

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

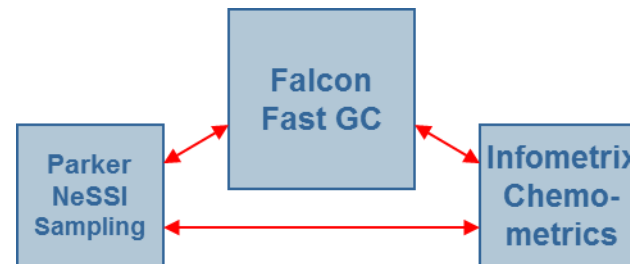
Mike Cost, Parker Hannifin

George Schreiner, Justice Laboratory Software

John Crandall, Falcon Analytical

10/16/2011

# Outline of Presentation



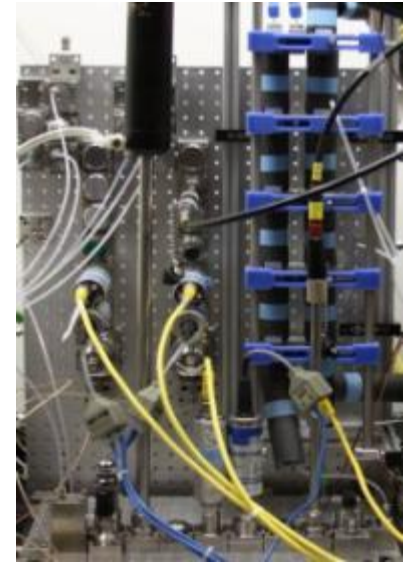
- NeSSI, Fast Gas Chromatography and Chemometrics are still (after all these years) considered new technology.
- Thought leaders and early adopters alike are excited, make lots of positive noise about these new technologies and have implemented to an extent.....a limited extent.
- However, to reach genuine 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

# 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

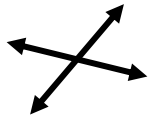
(Foundation of Modular Approach)

ISA/ANSI SP76.00.02  
Compliant



Same screw size  
throughout

Same plane  
flowpaths



Field connectors  
(top or end)

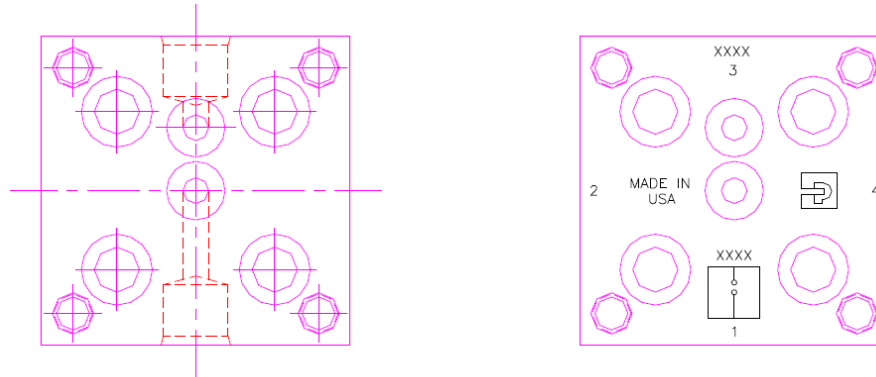
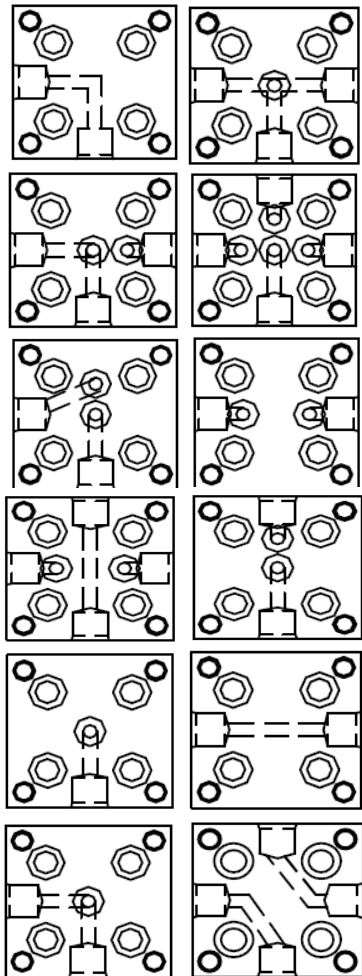
Mounting  
"Pegboard"

Slip-fit intra-fitting  
connectors

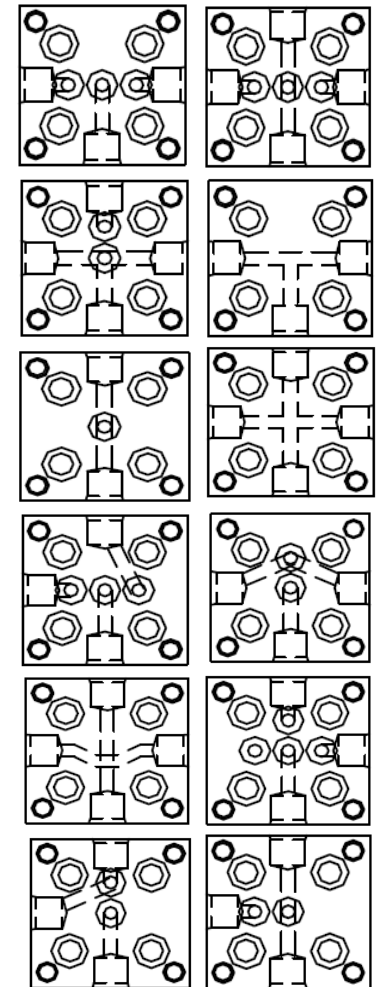
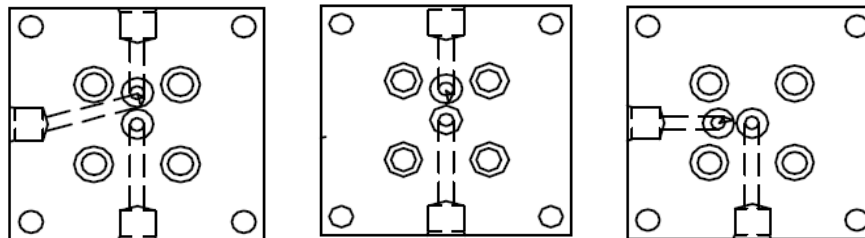
# Intraflow™ Substrates/Flowpath Options:

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

## Part Number Configurator/Generator



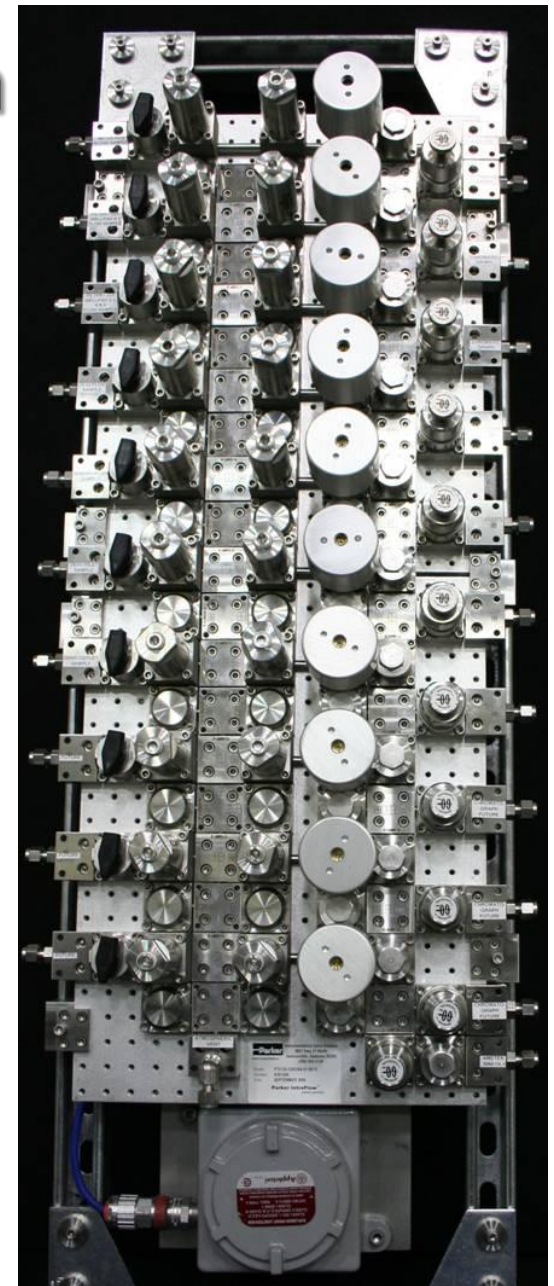
**IntraFlow™ Fitting**



# High Pressure Process Application

## 10-Stream Natural Gas BTU Analysis System

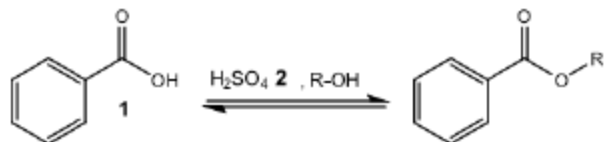
- Coalescing & Membrane Separator Drain Header
- Restricted Orifice Header Pressure Control
- Freeze Protection Heating
- Sample pressure 1,500 – 3,000psig





# Micro Reactor Fluid Control with Intraflow™

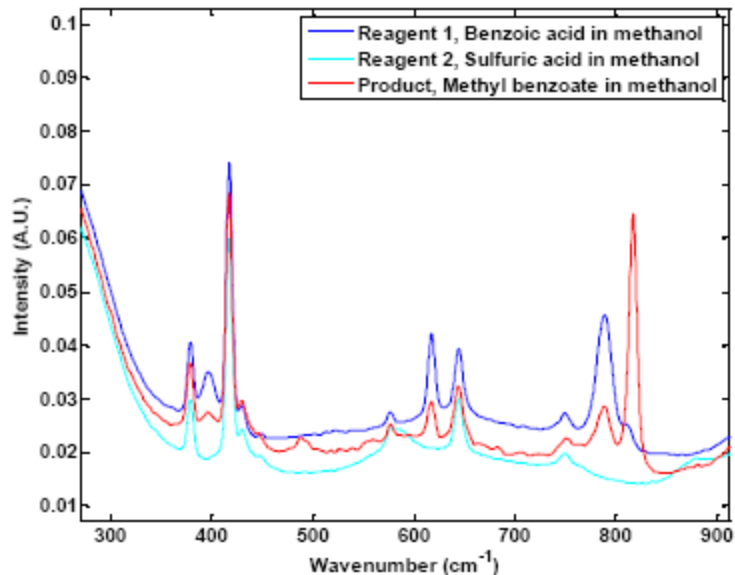
## Esterification of Benzoic Acid



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  $815\text{ cm}^{-1}$  indicates the reaction proceeded successfully.



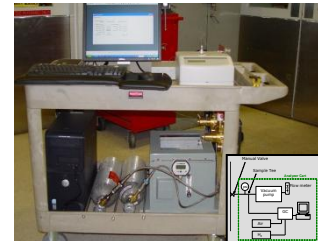
# Coolant Leak Detection into Blood Product Freeze Dryers (batch process)

- 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](http://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

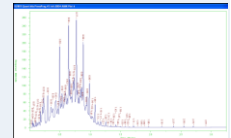




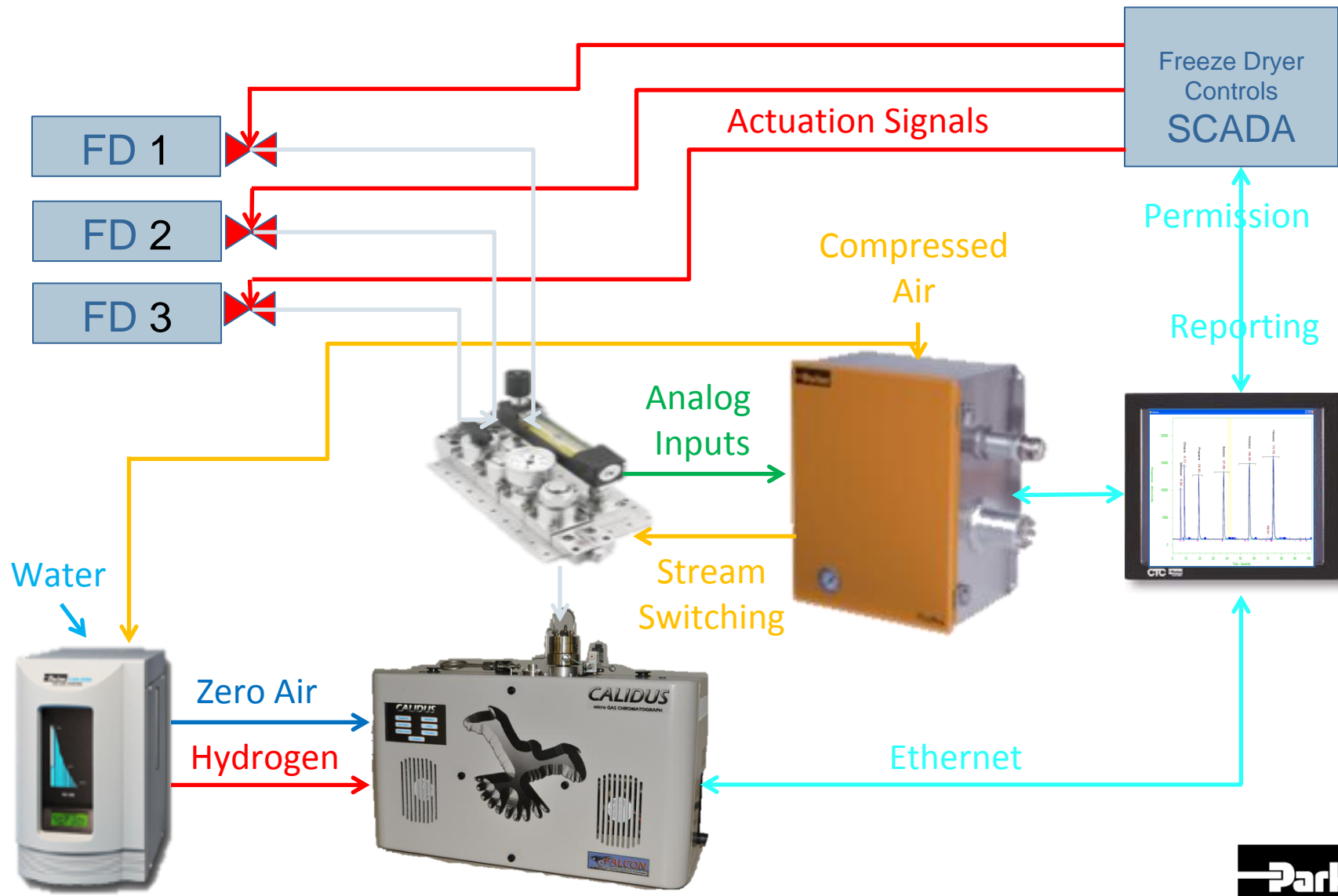
# Solution (aka future state): NeSSI, Fast GC and Chemometrics with Full Automation

- 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<sup>tm</sup> 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 concentrationAssessment 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

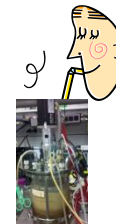




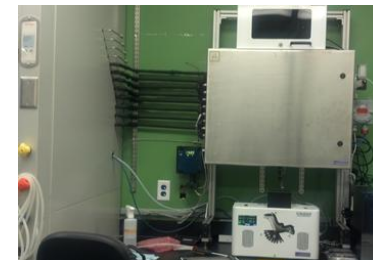
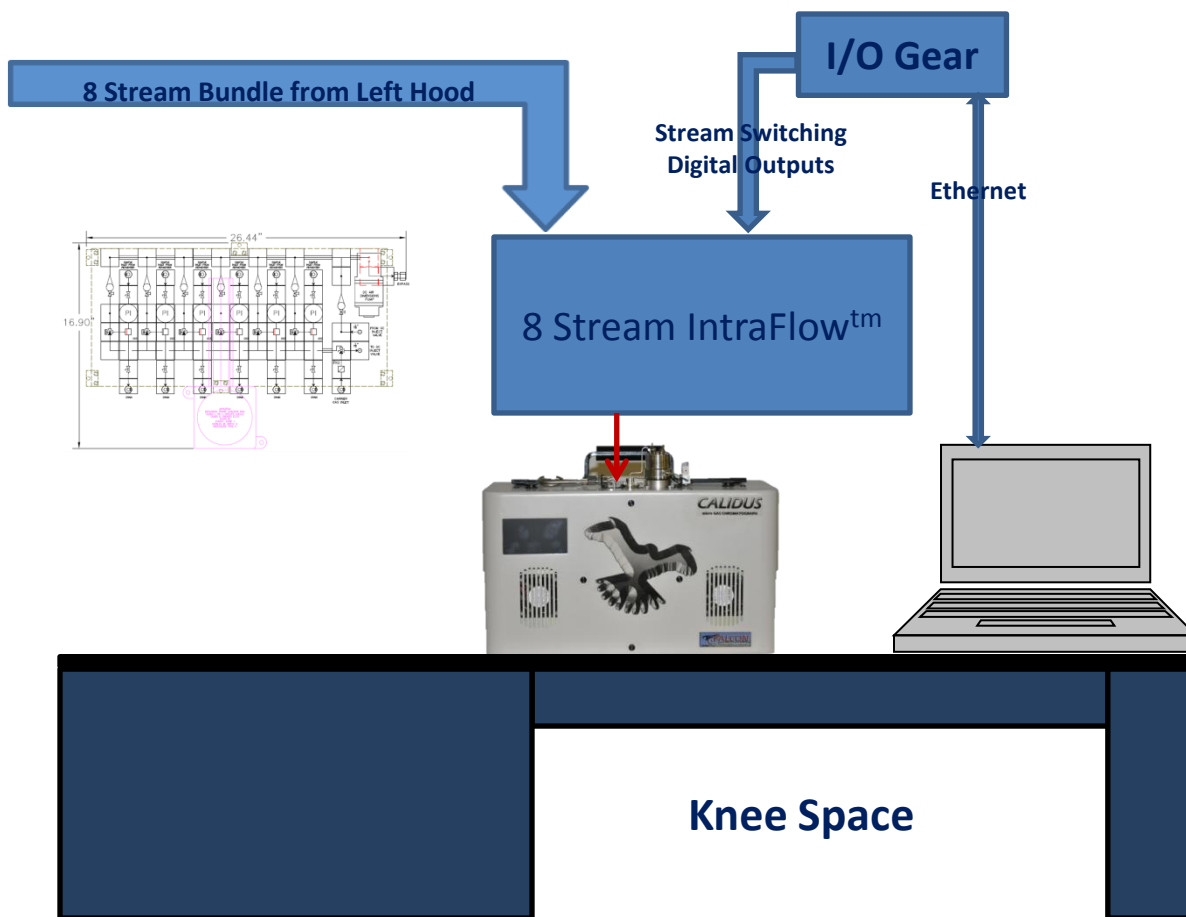
# Automation Strategy



- 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<sup>tm</sup> 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”

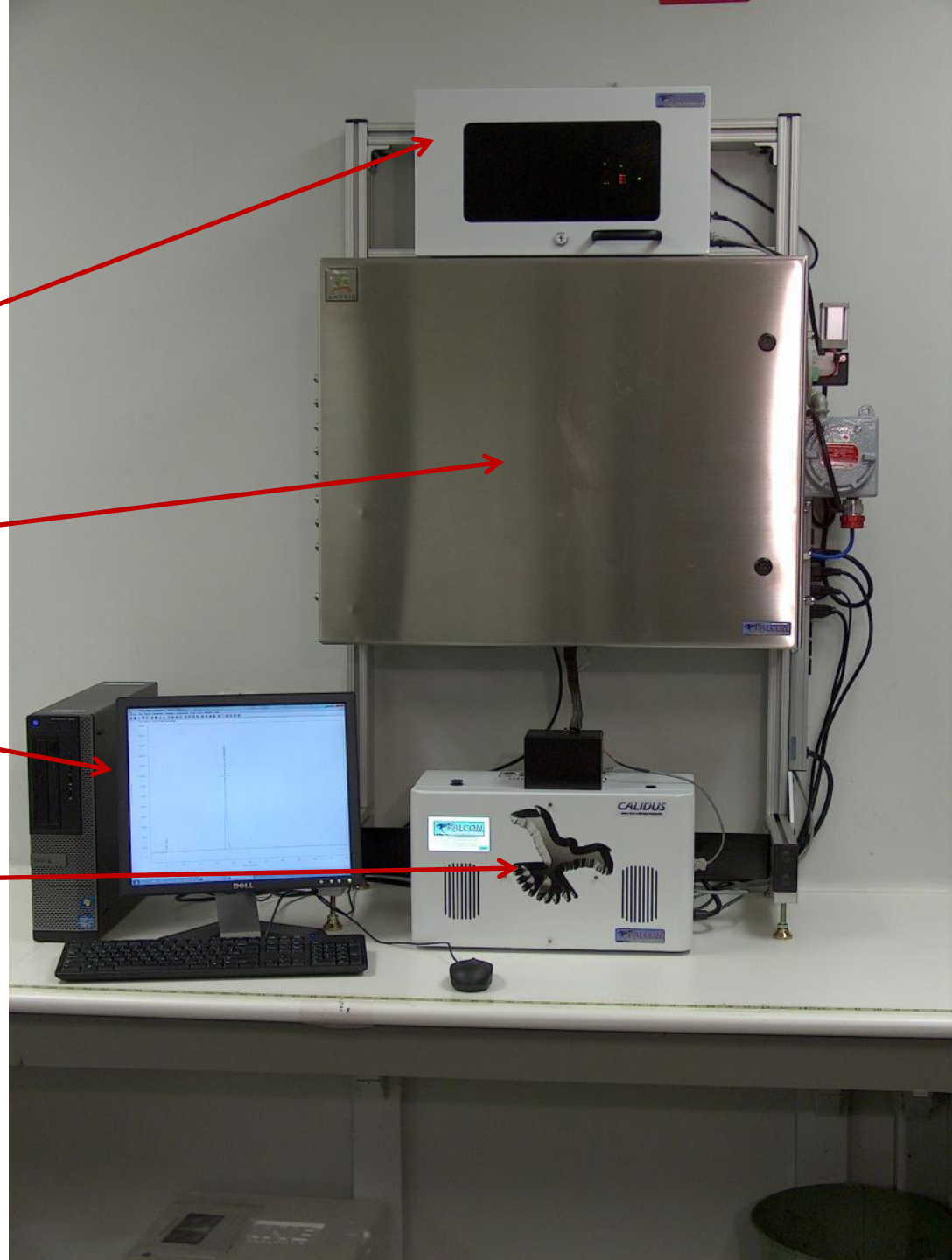


# System Conceptual Overview for the 8 Stream Continuous NeSSI/ Fast GC/Chemometric System (not to scale)



# 8 Stream Gas Analysis System

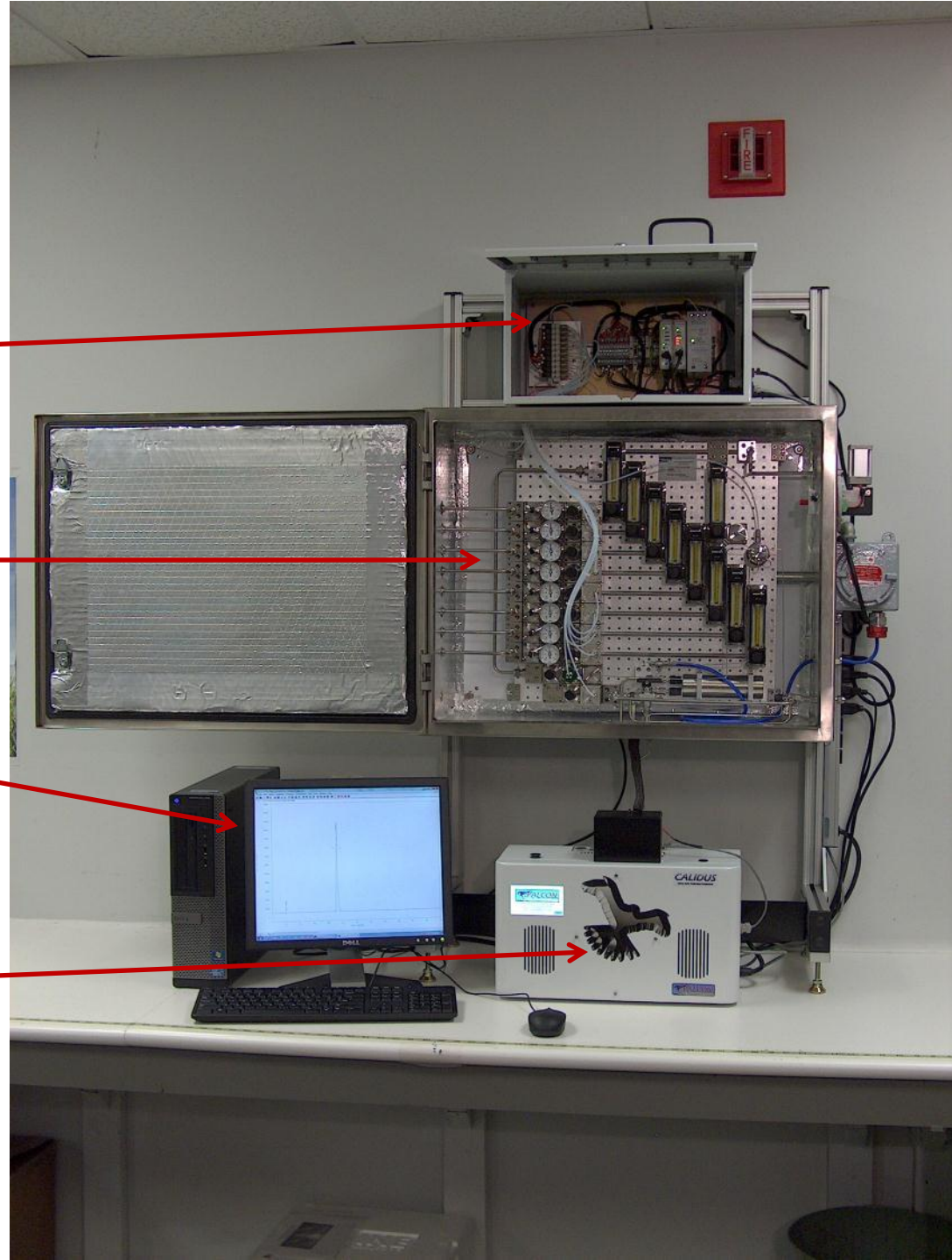
- Electronics, I/O
- 8 Stream Sample System
- System Computer
- Calidus Fast Gas Chromatograph





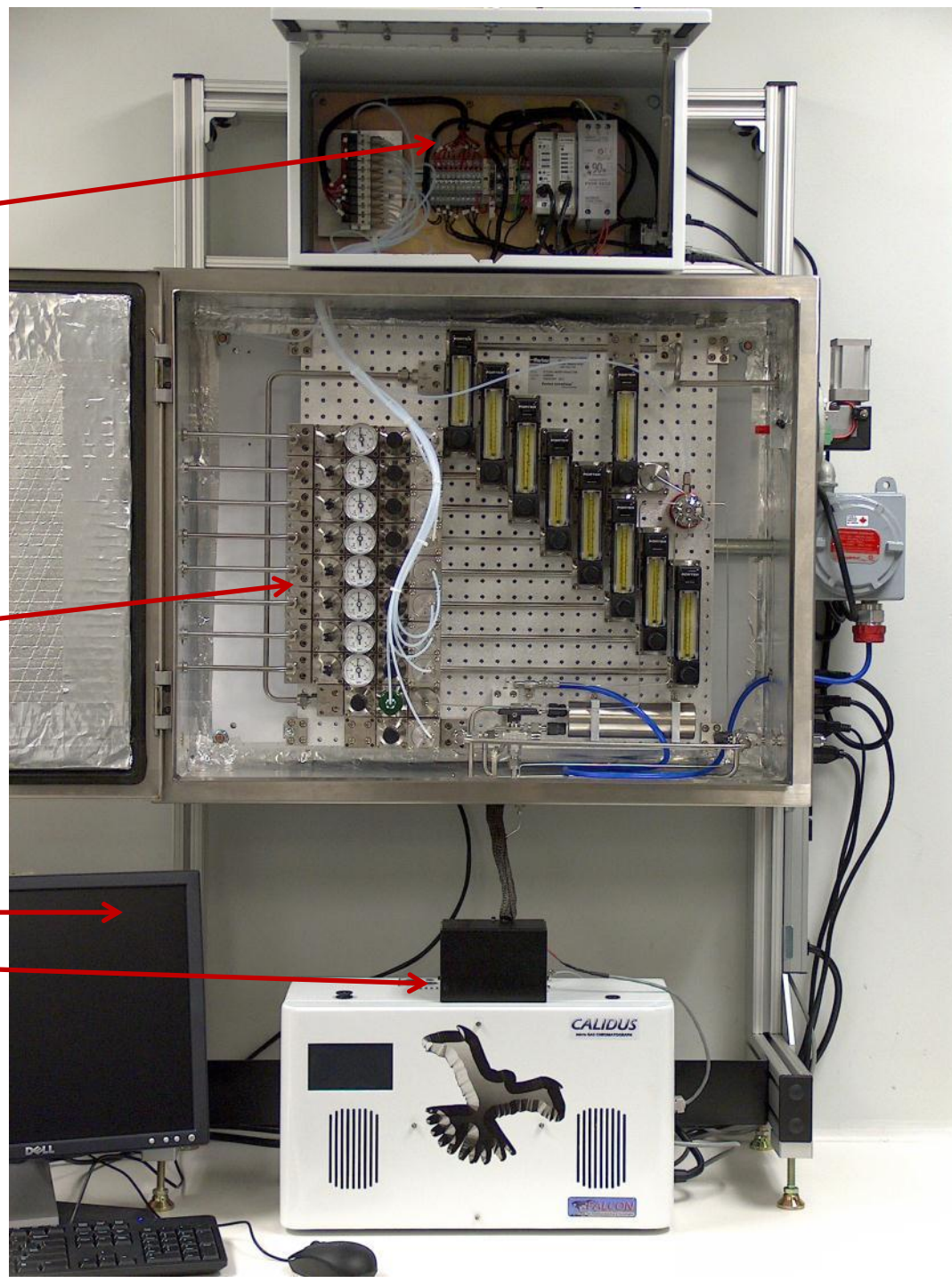
# Enclosures View

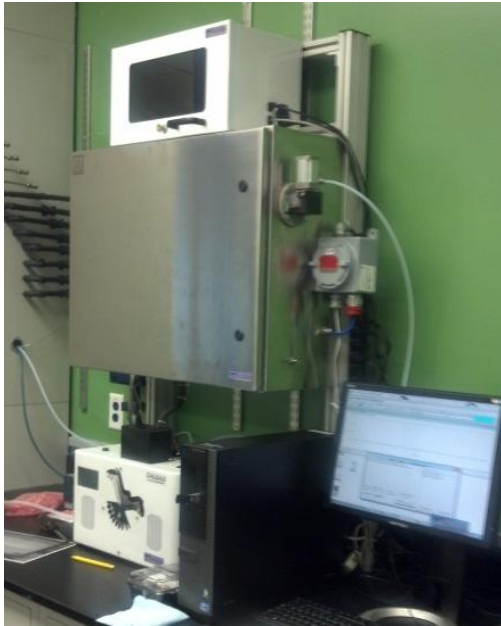
- Electronics, I/O
- 8 Stream Sample System
- System Computer
- Calidus Fast Gas Chromatograph



# Component Description

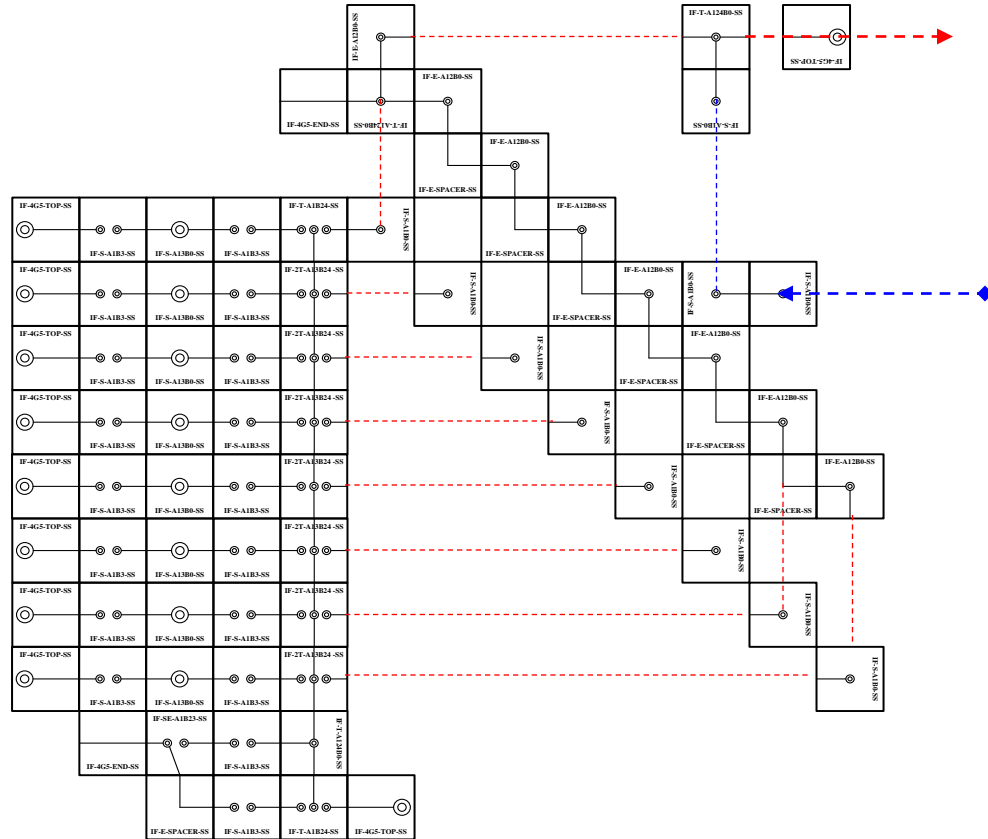
- Electronics, I/O
  - Power supply
  - Ethernet switch
  - 24 VDC outputs
  - Electronic to pneumatic switching
  - MODBUS modules are available to fit here
- 8 Stream Sample System
  - Block valves
  - Pressure gauge
  - Flow rotameters
  - Permeation tube calibrator
- System Computer
- Calidus Fast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



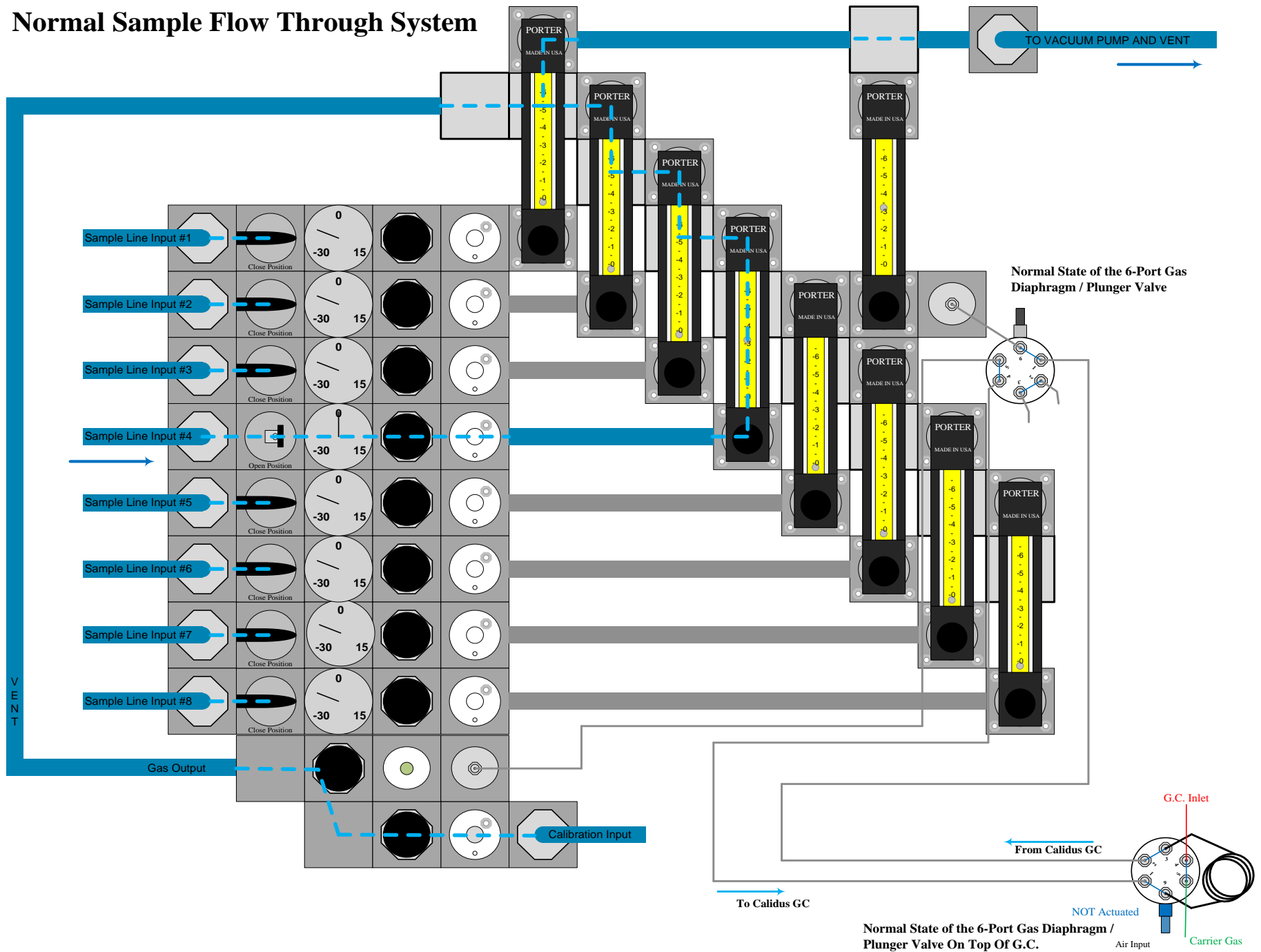


# Sample Flow Design

Block Diagram of Parker Interflow System

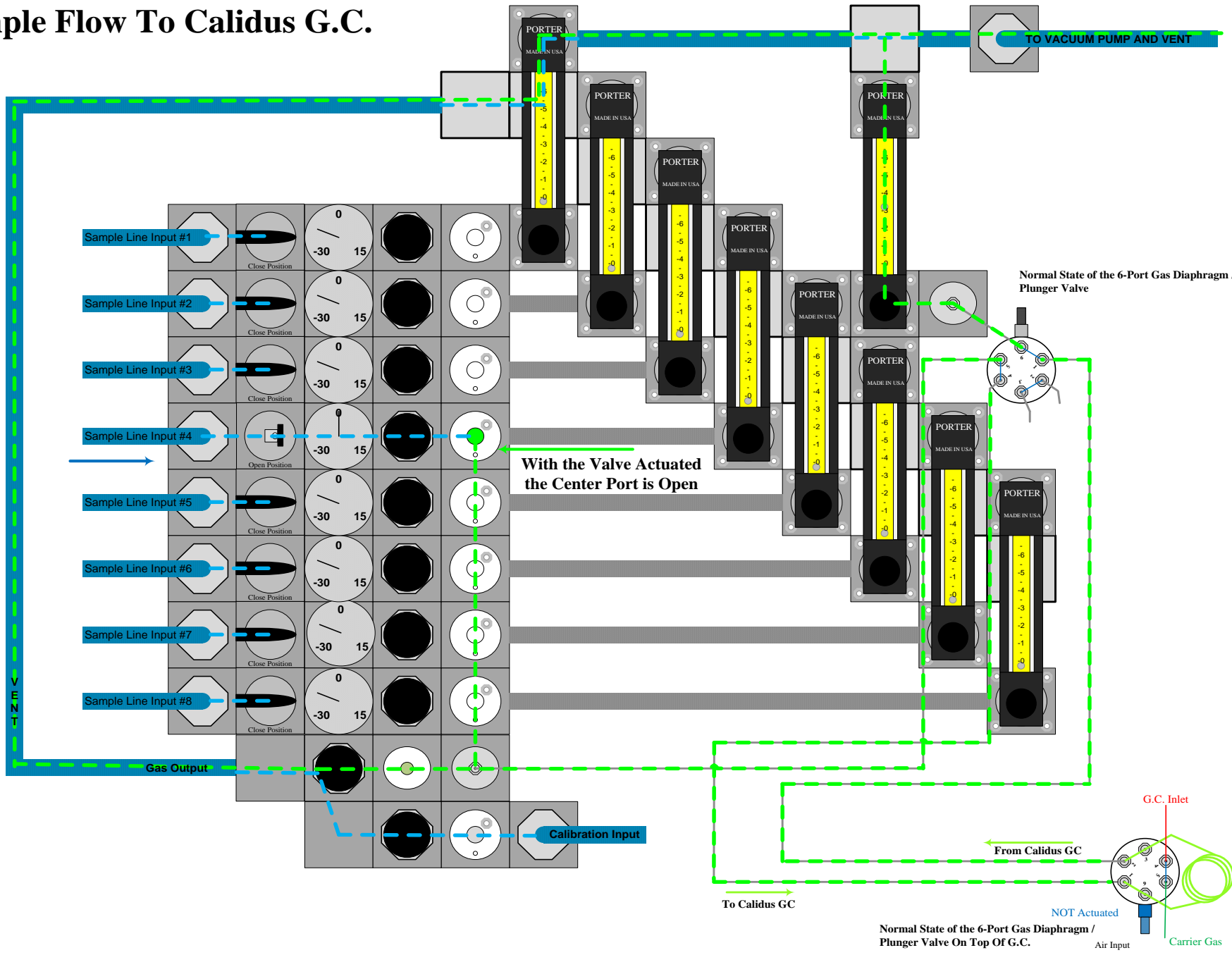


# Normal Sample Flow Through System

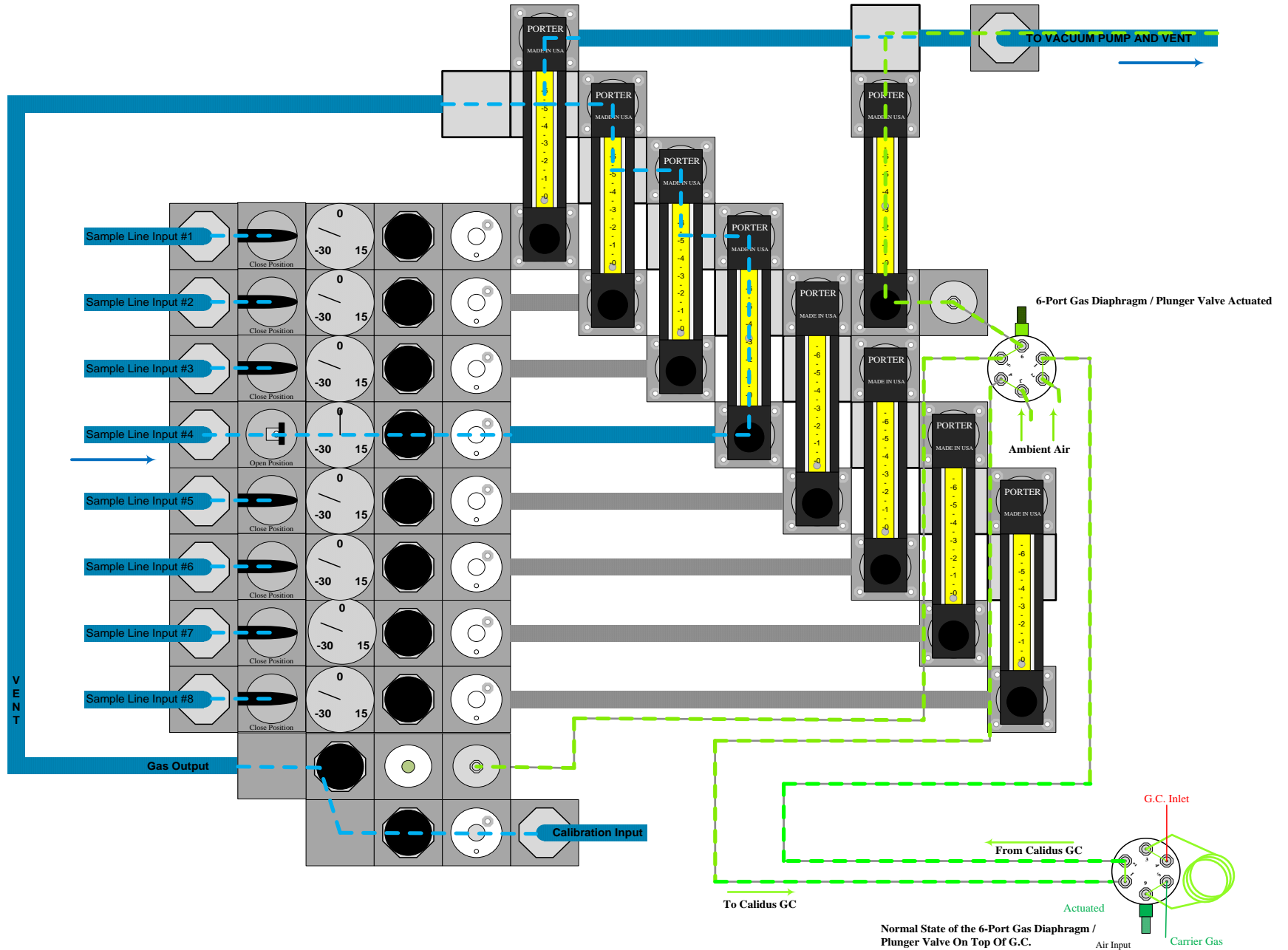




# Sample Flow To Calidus G.C.

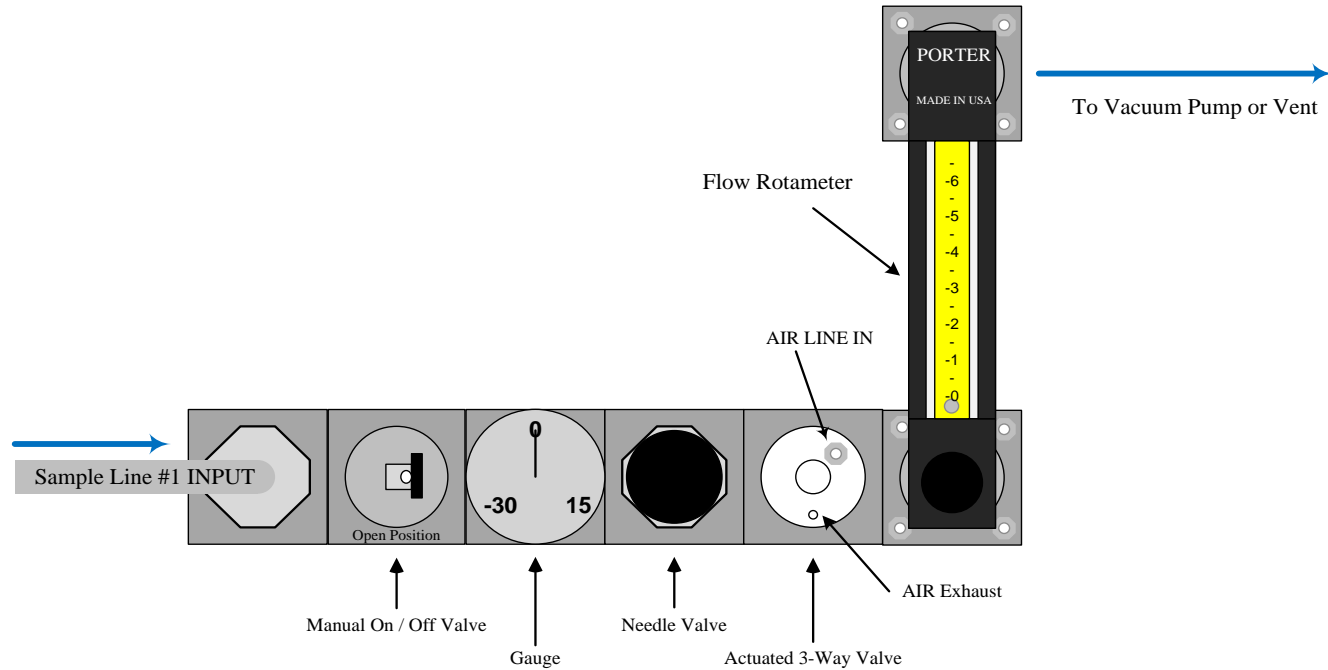


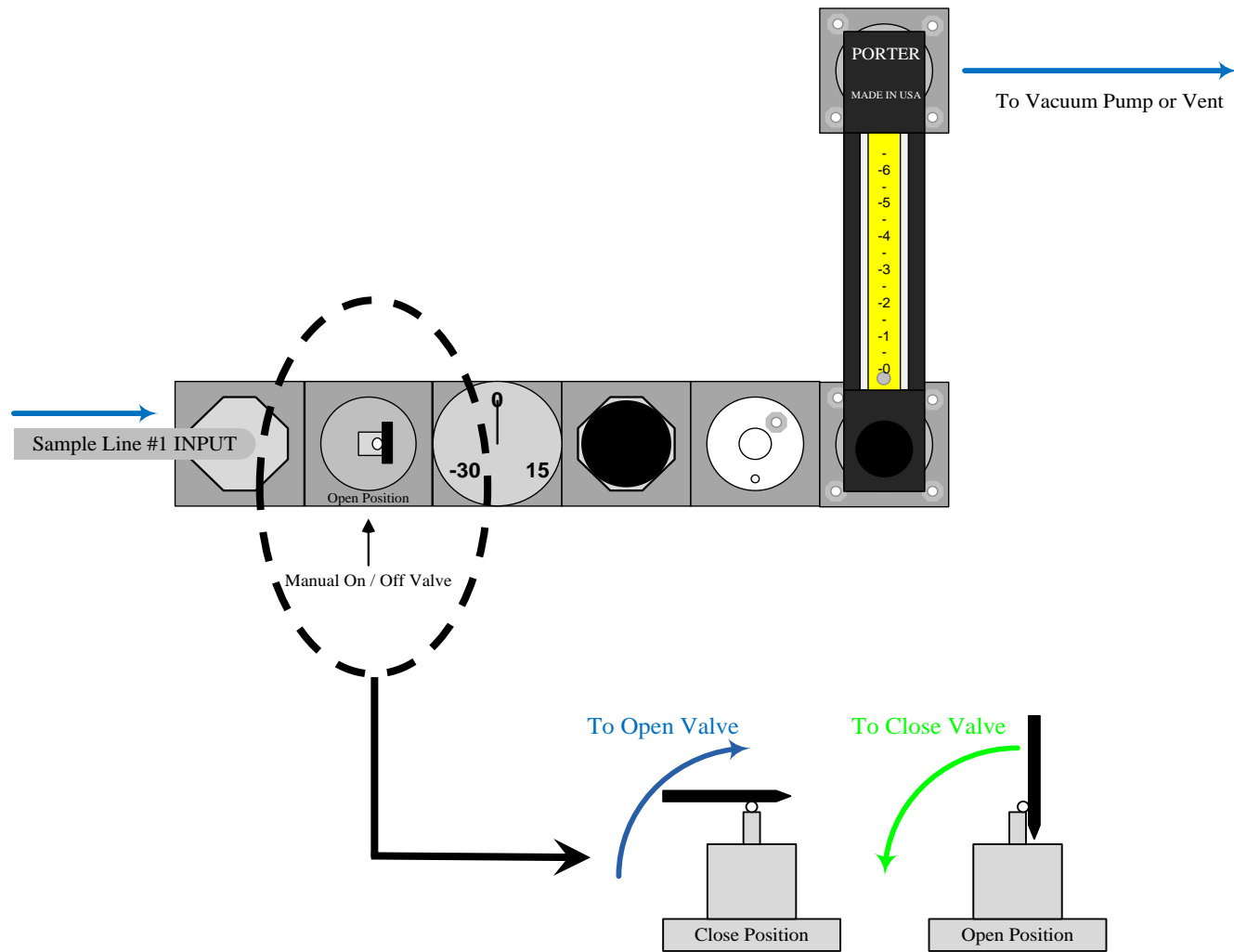
# Normal Sample Flow Through System With The 6-Port Gas Diaphragm / Plunger Valve Actuated





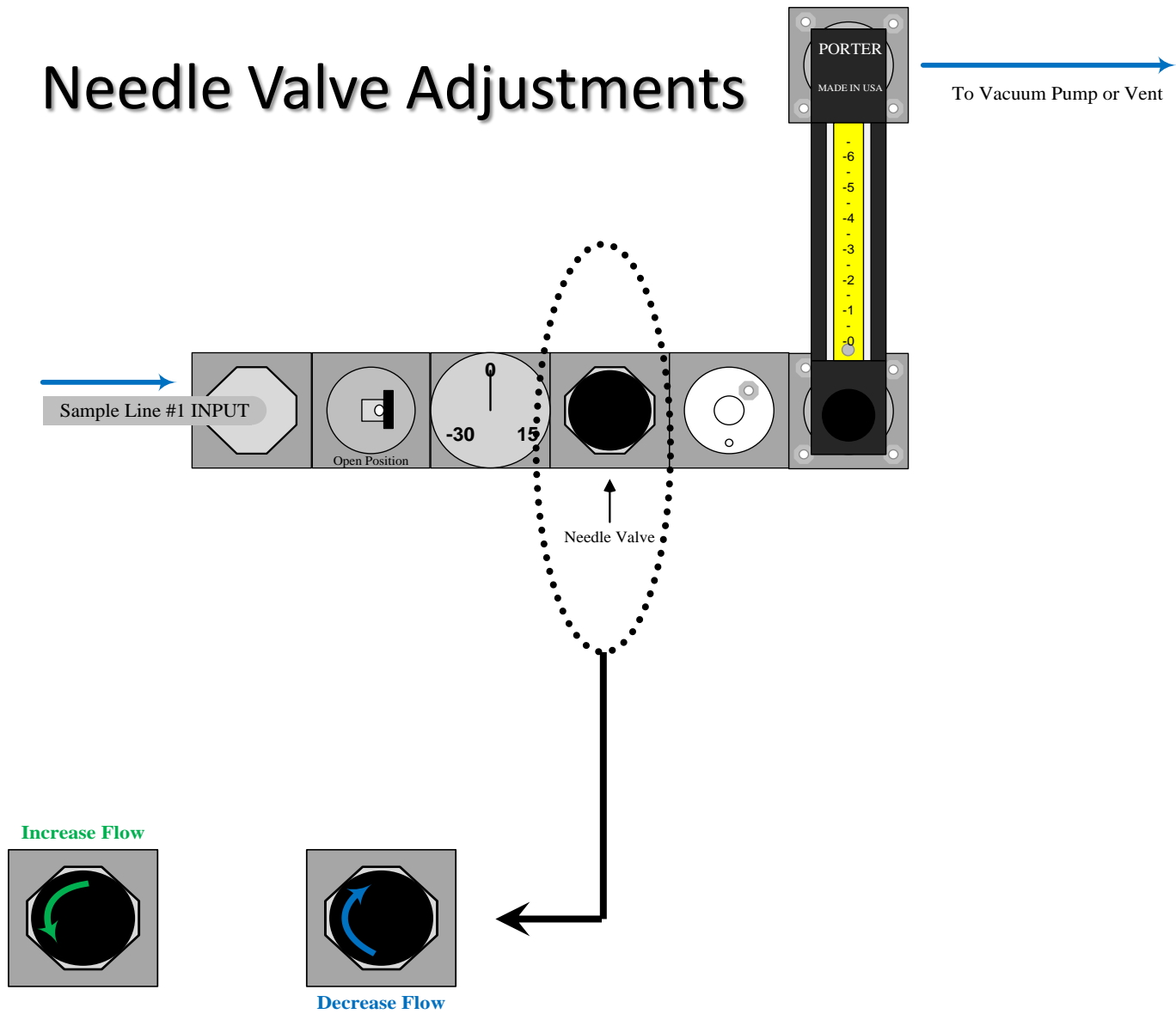
# Location and Identification of Parts on Sample Line #1

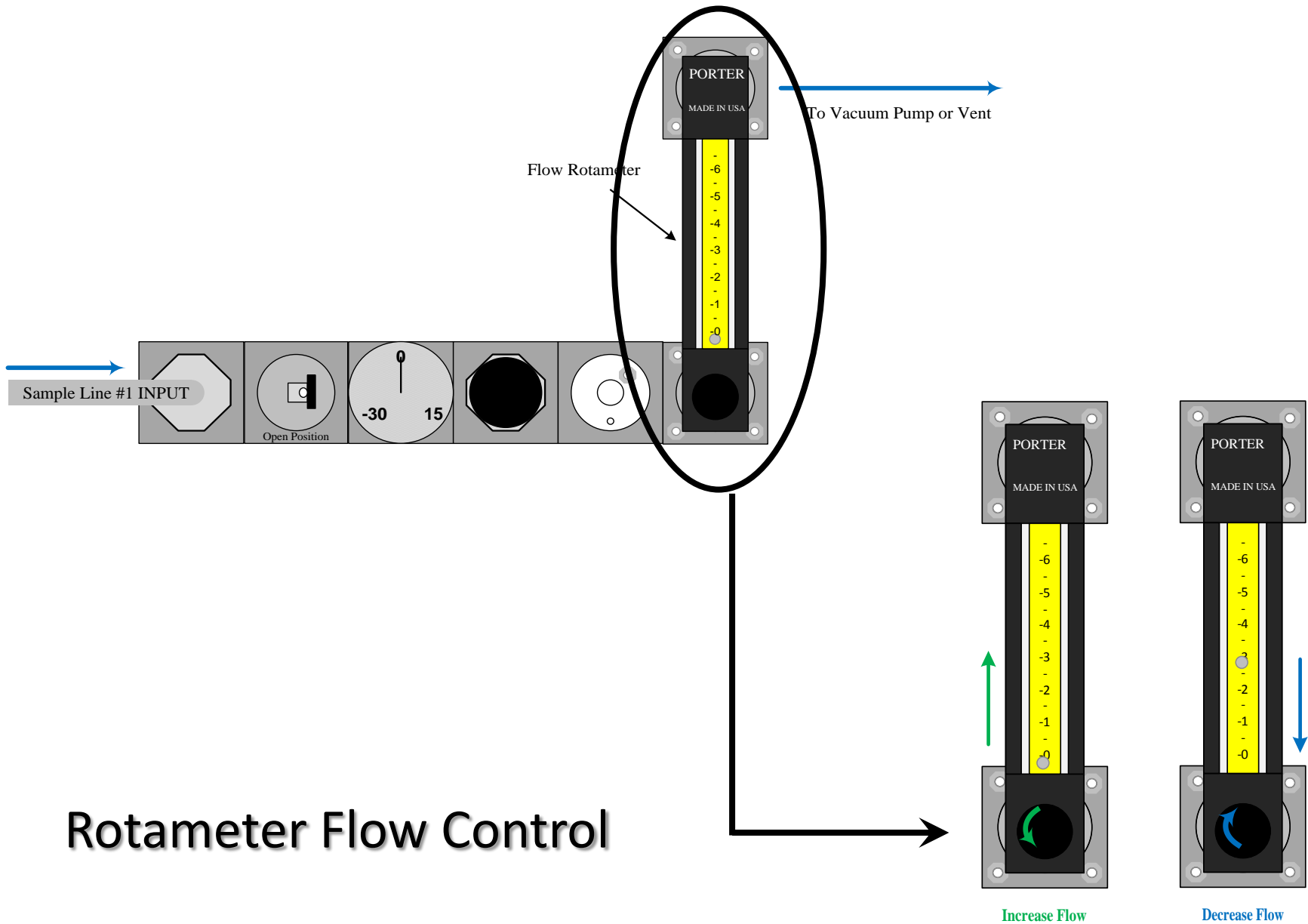




## Manual Valve Operation

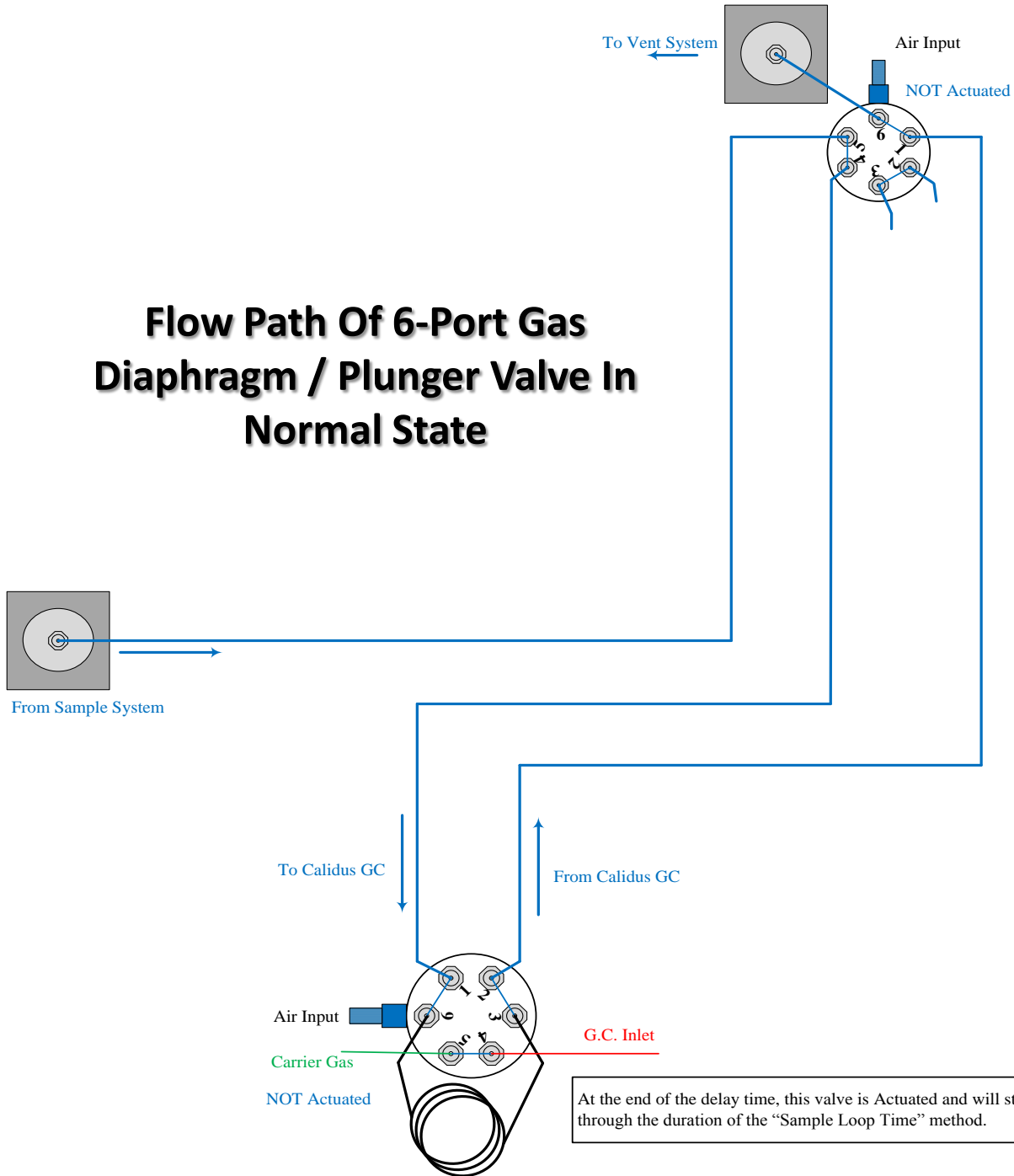
# Needle Valve Adjustments





# Rotameter Flow Control

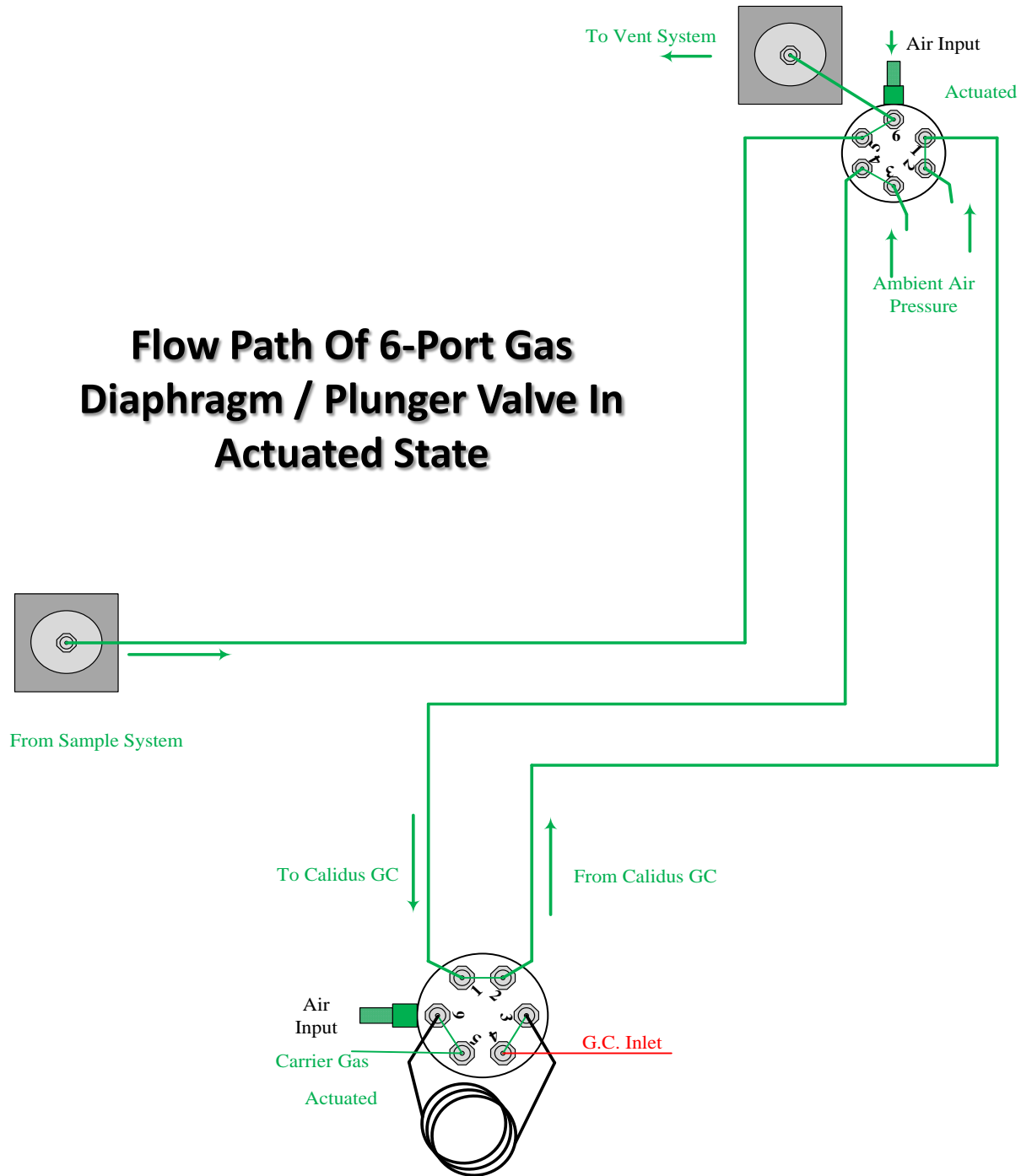
# Flow Path Of 6-Port Gas Diaphragm / Plunger Valve In Normal State



This valve is NOT Actuated until it receives the start signal from the software (CPPC). After the valve is Actuated it will stay so through the duration of the delay time (5 seconds) plus 2 seconds.

At the end of the delay time, this valve is Actuated and will stay so through the duration of the "Sample Loop Time" method.

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





# Calidus Chrom Perfect Process Control (CPPC) and Software Review

The screenshot displays the Chrom Perfect software interface, which is divided into several windows. At the top, the 'Chrom Perfect Data Acquisition on FALCONCALIDUS [SingleUser-]' window shows a table of acquisition parameters. Below this is the 'Chrom Perfect Analysis [SingleUser-]' window, which contains a chromatogram plot. The plot shows a series of peaks over a 1.4-minute period, with the y-axis representing 'Response - Counts' ranging from 0 to 240. The x-axis is 'Time - Minutes'. A 'Process Control Monitor' window is overlaid on the bottom right, displaying an error message: '04/05/12 11:21:40 Error 12 connecting to Acromag unit at 0.0 0.0: Connection time-out'. The monitor also shows the current time as 11:27:16 AM and the instrument status as 'Awaiting Download'. The Windows taskbar at the bottom shows the system clock as 11:25 AM on 4/5/2012.

Instrument	Control	Detector	Status	Sample Name	Raw File	Method File	Method	Calib. File	Run Time	Response	Sequence File	Quan	Seq. #	Vial #	Relays	Reference File
1A	D 2887 Demc	FID	Awaiting Download				.O.					.O.				

Response - Counts

Time - Minutes

Process Control Monitor

04/05/12 11:21:40 Error 12 connecting to Acromag unit at 0.0 0.0: Connection time-out

Running since 4/5/2012 11:21:40 AM  
Current Time 11:27:16 AM 11:27:16

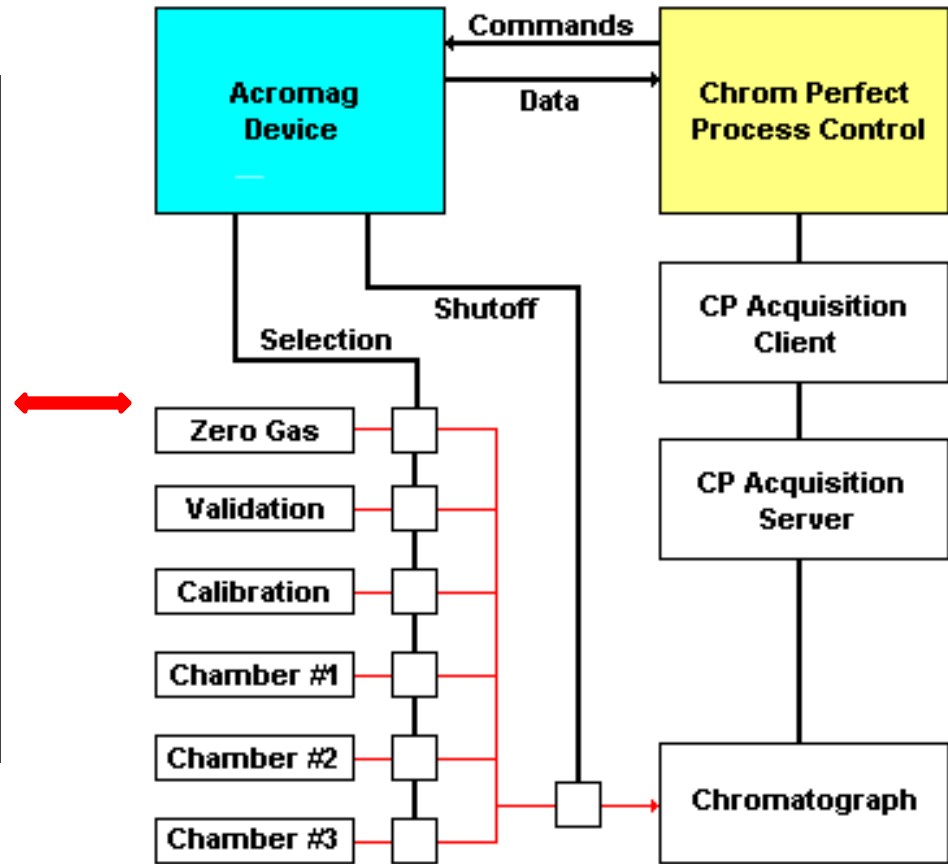
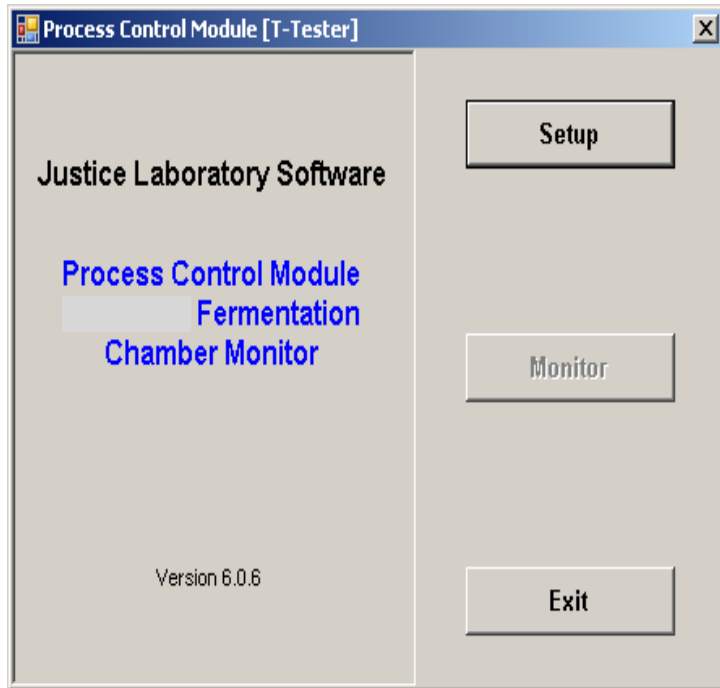
Monitor Status Waiting for next scheduled sampling  
Instrument Status Awaiting Download

Copy to Clipboard Enable Streams Abort Sequence Dismiss Alarm

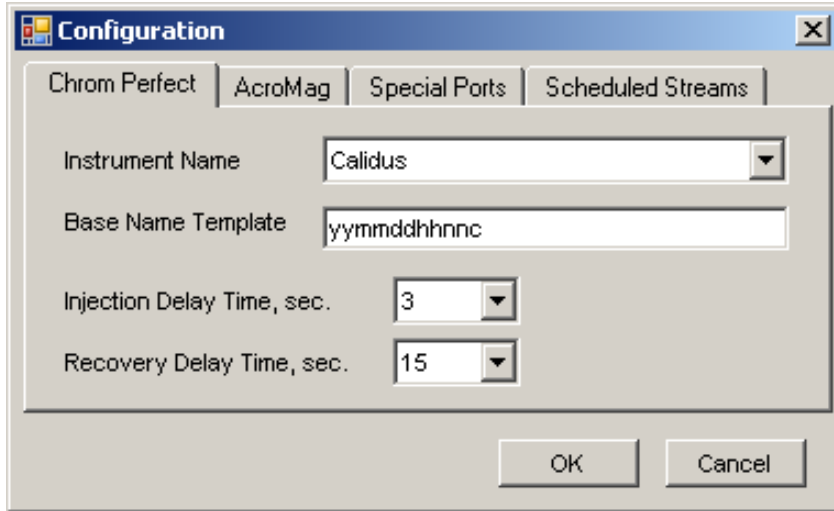
Copy to Clipboard Clear Process Log

11:25 AM 4/5/2012

# Chrom Perfect Process Control (CPPC)



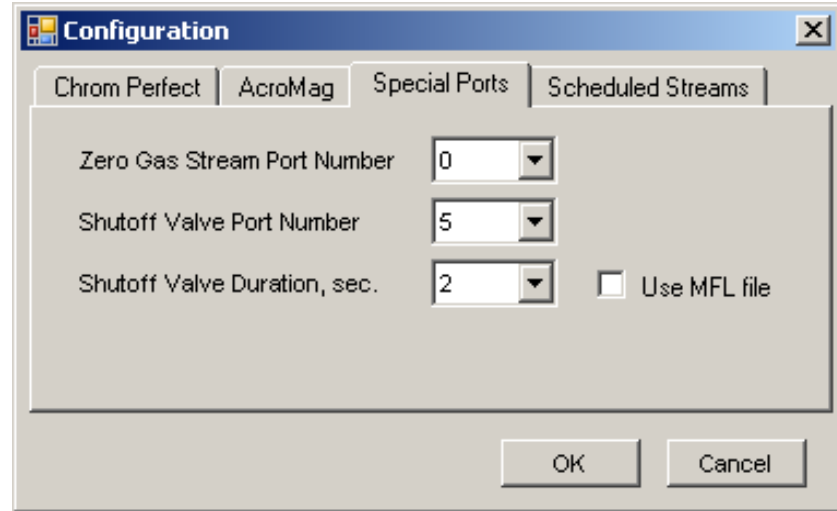
# Click on Setup to Configure the System



Configuration dialog box, Chrom Perfect tab. Fields include Instrument Name (Calidus), Base Name Template (yymmddhhnc), Injection Delay Time (3 sec), and Recovery Delay Time (15 sec).

Instrument Name	Calidus
Base Name Template	yymmddhhnc
Injection Delay Time, sec.	3
Recovery Delay Time, sec.	15

OK Cancel

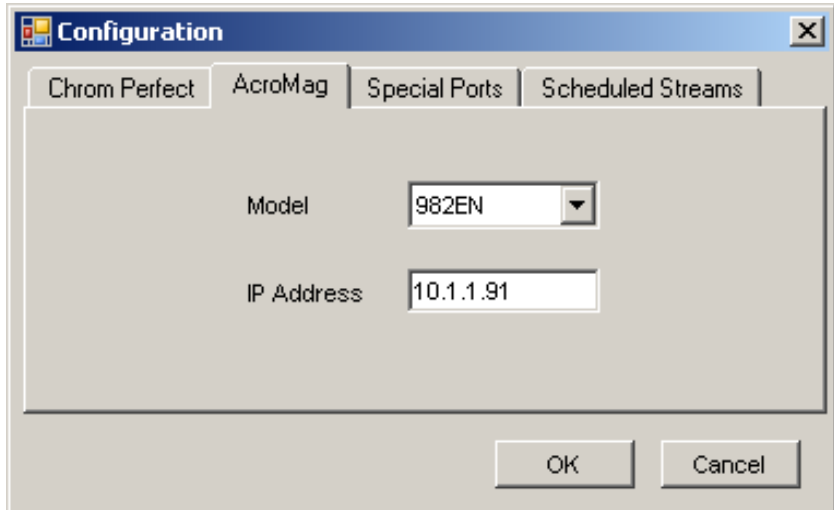


Configuration dialog box, AcroMag tab. Fields include Zero Gas Stream Port Number (0), Shutoff Valve Port Number (5), and Shutoff Valve Duration (2 sec). A checkbox for Use MFL file is present.

Zero Gas Stream Port Number	0
Shutoff Valve Port Number	5
Shutoff Valve Duration, sec.	2

Use MFL file

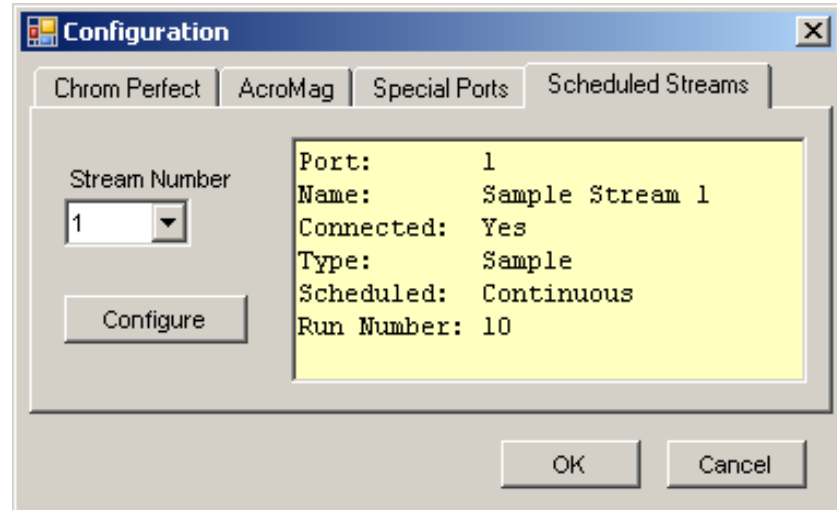
OK Cancel



Configuration dialog box, Special Ports tab. Fields include Model (982EN) and IP Address (10.1.1.91).

Model	982EN
IP Address	10.1.1.91

OK Cancel



Configuration dialog box, Scheduled Streams tab. Fields include Stream Number (1) and a Configure button. A yellow box displays stream details.

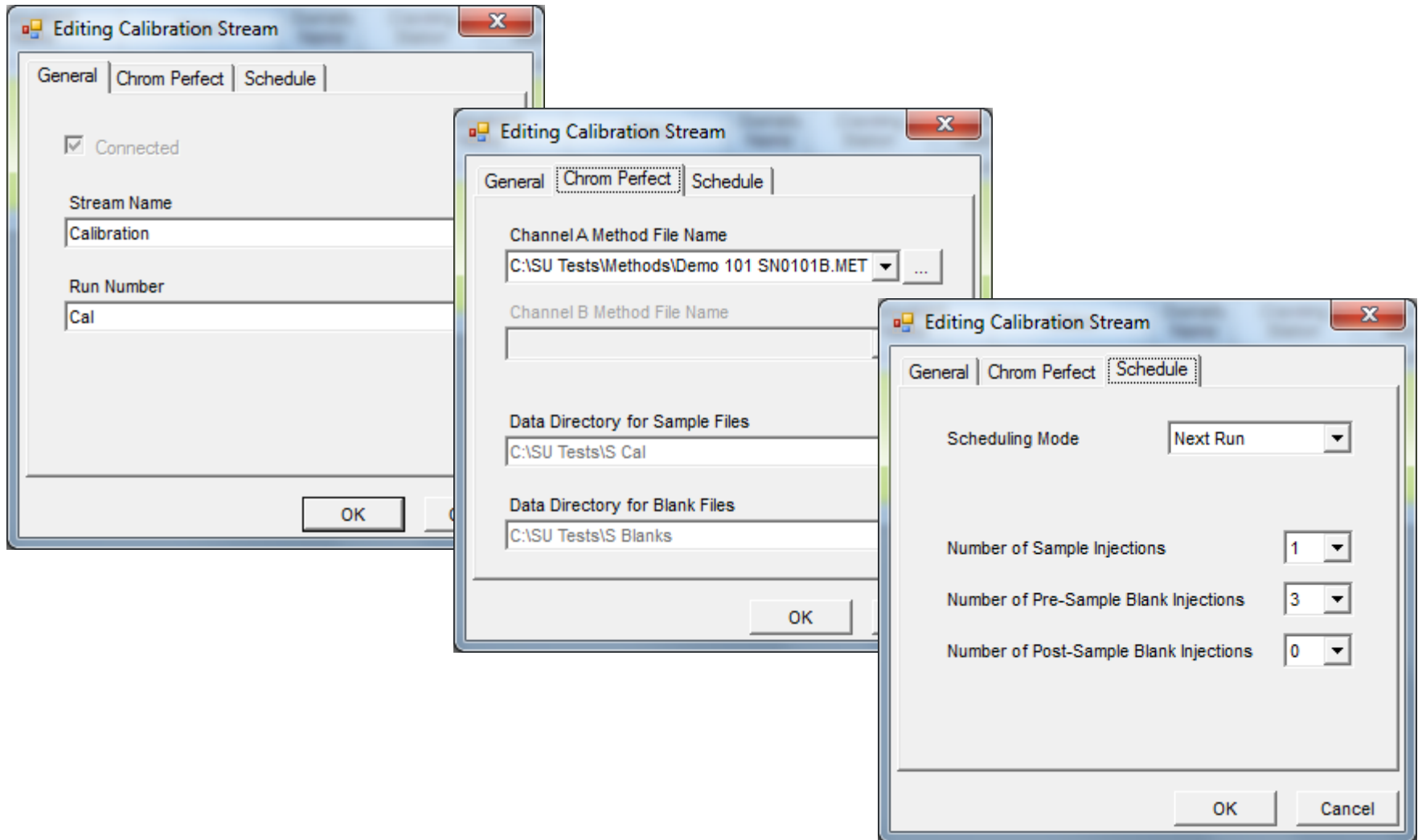
Stream Number	1
---------------	---

Configure

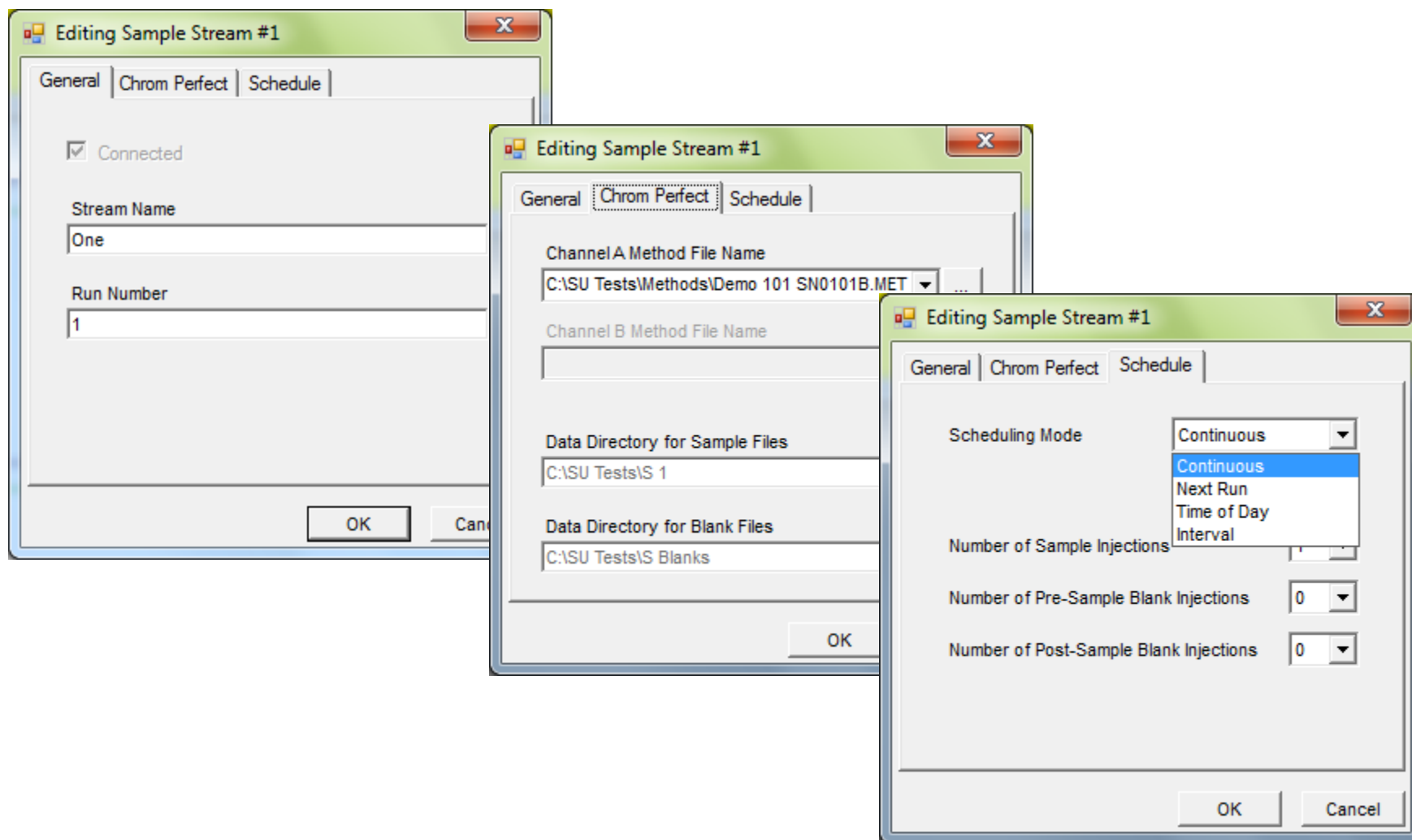
```
Port: 1
Name: Sample Stream 1
Connected: Yes
Type: Sample
Scheduled: Continuous
Run Number: 10
```

OK Cancel

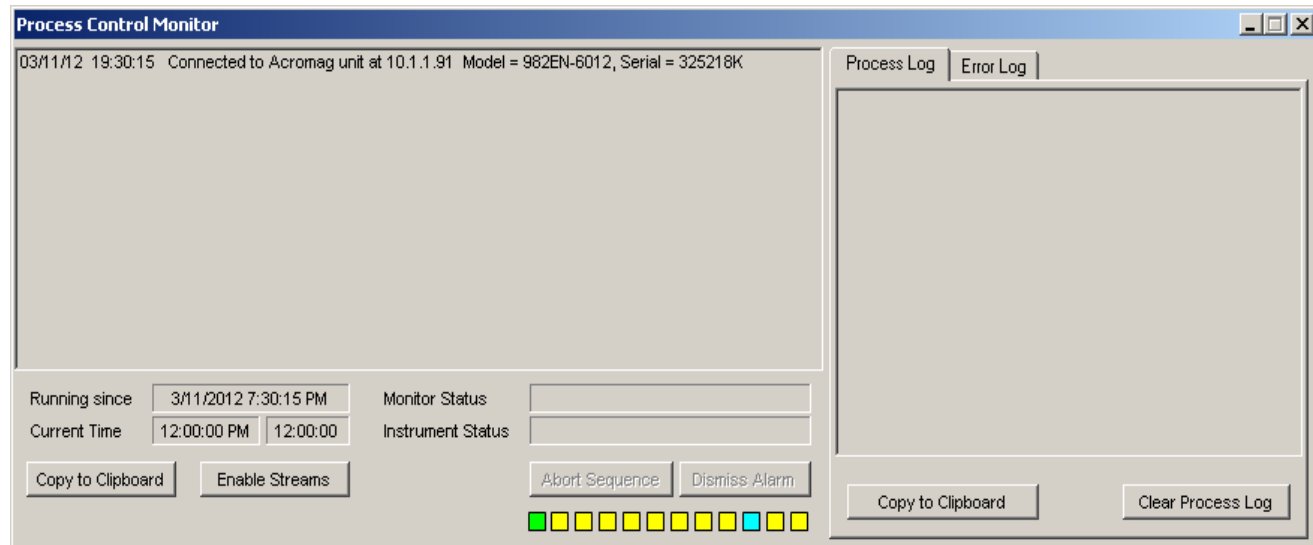
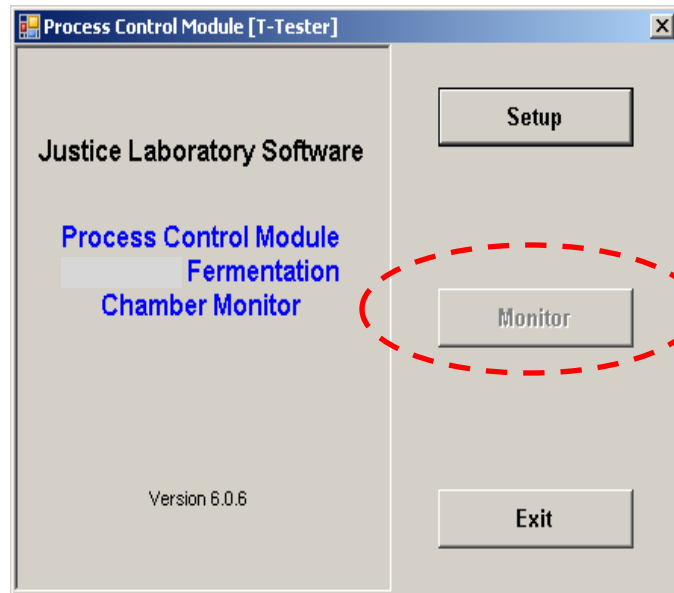
# The Calibration Configuration Functions



# The Stream Configuration Functions



# Chrom Perfect Process Control (CPPC)



# GC Operational Information

**Process Control Monitor**

03/11/12 19:35:20 Downloading Method file <C:\CPData\junk.MET>  
03/11/12 19:35:20 Instrument is busy, cannot download. [RunState = 11]  
03/11/12 19:35:23 Downloading Method file <C:\CPData\junk.MET>  
03/11/12 19:35:23 Instrument is busy, cannot download. [RunState = 11]  
03/11/12 19:35:26 Downloading Method file <C:\CPData\junk.MET>  
03/11/12 19:35:29 Selecting sample stream #1  
03/11/12 19:35:37 Starting run #1 (of 1)  
03/11/12 19:35:46 Start of run detected  
03/11/12 19:36:12 End of run detected  
03/11/12 19:36:16 Processing Raw file <C:\CPData\JunkRawFiles\Samples1\1203111935A.0001.RAW>  
03/11/12 19:36:16 Processing Raw file <C:\CPData\JunkRawFiles\Samples1\1203111935B.0001.RAW>  
03/11/12 19:36:46 Downloading Method file <C:\CPData\junk.MET>  
03/11/12 19:36:49 Selecting zero gas stream #0  
03/11/12 19:36:55 Starting run #1 (of 1)

Running since: 3/11/2012 7:30:15 PM  
Current Time: 7:36:55 PM 19:36:55

Monitor Status: Starting acquisition  
Instrument Status: Ready to Go

Buttons: Copy to Clipboard, Enable Streams, Abort Sequence, Dismiss Alarm

Process Log / Error Log

03/11/12 19:32:41 STARTED: Permeation tube B  
03/11/12 19:33:54 COMPLETED: Permeation tube B  
03/11/12 19:33:59 STARTED: Fermentation tank 1

Buttons: Copy to Clipboard, Clear Process Log

Indicator lights: 12 small squares, the 11th from the left is lit cyan.

Monitor Status: **\*\*\* ALARM \*\*\***

Instrument Status: In Run

Buttons: Abort Sequence, Dismiss Alarm



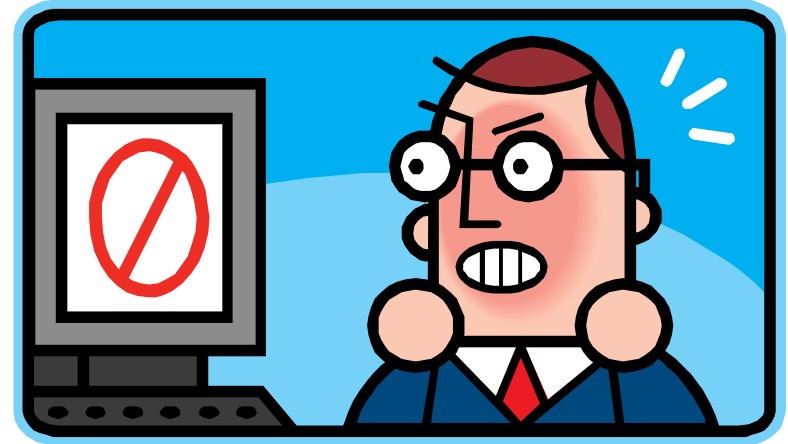
# Change Operations

Streams						
	Name	Enabled	Run Number	Type	Mode	Config
0	Zero gas stream	<input type="checkbox"/>				
1	Fermentation tank 1	<input checked="" type="checkbox"/>	10	Sample	Continuous	...
2	Fermentation tank 2	<input type="checkbox"/>	444	Sample	Continuous	...
3	Fermentation tank 3	<input checked="" type="checkbox"/>	14	Sample	Continuous	...
4	Fermentation tank 4	<input type="checkbox"/>	567	Sample	Continuous	...
5	Fermentation tank 5	<input type="checkbox"/>	678	Sample	Continuous	...
6	Fermentation tank 6	<input type="checkbox"/>	468	Sample	Continuous	...
7	Permeation tube A	<input type="checkbox"/>	45	Calibration	Time	...
8	Permeation tube B	<input checked="" type="checkbox"/>	334	Validation	Priority	...
9	Shutoff valve port	<input type="checkbox"/>				
10	[Not Connected]	<input type="checkbox"/>				
11	[Not Connected]	<input type="checkbox"/>				

Apply Close

# Is This Proof Enough?

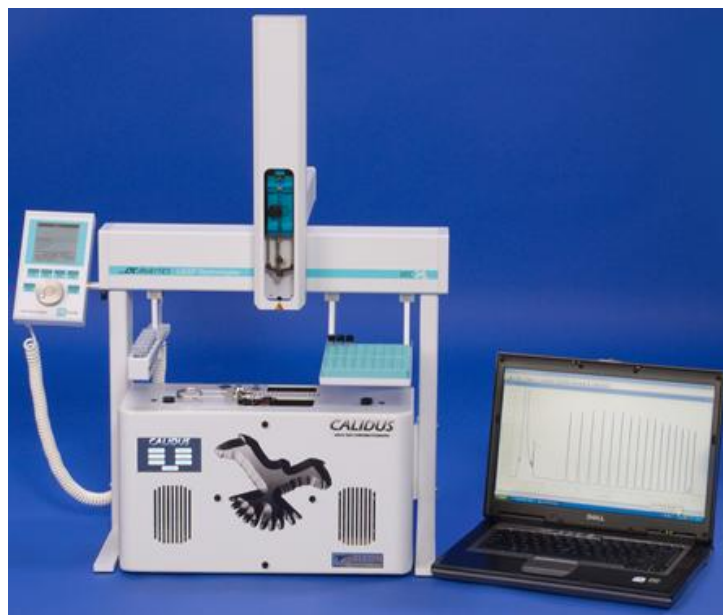
- Probably not...  
... but we're getting closer!
  - Our experience
    - with micro scale fluidics, leaks are more problematic than the “dreaded” plugs
    - with micro GC, the application capability is about 80% of the market need
    - with chemometrics, it doesn't take a PhD to take big advantage 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



**Justice Laboratory Software**

Thanks to our strategic friends at...

