



# Buffer Dilution

YMC PT - experienced integrated and standalone BID solutions provider. We offer standard & customized solutions that meet specific customer process requirements and control integration needs.

YMC Bio / Pharma Systems Group, Devens, MA USA

# Buffer In-line Dilution – YMC “intellidrive” approach



## Cost Savings:

- Reduced Capital Expense:
  - 200L Tank (typical): \$60,000
  - 2,000L Tank (typical): \$89,000
  - Savings: ~33%

## Space Savings:

- Reduced Floor space Requirements:
  - 200L Tank Diameter (typical): 26” dia
  - 2,000L Tank Diameter (typical): 54” dia
  - Savings: ~75%
- Ability to incorporate disposable technology



From  
this to  
only  
this



# Standard Buffer In-Line Dilution System



A buffer management platform



<p>Flow Rate and Dilution Factor Ranges</p> <p>Recommended system flow rate and dilution factor to achieve +/-1% flow accuracy and precision.w</p>	<table border="1"> <thead> <tr> <th>Total Flow (L/min)</th> <th>5X</th> <th>10X</th> <th>20X</th> <th>50X</th> </tr> </thead> <tbody> <tr> <td colspan="5"><b>17 LPM System</b></td> </tr> <tr> <td>4</td> <td>✓</td> <td>x</td> <td>x</td> <td>x</td> </tr> <tr> <td>6</td> <td>✓</td> <td>✓</td> <td>x</td> <td>x</td> </tr> <tr> <td>8</td> <td>✓</td> <td>✓</td> <td>x</td> <td>x</td> </tr> <tr> <td>10</td> <td>✓</td> <td>✓</td> <td>x</td> <td>x</td> </tr> <tr> <td>12</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>x</td> </tr> <tr> <td>15</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>✓</td> </tr> <tr> <td>17</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>✓</td> </tr> <tr> <td colspan="5"><b>33 LPM System</b></td> </tr> <tr> <td>8</td> <td>✓</td> <td>x</td> <td>x</td> <td>x</td> </tr> <tr> <td>12</td> <td>✓</td> <td>✓</td> <td>x</td> <td>x</td> </tr> <tr> <td>16</td> <td>✓</td> <td>✓</td> <td>x</td> <td>x</td> </tr> <tr> <td>20</td> <td>✓</td> <td>✓</td> <td>x</td> <td>x</td> </tr> <tr> <td>25</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>x</td> </tr> <tr> <td>29</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>✓</td> </tr> <tr> <td>33</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>✓</td> </tr> </tbody> </table>	Total Flow (L/min)	5X	10X	20X	50X	<b>17 LPM System</b>					4	✓	x	x	x	6	✓	✓	x	x	8	✓	✓	x	x	10	✓	✓	x	x	12	✓	✓	✓	x	15	✓	✓	✓	✓	17	✓	✓	✓	✓	<b>33 LPM System</b>					8	✓	x	x	x	12	✓	✓	x	x	16	✓	✓	x	x	20	✓	✓	x	x	25	✓	✓	✓	x	29	✓	✓	✓	✓	33	✓	✓	✓	✓
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# Customized In-Line Dilution Systems: EcoPrime BID



## Location

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Global

## Application

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Buffer dilution for central system distribution to downstream biopharmaceutical processes

## YMC solution

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YMC original design. Employs YMC intellidrive ecodos pumps with system design and manufacture by YMC.

YMC proprietary volume control out performs sensor feedback control (e.g. pH or conductivity) assuring 99.5% accuracy of buffers with no sensor drift.

# Selection of optimal components & fluid dynamic design

## Buffers and mixing

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- **In-line vs Batch make-up**
  - In-line more rigorous, less room for error
  - Batch can “absorb” small variations (batch release)
- **Control of mixing:**
- Flow control: Flowmeters more accurate and stable than pH or conductivity detectors
- pH or conductivity: Cascade design - control with flow meters

BID often used with 5-10X concentrated buffers

## Optimal design regarding fluid dynamics

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- **Accurate flowrates**
  - Valve mixing:  $\pm 2\%$  mixing variation (& lobe pumps) lower dynamic range
  - Ecodos:  $\pm 2\%$  Flow variation
  - Ecodos-intellidrive:  $\pm 1\%$  or less Flow variation  
large dynamic range
- **Backpressure valve**
  - Increase pump performance and secure constant flow across system
- **Optimal mixing**
  - Static mixer and/or Filter housing and/or Bubble trap

# BID systems with volume-based control

## Volumetric Flow Control

Flow meters and pumps are more accurate and stable than pH or conductivity detectors

Peristaltic pump

- Accuracy  $\pm 5\%$

LEWA ecodos pump

- Accuracy  $\pm 2\%$

ecodos pump with intellidrive

- Accuracy  $\pm 0.5\%$



Volumetric flow control delivers sustainable performance for consistent buffer preparation.

## pH Control

- Accuracy,  $\pm 1\%$
- In addition:
  - Tendency to drift
  - Memory effect often observed
  - Frequent calibration required

## Conductivity Control

- Accuracy,  $\pm 1\%$
- In addition:
  - Frequent calibration required

# BID systems with volume-based control

Pharmaceutical Buffer | An Integrated Approach to Buffer Dilution and Storage | Pharmaceutical Manufacturing

6/10/10 8:00 PM

## PharmaManufacturing.com

THE DIGITAL RESOURCE OF PHARMACEUTICAL MANUFACTURING MAGAZINE

### An Integrated Approach to Buffer Dilution and Storage

Genentech engineers illustrate an advanced, integrated approach to inline dilution of buffer concentrates and the use of disposable bioprocess bags for buffer storage.

BY TIM MATTHEWS, BRYAN BEAN, POONAM MULHERKAR, AND BRAD WOLK, GENENTECH, INC.

**Conclusion:** “We determined that inline control of pH and conductivity is not necessary to guarantee accurate blends since tracking flow rate through a Coriolis mass flow meter is inherently more accurate.”

BID with accurate volumetric flow control delivers predictable and consistent buffer composition and pH

# Buffer-In-Line and Caustic Dilution

## General Points to Consider:

- Hardware:
  - o Consider intellidrive for maximum effective range
    - Digital servo motor provides 180:1 operating range
  - o Multiple inlets to maximize flexibility/automation
- Use considerations:
  - o Batch vs. continuous
  - o Central location vs. near POU (piping flush, remote operation)

## Buffer dilution considerations:

- Chemistry
  - o Impact of operating at boundary of buffering capacity (dilution vs. conditioning)
  - o Flow control (monitor conductivity and pH)
  - o pH and Conductivity Control (start/stop considerations)

## Caustic Dilution Considerations:

- Heat of dilution
  - o Consider HX or cool PW to account for temperature rise (typically only with concentrated caustic)





## System requirement drives design:

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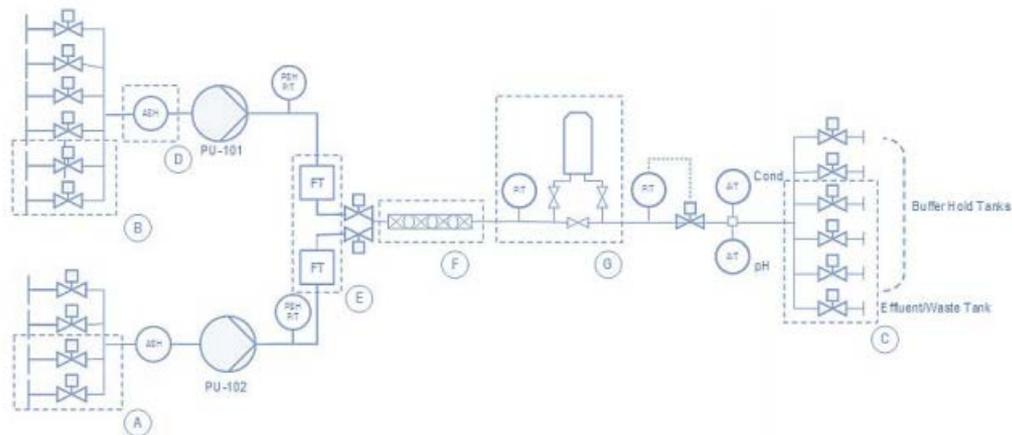
- **Low flow systems** – utilize Ecodos for WFI and concentrate flow
- **High Flow systems** – utilize Rotary Lobe for WFI flow and Ecodos for concentrate flow
- **Cascade flow meter control** - WFI signal -> Ecodos pump to adjust concentrate flow
- Design provides most accurate concentrate control
- pH or Conductivity through cascaded flow control (all parameters are user selectable).

# Buffer In-Line Dilution flow scheme



## YMC EcoPrime BID

### Flow schematic for standard platform



# Buffer In-Line Dilution Strategy Summary (pg. 1 of 2)



- Accurate dilution and flow control.
- Diluent and concentrate delivered through separate pumps to form final concentration
  - Can be set through PLC controller.
- Feedback control of a dedicated mass flowmeter in the diluent and concentrate flow paths
  - prior to combining the flow streams.
- Accurate concentration control - diluent flow meter feedback to controller which utilizes input signal to control / adjust flow of concentrate pump set point.
  - Most critical for higher flow applications where rotary lobe is used for diluent pump.
  - Provides flow accuracy of greater than or equal to 1% of set point.
- Two inlets per pump provided to allow system flushing or cleaning.

# Buffer In-Line Dilution Strategy Summary (cont'd)



- Two outlets included to allow system to flow to drain until user selectable final concentration is achieved.
- Capability to monitor conductivity, pH, and temperature.
- User may preset flush volume or quality (conductivity) to be achieved prior diverting the system from drain to operation.
- During operation, system will monitor conductivity and pH and may be used as user selectable

- Alarm levels, to alert operators and/or divert product to drain.
- In addition, user specified totalized volume may be used to control system operation.



# Can Buffer In Line Dilution be directly designed into a YMC Chromatography system?

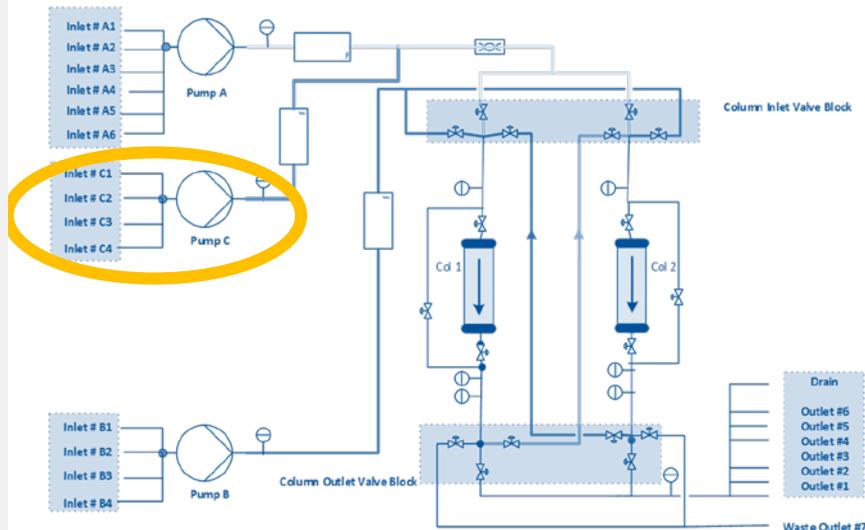
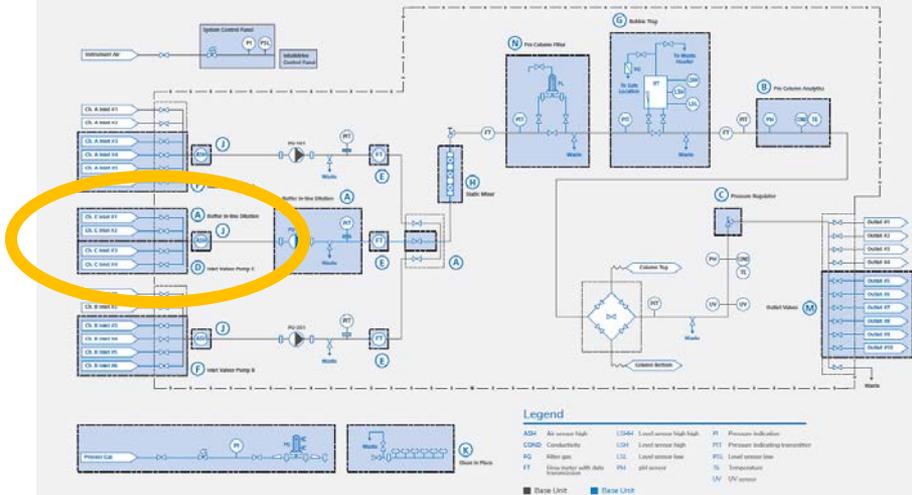
(Yes – absolutely)

# A 3<sup>rd</sup> pump can be added to either batch or continuous (TWIN) for in-line buffer dilution

EcoPrime TWIN (batch) LPLC with BID

Contichrom TWIN (continuous) LPLC with BID

EcoPrime LPLC  
Flow schematic for standard platform





# About YMC America

Biopharma & Pharmaceutical Systems Group,  
Devens, MA USA

# What we do: lab to GMP scale systems

## Batch chromatographic systems

**YMC EcoPrime®**  
**LPLC and HPLC**  
using digital pump  
drive technology



## Multi-column LPLC continuous chromatographic systems

**YMC Contichrom®**  
**TWIN LPLC**  
based on YMC  
ChromaCon's  
CaptureSMB patented  
processes.



## Multi-column HPLC continuous chromatographic systems

**YMC Contichrom®**  
**TWIN HPLC**  
based on YMC  
ChromaCon's  
MCSGP patented  
processes.



## Buffer dilution systems

**YMC buffer dilution**  
automated systems



## Custom downstream process systems

**TFF (Tangential Flow) systems**

Cassette or hollow fiber.

**Synthesis systems**

Your design, our fabrication.

**Filtration skids**

MF, PF and viral clearance.

**Bench top (lab) system**

Continuous and batch chromatography.

# About us



YMC America, Inc.  
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Web: [www.ymcpt.com](http://www.ymcpt.com)



Photo: portion of manufacturing hall  
YMC – Devens, MA USA

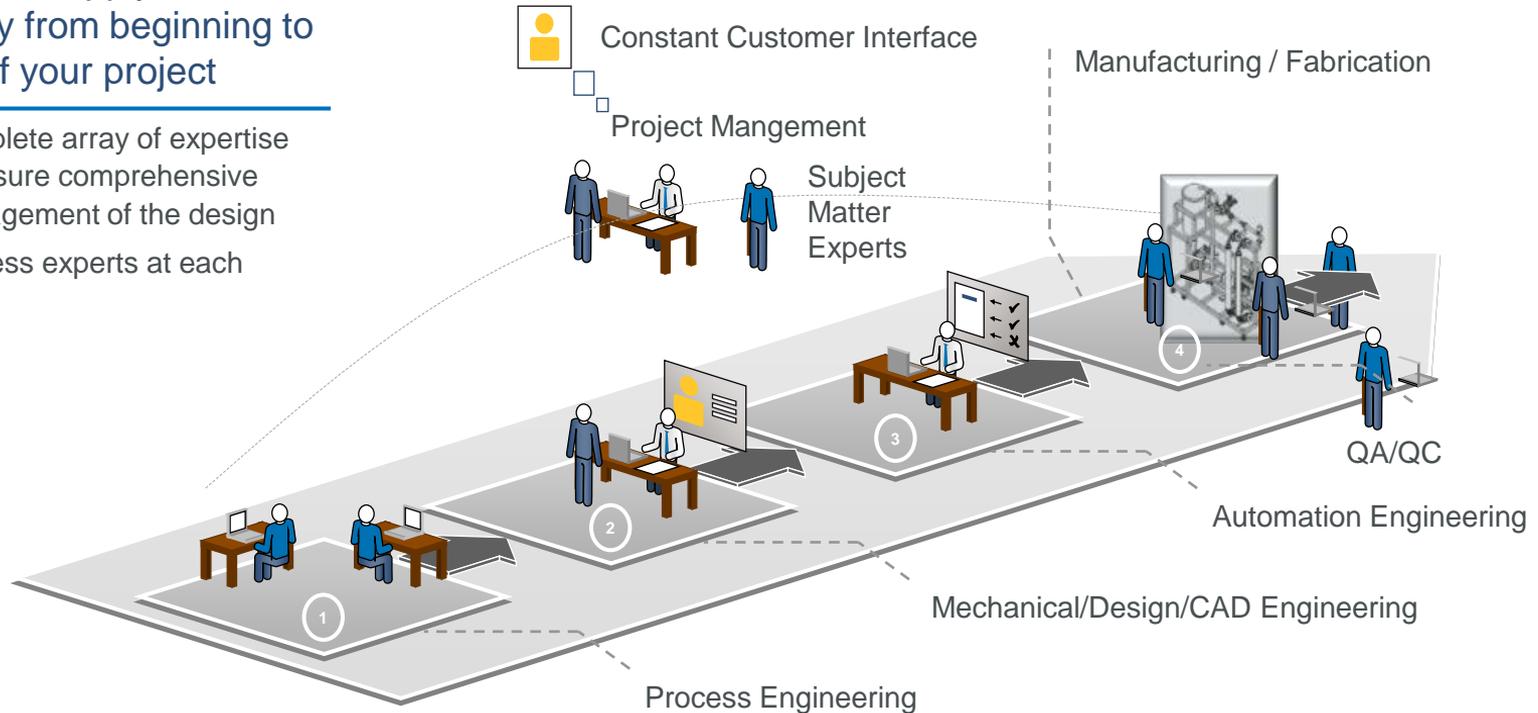
## YMC America, Inc.

Employees: ~50 Total	<ul style="list-style-type: none"><li>8 customer support / mktg.</li><li>20 engineering and quality</li><li>17 operations staff</li><li>5 general and administrative</li></ul>
Location	Devens, MA USA
Date of Establishment	2000
Ownership	100% subsidiary of YMC Co., Ltd.
Quality System	Quality: ISO 9001:2015
Footprint	35,000 ft <sup>2</sup> (~3,250 m <sup>2</sup> )
Target markets	Biopharmaceutical Pharmaceutical OEM (bio/pharma)
Core business	GMP scale systems engineering, manufacturing & automation; <ul style="list-style-type: none"><li>Chromatography</li><li>Buffer In-line Dilution</li><li>Downstream process skids</li></ul>
Exec staff	CEO – Mark Dymnt CMO – Gerard Gach GSD – Wayne Nettnay

# Work Flow For YPT; - design, automate, manufacture

## Vertical Supply – Controls quality from beginning to end of your project

- Complete array of expertise to ensure comprehensive management of the design
- Process experts at each step.



YPT maintains a full compliment of departments that ensure the project has the right resources

# LPLC Chromatography System: Standard & Custom EcoPrime LPLC Systems



## Location

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Global

## Application

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Low Pressure Chromatography skids for monoclonal antibody production for GMP suites.

## YMC solution

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YMC original design. Employs intellidrive enabled ecodos pumps with system design and manufacture by YMC.

Range of two conventional skids and unique buffer in-line dilution option consolidates two unit operations into single skid.

[Video Link Here](#)

# Continuous Multi-column Chromatography Systems

## 2-PCC (continuous batch twin column) – With Integrated BID



YMC Contichrom TWIN LPLC

### Location

Global

### Application

Continuous processing for monoclonal antibody production at GMP scale.

Performs batch and integrated batch in addition to periodic counter current chromatography.

### YMC solution

YMC design from ChromaCon licensed technology. Employs digitally controlled Ecodos pumps.

EcoPrime Twin is GMP scale up version of Contichrom lab scale instrument (shown on cart to left of EcoPrime Twin).

[Video Link Here](#)

# YMC Control Systems – done internally for quality control



## Location

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USA, EU, Asia (GMP Bio/pharma Facility).

Delivered Regularly

## Application

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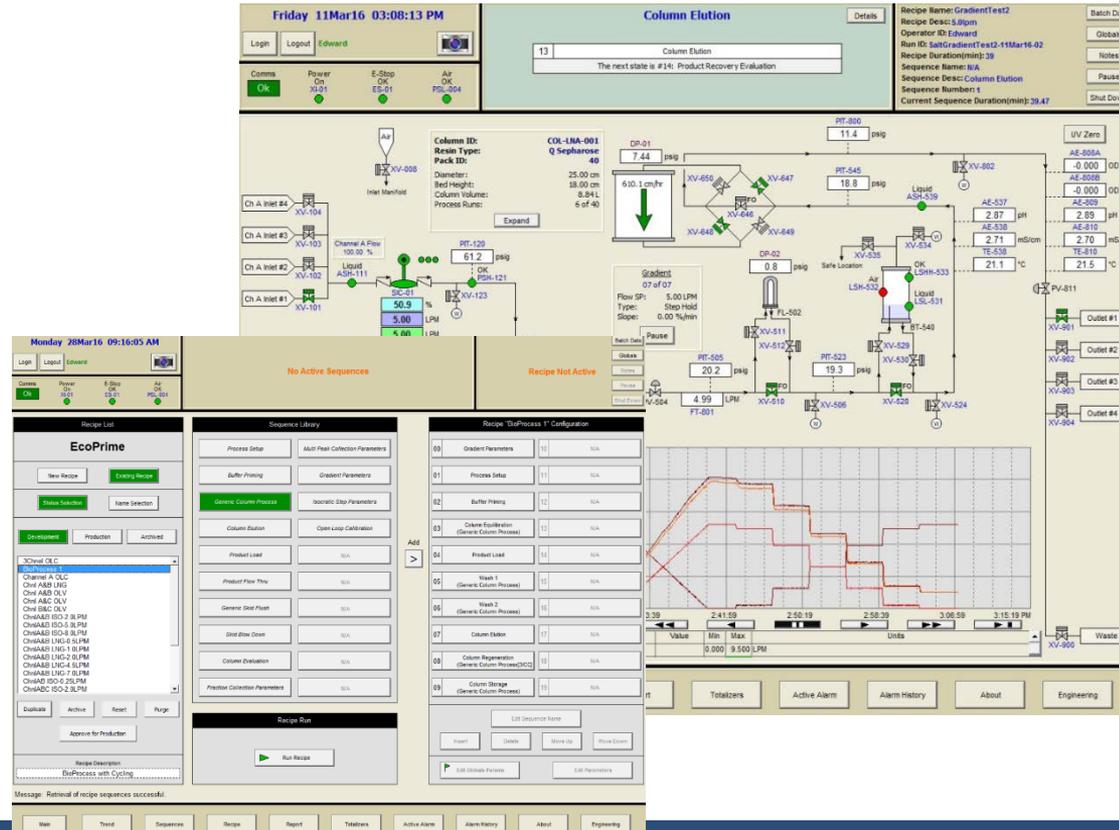
Control of pharmaceutical manufacturing processing, F&B systems, electronics manufacturing skids...

## YMC solution

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YMC designs and manufactures control systems / panels to meet most any system design such as ATEX, CE, ExP....

# YMC HMI / Software Development – done internally for quality control ... or bring third party software to us



Location

Global

Delivered Regularly

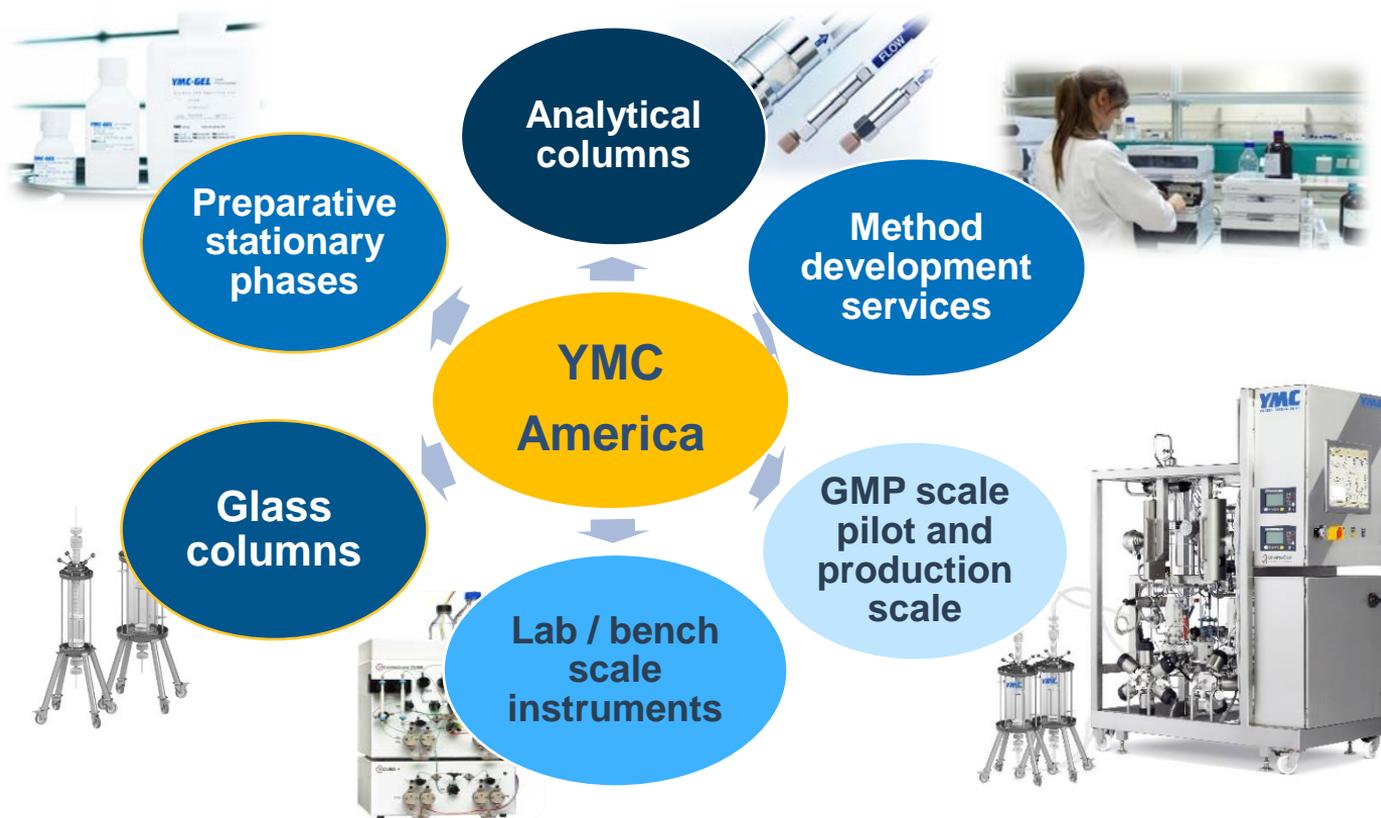
## Application

Control of pharmaceutical manufacturing processing, ROCKWELL BASE systems, DeltaV connectivity...

## YMC solution

YMC Process Technologies designs and manufactures control systems / HMI panels to meet most any system design such as ATEX, CE, ExP...

# Summary: Full line of lab to production purification technologies **YMC**



## **YMC Corporate mission:**

*“Strive to contribute to the future of science and society by separation and purification technologies.”*

## **YMC Vision:**

*As a global leader of separation and purification technologies and products.*

## The future provides broader solutions for our customers



YMC Co., Ltd. assumed all rights and production for the EcoPrime suite of systems in late 2018 from LEWA-Nikkiso America, Inc. and the Contichrom portfolio from ChromaCon AG in 2019. These acquisitions bring a broad spectrum of chromatographic resins, and columns ideal for large and small molecule purification in a continuous process format.

**Ordering information** To order the products, please contact your regional sales representative.

### YMC America, Inc. Process Technologies Group

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