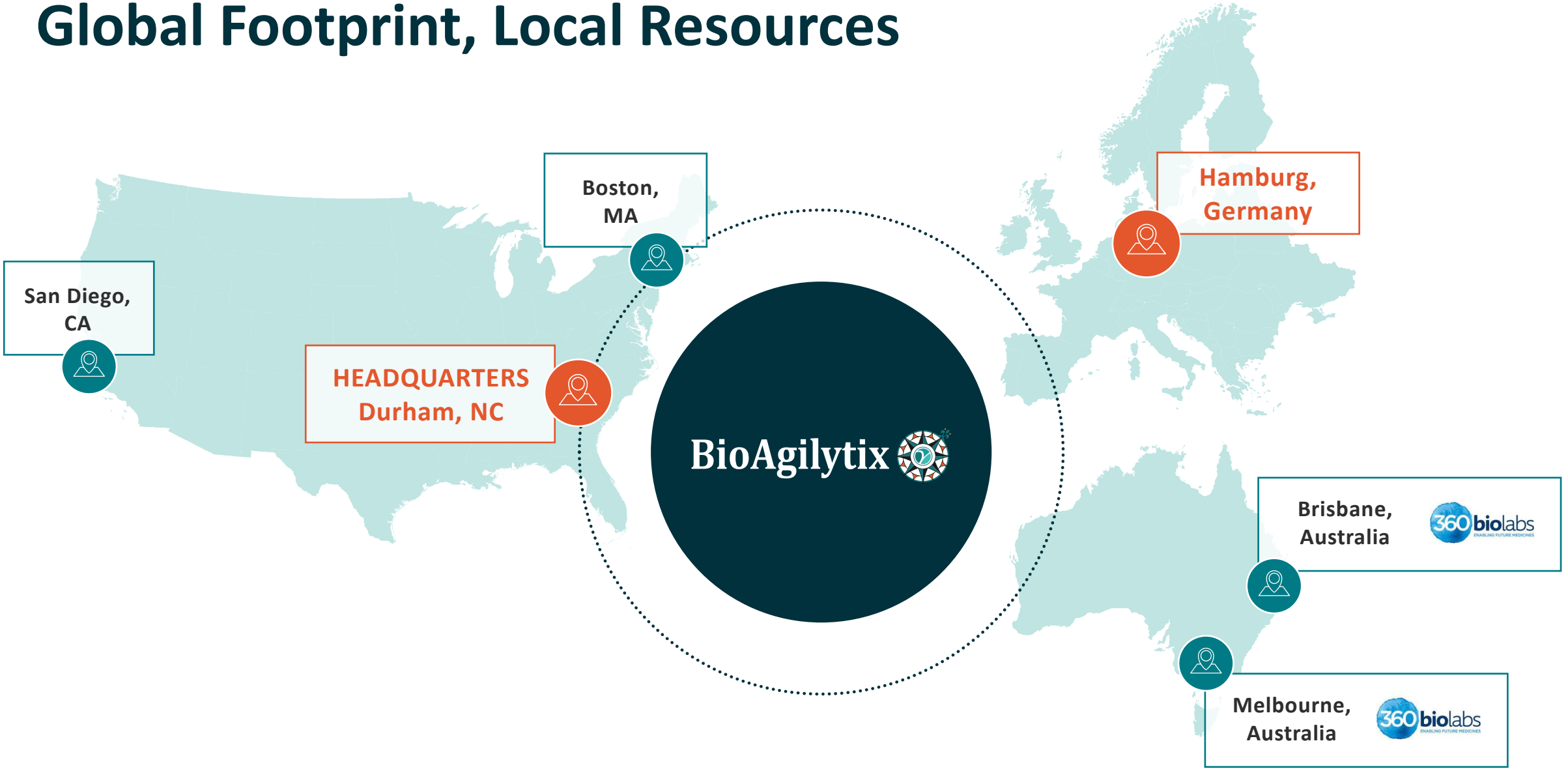
BioAgilytix

Global Footprint, Local Resources



CMC Analytical Services

Plate-Based Assays

- HCPs, HC DNA, process-related impurities
- Enzyme and functional activity
- Target-binding

Molecular Assays

- Residual DNA
- Host cell DNA
- Vector copy number
- Gene Expression

Concentration and Characterization

- Characterization, purity, product-related
- Impurities, PTMs, isoform analysis
- Compendial testing

Potency Assays

- Cell-based/plate-based
- Readouts: ELISA, MSD, PCR, flow cytometry
- LC/HRMS, imaging

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CMC Analytical Instrumentation

Beckman CytoFLEX, BD FACS Canto II, BD FACSLyric™
(Flow Cytometry)

QuantStudio 5/7 Flex
(qPCR)

Maurice
(cIEF, purity)

Spectrophotometer SoloVPE
(UV-Vis)

Sciex: PA 800 Plus
(cIEF, purity)

Thermo Scientific Orbitrap Exploris
(HRMS)

QX200 and QXOne Droplet Digital PCR Systems
(ddPCR)

SpectraMax w/ SoftMax Pro
(Plate Reader)

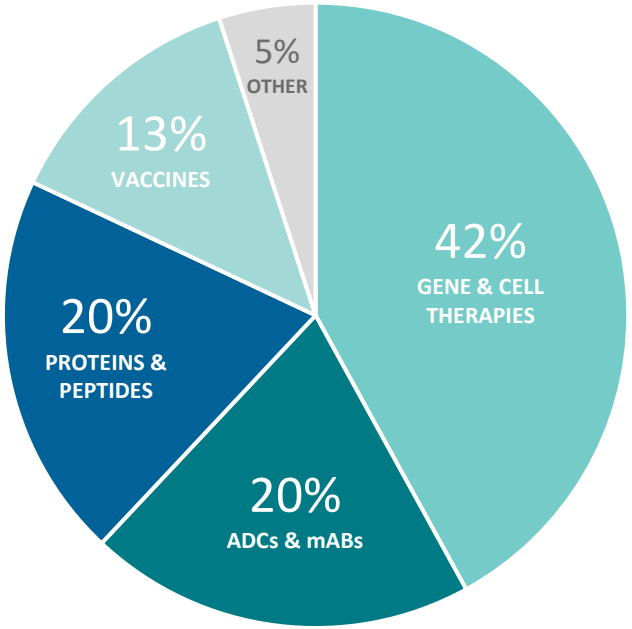
Arc Premier and HPLC System
(UPLC and HPLC)

MALS
(Size/Aggregate Analysis)

CMC Analytical Services

Modality Agnostic

(2020-2024) Modality profile



Consultative, Science Driven

Your partner for all phases

Quality support covering *de novo* assay creation through late phase method **validation**

From purity assessment to potency assays, BioAgilytix can support your molecule from concept to commercialization

Compliance Forward

(1st PAI in 2014, EU lab earned certification in 2022, no 483s to date)

Critical Reagent Management

Regulatory Considerations for Critical Reagent Management

ICH Q2(R2), ICH Q6B, USP <1033>, USP <1043> and comprehensive reagent tracking and qualification.

Characterization and Qualification

Ensure reagents are well-defined (source, purity, activity).

Lot-to-Lot Consistency

Minimize variability through rigorous control and qualification programs.

Change Control and Documentation

Implement robust change control procedures for reagent sourcing, handling, and storage

Stability and Expiry Dating

Monitor reagent stability over time and set appropriate retest periods.

Bridging Studies

Required when switching reagent lots or suppliers to demonstrate assay comparability.

Challenges and Solutions in Critical Reagent Management

1. **Reagent Variability**
   Challenge: Lot-to-lot variation impacting assay performance.
   Solution: Implement qualification criteria, trend historical performance, and conduct parallel testing when transitioning lots.
2. **Reagent Stability and Expiry**
   Challenge: Loss of reagent activity over time affecting potency readouts.
   Solution: Establish stability protocols, conduct real-time and accelerated stability studies, and define appropriate storage conditions.
3. **Supply Chain Issues**
   Challenge: Supplier discontinuation or delays impacting assay continuity.
   Solution: Establish secondary suppliers, maintain reagent stockpiles, and use risk-based procurement strategies.
4. **Change Management and Bridging Studies**
   Challenge: Unexpected performance shifts due to reagent changes.
   Solution: Implement pre-defined change control procedures, conduct side-by-side testing, and use statistical analysis to assess comparability.
5. **Documentation and Compliance**
   Challenge: Inadequate tracking of reagent usage and performance.
   Solution: Use electronic inventory management systems, maintain detailed reagent logs, and ensure compliance with regulatory expectations.

Visit the BioAgilytix booth and grab a copy of a recent poster on Navigating Critical Reagent Challenges in Cell-Based Potency Assays

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Navigating Critical Reagent Challenges in Cell-Based Potency Assays: Case Studies on Variability and Solutions

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BACKGROUND

A critical reagent is a key component of an assay that directly impacts the assay's performance. Critical reagents are often biological molecules like antibodies, proteins, or cell lines. They are the backbone of cell-based potency assays (CBA), as such their variability can create major challenges in assay development, validation, and routine sample testing. Issues such as lot-to-lot inconsistencies, supply chain disruptions, and reagent discontinuation can lead to unexpected changes in assay performance, potentially impacting result consistency over time and regulatory compliance. This poster presents two real-world case studies that highlight these challenges and discuss practical mitigation strategies to ensure long-term assay sustainability and robustness.

CASE STUDY #1 – mRNA FLOW CYTOMETRY ASSAY

A flow cytometry-based potency assay faced multiple changes for its reference standard lots as well as the assay control lots throughout its lifecycle—from development to validation and through routine sample analysis. Each lot transition introduced variability which impacted the reported potency. Assay control recoveries were consistently trending high. This made assay qualification difficult and complicated regulatory submissions. The case underscores the importance of proactive lot-change management to maintain consistency.

Possible Solutions: A) Identify critical reagents early and assess their impact on assay performance. Assess and project the needs for the assay and manufacture a batch of critical reagents which lasts longer. B). Conduct parallel testing and stability monitoring of new and old lots to evaluate variability before transitioning. **C) Perform regular and routine evaluation of reference materials as part of method Lifecycle Management.**

CASE STUDY #2 – FUSION PROTEIN FOR PHAGOCYTOSIS

A flow cytometry potency assay relied on an in-house critical reagent (engineered cells), but as the project scaled up, outsourcing became necessary to meet requirements for volume of reagent. Finding a suitable vendor proved difficult due to differences in reagent quality and sourcing. A custom manufacturing approach was ultimately chosen, but the new lots introduced additional variability, requiring extensive method and reagent requalification efforts.

Possible Solutions: A) Conduct early risk assessments to identify potential sources. B) Develop backup strategies, including alternate suppliers. C) Establish long-term agreements with suppliers to ensure batch-to-batch consistency. D) Consider custom manufacturing with strict quality control measures.

CONCLUSIONS

By taking a proactive approach to critical reagent management, companies can: A). Improve assay reliability & maintain consistency during drug development. B). Reduce the burden of frequent requalification and regulatory delays. C). Strengthen supplier agreements to mitigate risks associated with reagent variability. Early risk assessment, robust supplier partnerships, and long-term reagent planning are essential to ensuring sustainable potency assay performance.