CORNING | Advanced-Flow™ Reactors

Flow-Chem revolution: Seamless scale-up from Lab to 10000 TPA

Indian Institute of Chemical Engineers

Northern Regional Centre – New Delhi

C K Sethia

30th July 2022

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Presentation Outline

Corning & Corning AFR

Advanced-Flow reactors

Seamless Scaleup from Lab
to 10000's TPA

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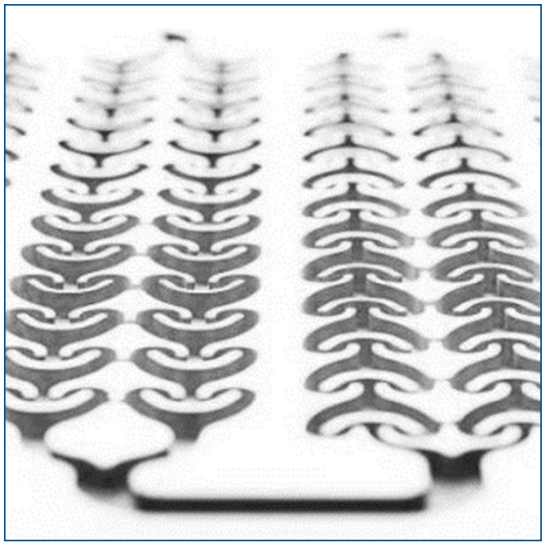
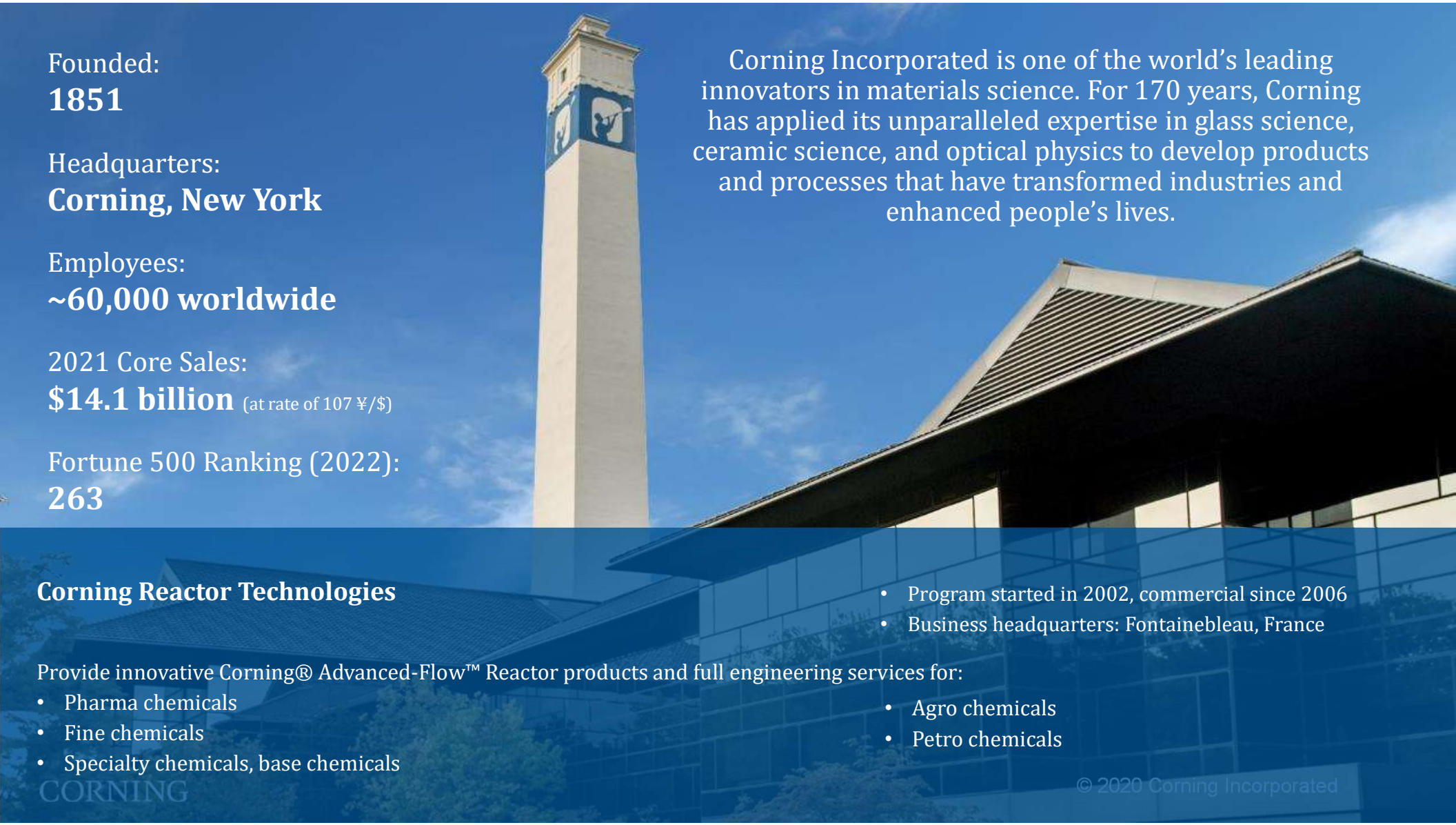


Corning & Corning AFR



Founded:
1851

Headquarters:
Corning, New York

Employees:
~60,000 worldwide

2021 Core Sales:
$14.1 billion (at rate of 107 ¥/$)

Fortune 500 Ranking (2022):
263

Corning Incorporated is one of the world's leading innovators in materials science. For 170 years, Corning has applied its unparalleled expertise in glass science, ceramic science, and optical physics to develop products and processes that have transformed industries and enhanced people's lives.

Corning Reactor Technologies

- Program started in 2002, commercial since 2006
- Business headquarters: Fontainebleau, France

Provide innovative Corning® Advanced-Flow™ Reactor products and full engineering services for:

- Pharma chemicals
- Fine chemicals
- Specialty chemicals, base chemicals
- Agro chemicals
- Petro chemicals

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Corning® Advanced-Flow™ Reactors Innovation timeline

2002
Concept development & customers collaborations

2006
G1 reactor

2007
Collaboration with European platform

2008
European Application Lab

HEART design

G2 bank concept

2009
MIT collaboration

Low-Flow reactor

2010
Chinese Application Lab

G3 reactor

2011
G4 SiC reactor

2012
Indian Application Lab

2013
G2 SiC reactor

2014
G1 Photo reactor

Turn key industrial solutions

2015
New Corning AFR Qualified Lab:
Nalas Engineering (USA)

G1 SiC reactor

2016
New Corning AFR Qualified Lab:
- Shanghai Hybrid-Chem (China)

2017
New Corning AFR Qualified Lab:
- CiTOS (Belgium)
- Shandong Chambroad (China)

Lab Reactor

Lab Photo

2018
New Corning AFR Qualified Lab:
- Fuzhou University (China)
- Sinochem International (China)

G3 Photo reactor

Full automated industrial unit

2019
Chinese Head-Quarter:
Corning Advanced-Flow Reactor Technology Co., Ltd.

Education kit for Academia

2020
G5 SiC reactor

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Corning® Advanced-Flow™ Reactors

Inherently safer technology offering full scale production

- AFR technology enables reduced time to full scale production and improve yield
  - The AFR flow channel design enables intense mixing and heat transfer while providing a narrow residence time distribution
  - Our reactors provide seamless scale up from laboratory reactors to production reactors (5MT to 10,000MT annual flow throughput/unit)
- AFR is a commercially deployed technology
  - 600+ AFR units installed worldwide
  - 100+ production units
  - 30+ production units in pharma and CDMO
  - 35,000+hr continuous run milestone reached
  - Rich experience in AFR flow chemistry process development (tested more than 2,500+)

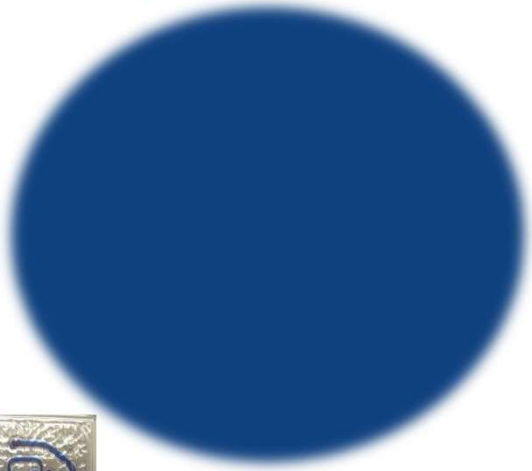
Advanced-Flow Reactor Technologies

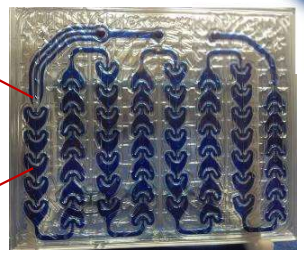
Advanced-Flow reactors

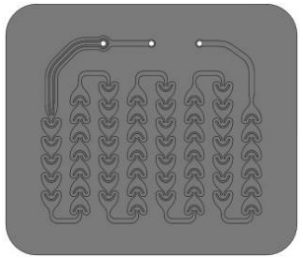
Corning Patented “HEART-Cell” Fluid Module Designs

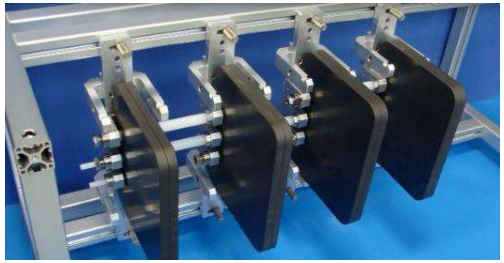
Offer excellent mixing (100X better),superior heat transfer (1000X enhancement)

Mixing of Two Liquid Phases
Liquid 1: Blue
Liquid 2: Yellow
Mixture: Green

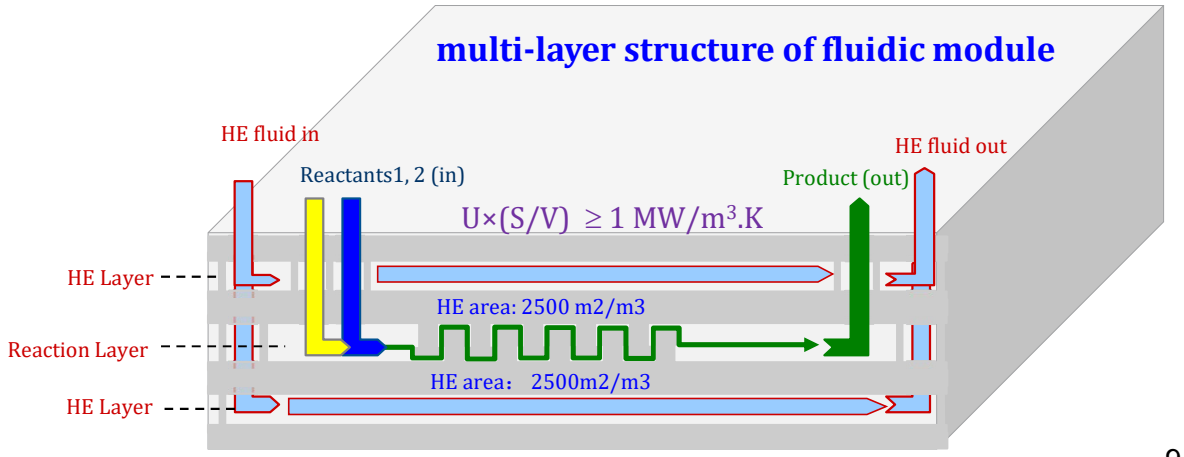








Corning® AFR™ G1 Platform



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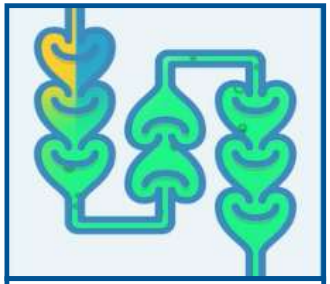
Corning® Advanced-Flow™ Reactors

Key benefits and advantages

High Mixing

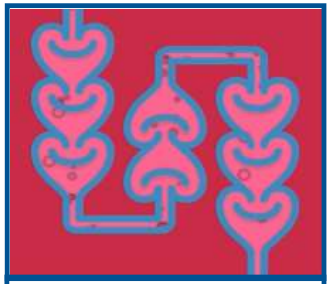


Patented HEART shape

Provides intense mixing, heat exchange and narrow residence time distribution

SCALABILITY/ SELECTIVITY

High Heat Exchange

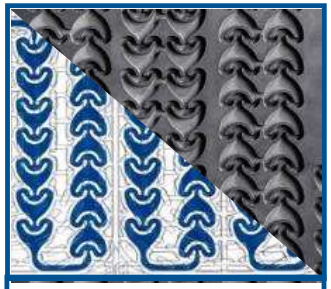


Independent thermal control

Improved heat removal offers excellent temperature control

SCALABILITY/ SELECTIVITY/ SAFETY

Durable Materials



Constructed of Glass and Ceramic material

Superior corrosion resistance & compatible with broad range of reagents

VERSATILITY

Seamless Scale-Up

Reactors are designed for seamless scale-up

Direct from Lab to Production

SCALABILITY/ SELECTIVITY

Complete Units

Complete turn-key solutions tailormade to the process

Configured with support from engineers

SCALABILITY/ SAFETY

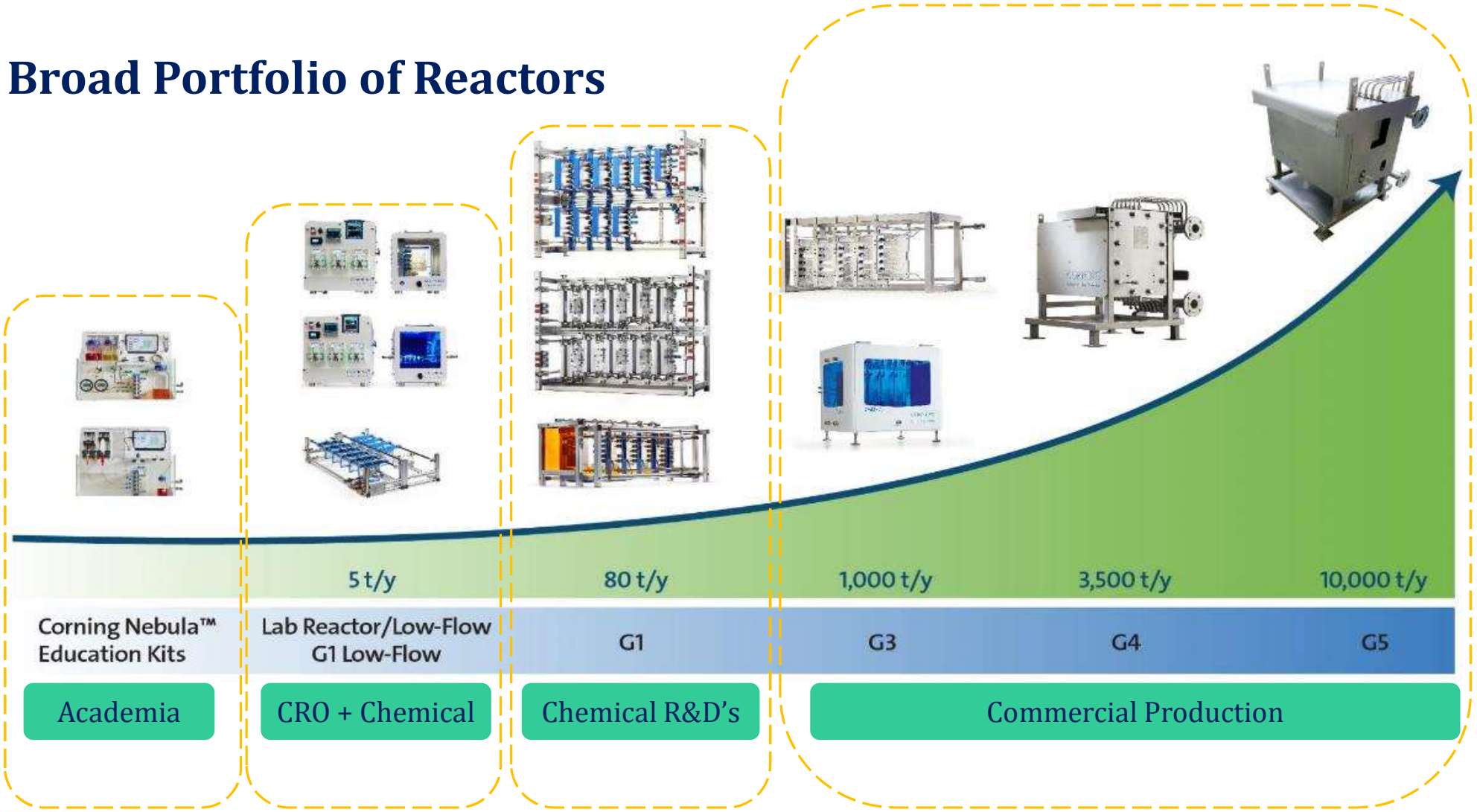
Mass transfer 100x better* | **Heat Exchange 1000x better*** | **Residence time distribution 50x better*** | **Reaction volume 100x lower***

***Compared to batch reactors**

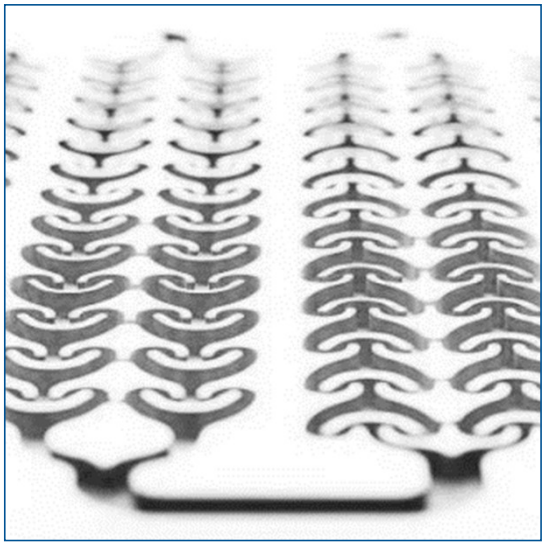
Successfully tested 2500+ Chemistries Globally

- **Nitration Reactions**
  - Reduced solvent usage, higher yield of safer operation
- **More Nitration Reactions in AFR**
  - Mixing quality vs. conversion, and selectivity
- **Selective Hydrogenation of Slurry**
  - 98%+ conversion & selectivity (impurity profiles within spec.)
- **Gas/Liquid Hydrogenation**
  - High catalyst activity enabling short reaction residence times
- **Green Process: Glycerine to Fuel Additives**
  - Successful feasibility demonstration for industrial production
- **Sulphonation Reaction**
  - Full conversion achieved with high purity in shorter time
- **Beckmann Rearrangement: Process Intensification**
  - Stable and better results meeting performance targets
- **Photochemical Reactions**
  - Can be very efficient
- **Liquid/Liquid Amidation (Schotten-Baumann)**
  - Improved yield through continuous mixing
- **Dipeptides Synthesis**
  - Avoiding precipitates in biphasic solvent for amine bonding
- **Dibal Reaction**
  - Same results achieved with much higher temperature
- **Diasteroselective Ritter Reaction**
  - Increased productivity with easy & safe zoperation
- **Accelerating Reactions**
  - An alternative to microwave heating
- **Low Temperature Applications**
  - Energy Saving and/or Better Yield (DCM-B-Pin)
- **Chloroformate Chemistry**
  - Better yield easily followed by on-line Raman PAT
- **Grignard Reagent (RMgX) Preparation**
  - Precise controls lead to better purity of final products
- **Particle Handling**
  - Enable slurry reactions

Broad Portfolio of Reactors



Seamless scaleup from Lab for 10000's TPA



Commercial Case Studies

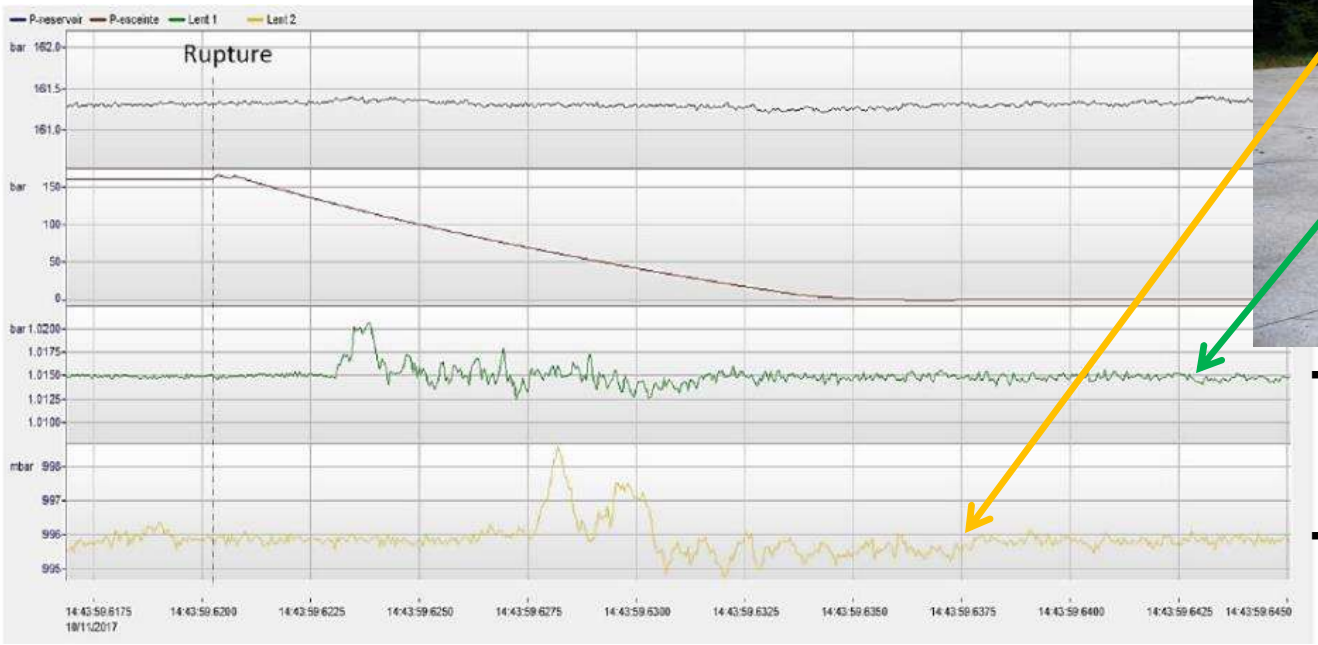
Corning Advanced-Flow™ G4 & G5 Reactors

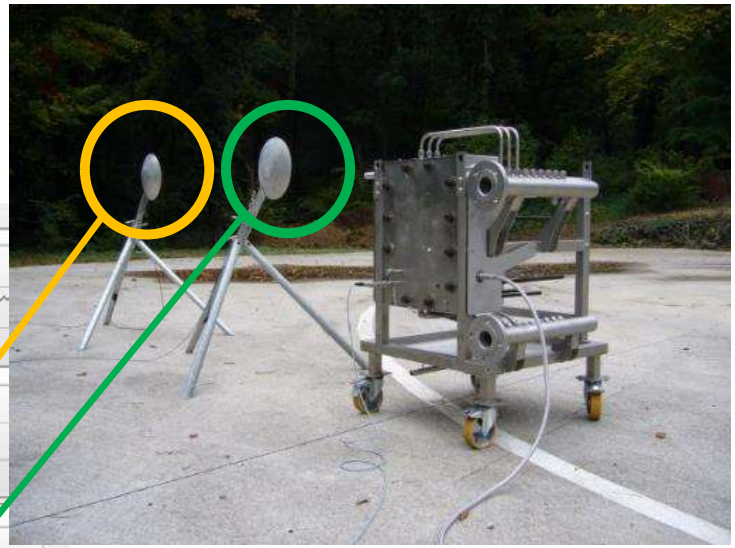
- ✓ Seamless scaleup
- ✓ Modular design
- ✓ 100x mixing
- ✓ 1000x heat transfer
- ✓ High chemical durability
- ✓ Thermal cycle of over 110^{0}C
- ✓ No retention zone
- ✓ Shorter Time to market
- ✓ Turnkey solution
- ✓ Inherent Safer design
- ✓ 100+ commercial reactors

Inherently Safer reactor

G4 explosion test (done by INERIS)

Shock wave





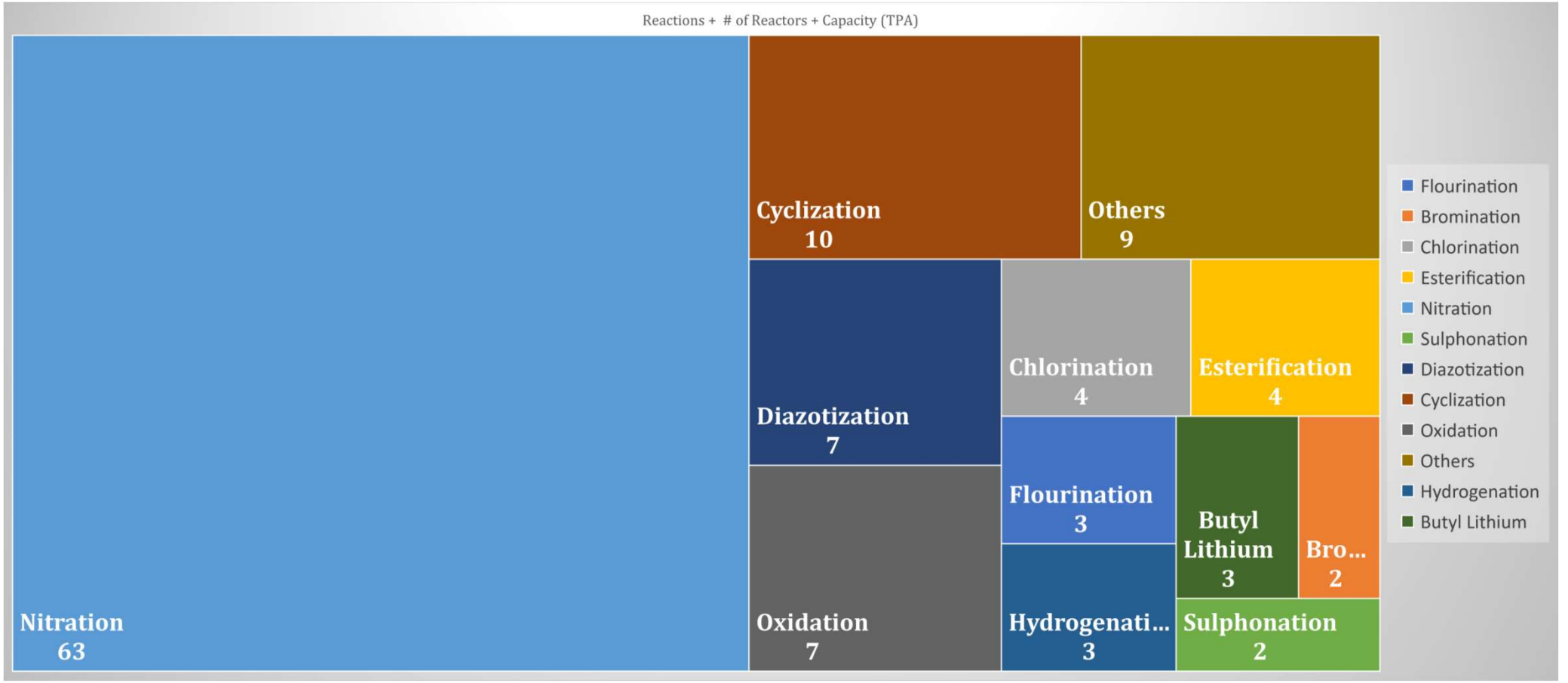
➔ Max : 6 mbar

➔ Max : 2 mbar

- *20 mbar : possible indirect effet on people (windows broken…)*
- *140 mbar : serious direct effect on human being*
- *200 mbar : potential lethal effect on human being*

NO risk in terms of shock wave

Commercial Reactors: Treemap (105+)
1,000 to 1,00,000 TPA



Sun Pharmaceuticals, India

Corning delivered its promise of seamless scale-up from Lab to production for multi Step chemical Synthesis for pyrophoric & hazardous chemicals

For detailed article, please visit :
https://www.corning.com/worldwide/en/innovation/corning-emerging-innovations/advanced-flow-reactors/corning-advanced-flow-reactors-collaborates-with-sun-pharmaceutical-industries.html

Anupam Rasayan, India

Corning AFR G4 installation @ Anupam Rasayan, India

Corning G4 reactor system with 3 dosing lines, 1 temperature zone control and Electrical Panel with a footprint of 15m2 for a multipurpose chemical plant upto 2000 TPA installed since Dec 2016

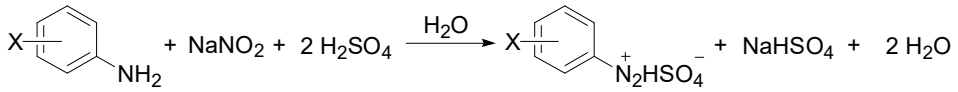
Nitration + Multiple Reactions

Agro-chem continuous manufacturing with AFR at 10 000 MT/Yr flow throughput via X-Aniline diazotization & hydrolysis

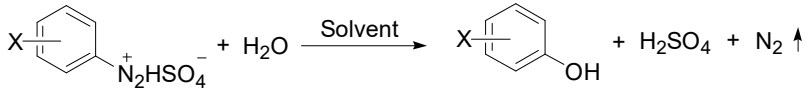
惠和化德生物科技 HYBRID-CHEM TECHNOLOGIES

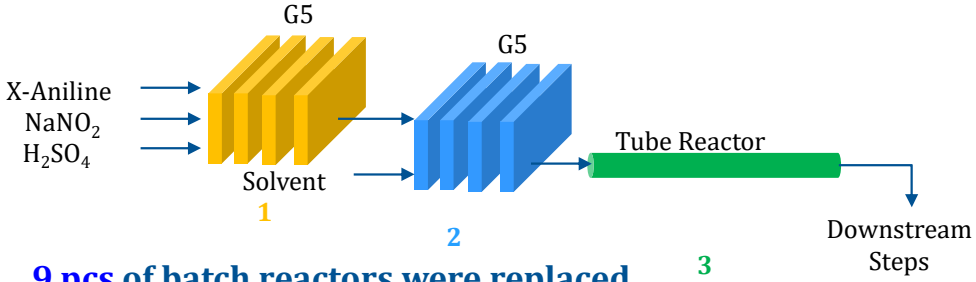
CORNING  WEIHUA NEW MATERIAL 巍华新材

Step 1



Step 2





9 pcs of batch reactors were replaced
Volume 36,000 L ➔ 2x2L AFR + 2x270L Tube

Traditional reactor s: 9 pcs
- ✓ 6 pcs of 3000L batch reactor (diazotization)
- ✓ 3 pcs of 6000L batch reactor (hydrolysis)

Reaction time:
Diazotization: 8 hrs /batch ➔ <5s (flow)
Hydrolysis: 4 hrs/batch ➔ <10min (flow)

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Total yield increased by 15%
# of operators reduced by 30
Solid waste reduced 75%
Process footprint reduced by 90%

15 000 hrs

Shandong Efirm Biochemistry and Environmental Protection Co., Ltd.

Nitration in G4 Reactors for Fine Chemicals Manufacturing

- **Customer**: Shandong Efirm is a manufacturer of fine chemicals located in Binzhou, Shandong Province

- **Project:** 10 000+ ton/year continuous flow nitration plant for safety (hazardous batch process), increased product purity, and reduced footprint (equipment and manpower) for production of 2-ethyhexyl nitrate (EHN) for use as diesel additive

- **In Service Date:** 24/7 operation since **October 2018** (four G4 reactors); additional G4 reactors added April 2019

- **Footprint reduction** for continuous flow**:**
  - **4,000 m^2 (batch) → 400 m^2 (Five G4 reactors)**

- **OpEx improvement:**
  - **Increased product purity and product color**
  - **Reaction time decrease: hours/batch → residence time of seconds (flow)**
  - **Reduction in manpower: 2 operators/shift with centralized monitoring & control**

Corning 6×G4: 12 000 mt/yr stable operation over

Nitration: Ethyl Hexyl Nitrate

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Organometallic reaction: from home-made to G1 and to G4

Learning: Spent lot of time with home-made with local university feasibility study, but at the end, no way to scaleup!
Merit: Seamless scale up from G1➔G4, 1 year, 3 validation batches, ROI 1 year
Solutions: Handling solid, run 16 hrs, auto-clean 5 min

Similar yield / impurity profile as feasibility trials
COGS reduction by 30-40 % vs sourced intermediate
Reduction of amount of raw materials and solvents

30X

3 pilot batches validation in G4 Sic 2000 T/y

Spent 6 month

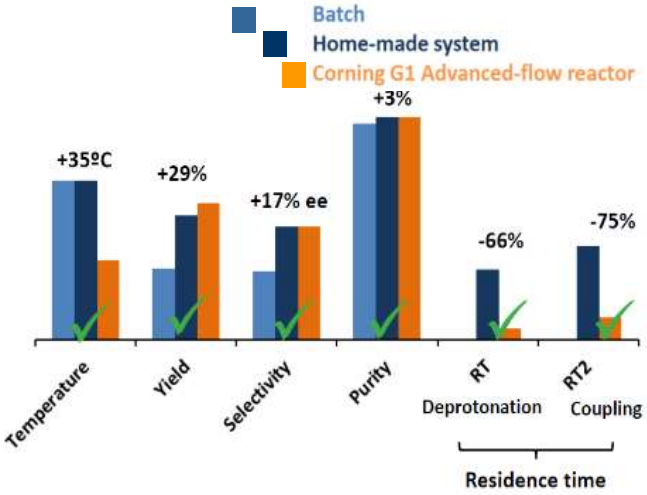
3X

Process optimization & scaleup in G1 glass 80 T/y

Spent 6 month

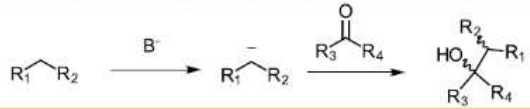
Home-made lab with University feasibility test, 1/8" tube

Spent 1.5 Yr



Organometallic reaction

Fast and highly exothermic, cryogenic, unstable intermediates



- Heat transfer
- Mixing
- Extreme reaction conditions

Organometallic Reactions

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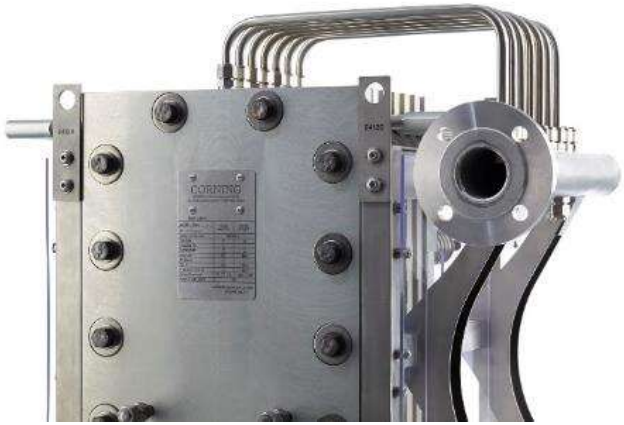
cGMP and FDA G4 Reactor for API Manufacturing

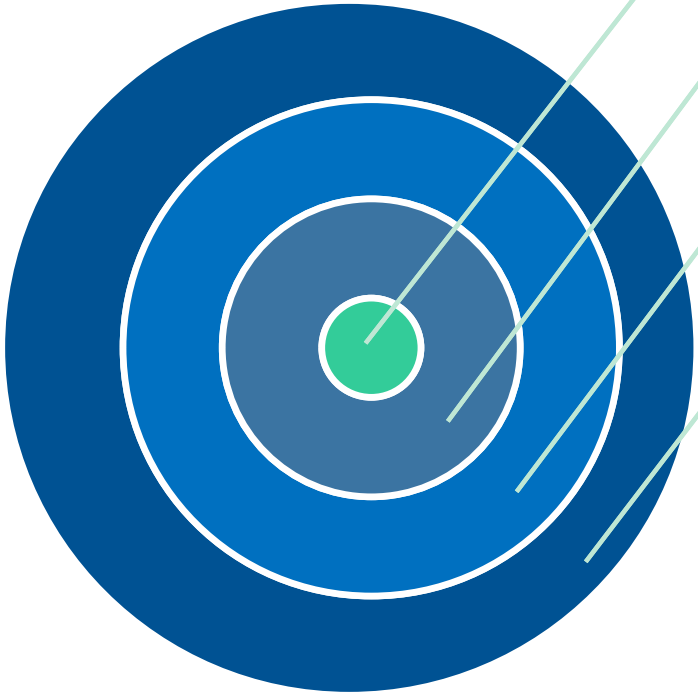
ANGELINI

- Multipurpose G4 Platform
- Dosing lines with automation
- ATEX design, DCS control
- Corning supplied whole system including reactor, dosing lines and control system

Courtesy of Angelini

Corning AFR can change the industry – and lives





Inherently
Safer Technology

Over 600 + Customers

Over 100+ Commercial
reactors

Seamless scaleup from Lab to
Production

Growing list of industry & academic AFR India customers*

INDIA

* Partial list

ANUPAM RASAYAN INDIA LTD.

Divis

SUVEN Life Sciences

JUBILANT LIFESCIENCES

AUROBINDO Committed to healthier life!

ARAGEN A GVK BIO Company

Dr.Reddy's

SRF We always find a better way

SRAVATHI ...Continuous innovation

Cipla Caring for life

LUPIN

Piramal knowledge action care

sabic

MOMENTIVE inventing possibilities

Deepak Nitrite Limited

NIT Warangal

JNTU, Hyderabad

IIT Madras

Osmania University
Chemical Technology

IIT Delhi

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ACHEMA
4.0/ Stand J58 | 9.1/Stand E64-03
Messse Frankfurt, Germany
August 22 – 26, 2022

Flow Chemistry India
Hotel Sahara Star, Mumbai
September 15 – 16, 2022

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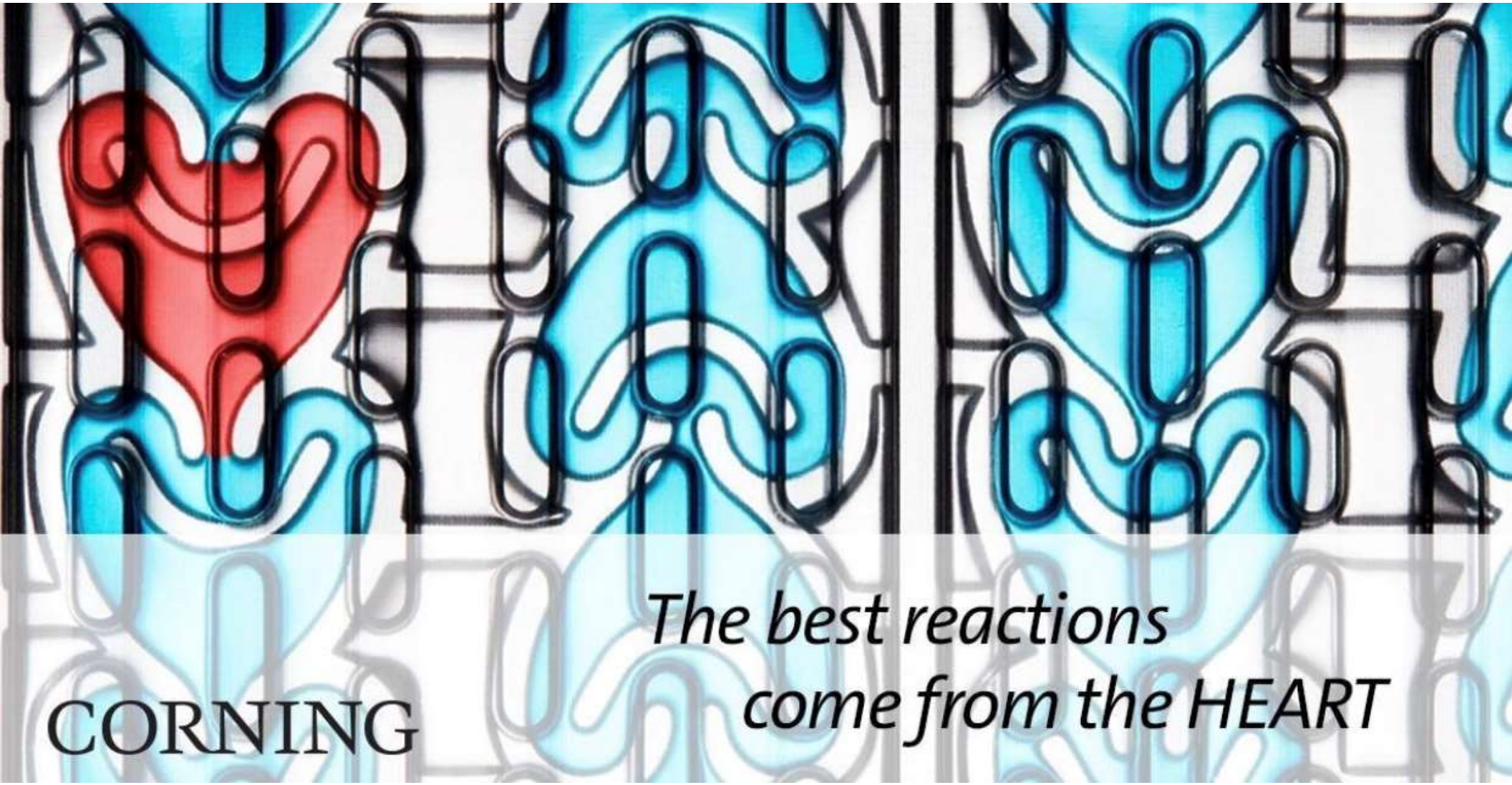

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