

Evolution of Discoverant Usage at Biogen Idec

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Biogen Idec

Discover 2011

Outline

- APC Vision
- Phase 1: Commercial Drug Substance (DS) Manufacturing Hierarchies
- Phase 2: Generic Hierarchy and Expansion to Clinical DS Manufacturing
- Phase 3: Expansion to Drug Product (DP) and Stability Hierarchies
- Vision for future

APC Charter

APC: The Advanced Process Control (APC) program at Biogen Idec is focused on providing and delivering in a timely manner, advanced data management tools that will facilitate the availability of data, through the trending program, to various internal customers (MFG, QA, Tech Transfer, RA, MS) to help ensure uninterrupted drug supply to patients.

The APC program has standardized on 2 main data management/availability tools:

- **Data Management Tool:** Powerful data management/analytical tool that provides connectivity to multiple data sources (OPM, LIMS, Pi, Batch record data). In addition it has powerful analytics (SPC, Transition Analysis, Overlay continuous points) for trending.
- **Online Multivariate tool:** Monitors batch evolution in real time by taking data from the Distributed Control System and using multivariate analysis techniques (MVA) combined with conventional Statistical Process Control (SPC) and plots data against a pre-developed model

The Evolution of Biogen Idec Discoverant Usage

Phase 1: Commercial Drug Substance Manufacturing

2003 – 1st Commercial Custom Hierarchy and PRIMR pages

- Proof of concept – Could Discoverant be successfully implemented to meet our manufacturing “offline” data needs?
 - Batch record (BPR) and solution lot record (SLR) data repository using PRIMR
 - Connections to LIMS, OPM, and PI Systems to have one-stop-shop for data
 - Basic data trending
- 9 month development timeline – Aegis and Biogen Idec Collaboration

2006 – 2nd Commercial Custom Hierarchy and PRIMR pages

- 11 month development timeline – Aegis and Biogen Idec Collaboration
- Began to showcase data trending capabilities
 - Weekly Manufacturing updates, reports
 - Manufacturing began to understand the process in ways they hadn't previously
 - Correlations between process inputs and outputs were easily determined.
 - Focus on ensuring process is in control, not simply free of deviations

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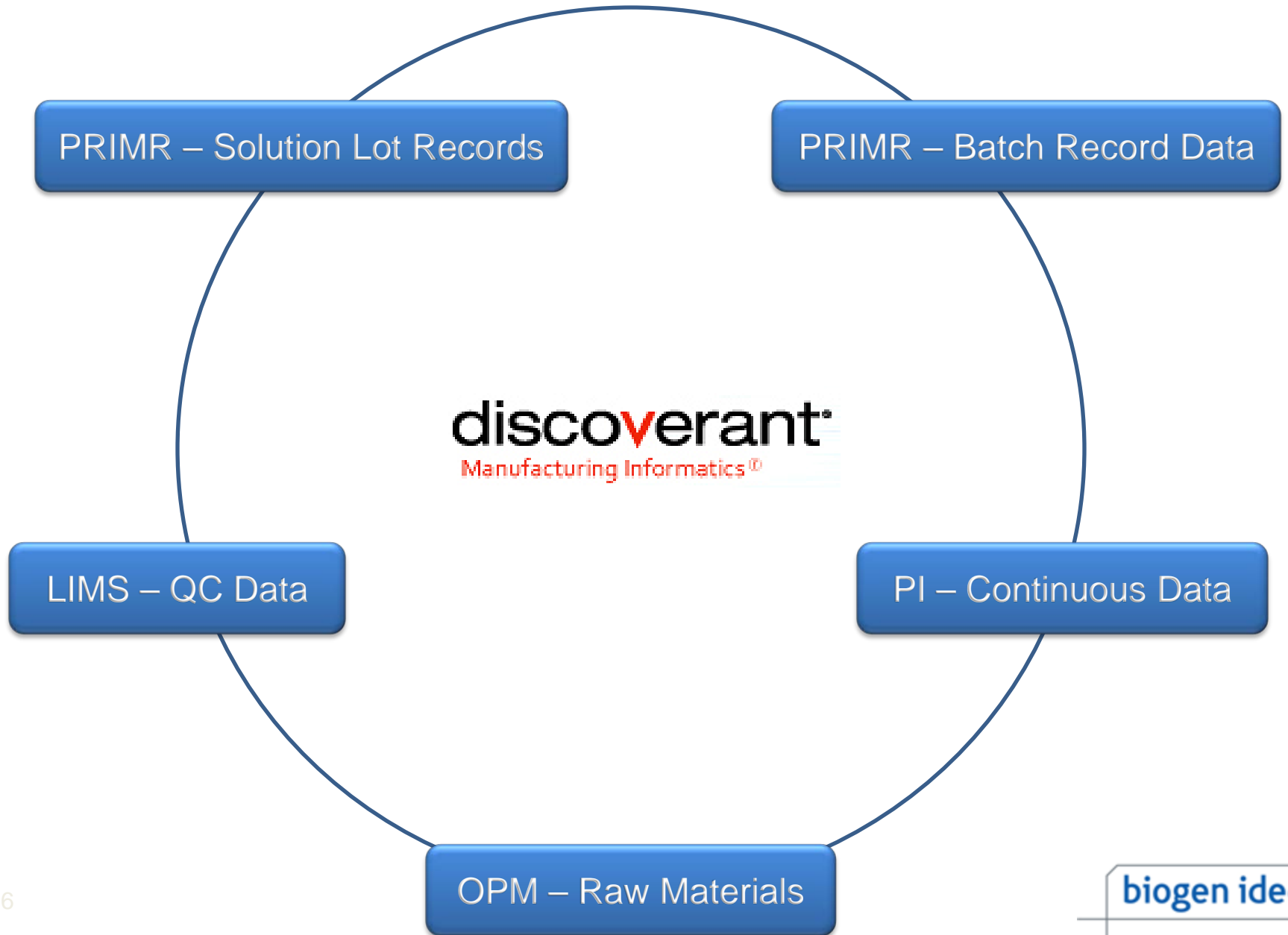
Phase 1: Commercial Drug Substance Manufacturing

Manufacturing Sciences

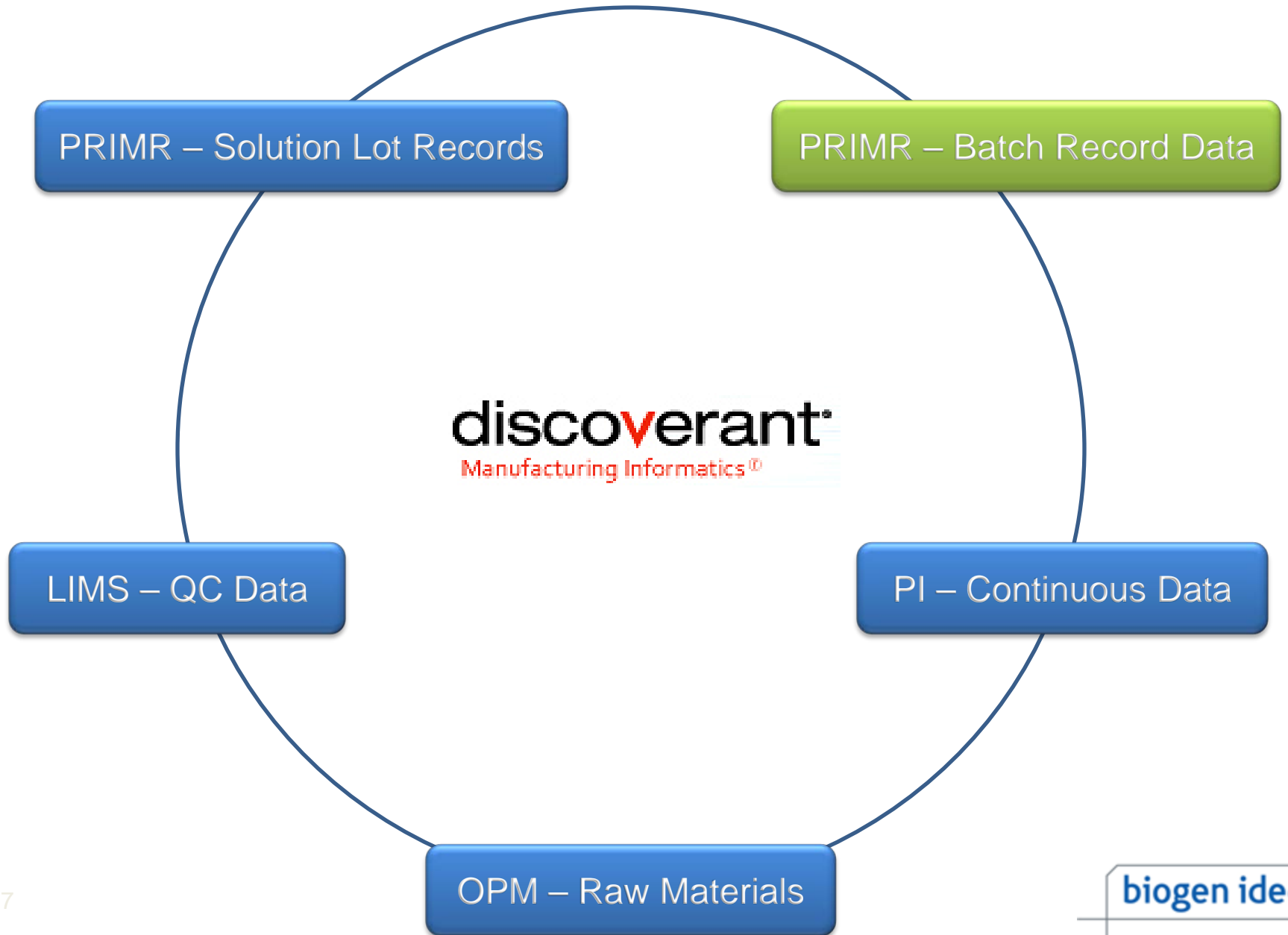
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Discoverant Data Connections



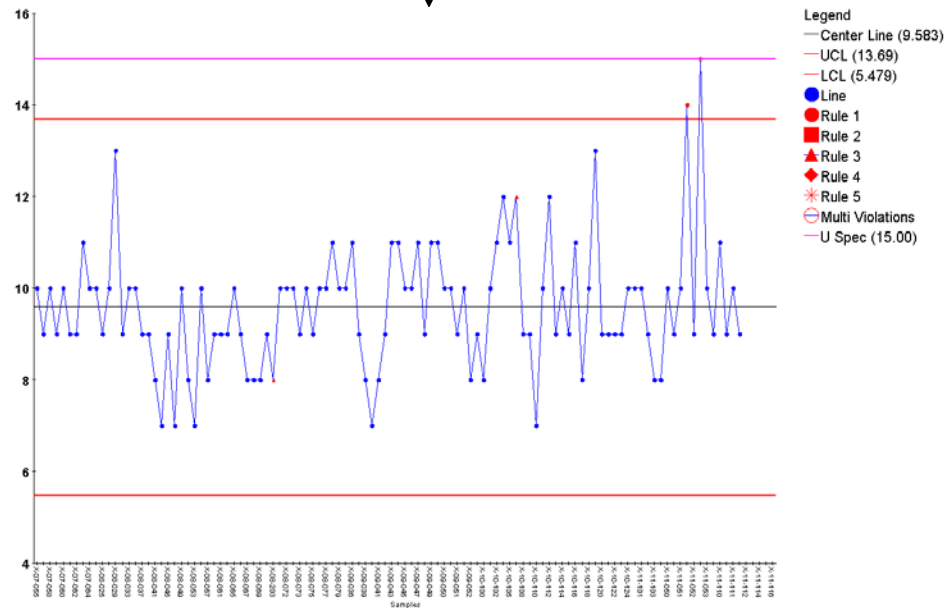
Discoverant Data Connections



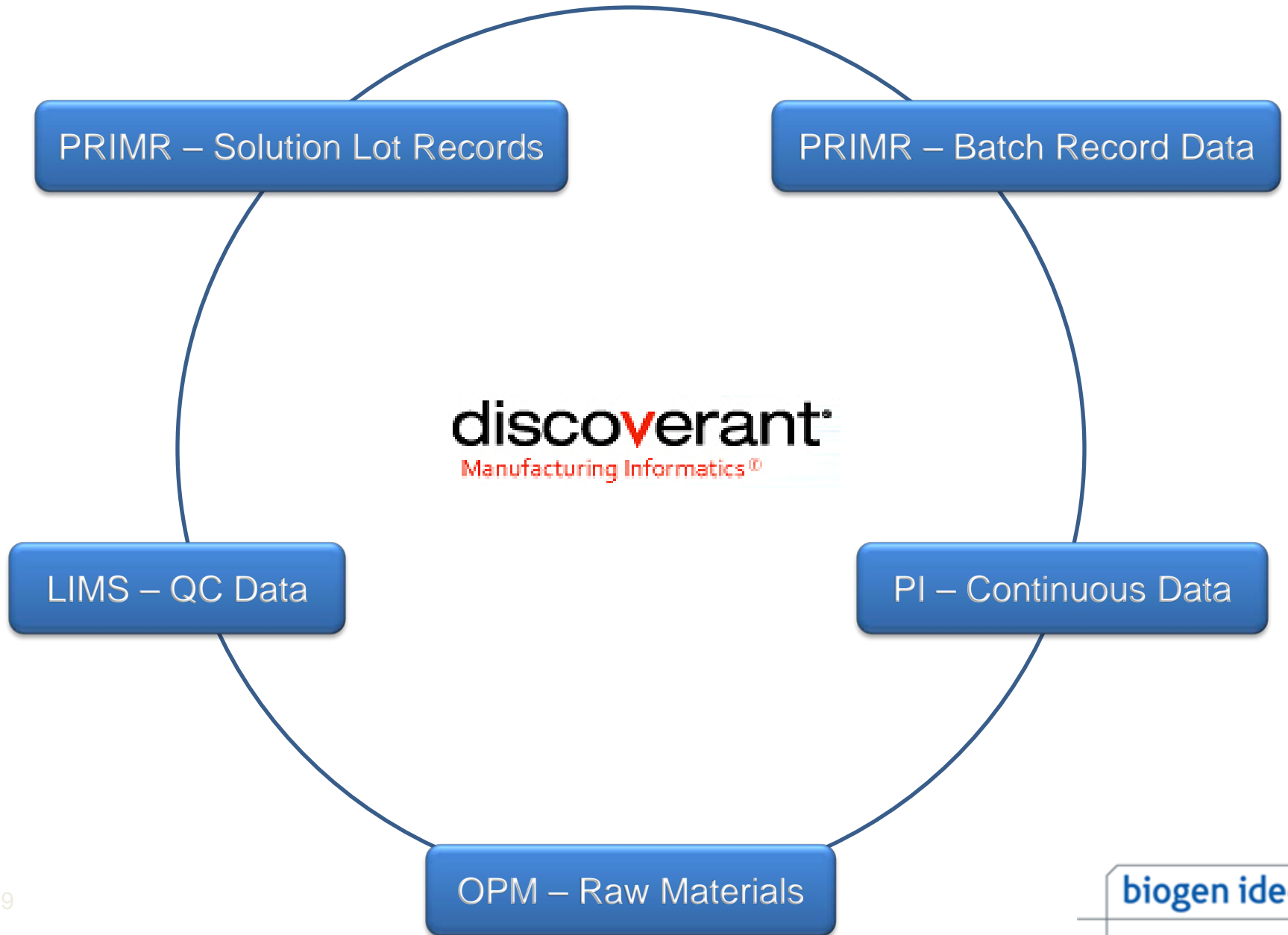
Batch Record Data

- ✓ Discoverant used for investigational purposes
- ✓ Control charts were a tool used to demonstrate process consistency and trends in reports and regular manufacturing meetings.

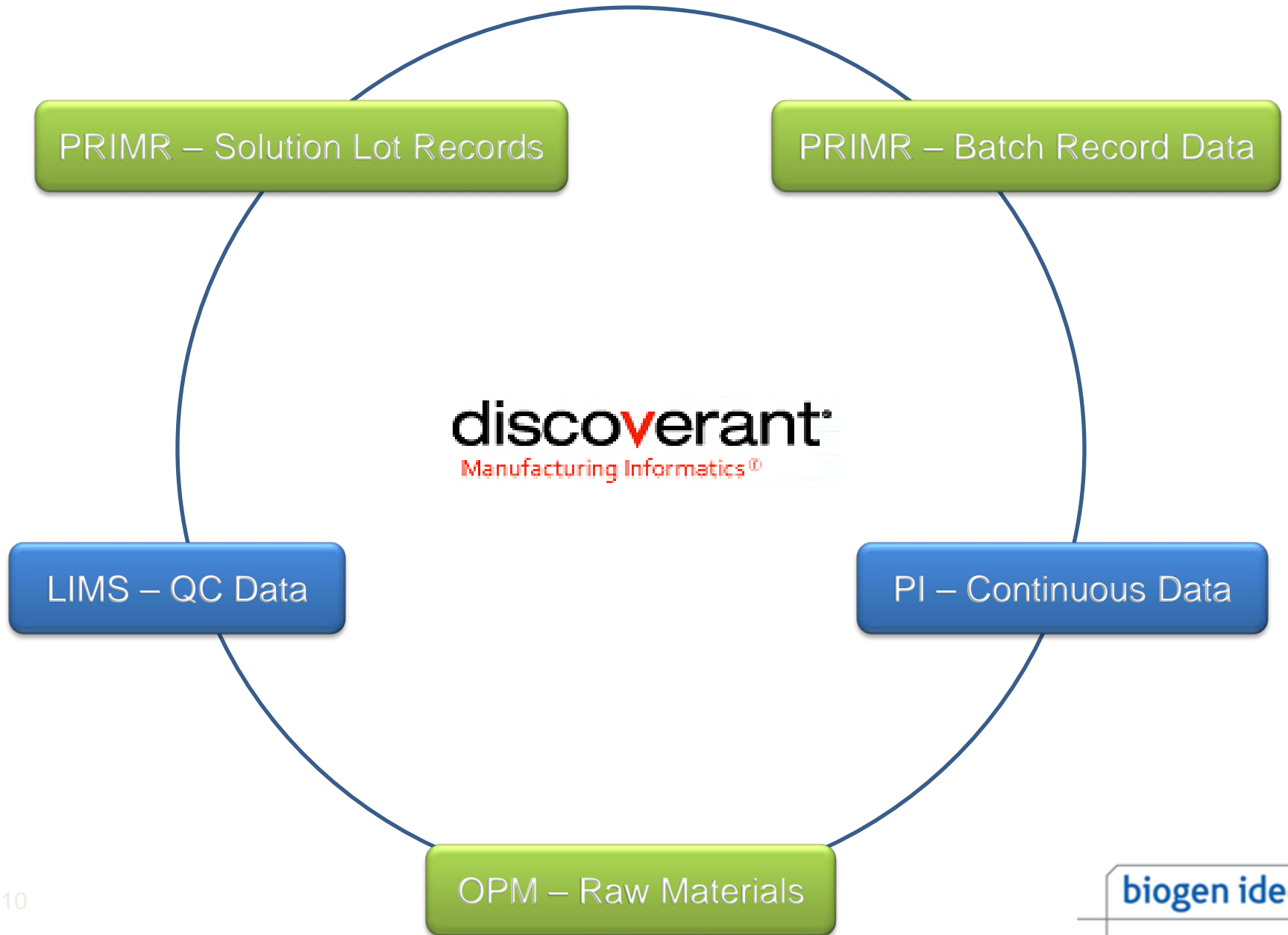
PRIMR – Batch Record Data



Discoverant Data Connections

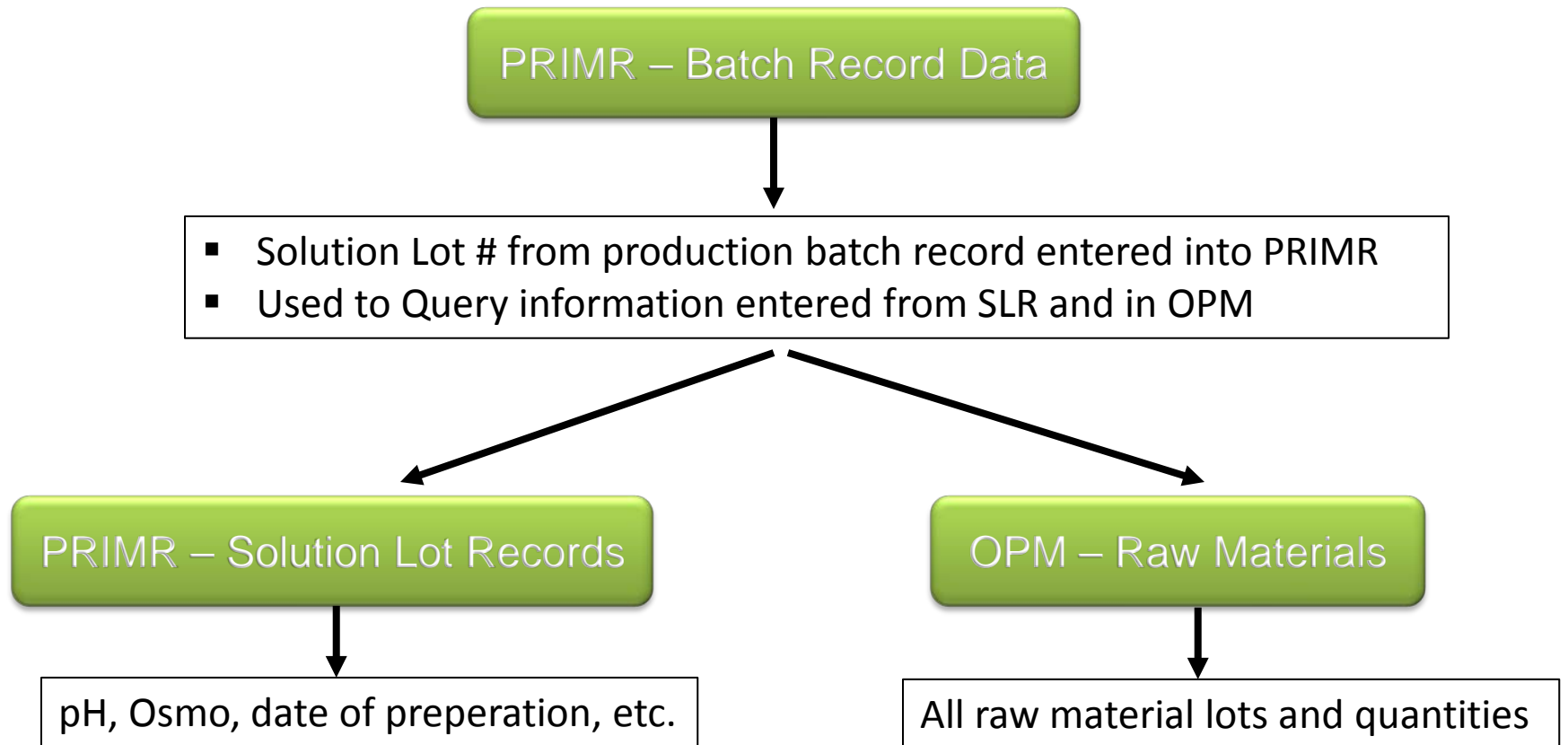


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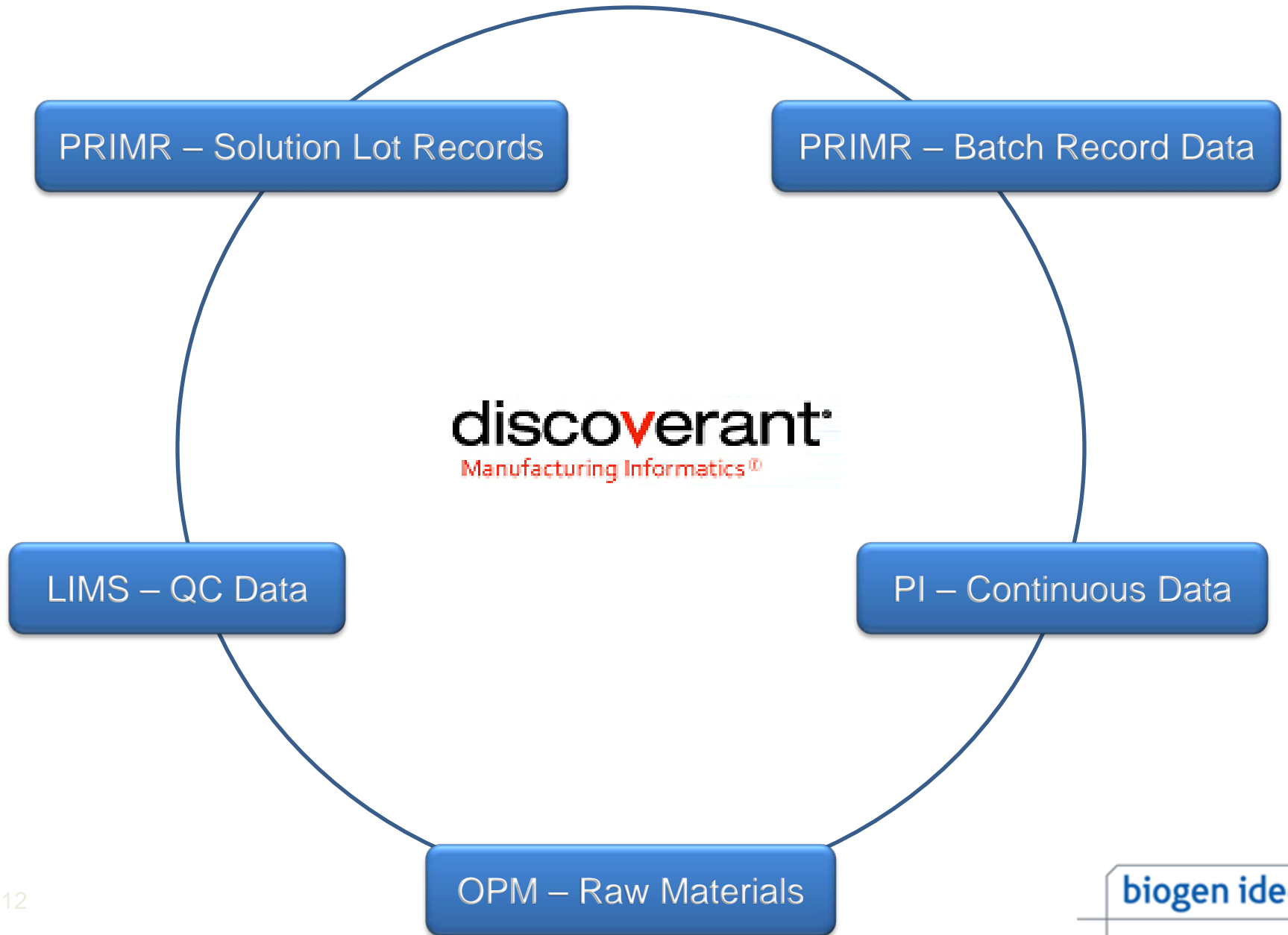


Solution Raw Materials and Analytical Testing

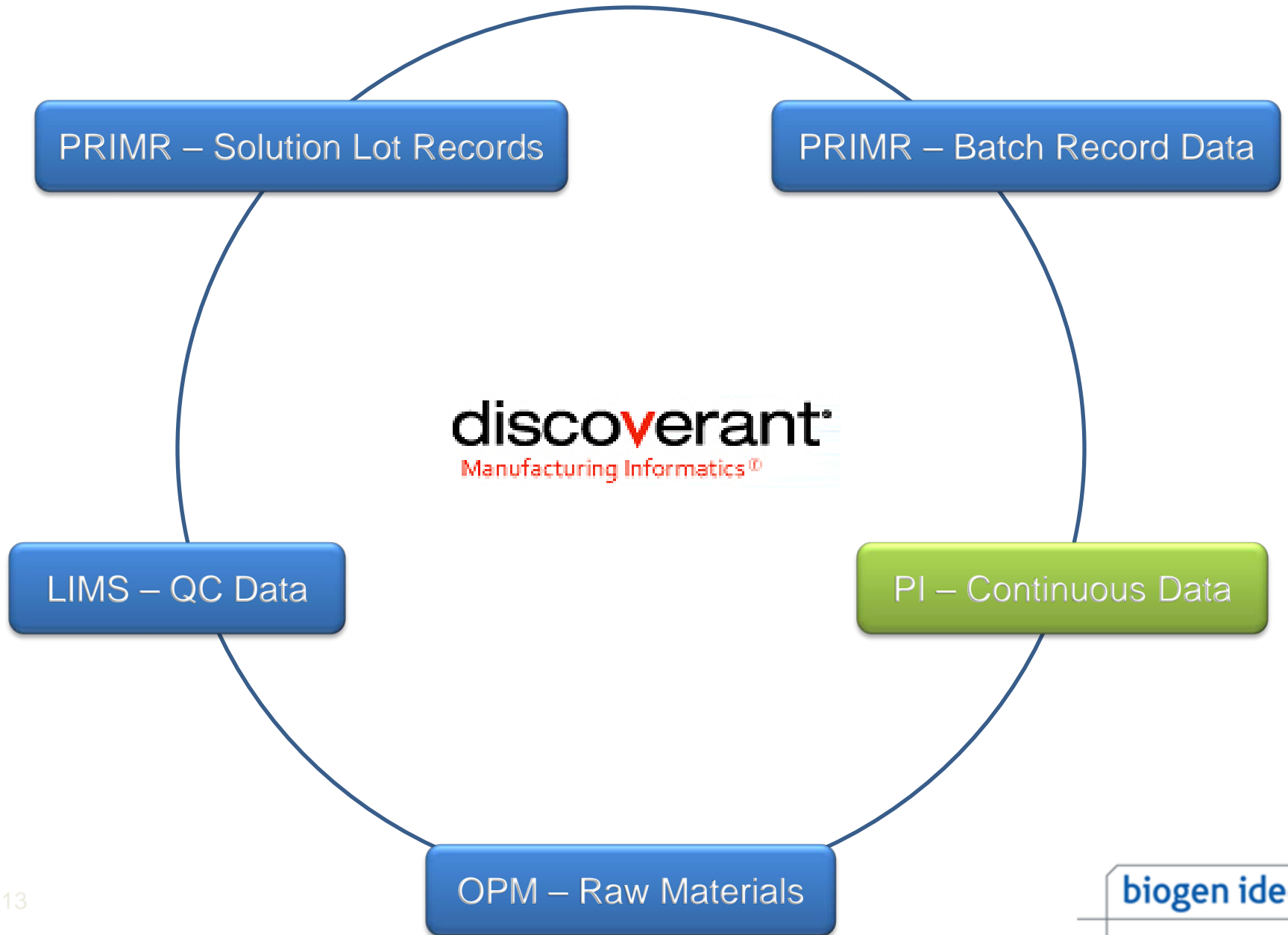
- ✓ Raw material and analytical data available for every solution used in a commercial production batch
- ✓ Essential for rapid response to process abnormalities with a small fraction of resources to gather raw material information



Discoverant Data Connections

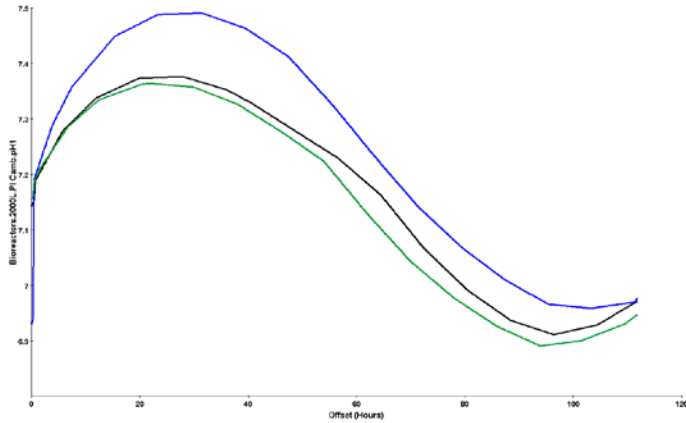


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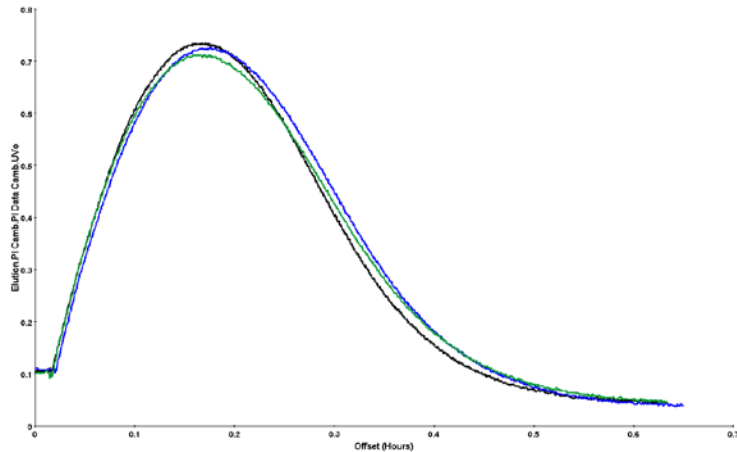


PI Connections for Continuous Data

- ✓ Historical Trends for Bioreactors and Purification of commercial processes



PI Connections



The Evolution of Biogen Idec Discoverant Usage

Phase 2: Generic Hierarchies and Expansion to Clinical DS Manufacturing

2007 – Generic Hierarchy 1.0

- Built w/ Aegis support
- One hierarchy and set of PRIMR Pages encompassing all process needs
- Allowed expansion of Discoverant use for Clinical campaigns w/o building new hierarchies
- Became too large, not streamlined. 90% empty data
- Difficult for users to find data of interest

2009 – Generic Hierarchy 2.0 Internally

- Allowed Biogen Idec to build all clinical hierarchies in house
- Copy of the library was used to make process specific hierarchies
- Process experts provide specifications that use only subset of generic library. Only new parameters need to be validated
- Now only takes 4-6 weeks to build, regardless of connections requested
- Over time, hierarchy specs have advanced from “page” level to “parameter” level

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Phase 2: Generic Hierarchies and Expansion to Clinical DS Manufacturing

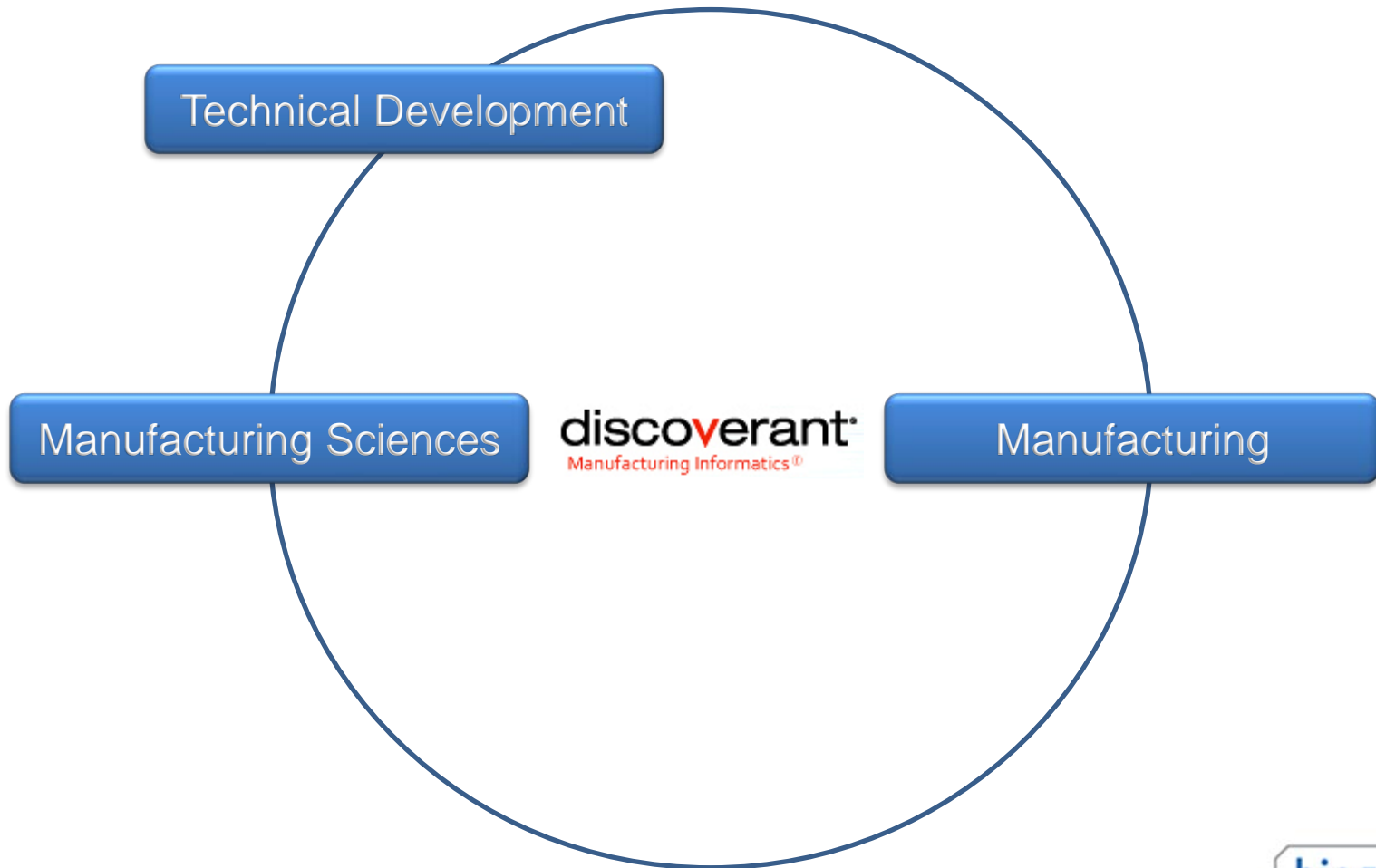
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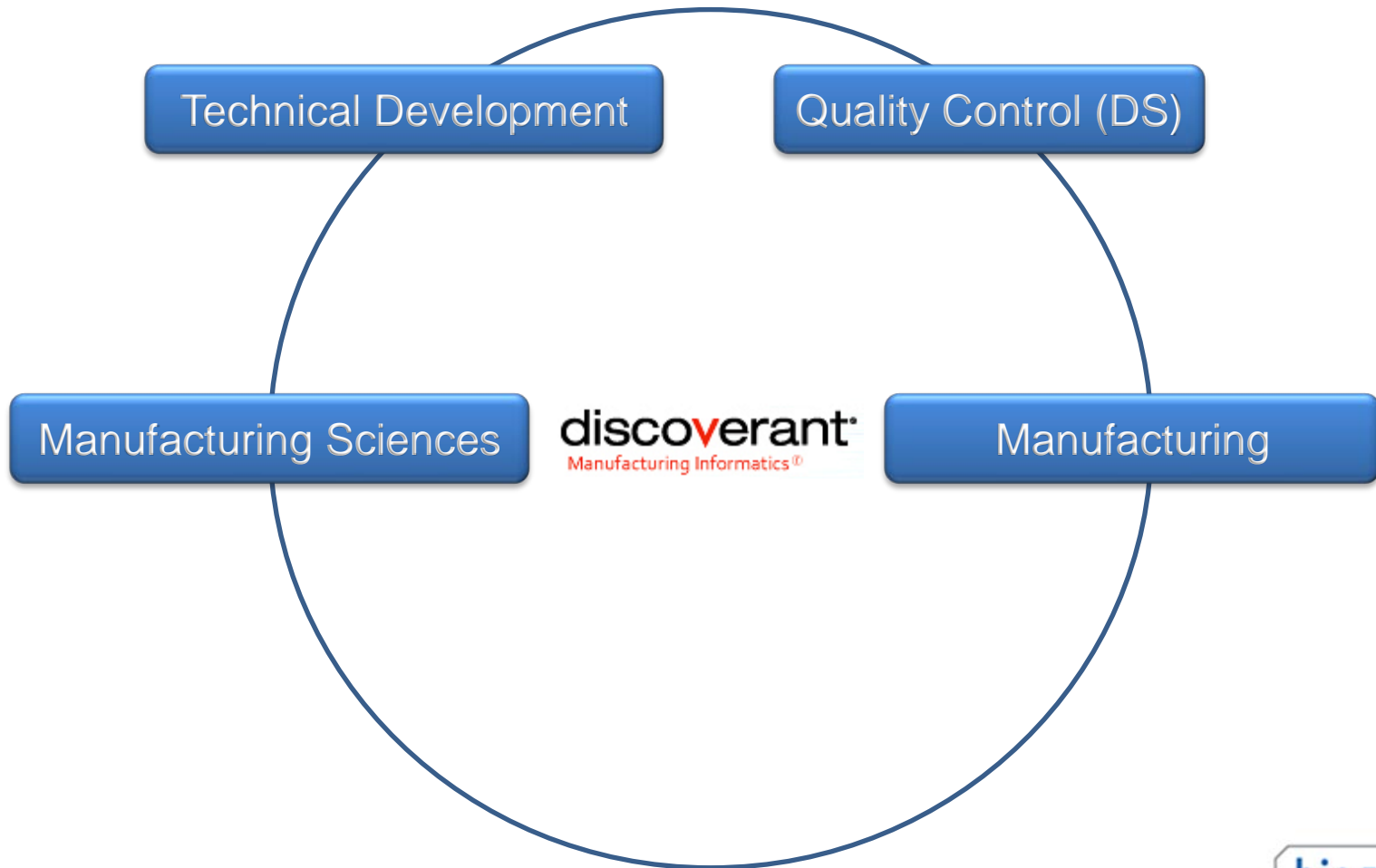
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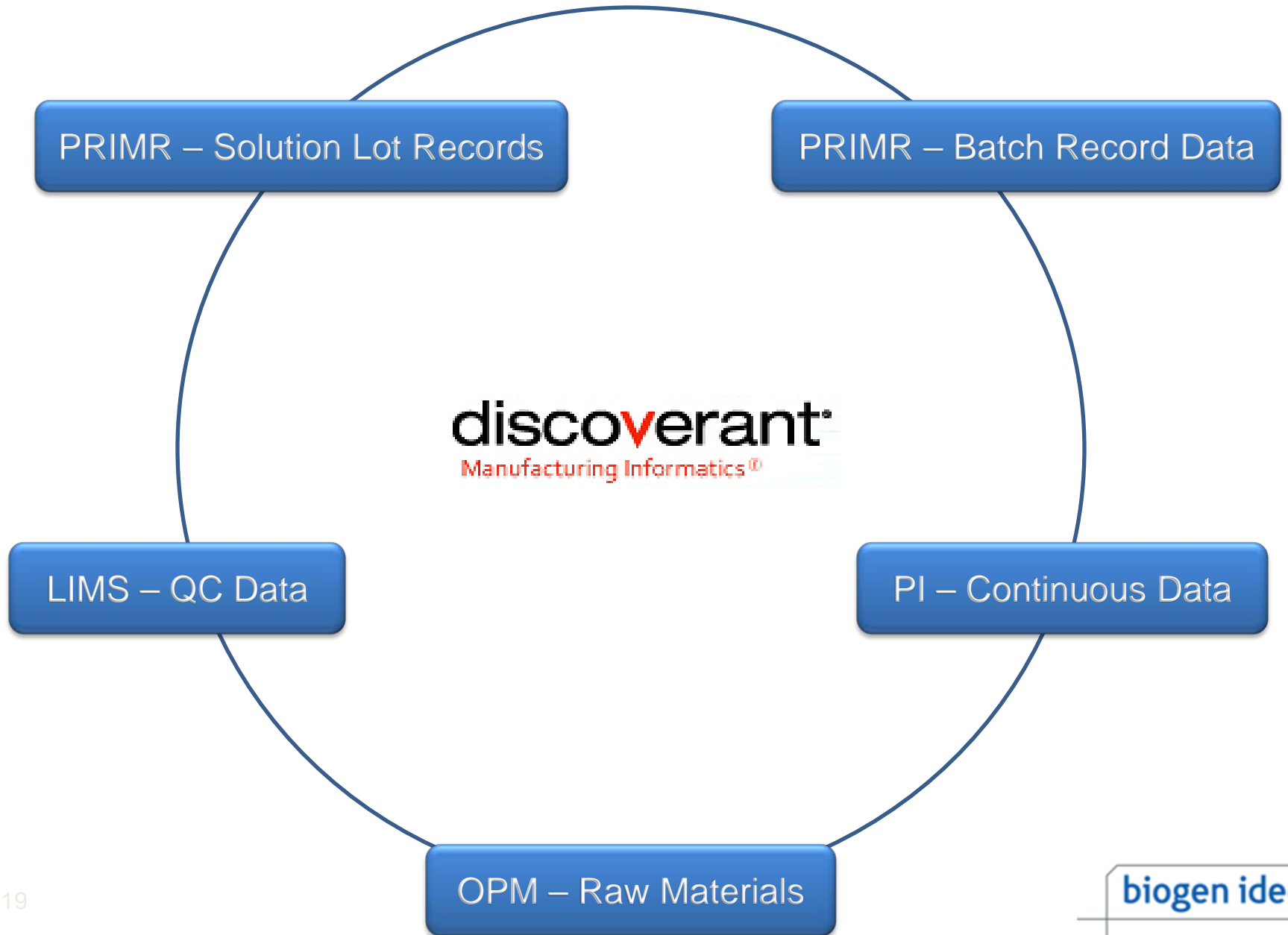


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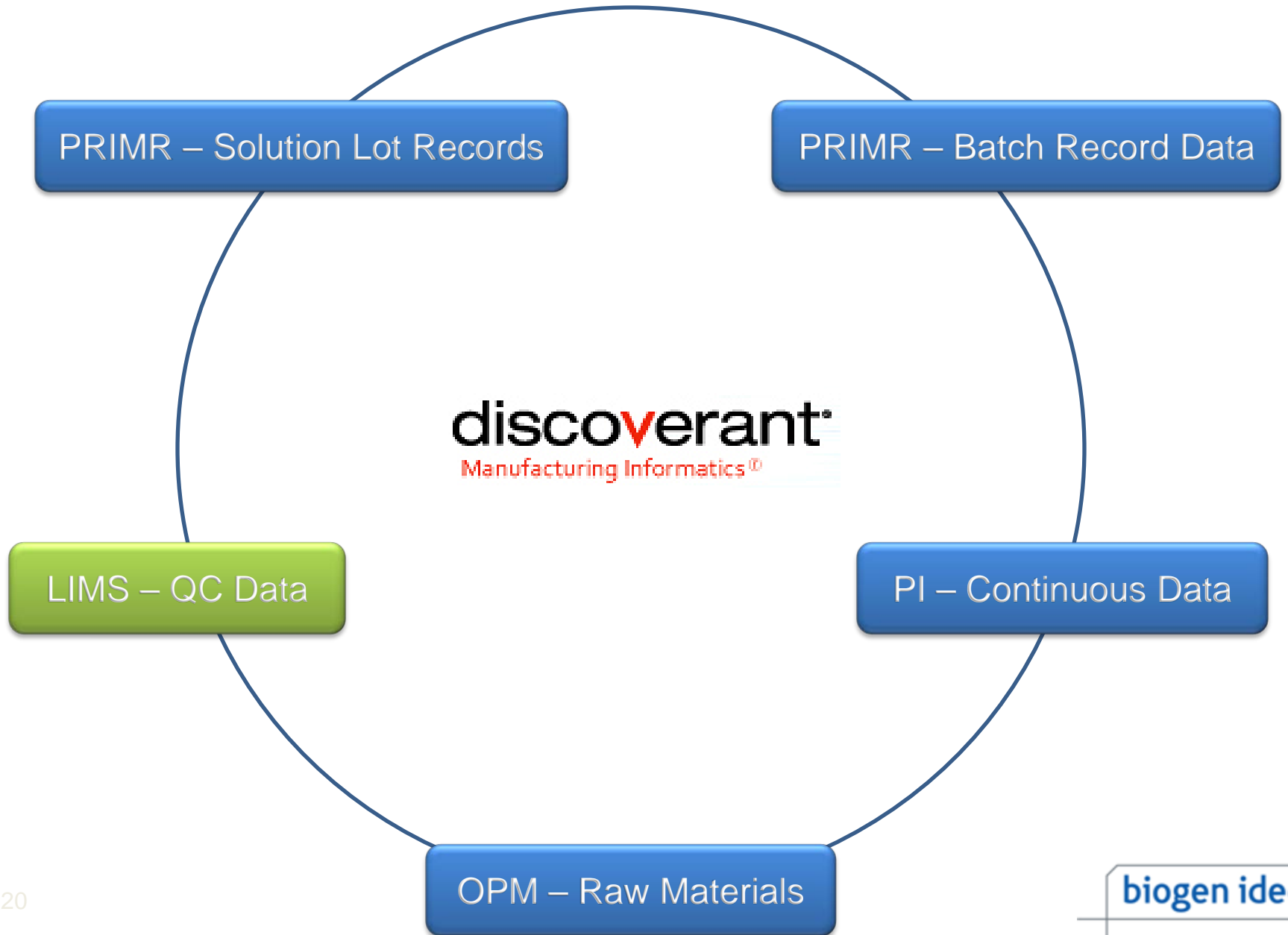
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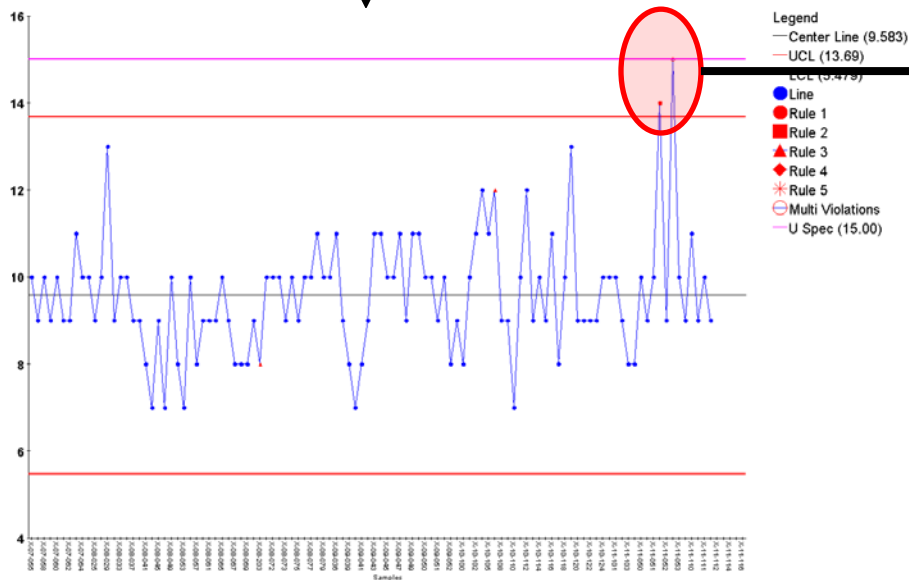
Discoverant Data Connections



Quality Control Monitoring

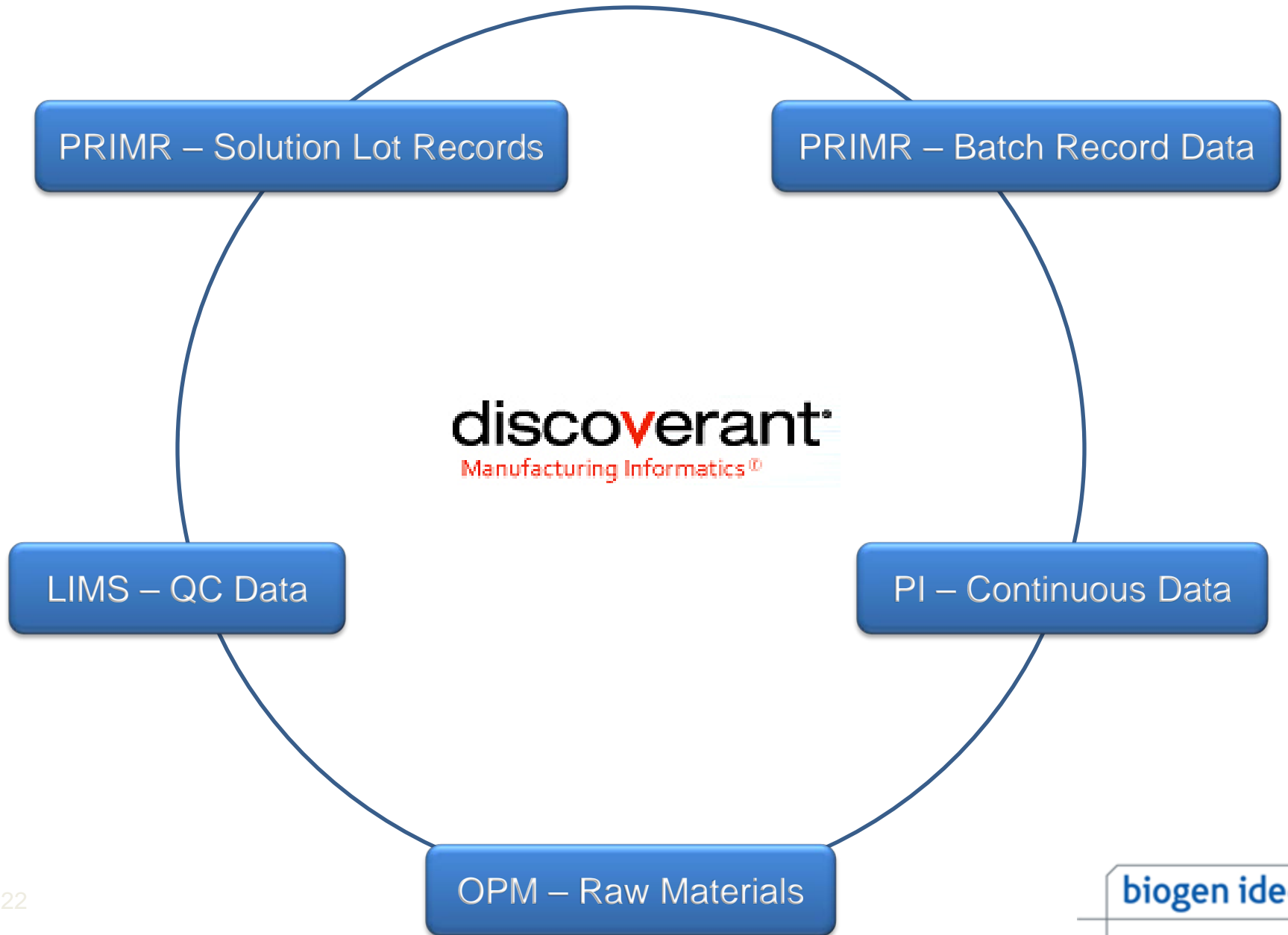
- ✓ Control trending used by Quality Control and Manufacturing to monitor product quality and identify anomalous results.
- ✓ Allows users to bypass cumbersome LIMS software to quickly access historical data for investigations.
- ✓ Initially available for only Commercial Campaigns

LIMS – QC Data

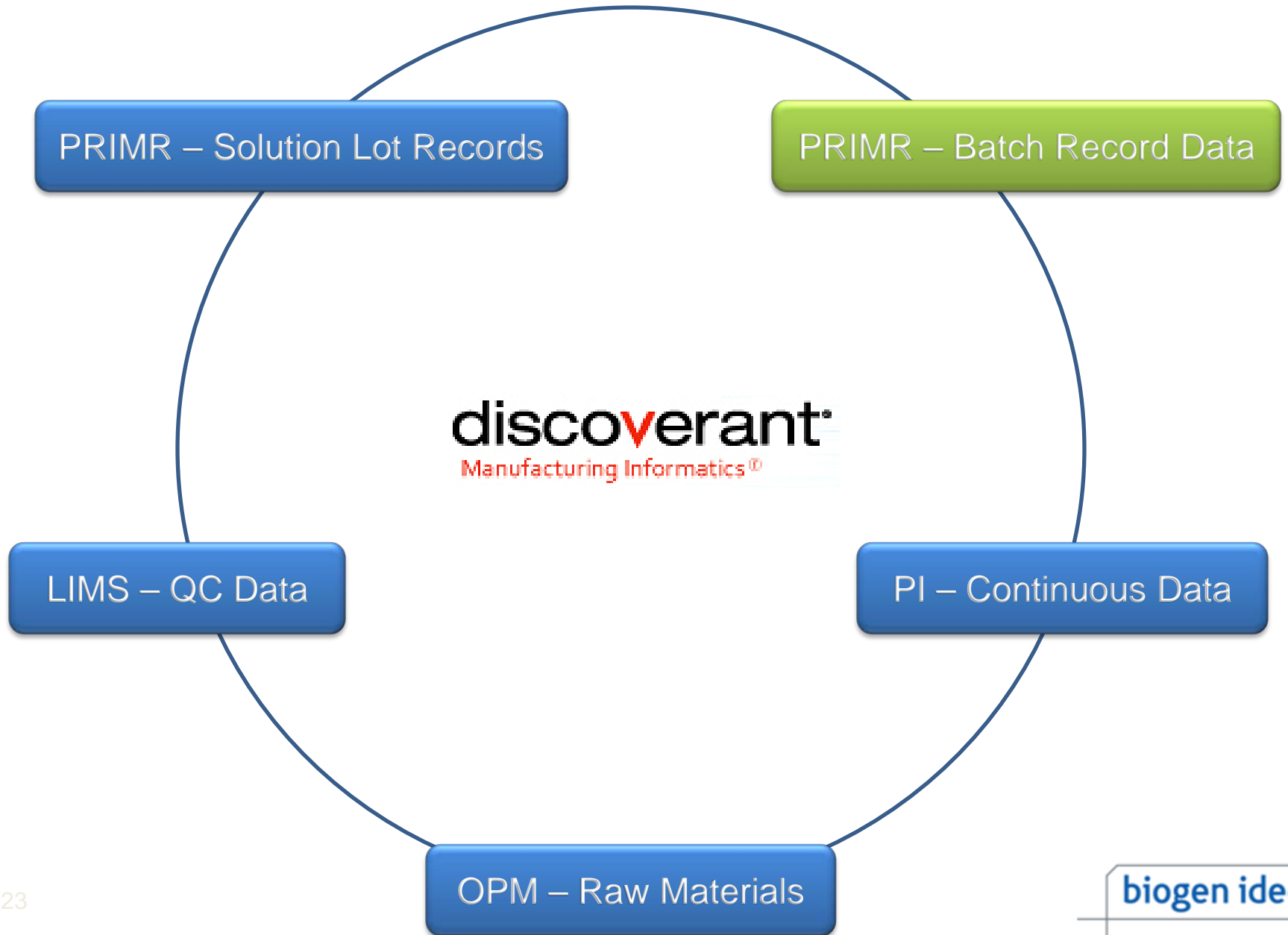


Outliers trigger email notifications to appropriate individuals or groups.

Discoverant Data Connections



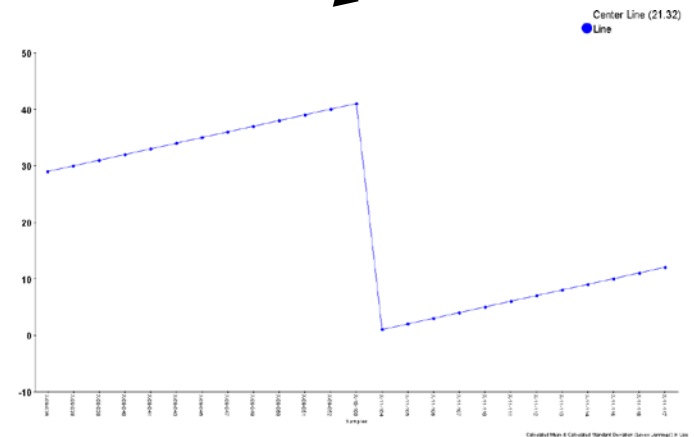
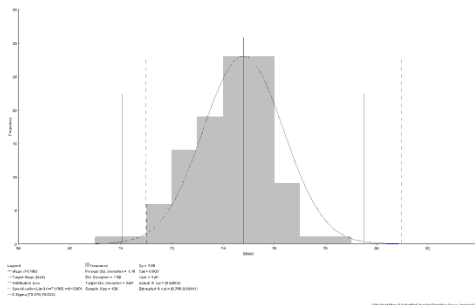
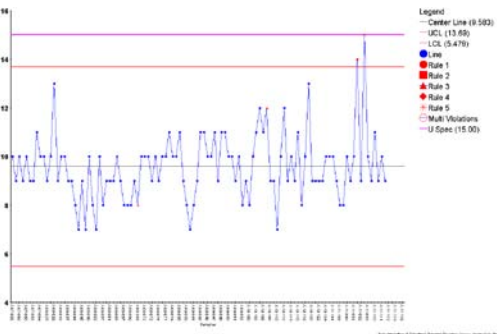
Discoverant Data Connections



Batch Record Data

- ✓ Daily, weekly, monthly trending programs
- ✓ Control charts remain a key tool for process monitoring – increased use of ARMs and email alert functionality
- ✓ Capability analysis and calculated variables are common practice

PRIMR – Batch Record Data



Control charts, process capability (cpk)

Use of calculated variables to trend column lifetime, cICG and growth rates

The Evolution of Biogen Idec Discoverant Usage

Phase 3: Expansion Outside DS Manufacturing and Continuous Improvement

2009 – Drug Product Hierarchies

- New generic hierarchy created to support Drug Product trending.
- LIMS and PRIMR (DS lots, dates of mfg, facility)
- APR's and regular trending/alerts
- Process Validation and Commercials

2010 – Stability Hierarchies

- New generic hierarchy created to support Stability data trending
- Uses Discoverant stability module
- DS and DP hierarchies for all commercial campaigns

Continuous Improvement of DS Hierarchies

- Generic LIMS and OPM connections for Clinical campaigns (previously only for Commercials)
- Discrete multivariate models pulled via ODBC
- Campaign Dashboards via ODBC
- Double Data Entry for PVR and Commercials – Discoverant used as source of verified data
- Connections to Delta-V to replace batch record entry

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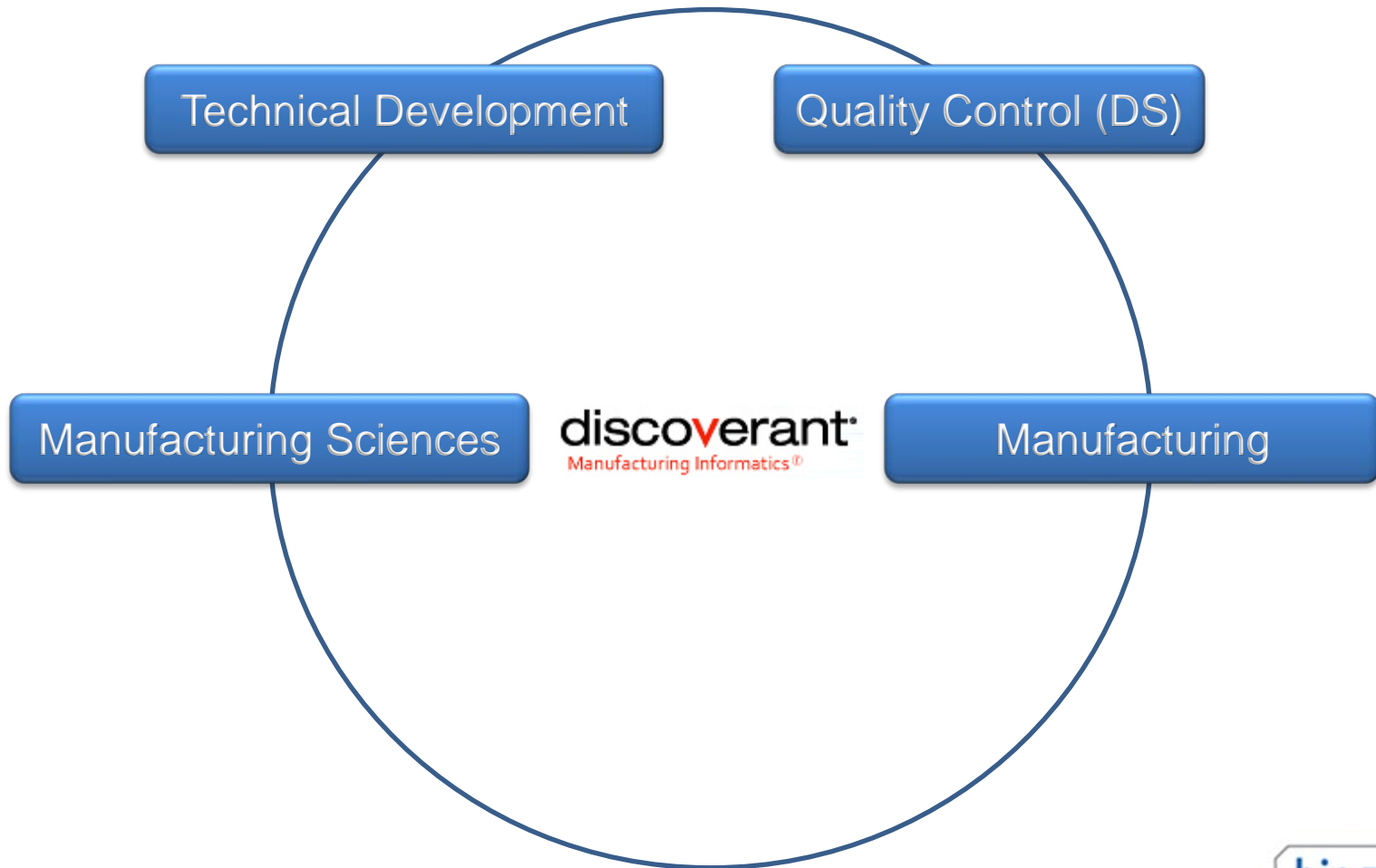
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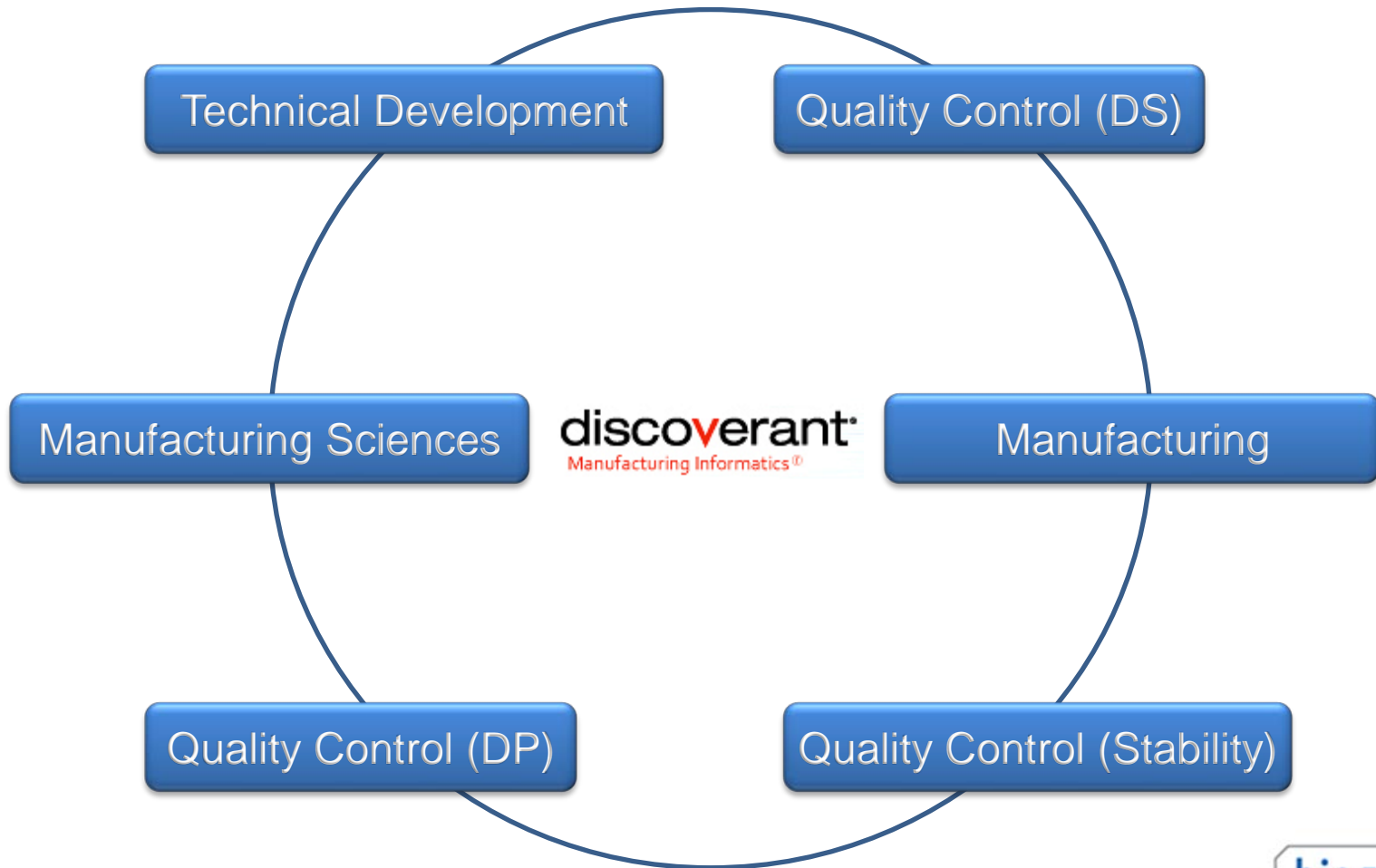
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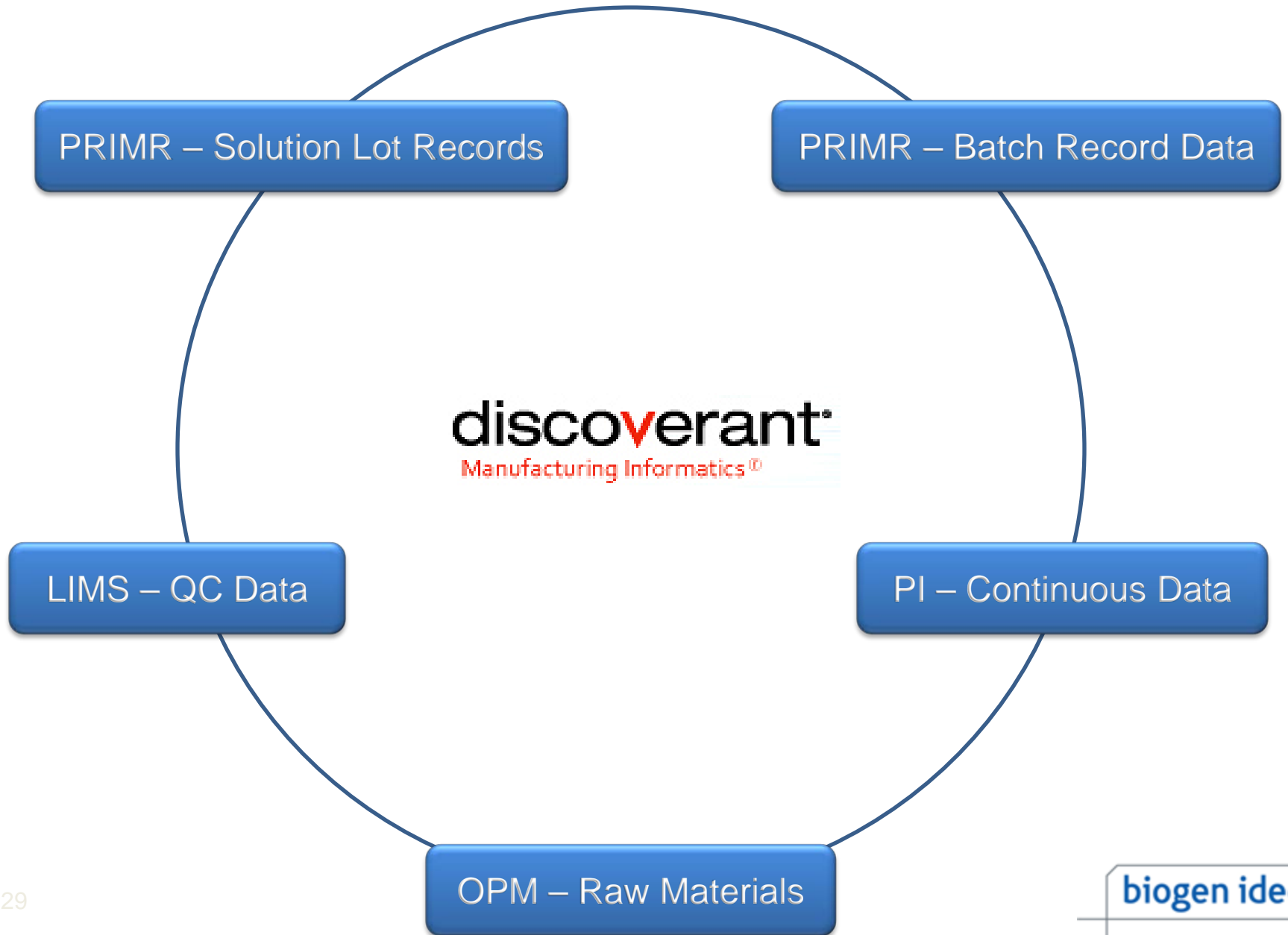


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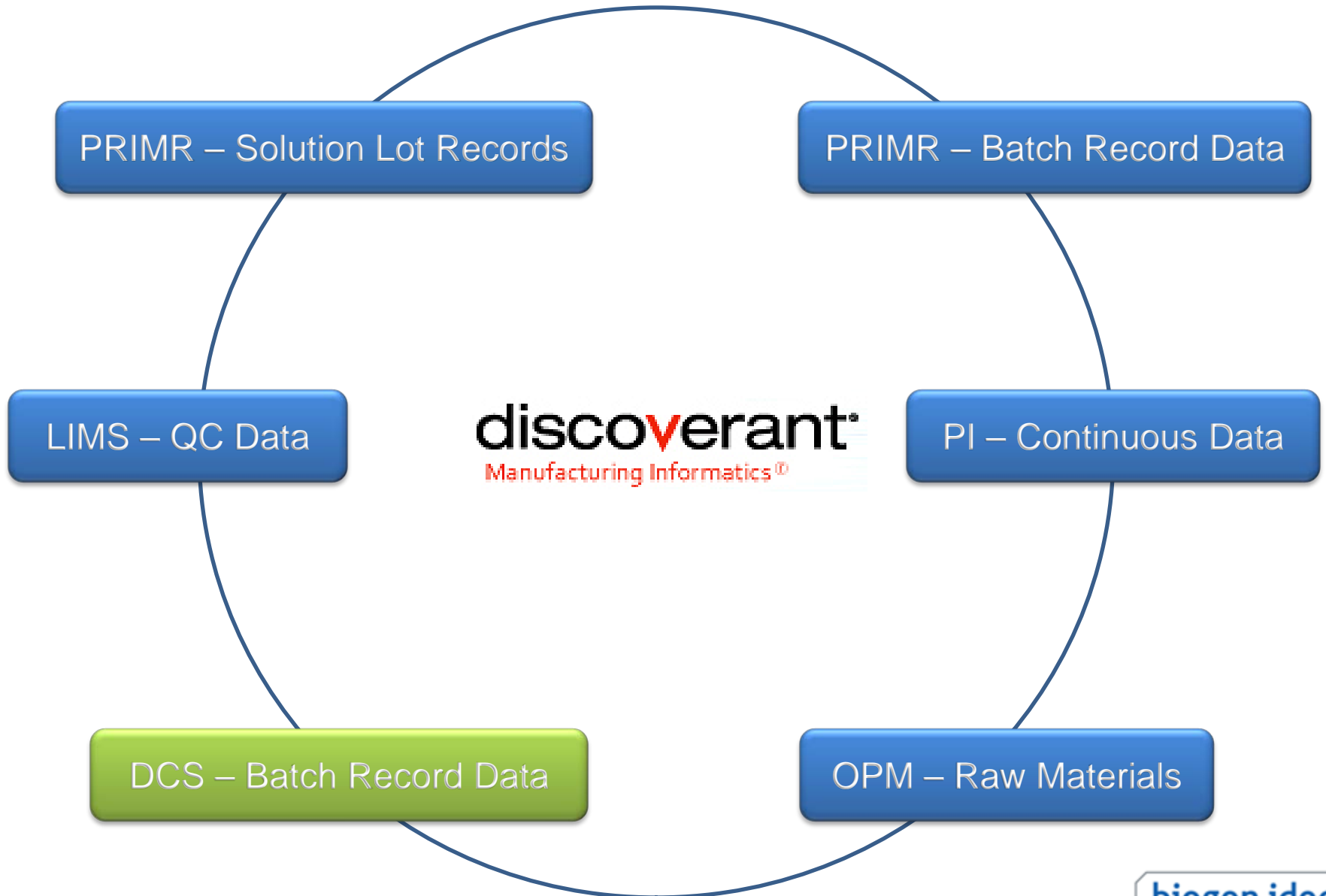
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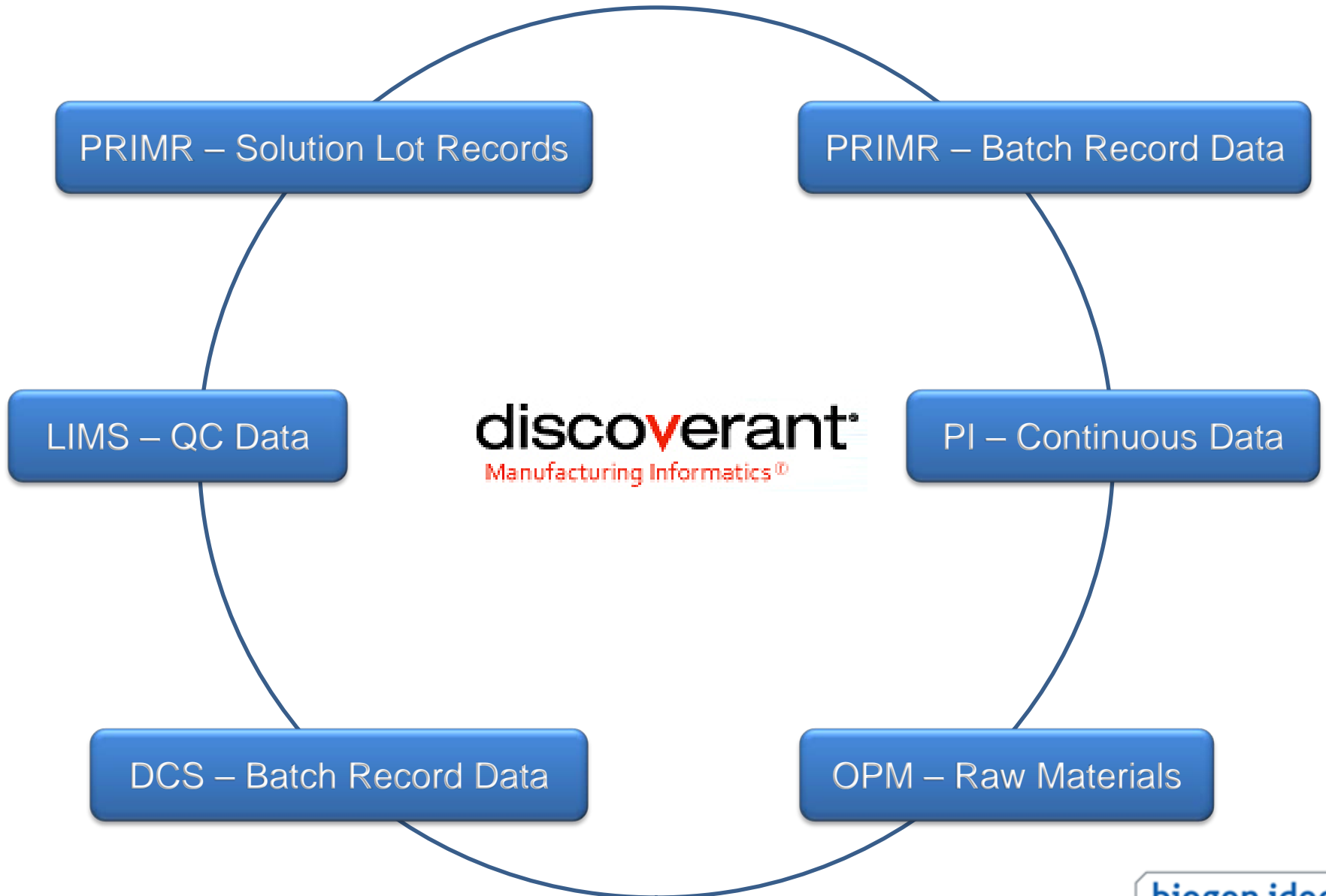
Discoverant Data Connections



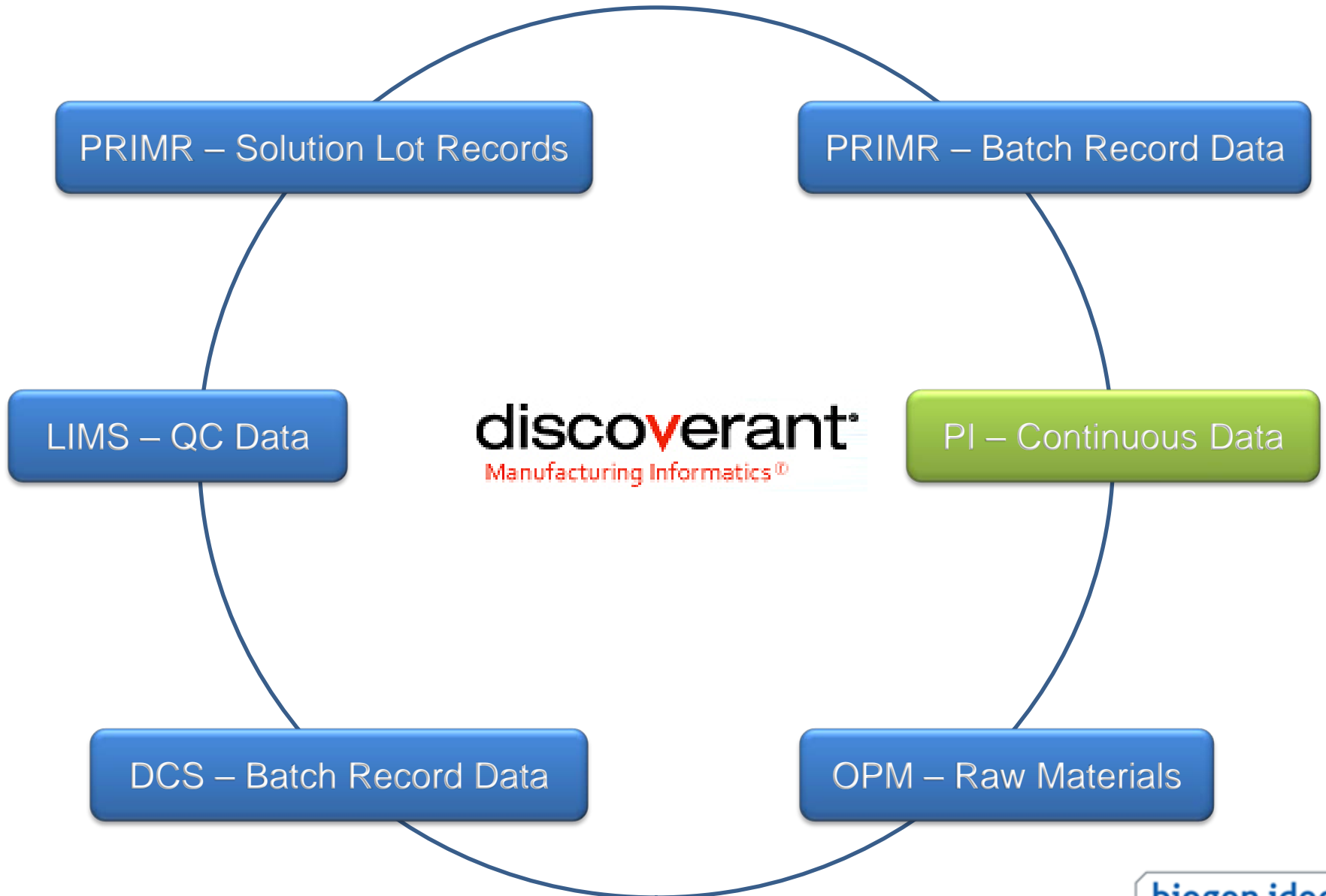
Discoverant Data Connections



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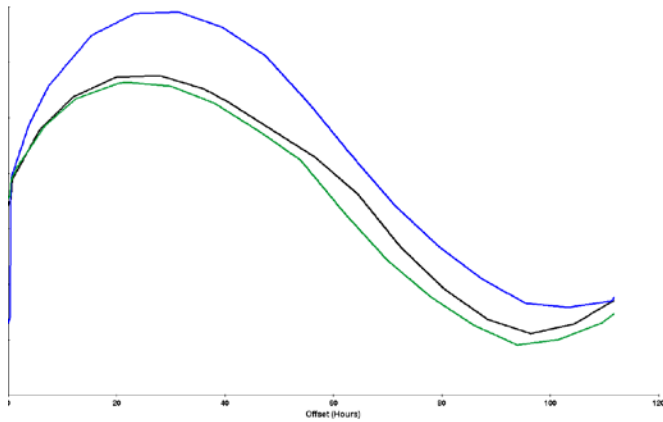


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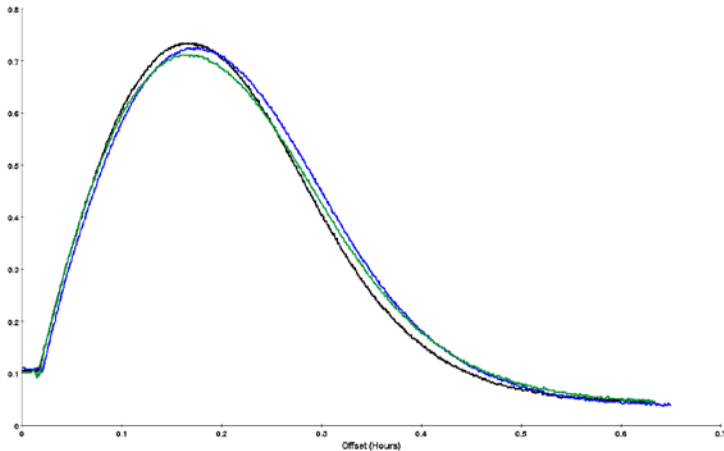


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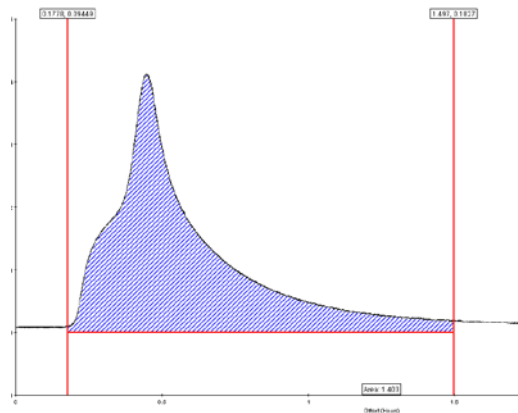
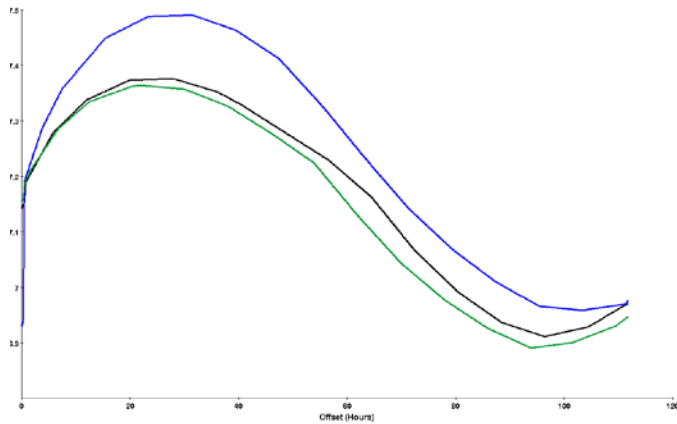


PI Connections



PI Connections for Continuous and Discrete Data

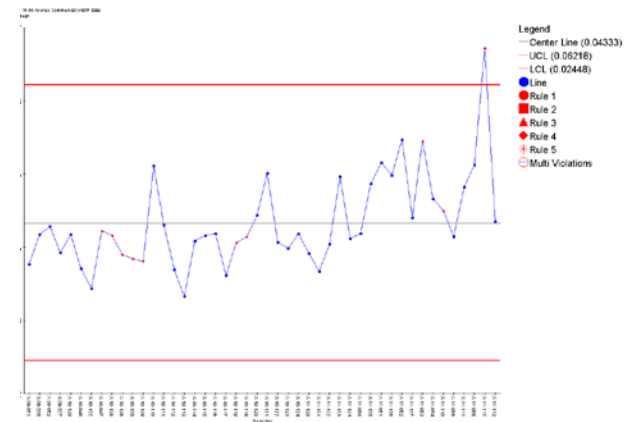
- ✓ Historical Trends for Bioreactors and Purification of commercial processes



PI Connections

- ✓ Discrete parameters calculated in DCS and stored in PI:
 - HETP
 - Asymmetry Factors

- ✓ Feature Extraction



Future Hierarchies

Raw Materials Hierarchy (in progress)

- Ability to track raw materials (resins, critical raw materials) across programs
- CoA info (PRIMR) and analytical data (LIMS)
- Eventually expanded to small molecule production
- One-stop-shop for Raw Material Data

Environmental Monitoring (2012)

- Track all environmental data throughout facilities
- LIMS – Test results, e.g. Bioburden
- PRIMR – dates of testing, locations
- PI – Online data, e.g. airflows or pressures

A Look Back

Discoverant started in 2003 as a data repository and analytical tool for DS Manufacturing

- Successful in building commercial hierarchies that created one stop shop for offline data.
- Data used for day-to-day trending and reports such as APRs

Expanded Use to Clinical DS Manufacturing in 2007-2009

- Building generic hierarchies allowed for use in clinical campaigns

Expansion Throughout Operations Organization 2009-Present

- As other groups became exposed to advantages of Discoverant, developed hierarchies in DP and Stability groups
- Discoverant now recognized throughout organization as an effective data management tool, will continue to expand as needs arise

Keys to Success

- Tight collaboration between IT and Business users
- Pull vs. Push approach to adoption in other areas