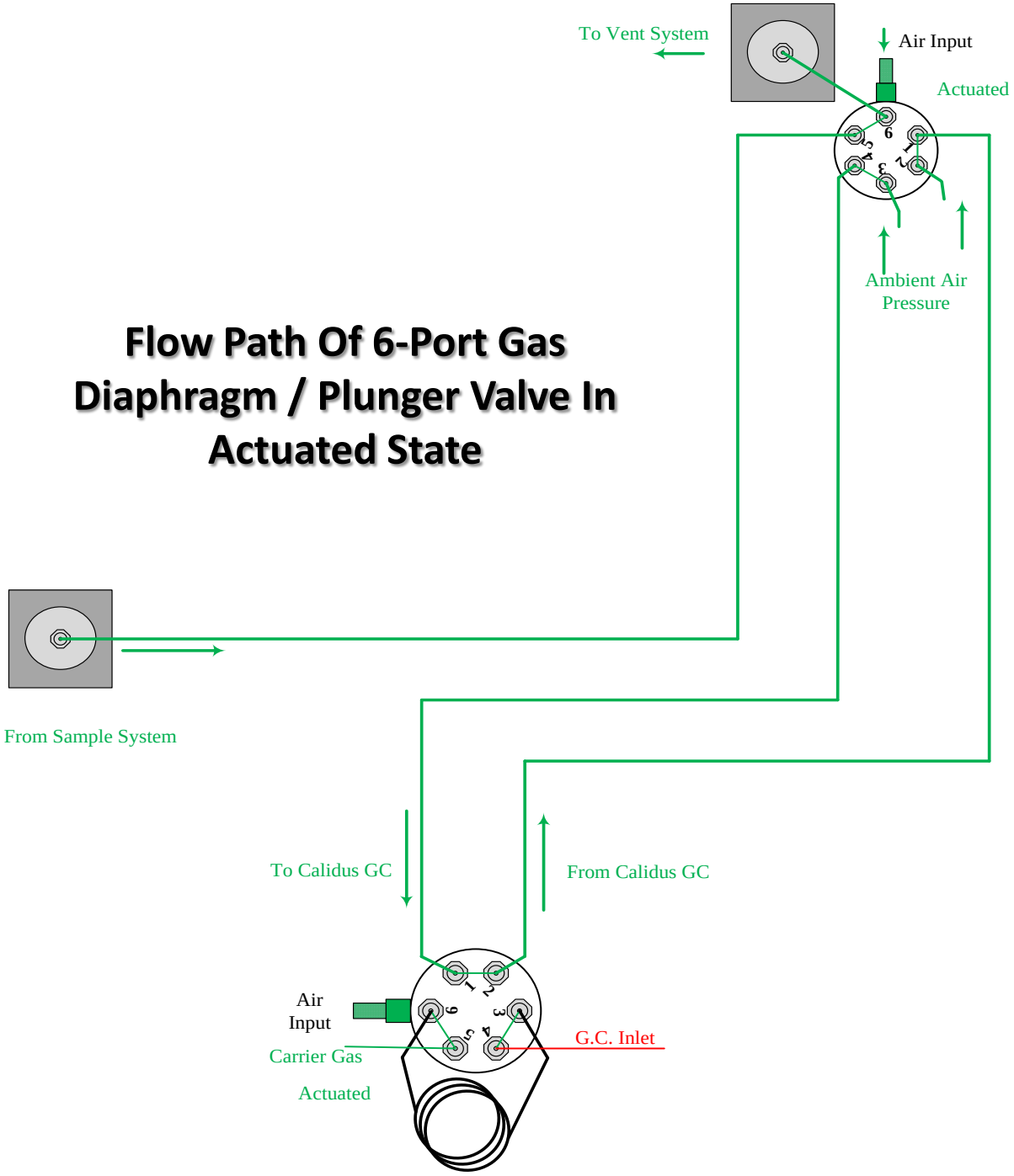


Rotameter Flow Control

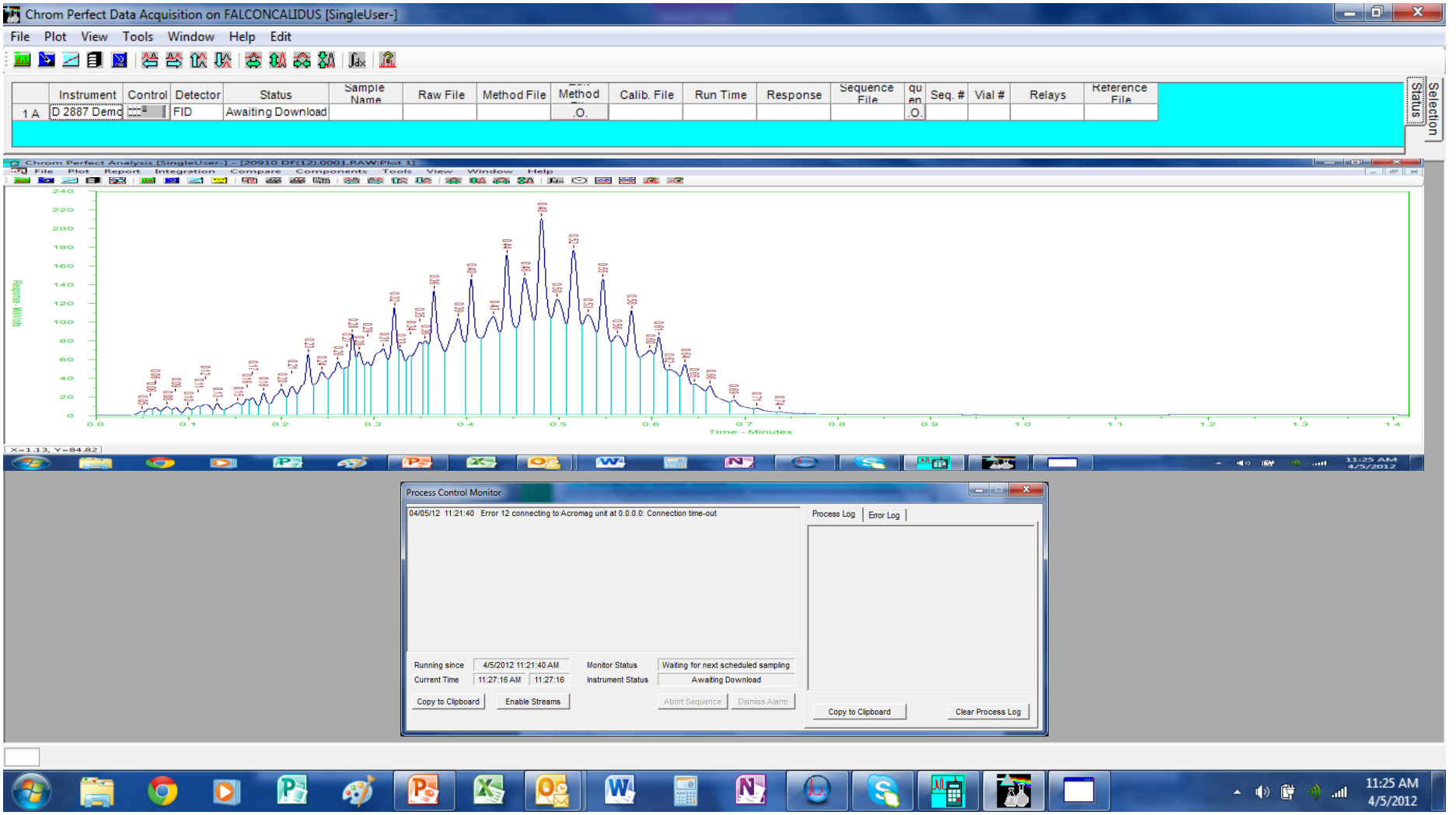
Flow Path Of 6-Port Gas Diaphragm / Plunger Valve In Normal State



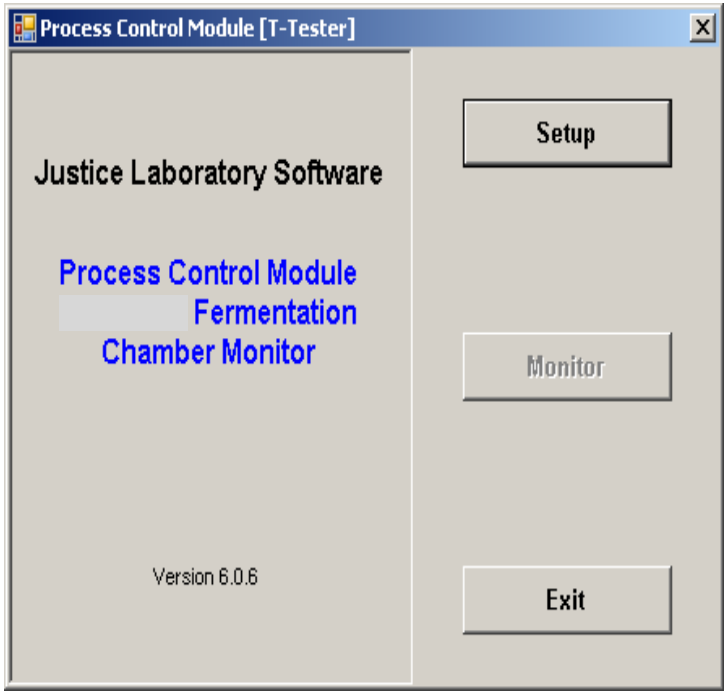
Flow Path Of 6-Port Gas Diaphragm / Plunger Valve In Actuated State

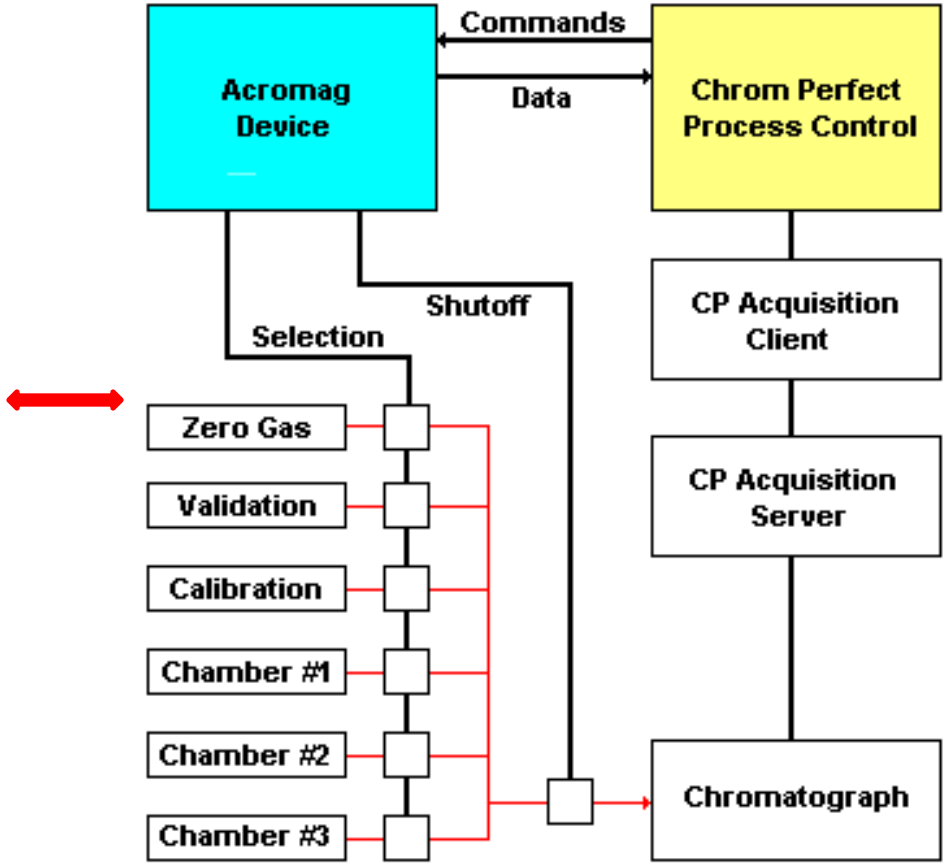


Calidus Chrom Perfect Process Control (CPPC) and Software Review

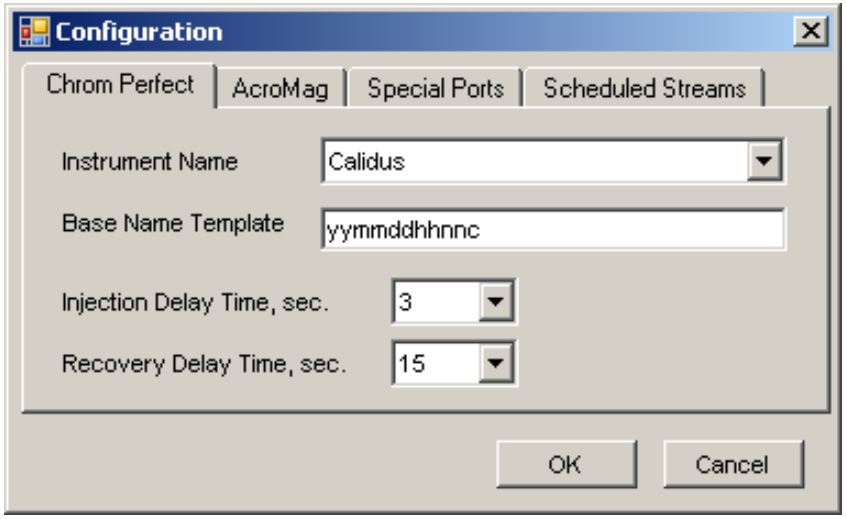


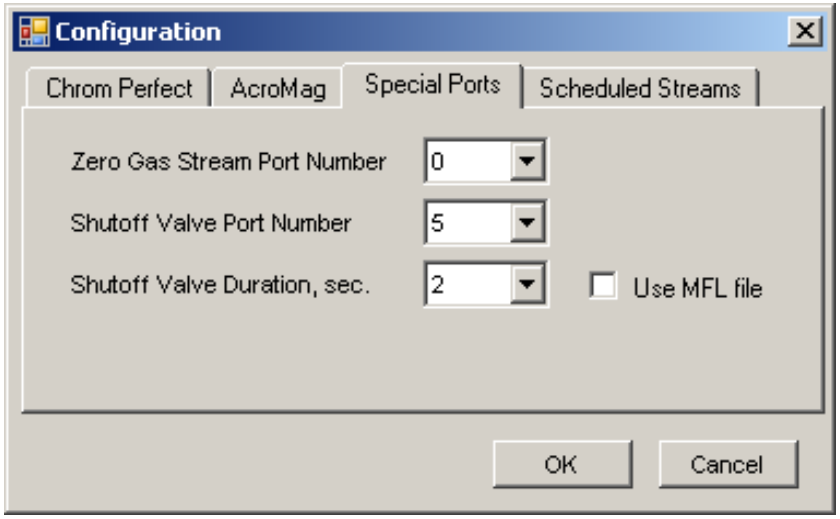
Chrom Perfect Process Control (CPPC)

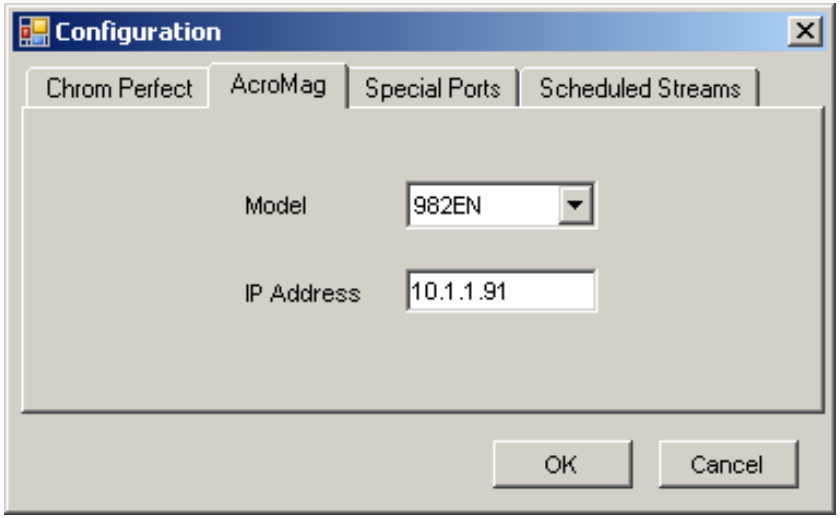


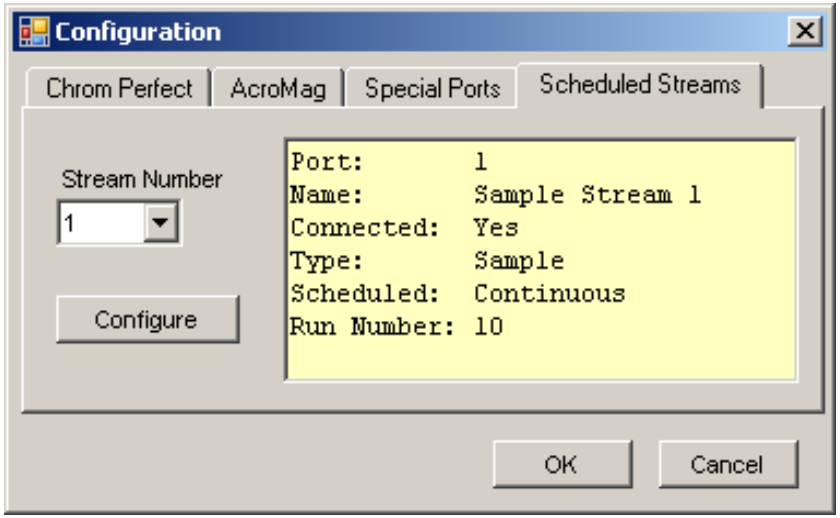


Click on Setup to Configure the System

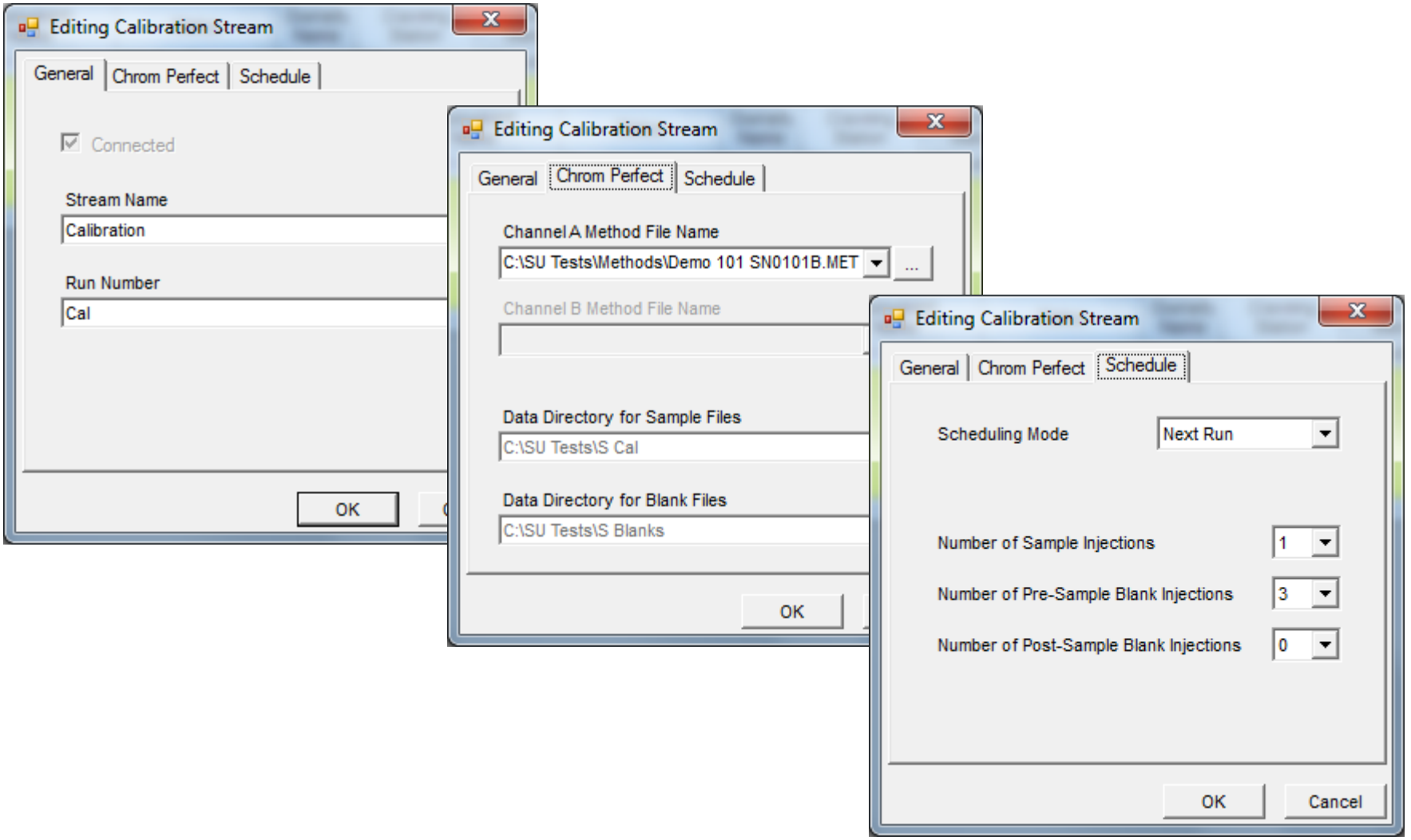




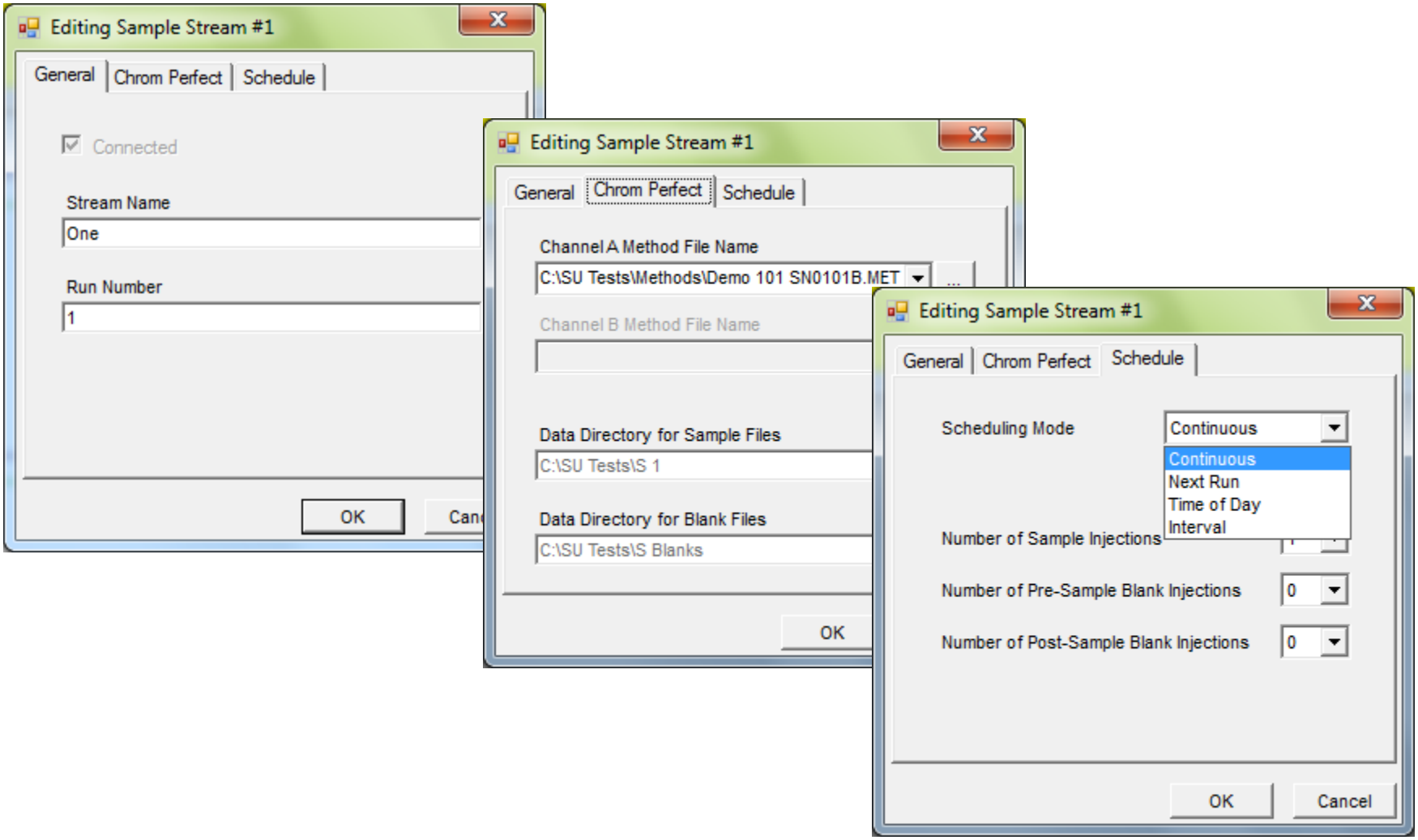




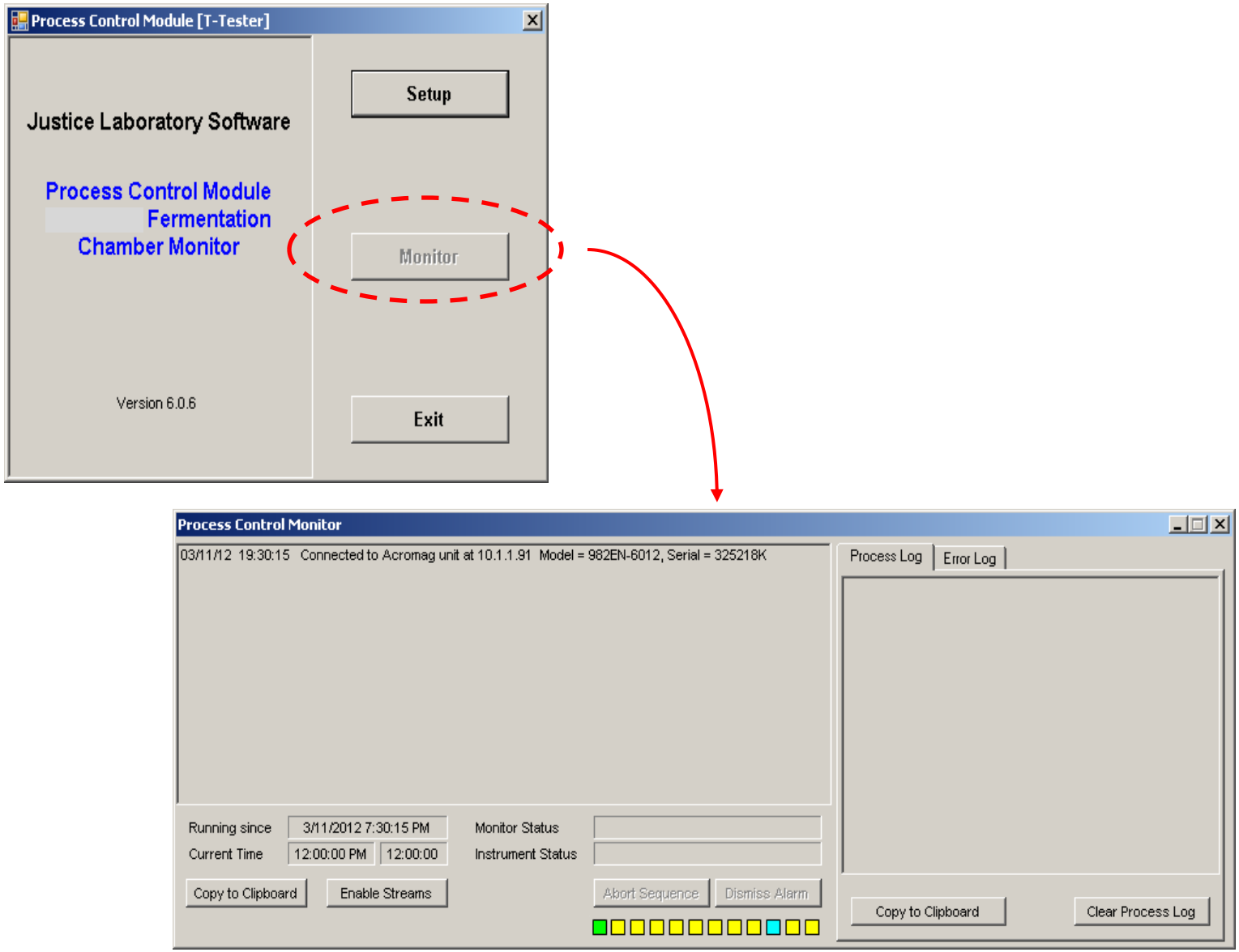
The Calibration Configuration Functions



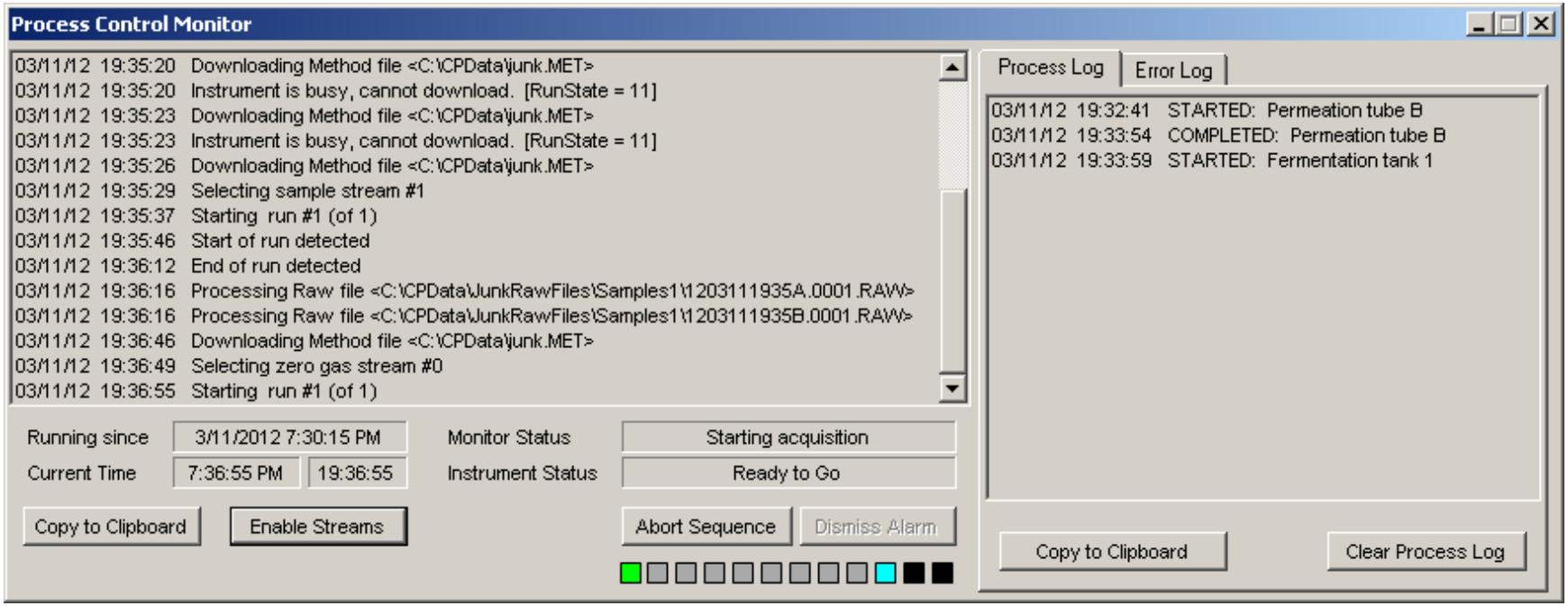
The Stream Configuration Functions



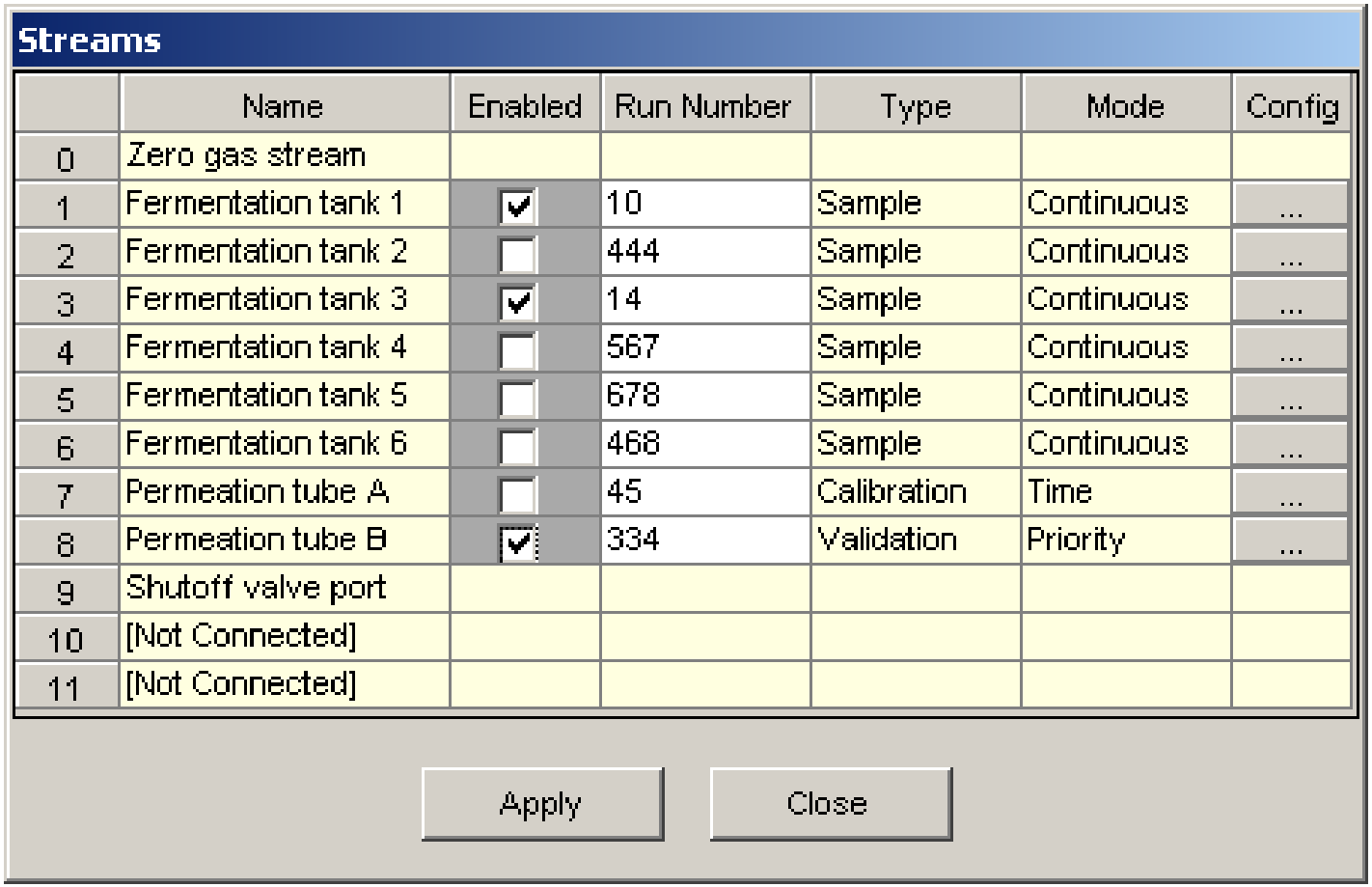
Chrom Perfect Process Control (CPPC)



GC Operational Information

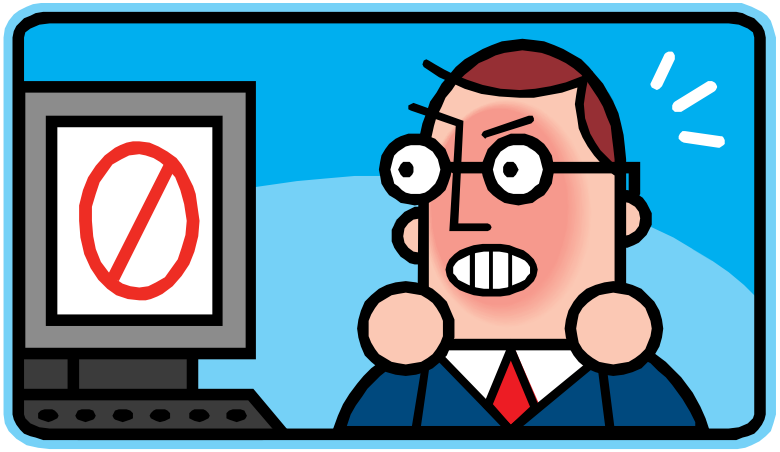


Change Operations



Is This Proof Enough?

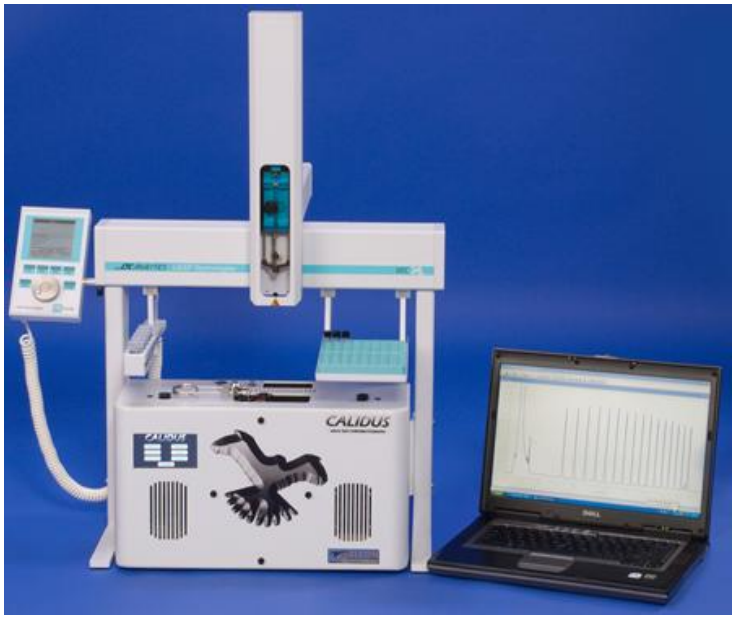
- Probably not…
  … but we're getting closer!
  - Our experience
    - with micro scale fluidics, leaks are more problematic than the "dreaded" plugs
    - with micro GC, the application capability is about 80% of the market need
    - with chemometrics, it doesn't take a PhD to take big advantage of the benefits
  - And orders are beginning to flow… the real PROOF!



- RISK is a four letter word!
  - Users are reluctant
    - Doesn't NeSSI mean NEW?
    - Who the heck are Falcon and Calidus and what do you mean micro?
    - Chemometrawho? Isn't that the smoke and mirror stuff from NIR?

CALIDUS

micro GAS CHROMATOGRAPH



Easier, Smaller, Smarter, Faster, Greener

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