charles river

Forum on Regenerative Medicine Workshop

SESSION IV: Quality Control and Regulatory Considerations

Matthew M Hewitt B.A. Ph.D.
VP, Technical Officer CGT & Biologics

10/31/2023

charles river

Our mission is to create healthier lives

We currently operate

120+ Facilities **IN** **20+** Countries

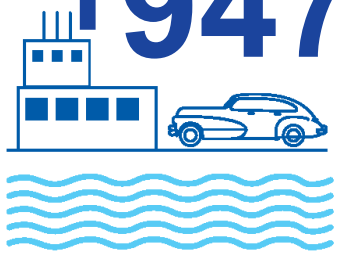
We supported the development of

86%

of novel FDA-approved drugs in 2021

Founded

1947



DIVISIONS

- RESEARCH MODELS & SERVICES
- DISCOVERY SERVICES
- SAFETY ASSESSMENT
- LABORATORY SCIENCES
- BIOLOGICS SOLUTIONS (CDMO AND TESTING)
- QC MICROBIAL SOLUTIONS

Past and Current Regulatory Successes

Regulatory inspections continue at our CDMO facilities for subsequent program(s) going commercial

businesswire
A BERKSHIRE HATHAWAY COMPANY

HOME SERVICES NEWS EDUCATION ABOUT US

Charles River Laboratories is First CDMO in North America to Receive EMA Approval to Commercially Produce an Allogeneic Cell Therapy Drug Product

Company awarded commercial GMP license following successful EMA inspection of Memphis CDMO facility

August 09, 2022 08:00 AM Eastern Daylight Time

MEMPHIS, Tenn.--(BUSINESS WIRE)--Charles River Laboratories, International Inc. (NYSE: CRL) announced it has received regulatory approval, in the form of Good Manufacturing Practice (GMP) certification, to commercially produce allogeneic cell therapy drug products for distribution in Europe, from the European Medicines Agency (EMA).

Charles River is first #CDMO in North America to receive EMA approval to commercially produce an #allogeneic #celltherapy drug product. @criverlabs

The approval follows an inspection by the cell and gene therapy experts from the Italian inspectorate, Agenzia Italiana del Farmaco (AIFA), performed on the EMA's behalf. The GMP certification of Charles River's Memphis contract development and manufacturing (CDMO) facility complements an existing GMP license for Investigational Medicinal Product (IMP) production. The Memphis site can manufacture and ship drug

Successful CDMO Operational and Regulatory Track Record

https://www.businesswire.com/news/home/20220809005319/en/Charles-River-Laboratories-is-First-CDMO-in-North-America-to-Receive-EMA-Approval-to-Commercially-Produce-an-Allogeneic-Cell-Therapy-Drug-Product

charles river

Five (5) approved therapies in the US so far in 2023

Another 3 have US decision dates in 2023

	Therapy	Type	Indication	Status
Approved	**Hemgenix** *(uniQure and CSL Behring)*	Gene Therapy	Hemophilia B	Approved (February 2023)
Approved	**Omisirge** *(Gamida Cell)*	Cell Therapy	Reduce time to neutrophil recovery and infection in patients with hematologic malignancies	Approved (April 2023)
Approved	**Vyjuvek** *(Krystal Biotech)*	Gene Therapy	Dystrophic epidermolysis bullosa	Approved (May 2023)
Approved	**Elevidys** *(Sarepta Therapeutics)*	Gene Therapy	Duchenne muscular dystrophy	Approved (June 2023)
Approved	**Lantidra** *(CellTrans)*	Cell Therapy	Type 1 Diabetes	Approved (June 2023)
Approved	**Roctavian** *(BioMarin Pharmaceuticals)*	Gene Therapy	Hemophilia A	Approved (June 2023)
BLA/MAA Accepted	**CTX001** *(Vertex Pharmaceuticals & CRISPR Therapeutics)*	Gene Editing Therapy	Sickle cell disease, β-thalassemia	EU decision expected in the fall of 2023 FDA decision set on sickle cell disease for December 8, 2023 FDA decision for β-thalassemia expected March 2024
BLA/MAA Accepted	**Lifileucel** *(Iovance)*	Cell Therapy	Metastatic melanoma	FDA decision set for November 25, 2023
BLA/MAA Accepted	**NurOwn** *(BrainStorm Therapeutics Inc.)*	Cell Therapy	Amyotrophic lateral sclerosis (ALS)	FDA decision set for December 8, 2023
BLA/MAA Accepted	**Lovo-cel** *(Bluebird bio)*	Gene Therapy	Sickle cell disease	FDA decision set for December 20, 2023
BLA/MAA Submitted	**HPC Cord Blood** *(StemCyte)*	Cell Therapy	Unrelated Donor hematopoietic progenitor cell transplantation	BLA Pending

Clinical Trials

North America	Asia Pacific	Europe	Total
917	648	329	1,687

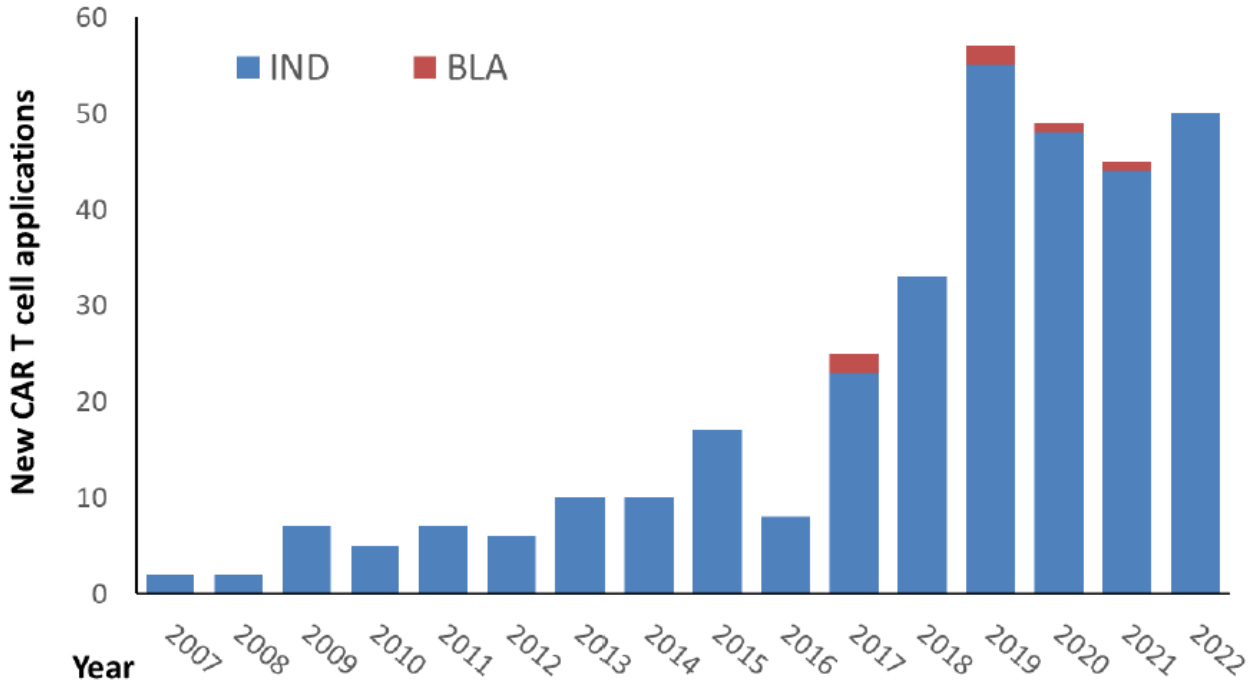
Transition from predominantly clinical-focused manufacturing to commercial

https://alliancerm.org/sector-snapshot/

charles river

INDs for Cell Therapy Continue to Climb

FDA increasingly signaling they are open to discuss how to increase manfuacturing



- Approximately 327 CAR T cell research INDs*
  - 62% are for hematologic malignancies
  - 86% are autologous products
  - >60 antigen targets
- 6 licensed autologous CAR T cell products

- Field continues to expand:
  - New targets
  - New indications
  - New manufacturing strategies
- FDA support:
  - Guidance
  - Town Halls
  - Workshops

Adapted from FDA slides from ISCT NA 2023, Kimberly Schultz, PhD

charles river

Therapeutic Demand is Outstripping Supply

Comments from Christi Shaw and an academia-led survey suggests therapies are in short supply

"After 5 years post-approval for diffuse large B-cell lymphoma, even today only 2 out of 10 patients who are eligible are actually receiving the therapy…43% of patients are alive five years after receiving this therapy"

Medscape

News > Medscape Medical News > Features

Patients Waiting Months for 'Last Chance' CAR T-Cell Therapy

Roxanne Nelson, RN, BSN
July 14, 2022

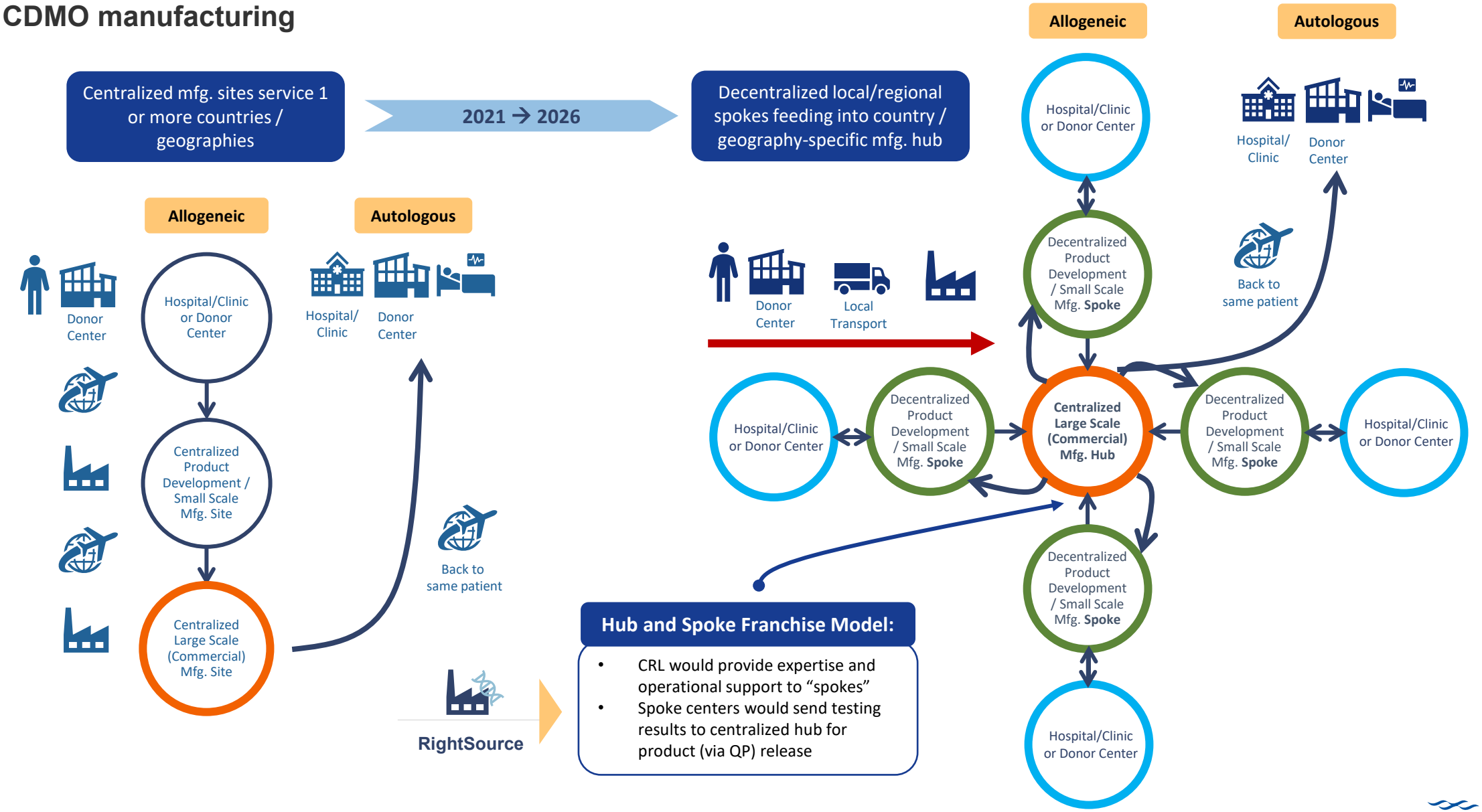
Survey published as an abstract at the 2022 ASCO meeting by Yi Lin, MD, PhD. The survey contacted 20 US centers and 17 responded.

- 6 month median waitlist time
- 25% of patients received CAR T-cell therapy
- 25% were able to enter a CAR-T clinical trial
- 50% of patients either were enrolled in a different type of trial, entered hospice, or died.

charles river

‘Picture of the Future’ – CGT CDMO/CMO Landscape

Options exist whether the future includes centralized and decentralized CDMO manufacturing



charles river

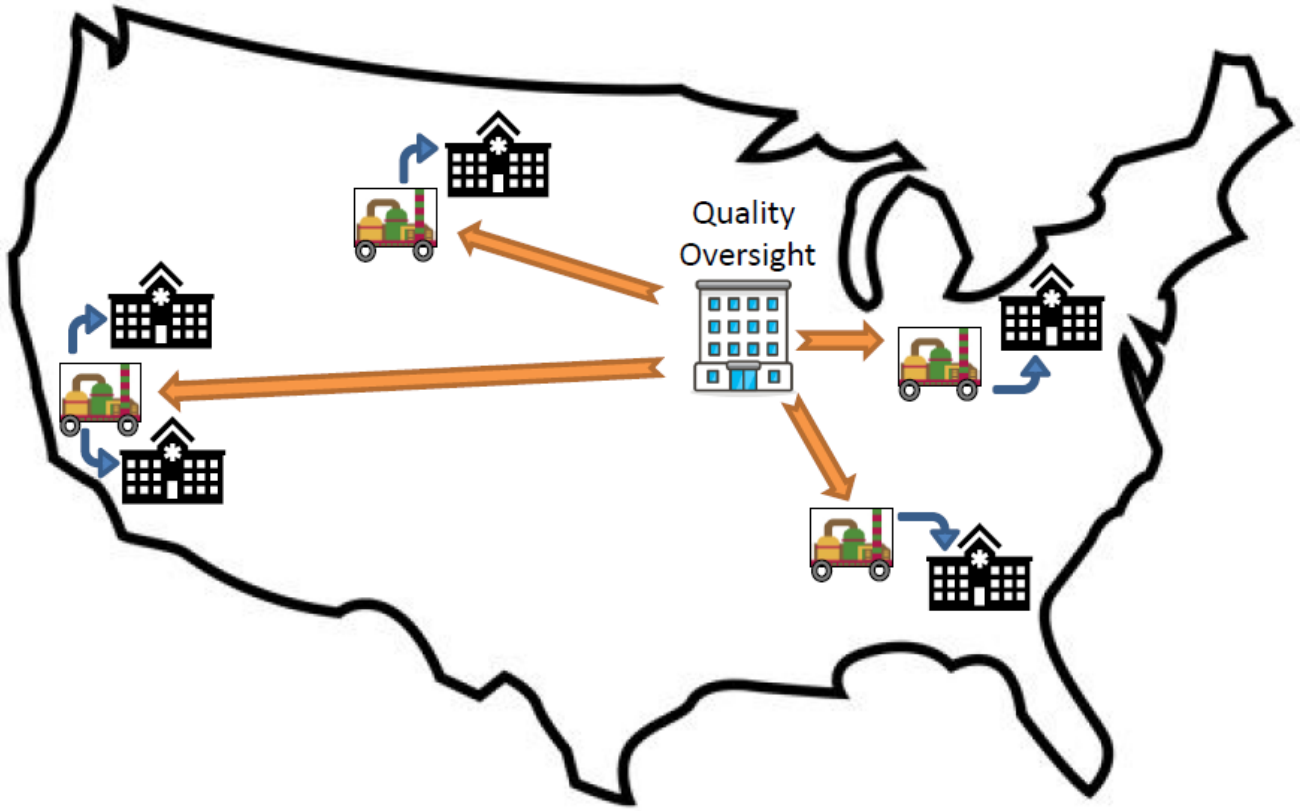
CRL's "Hub and Spoke" Franchise CDMO/CMO footprint

Conceptual blueprint illustrating how CRL's existing and planned centralized CDMO facilities can manage "franchised" decentralized CMO "spokes" for autologous cell therapies

charles river

Broad Industry and Regulatory Alignment

Multiple stakeholders are thinking similarly about decentralized manufacturing



- Centralized quality oversight

Adapted from FDA slides from ISCT NA 2023, Kimberly Schultz, PhD

A central CGMP facility

- Responsible for remotely releasing all drug product batches manufactured at local sites, and for identifying and handling deviations
- Establishes all standard operating procedures (SOPs) and the quality management system (QMS), which are duplicated at local sites

Small, local clones of the central facility

- Responsible for CGMP compliance and batch documentation
- Located close to the point of care
- Follow the central site's SOPs and QMS

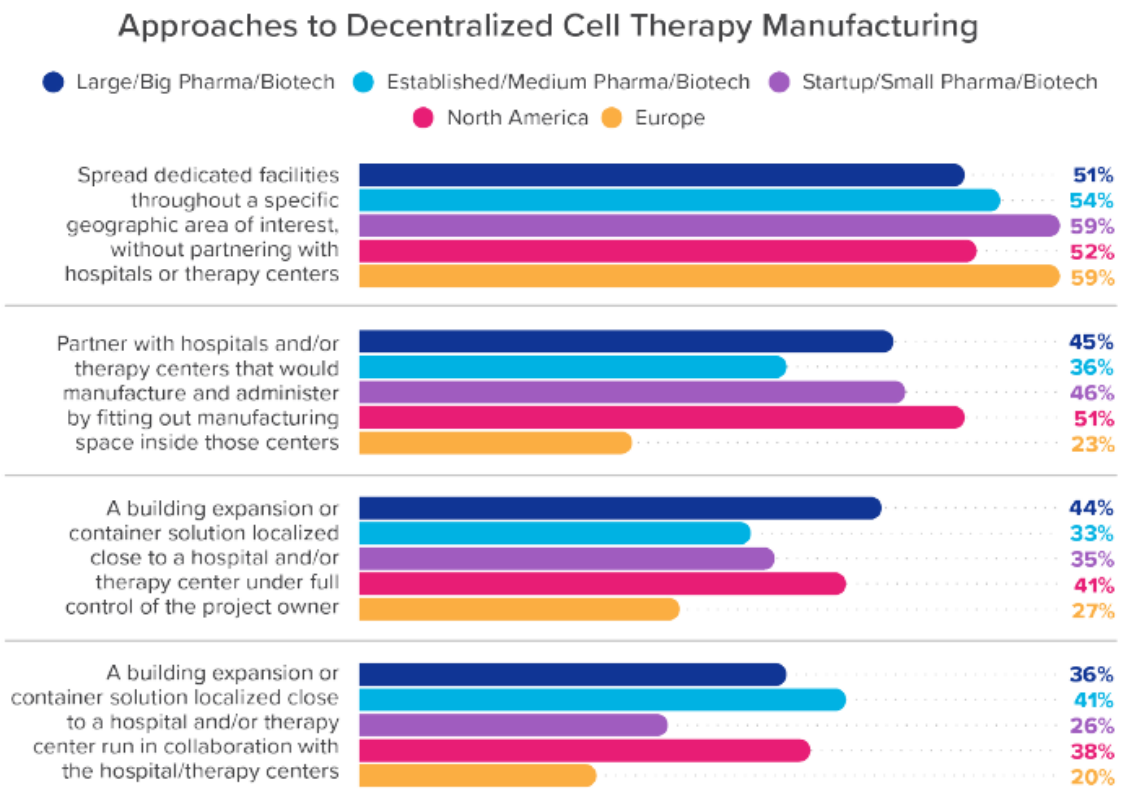
Adapted from CRB 2023 Horizons Report
https://go.crbgroup.com/2023-horizons-life-sciences-report

charles river

Enabling Decentralized/Distribute Manufacturing

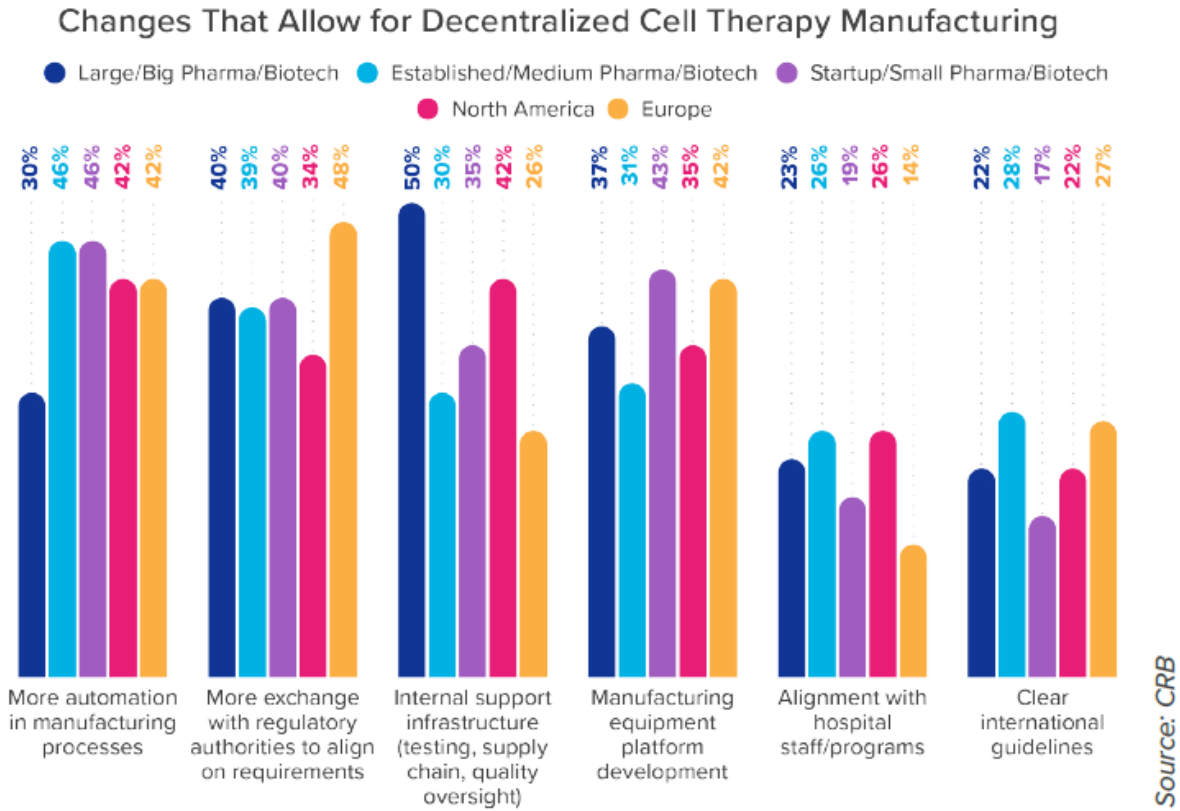
Different stakeholders have disparate opinions on what is needed to enable decentralized manufacturing

Would your company consider using any of the following potential approaches to decentralized manufacturing for cell therapy?



Source: CRB

What are the most important changes needed to allow for decentralized manufacturing for cell therapy?



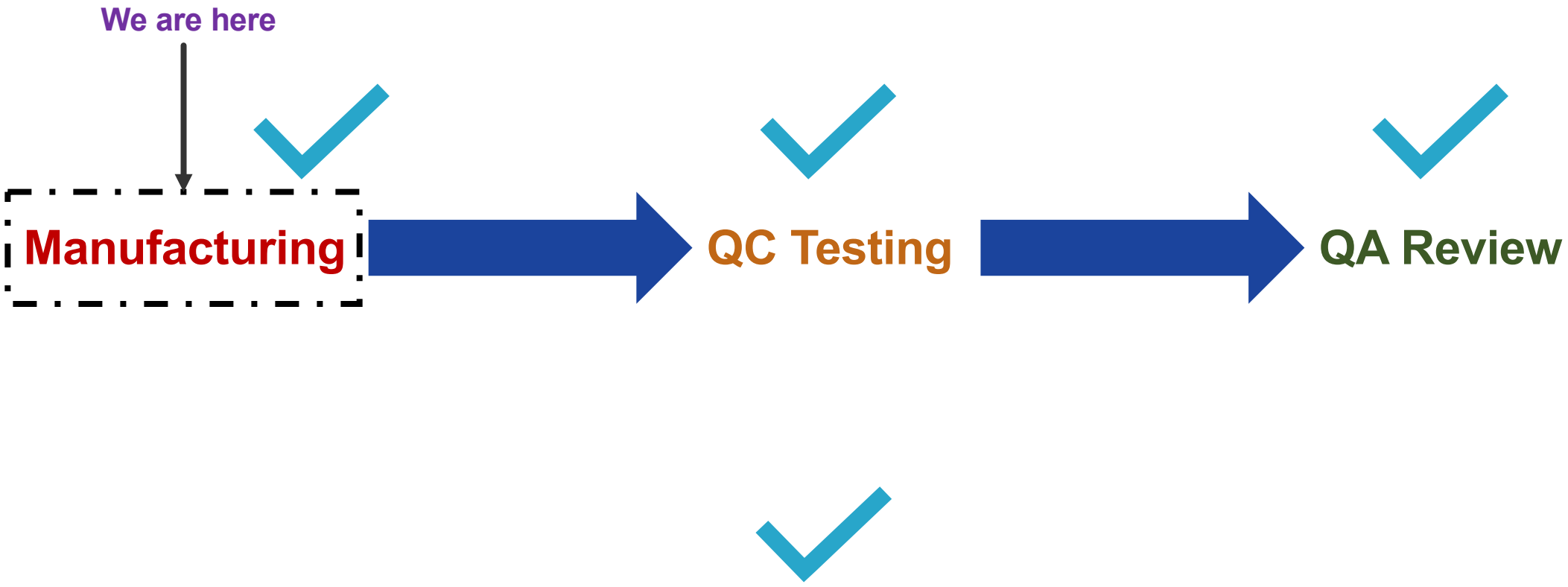
Source: CRB

Adapted from CRB 2023 Horizons Report
https://go.crbgroup.com/2023-horizons-life-sciences-report

charles river

Manufacturing is just 1 Challenge Facing the Field

Must get more proactive on solutions going forward to lower costs and increase patient access



charles river

charles river

Thank you for your attention

With so much at stake,

select a partner with the capacity and capability to deliver.

askcharlesriver@crl.com

www.criver.com

877.CRIVER.1