NIIMBL
The National Institute for Innovation in Manufacturing Biopharmaceuticals

NIIMBL Roadmapping Workshops: Project Descriptions

- Big Data Analysis for Biomanufacturing
- Robotics / Automation in Bioprocesses

Tuesday, Nov 19th
The Solution Center, 1101 Slater Road, Durham, NC 27703

Report Content

- Executive summary
- Participants
- Facilitators
- Workshop objectives & process overview
- High level agenda
- Project outputs
    - Big Data
    - Robotics and Automation

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Executive summary

- 52 delegates, from 35 organizations representing the biopharmaceutical industry, academia and government agencies met in Durham, NC for a 1-day workshop to develop the project ideas generated in the recent NIIMBL Technical Workshops (TW II and III)

- Two groups worked on the priority topics areas of Workshop
  - Big Data Analysis for Biomanufacturing
  - Robotics / Automation in Bioprocesses

- The big data group split into 5 teams each looking at a separate project
- Robotics group acted as a single team looking at 3 out of 4 projects

- Vision and scope for the projects were developed where necessary
- Deliverables were defined and interdependencies between projects were noted
- 5 Big Data and 2 Robotics projects were significantly advanced and are ready to enter the project writing stage

- All outputs were captured and the majority to that data is presented here. High definition photos and videos can be made available

Workshop Participants (i)

Organization at Campaign Start	Name
Advanced Robotics for Manufacturing	Cara Mazzarini
Amgen	Roger Hart
Applied Biosensors	Prashant Tathireddy
Artesyn BioSolutions USA LLC	Andrew Robinson
Biogen Inc	Saly Romero-Torres
Biogen Inc	Kaschif Ahmed
BioPhorum	Phil Evans
BioPhorum	James Colley
BioPhorum	Graeme Moody
Biospherix Ltd	Randy Yerden
Carnegie Mellon University	Burak Ozdoganlar
Clemson University	Jon Harcum
Clemson University	Sarah Harcum
DoD	Lana Hopkins
Federal Stakeholder: FDA	Jeffrey Baker
Federal Stakeholder: NIST	Kelley Rogers
Federal Stakeholder: NIST	Nenad Ivezic
Federal Stakeholder: NIST	Boonserm Kulvatunyou
Genentech	Govi Sridharan
GlaxoSmithKline	Fausto Artico
GlaxoSmithKline	Mark Polinkovsky
GlaxoSmithKline	Arthur Edge
GlaxoSmithKline	Chays Duraiswami
Janssen Research & Development, LLC	Karin Balss
Janssen Research & Development, LLC	Gene Schaefer
Kaiser Optics	Maryann Cuellar
LAND O'LAKES, INC.	Scott Nieman
Massachusetts Institute of Technology	Richard Braatz

Workshop Participants (ii)

Organization at Campaign Start	Name
Merck	Pamela Meadows
Merck	James Haag
Merck	Jeremy Ramont
Metalytics	Sam Yenne
Metalytics	Eric Cumming
MilliporeSigma/EMD Serono	Joshua Hays
NIIMBL	Chris Roberts
NIIMBL	Ruben Carbonell
NIIMBL	Dan Maiese
NIIMBL	Sheryl Jones
NIST	Serm Kulvatunyou
North Carolina State University	Ryan Barton
Northeastern University	Wei Xie
OAGi	Jim Wilson
ProMechSys-RLP, LLC	Ali Ilhan
ProMechSys-RLP, LLC	Alpay Hizal
Protein Metrics Inc	Eric Carlson
Purdue University	Martin Jun
Quartic.ai	Larry Taber
Rensselaer Polytechnic Institute	Glenn Saunders
Rensselaer Polytechnic Institute	Steven Cramer
Rensselaer Polytechnic Institute	Jason Davis
Sartorius Stedim	Jonas Austerjost
Sartorius Stedim	Robert Soldner
Sartorius Stedim	David Pollard
Southwest Research Institute	Branson Brockschmidt
Southwest Research Institute	Hakima Ibaroudene
The Research Foundation for the State University of New York, on behalf of State University of New York Polytechnic Institute	Susan Sharfstein
University of Delaware	Abraham Lenhoff
University of Massachusetts System	Huolong Liu
University of North Carolina, Chapel Hill	Matthew Verber
Villanova University	Zuyi Huang

The BioPhorum facilitation team

James Colley, NIIIMBL Roadmap Component Facilitator

Graeme Moody, NIIIMBL Roadmap Component Facilitator

Phil Evans, BioPhorum Facilitator

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Workshop objectives and process overview

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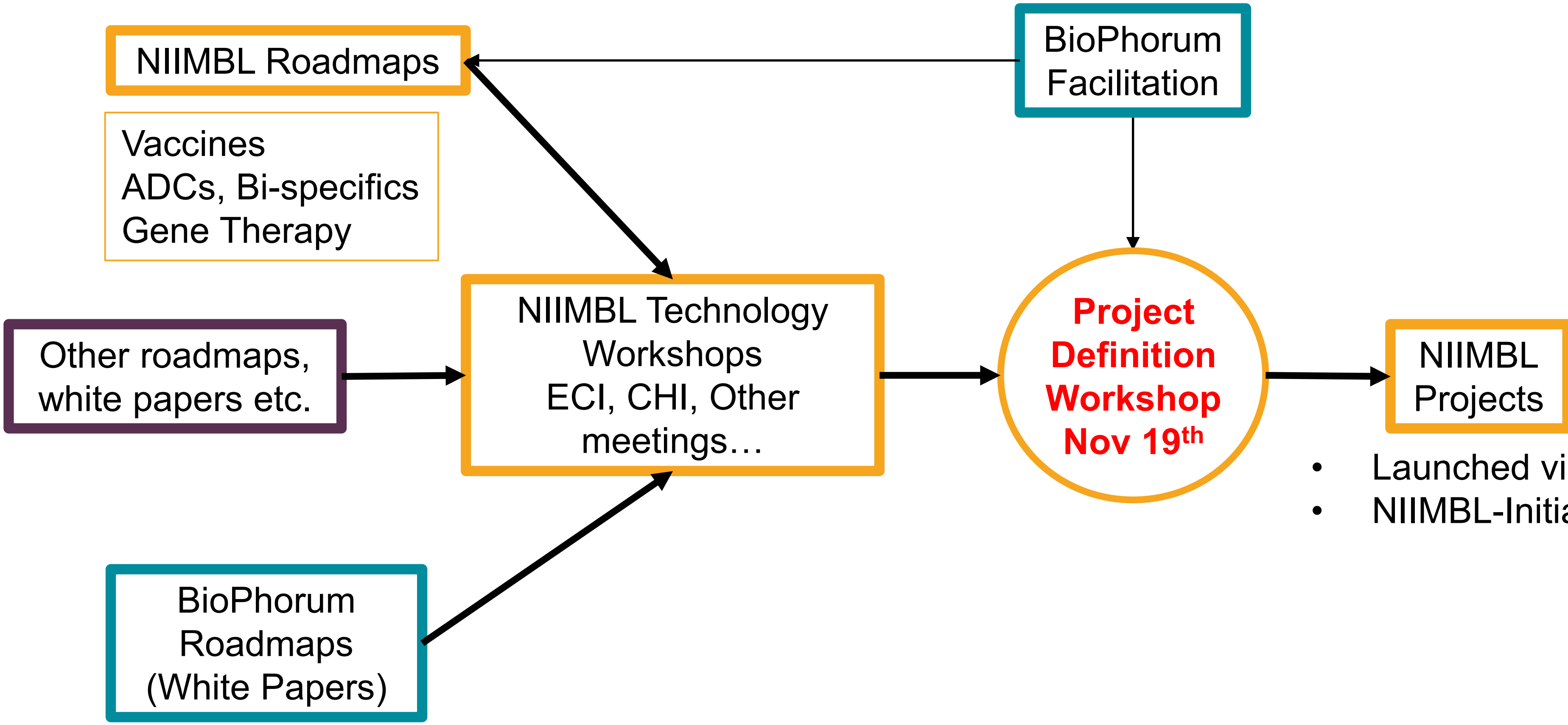
Workshop Objectives

Main goal: Develop the TWII and III project descriptions for NIIMBL to leverage existing investments in platforms and relationships with partner organizations such as ARM

High Level Agenda

Inputs	Agenda	Outputs
• Topic Heatmap exercise	▪ 08:30 Introduction & Welcome ▪ 09:30 - 12:30 Separate working sessions for the Big data and Robotics groups -- 12:30 - 13:00 Lunch --- ▪ 13:00 - 14:00 Continue topic scoping ▪ 14:00 - 15:30 Market place review & final topic selection ▪ 15:30 - 16:00 Next steps & wrap up	▪ Selection of topics for roadmapping ▪ High level topic scoping ▪ Identification of team leads/ members

NIIMBL project definition workshop pathway

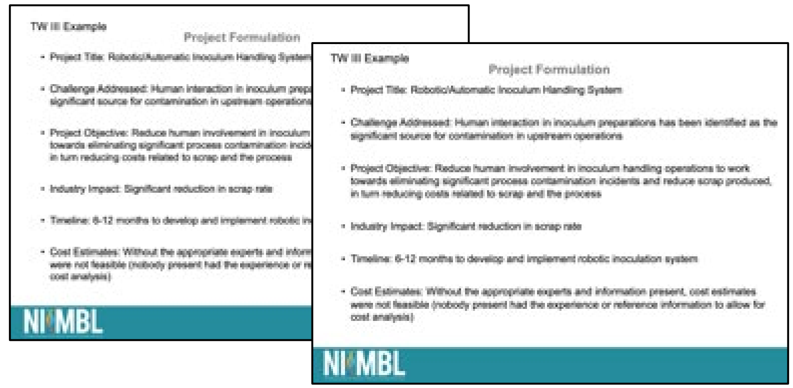


- Launched via RFP
- NIIMBL-Initiated

Workshop process overview

1.Deliverable: Develop the 5 Big Data and 4 Robotics project descriptions

2.Inputs: TWII and III



3.Progress Tracking

	Vision	Concept	Deliverables	Resources	Writing
Pr. 1					
Pr. 2					
Pr. n					

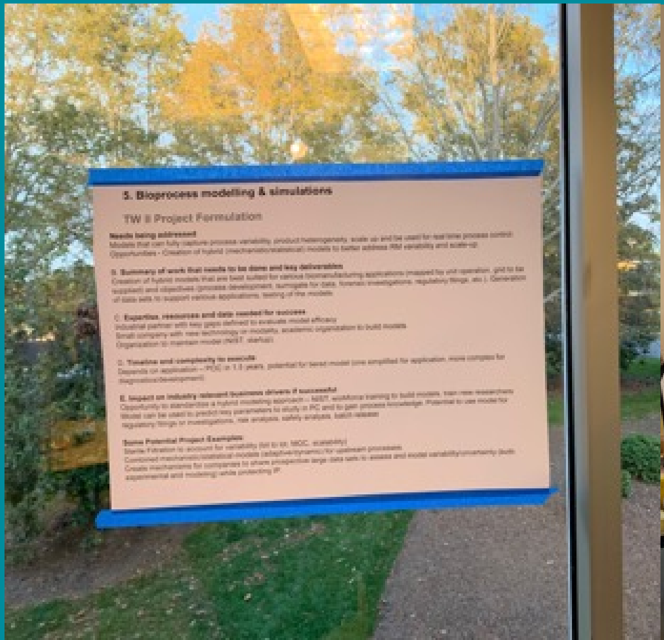
4.Templates

Working Agenda

Time	Item	
08:00 – 08:30	Registration	
08:30 – 09:00	Welcome, Introduction, Ice breaker. (NIIMBL and Facilitation team)	
09:00 – 09:30	Agree starting point for all projects	
09:30 – 10:45	Big Data working session 1 – Vision	Robotics working session 1
10:45 – 11:15	Big Data working session 2 – Vision summaries	Robotics working session 2
11:15 – 11:30	Coffee	
11:30 – 12:30	Big Data working session 3 - Dependencies	Robotics working session 3
12:30 – 13:15	Lunch	
13:15 – 15:00	Big Data working session 4 - Deliverables	Robotics working session 4
15:00 – 15:15	Coffee	
15:15 – 16:00	Big Data working session 5 - Deliverables	Robotics working session 5
16:00	Close Meeting	

Big Data Analysis for Biomanufacturing

Project Outputs



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Big Data

– project development tracker showing status of each project in the morning (AM) and at the end of the workshop (PM)

'?' And inverted 'AM" signifies a lack of clarity in the TWII information

Project concepts for Big Data

Data Standardization and Standardizations

Concept :

- Create an inustry standard for material data such that manual data entry at an OEM can be eliminated
- Enable a barcode system that once scanned retrieves all relevant data
- Achieve provenance use case

Real-time control of CQAs

Concept: Demonstrate robust, repeatable, lights-out operation of a downstream processing sequence consisting of one bioreactor and one other unit operation utilizing the facilities at BTEC

Multivariate sensors / data analytics

Concept :

- Roadmap on how to minimize off-line testing
- Work with Data Standardization, Modelling, RT control of process state to output consistency
- Generate relevant data and model CQA data flows with a bioreactor
- Build a CPV tool that will handle merged data set from a unit operation

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Project concepts for Big data, continued.

Machine Learning applications in biomanufacturing (data generation)

Concept : Generate a comprehensive data package collected for 24-bioreactor-in-parallel setup (ambr) with a series of carefully designed experiments varying multiple variables, observing and analyzing their effects. Work with the Data Standardization and Modelling project teams.

Bioprocess Modelling & Simulations

Concept : Creation of hybrid (empirical & mechanistic) models to better address RM variability and scale-up utilizing the data created by the above project 'Machine Learning applications in biomanufacturing (data generation)'

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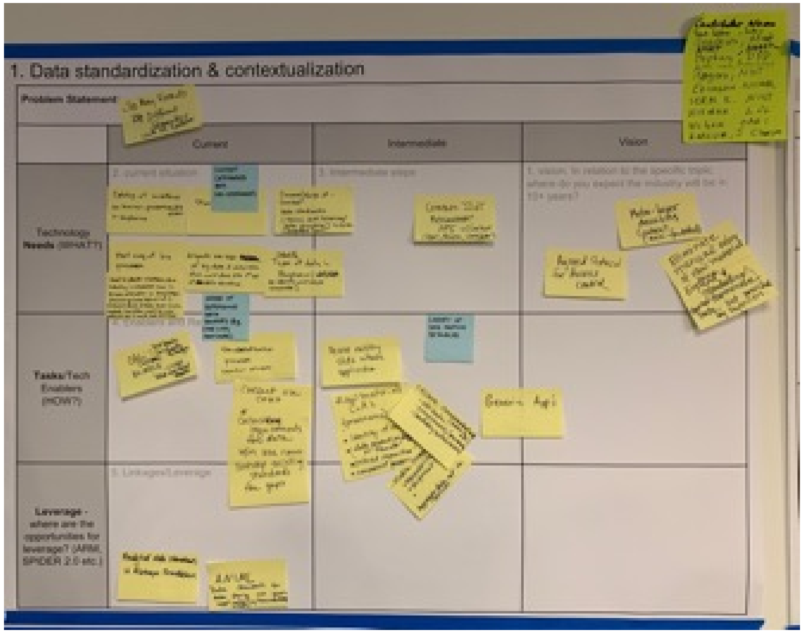
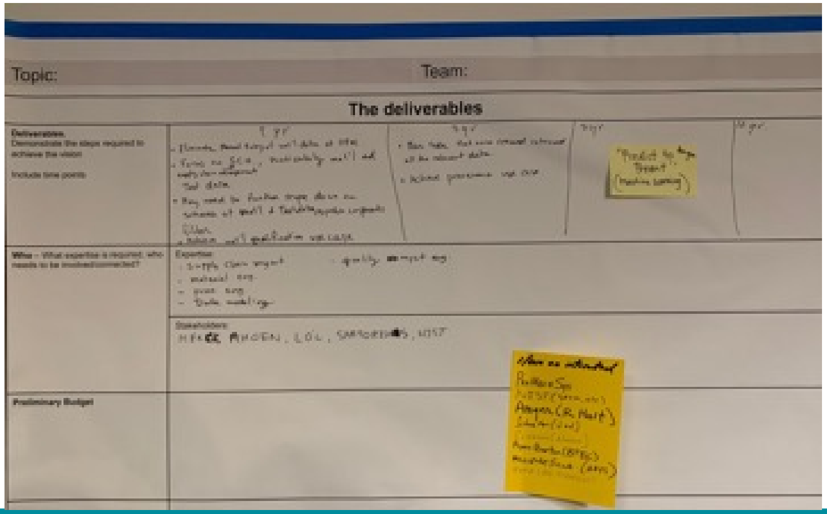
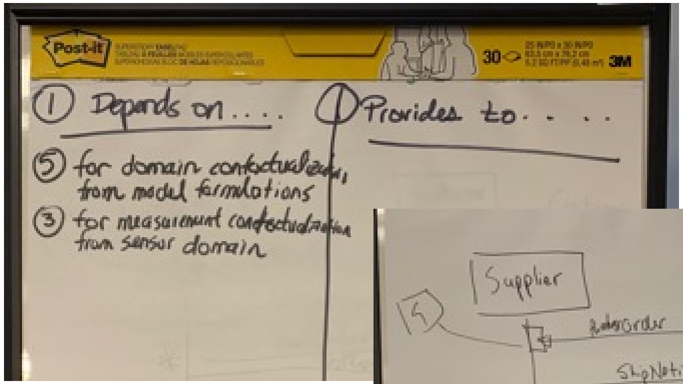
Project 1. Data Standardization & Contextualization

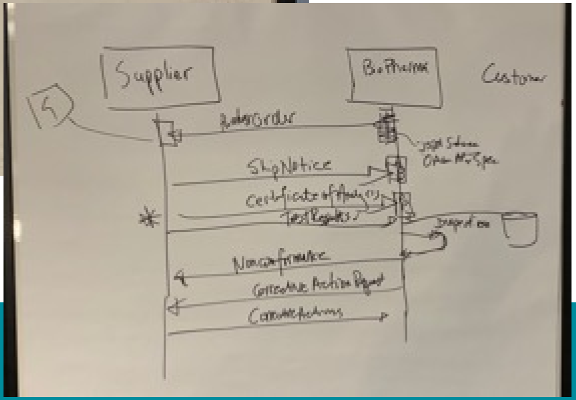
Contributors;

Robert Soldner	Sartorius Stedim
Pamela Meadows	Merck
Roger Hart	Amgen
Lana Hopkins	DOD
Alpay Hizal	ProMechSys
Kelley Rogers	NIST
John Erickson	NIIMBL
Serm Kulvatunyou	NIST
Scott Neiman	Land O'Lakes
Jim Wilson	OAGI
Jon Harcum	Clemson









Project 1. Data Standardization & Contextualization

<table>
<tr><td colspan="4">Problem Statement:</td></tr>
<tr><td></td><td>Current</td><td>Intermediate</td><td>Vision</td></tr>
<tr><td>Technology Needs (WHAT?)</td><td>- Catalogue of workflows or business processes in, biz area biopharma
- Heat map of biz process
- Need to decide whether the industry is interested more in process automation or knowledge discover (via logical inf.)
- Context Categories and sub categories
- Standard landscape
- A specific use case of big data & automation that would drive the 1st set of data standard
- Common curated Repo of - data standards [terms and schemes/data structure] in syntax independent form
- Different kinds of data standards maybe needed. The latter might be more difficult b/c it would need ontology
- Index of reference data sources (e.g. code lists, identifiers)</td><td>- Common industrial IoT measurement API w/context (Asset, process, work etc.)</td><td>- Agreed Protocol for access control
- meta-layer describes context (multi-faceted)
- Eliminate manual entry of raw material data
- Enrich & expand raw material (standardize/Harmonize) data set provided by suppliers.</td></tr>
<tr><td>Tasks/Tech Enablers (HOW?)</td><td>- OAGI; test results, certificates of Analysis MIMSOA
- CCOM DSA registered assets
- Standardization process curation process
- Collect use cases.
- Collect requirements for data w/in use cases survey existing standards for gaps</td><td>- Use existing standards where applicable
- Raw material CoAs….(provenance).
- identity of materials. Data protection/assurance on transfer. Critical impurities. Component Provenance
- Library of data mapping resources
- Media components. - traceability (to originated) - shipment temp.
- Aggregate data set in barcode……
- ? Filters: (compounded mat) - attribute (porosity etc.) - components/provenance - leachable/extractables
- Generic apps</td><td></td></tr>
<tr><td>Leverage - where are the opportunities for leverage? (ARM, SPIDER</td><td>- Analytical data standards in allotrope foundation
- ANIML Data standout for data sharing and generic applications/documentation analytics</td><td></td><td></td></tr>
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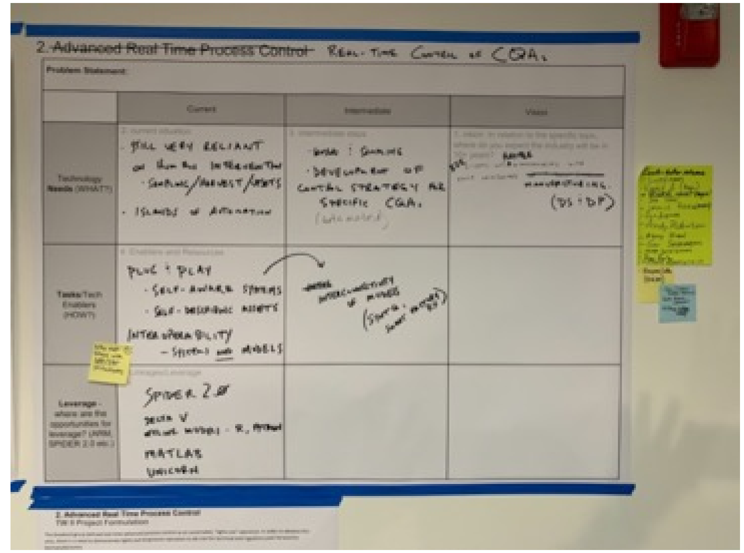
Project 1. Data Standardization & Contextualization

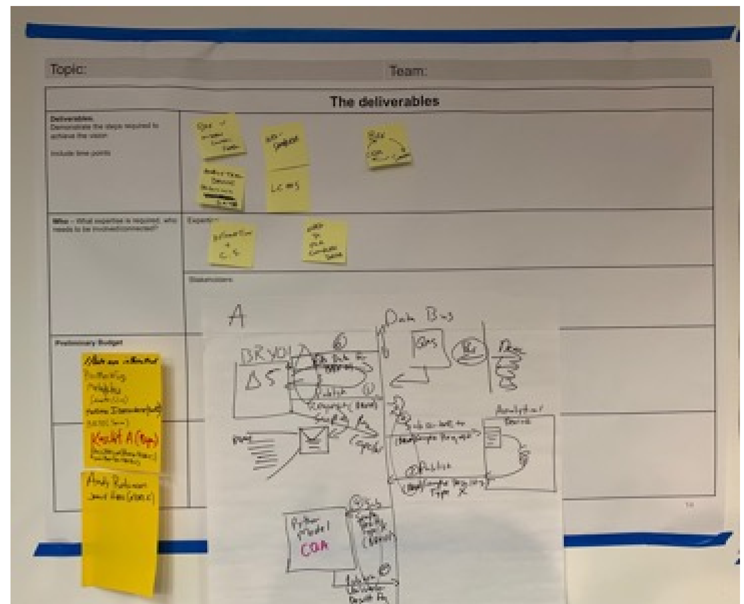
The deliverables			
	1 Year	3 Year	5 Year
Deliverables. Demonstrate the steps required to achieve the vision Include time points	Eliminate Manual entry of material data at OEM. Focus on SCM., particularly material and supply chain management. May need to further scope down on sub area of material & test data e.g. media components filter. Achieve material qualification use case.	Bar code that once scanned retrieved all the relevant data. Achieve provenance use case	"predict to prevent" (Machine learning) Amgen
Who – What expertise is required, who needs to be involved/connected?	Expertise: Supply chain management, material eng. Proc. Eng. Data modelling. Quality management eng.		
	Stakeholder: Merck, Amgen LOL, Sartorius, NIST		

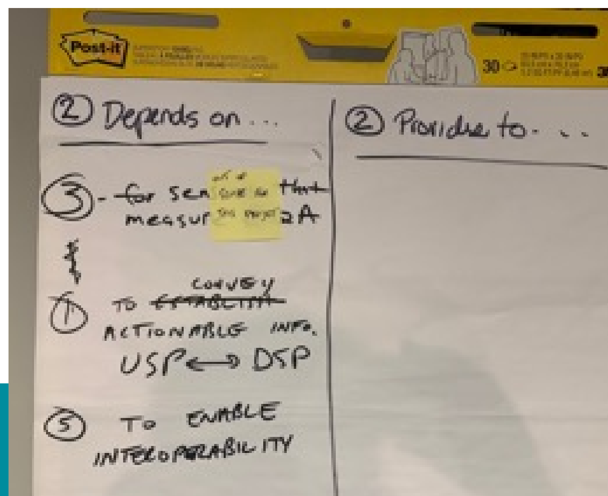
Project 2. Real-time control of CQAs (formerly Advanced real-time process control)



Contributors;

Scott Neiman	Land O'Lakes
Kaschif Ahmed	Biogen
Josh Hays	MilliporeSigma/EMD Serono
Jamie Haaag	Merck
Sam Yvenne	Metalytics
Andy Robinson	Artesyn BioSolutions
Alpay Hizal	ProMechSys
Govi Sridharan	Genentech
Chaya Dvraiswani	GSK
Ryan Barton	NC State. BTEC
Richad Braatz	MIT
Maryan Cullen	Kaiser Optics
Eric Carlson	Protein Metrics
Sarah Harcum	Clemson Uni
Arthur Edge	GSK





Project 2. Real-time control of CQAs (formerly Advanced real-time process control)

Problem Statement:

	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	- Still very reliant on Human intervention. Sampling/Harvest/Upsets - Islands of automation	- sensors : sampling - development of control strategy for specific CGAs (automated)	- E2E - Lights out flexible manufacturing with fully integrated manufacturing. (DS : DP)
Tasks/Tech Enablers (HOW?)	- Plug & play. - Self aware systems. - self describing assets - Interoperability - systems and models - Pr 1 Comment: why not start with S88/S95 structures	- Interconnectivity of models (SYNT Q, smart factory Rx)	
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)	- Spider 2.0 delta V offline models - R, Python - Matlab - Unicorn		

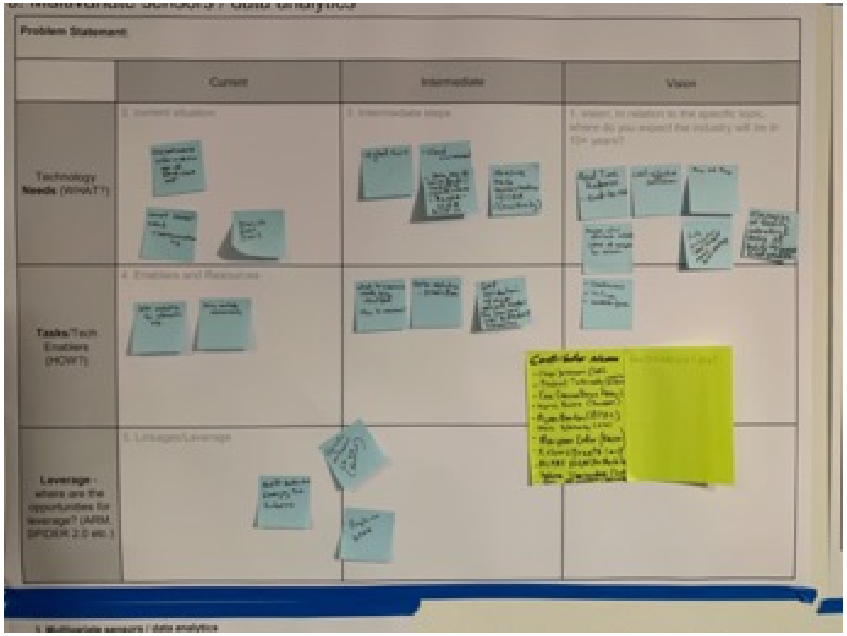
Project 2. Real-time control of CQAs (formerly Advanced real-time process control)

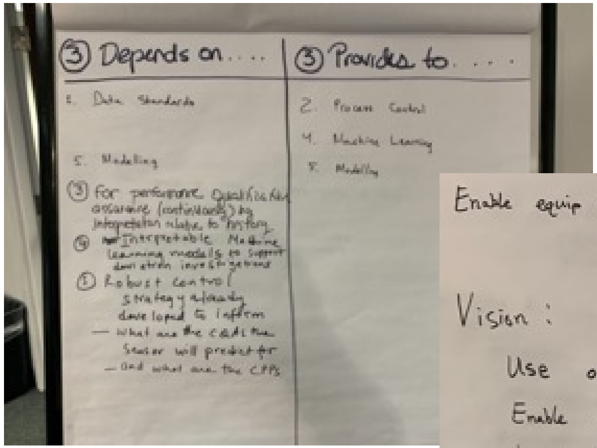
The deliverables			
Deliverables. Demonstrate the steps required to achieve the vision Include time points	- BRX w1 modern control system - Analytical device producing data - Autosampler - LCMS - BRX > Sample > CQA > BRX > …		
Who – What expertise is required, who needs to be involved/connected?	- Automation + C.S. - Need P: for complex data		
Preliminary Budget			

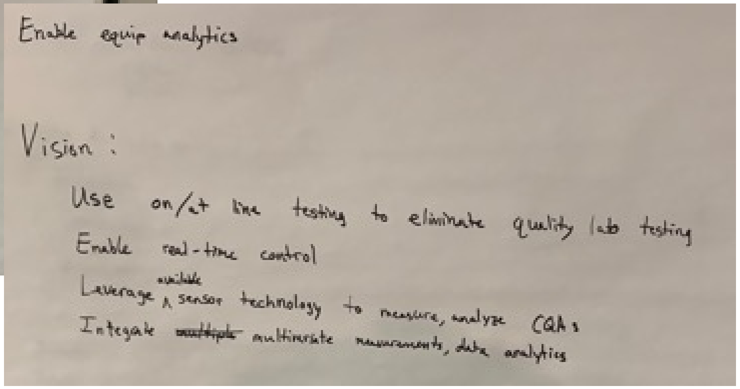
Project 3. Multivariate sensors / data analytics

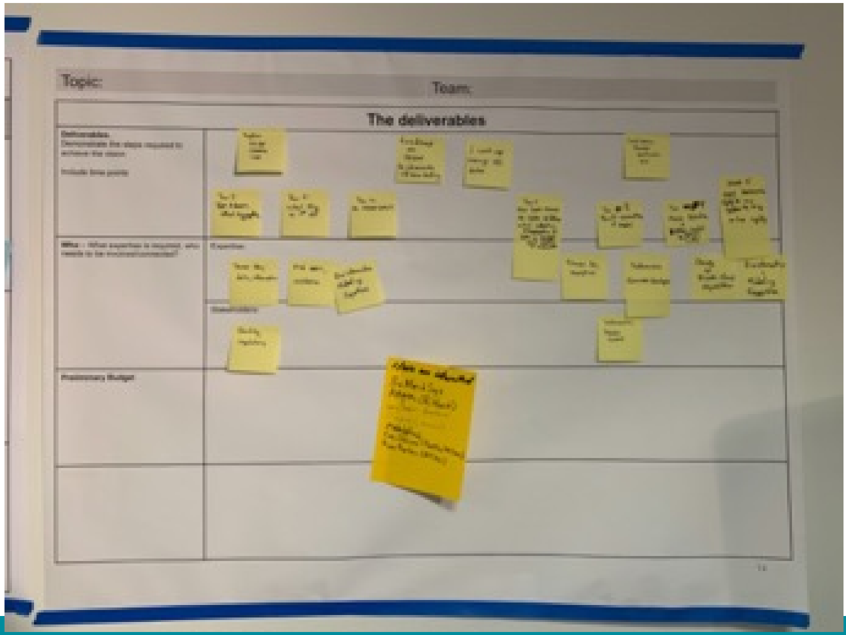
Contributors;

Chaya Duraiswami	GSK
Prashant Tathireddy	Applied Biosensors
Eric Carlson	Protein Metrics
Karin Balss	Janssen
Ryan Barton	NC State. BTEC
Mark Polinkovsky	GSK
Maryann Cuellar	Kaiser Optical
Richard Braatz	MIT
Alpay Hiza	ProMechSys
Hakima Ibaroudere	SwRI
Govi Sridharan	Genentech









Project 3. Multivariate sensors / data analytics

Problem Statement:

	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	- Discontinuous information, one off, stand alone - Unmet sensor need - contamination e.g. - Discrete QMS (silos)	- digital twin - cloud environment - data has to have (data) integrity requirements – ALCOA - CCEA built in - Measure trace concentration of CQA (sensitivity)	- real time release - end to end - measure actual attribute (CQA) - instead of surrogate for release - cost effective solution - fully integrated QMS designed around control strategy - plug and play - Elimination of quality laboratory testing. All testing via sensor in/at process
Tasks/Tech Enablers (HOW?)	- Data analytics for information only - Using available measurements	- what to measure needs to be identified - How to measure? - data analytics – prediction - GMP validation of multi variate model the sensor uses to predict outcomes	- Continuous - in-line - contact-free
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)	- Health authorities - Emerging tech initiatives	- Specific initiatives like e.g.(Sentinel) - BioPhorum	

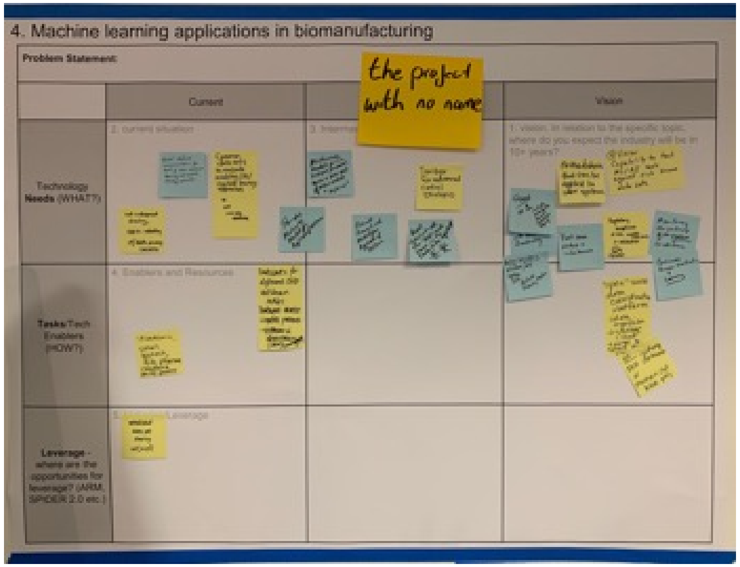
Project 3. Multivariate sensors / data analytics

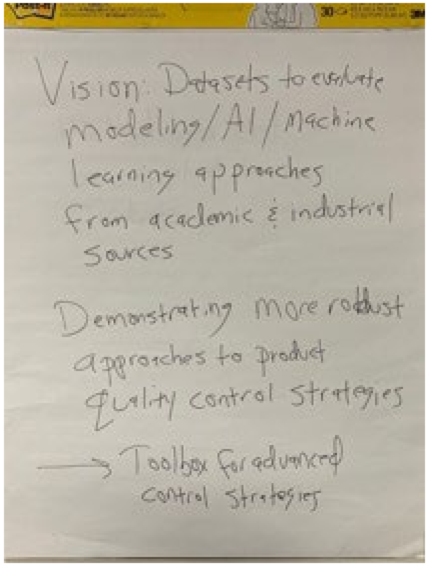
The deliverables			
	1 Year	3 - 4 Year	5 Year
Deliverables. Demonstrate the steps required to achieve the vision Include time points	- Replace DS/DP identity test - Year 1: MAP DATA FLOWS - ID CQAs to follow initial collection & aggregation & data in model unit operation or bioreactor - Year 1: Test & Learn - Initial algorithm	- Year 3. Build connections & model - Year 4 - Make prediction, Offer control to Project #2 - Roadmap on HOW to eliminate offline testing	- 1 unit op merge all data - Year 5: Make prediction - Apply to new system to bring online rapidly - Year 5: Initial filing on first API - Year 10: NO MORE GELS!
Who – What expertise is required, who needs to be involved/connected?	- Sensor devs, data informatics	- End users, validation - Bioinformatics - Modelling expertise	- Process dev, Analytical - Informatics - sensor developers - Cloud vs private cloud capabilities - Bioinformatics & modelling expertise
	- Quality, regulatory		
Preliminary Budget			

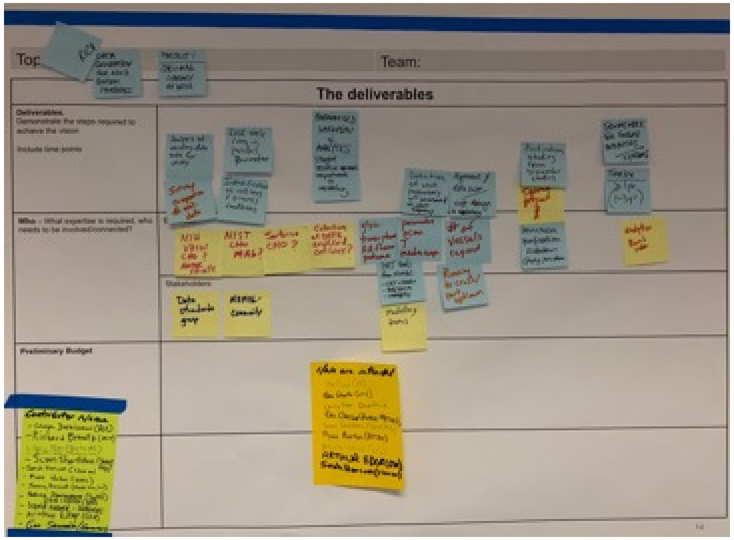
Project 4. Machine Learning (ML) applications in biomanufacturing

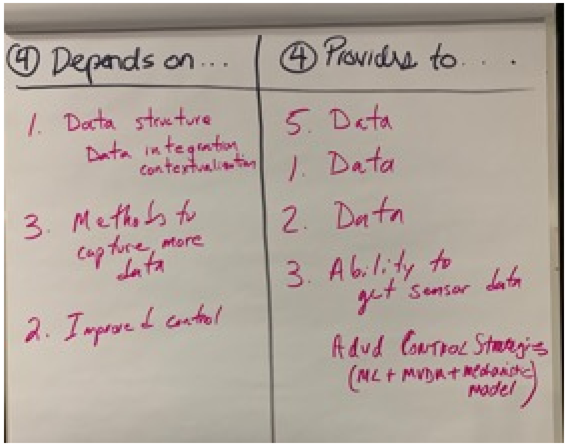
Contributors;

Chaya Duraiswami	GSK
Richard Braatz	MIT
Larry Taber	Quartic.ai
Alpay Hizal	ProMechSys
Susan Sharfstein	SUNY Poly
Sarah Harcum	Clemson
Matt Verber	UNC
Jeremy Ramant	Merck + Co Inc
Hakima Ibarroudere	SwRI
Steve Cramer	RPS
David Pollard	Sartorius
Arthur Edge	GSK
Govi Sridharan	Genentech









Project 4. Machine Learning (ML) applications in biomanufacturing

Problem Statement:			
	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	- Need defined success criteria for levels of more advanced learning and control strategy execution - Not widespread sharing, esp. in industry IP/data, privacy concerns - Common datasets to evaluate modelling/AI/machine learning approaches ex: NIH RNAseq database	- Mechanistic models for C&G biological process as a base set of AI/ML models - "Hybrid" - Overall hierarchical model for application of AI/ML - Toolbox for advanced control strategy - Must include all the additional needs shown on the charter to the left ****	- Goal = 1 - multiple participants to move industry & agency - Process control - Product Control Strategies are augmented with AI/ML functionality - Active learning machine/AI cycles - Reliable training models - Methodologies that can be applied to new systems - Root cause analysis is instantaneous - Continuous process verification & learning - 4 Vision: Capability to test ML/AI tools against rich known datasets - Regulatory acceptance of ML models and data sharing and validation (picture of smiley face) regulator - Monitoring the entirety of the system for all time
Tasks/Tech Enablers (HOW?)	- Academic, small biotech, Big pharma company participants - Data sets for different CHO cell lines and mAbs - Data set across complete process - upstream & downstream chromatography (ctoin)		- Open source data coordination platform => data ingestion => storage cloud portal to share analysis visualisation ex. RNAseq NIH database or human cell atlas project
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)	- Established data set sharing ex: (NIH)		

Project 4. Machine Learning (ML) applications in biomanufacturing

- Rich Data Generation for ADVD control strategies

- **Project 1: CHO & mAb library of data**

The deliverables			
- Timeline >= 1 yr (1-3 yr)			
Deliverables. Demonstrate the steps required to achieve the vision Include time points	- Analysis of existing data sets for utility - Survey companies for avail data	- Harmonized workflow & analytics staged iterative approach - experiments to modelling - Definition of what parameters will be measured at what frequency - alignment of data size/expt design with modelling	- purification studies from bioreactor studies - separate project $ - Downstream purification scaled own - (phytip, minicolumn) - Framework for future modalities/systems
Who – What expertise is required, who needs to be involved/connected?	- NIH VRCO/CHO AMBIC ref cells - NIST CHO mAb? - Sartorius - CHO?	- glyco. Transcriptome, AA fluxes, proteome - PAT tools from NIMBL - clef = intabio - 908 device – metalytics - Parameters osmo T media comp. - # of vessels required - running to crash past optimum	- Analytics round robin
	- Data standards group - NIIMBL community	Modelling teams	
Preliminary Budget			

Project 5. Bioprocess Modelling & Simulations

Contributors;

Chaya Duraiswami	GSK
Richard Braatz	MIT
Larry Taber	Quartic.ai
Alpay Hizal	ProMechSys
Susan Sharfstein	SUNY Poly
Sarah Harcum	Clemson
Matt Verber	UNC
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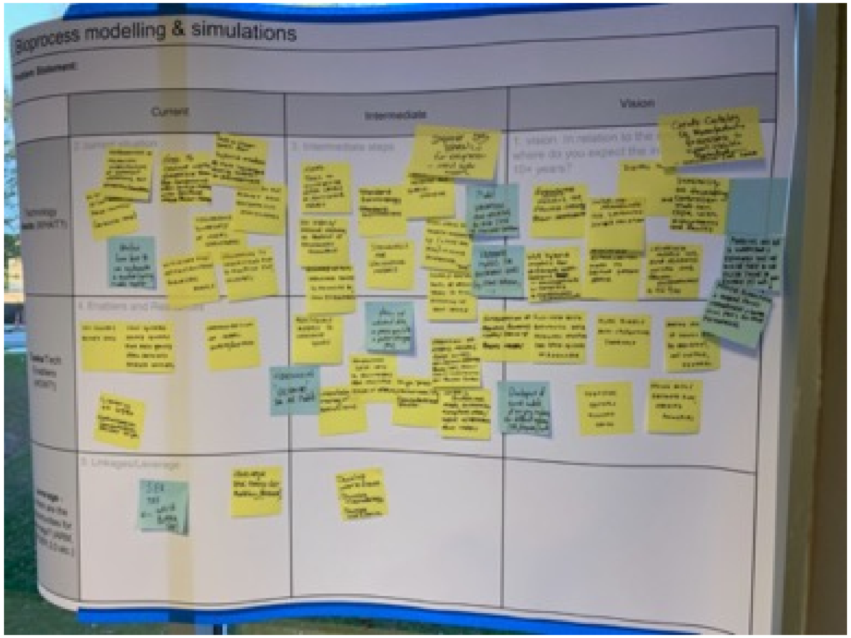
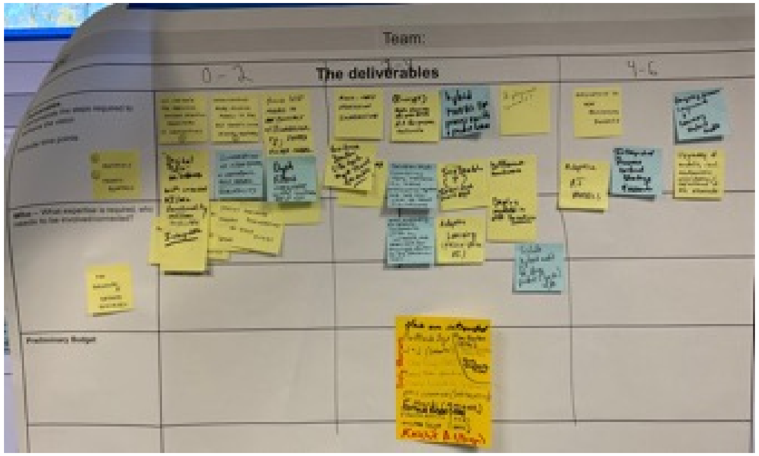
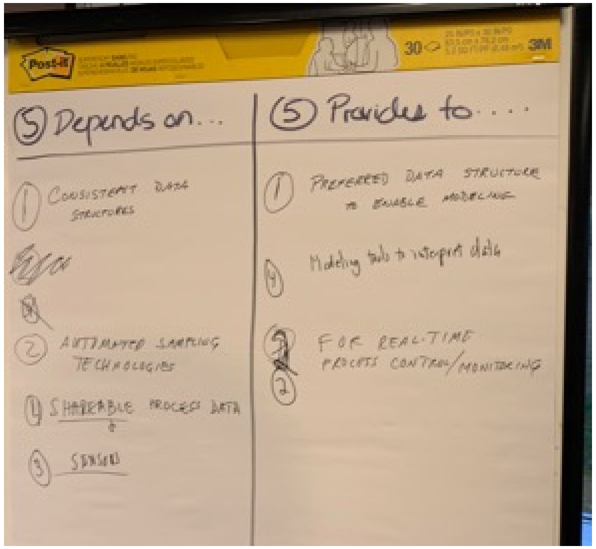
Saly Romero-Torres	Biogen
Fausto Artico	GSK







Project 5. Bioprocess Modelling & Simulations. **Part 1. Current to Intermediate**

	Current			Intermediate			
Technology Needs (WHAT?)	Heterogeneity of mechanistic understanding of different operations esp. upstream/ downstream	Need to define useful interface between pre-competitive open source models with bespoke unique product models	1. Not a clear path for hybrid models. 2. not leveraged during control or development	Need: tools to integrate across levels in multiscale models		Improve OMG BPMN 2.0 for subprocess - need better support	connect multiple units of operations to discover hierarchy of root causes
	No Holistic view of the manufacturing process (no digital twin)	Tremendous diversity of model structures	Models do not always have mechanistic explanations	Use Hybrid/machine learning in absence of mechanistic knowledge	Standard terminology Standard expectations	standardize methods for coarse-graining	mode validation and updating in real-time
	Unclear how best to use mechanistic and machine learning models together	no plug and play infrastructure for AI/ML models	challenging to understand how to minimize experiments	Discovery of more important causes to prioritize design experiments	standards for validating models	start small and grow organically (->plug and play) to reach framework 'goal'	separate models for different goals (e.g. Fault detection, …)
Tech Enablers (HOW?)	HCP Cluster Big Data ENVs	Silos systems. Legacy systems Poor Data Quality Small Data sets incomplete data sets	Harmonization of model Inputs/Outputs	Multiscale models to integrate levels	obtain and understand data on process variability & product heterogeneity (#4)	Creating of hybrid models best suited for various objective process Dev, product quality investigational Int. Process Control	
				Harmonizing 'vocabulary" for AI models	Generating data sets to test models from multiple scales o operation		
	Libraries of ODEs Optimization computation power High			Knowledge Management solutions	High process observability Computational power	Hybrid bioreactor model integration mixing/mass Xfer/shear w/metabolic flu models	
Leverage Opportunity	See the white board	Leverage total process cost modelling (BioSolve)		Develop workflows. Develop methodology Develop workforce			

Project 5. Bioprocess Modelling & Simulations **Part 2. Vision (long term)**

	Vision			
Technology Needs (WHAT?)	Hybrid models for process variable product heterogeneity	digital twins	Create catalogue of manufacturing process to support flexible manufacturing - understand root cause	modelling will be so understood & developed that we will be able to se digital twins to enable PD with minimal experiment and ongoing process improvement & control using fully (?) in-silico methods
	Use hybrid models for different applications. 1 - development 2 - controls 3 - continuous improvement	modelling framework for defining interrelationships	possibility of developing controller that can cope with disturbances and faults	
		minimize experimental work to define design space	leverage models for both advanced control and process improvement in real time	
Tech Enablers (HOW?)	Integration of process economics & supply chain of process models	Full view with automatic data pipelines updating the data systems in real-time	Adding sensors if causes point to important, not capture, features	
	Development of tiered models of varying complexity for different applications (PD, Diagnostics, Manufacturing)	AI/ML models auto-improving themselves	cognitive systems discovery causes	
		cognitive systems discovery causes	strong data/software engineering principles	
Leverage Opportunity				

Project 5. Bioprocess Modelling & Simulations

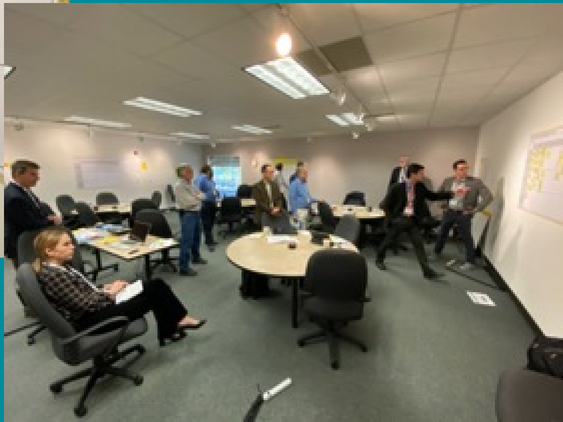
The deliverables			
	0 - 2 Year	2 - 4 Year	4 to 6 Year
Deliverables. Demonstrate the steps required to achieve the vision Include time points	- 1.Get the data TRV classical feature selection algorithms => correlations - 2. Infrastructure AI/ML existing models to predict targets using selected features - Build DSP models to connect of bioreactor e.g. depth filter model - 'Digital twin" milestones with embedded AI/ML functionality real time deployable - Integration of hydrodynamic & metabolic flux models. Scalability - Depth filters integrate with bioreactor end of run - Sensors and AI/ML	- Multi-unit operations integration - (encrypt) open source to members for purpose, tailorable - Hybrid models for process variables and product hetero. - A physical contract? - Guidance doc for life cycle management thereof of the models - Solution that combines many mechanistic ordinal differential equations and let the user to select the relevant ones depending on process constraints with a wizard and then ask for the right data to fit parameters - Best unit op modelling library - Scalable (?) Individual unit ops - Different hardware - adaptive learning (prescriptive AI) - Deploy model if different locations - Scalable hybrid models for drug product (lyo. Etc) UF,DR	- Applications to new biologic products - Adaptive AI models - Integrated process control strategy exe????????? - Ongoing process improvement and learning hybrid models - Upgrading of model incl. mechanistic elucidation/replacement of ML elements
Who – What expertise is required, who needs to be involved/connected ?	- Machine learning SMEs and APC enginesers - Data engineer HPC expert - Software engineer engine expert - Data modeller cluster administrator - Statistician program manager informatics - 1. Materials. 2. Process dynamics and hardware and software resources		
Preliminary Budget			

Robotics / Automation in Bioprocesses

Project Outputs

Contributors:

Glenn Sanders	RPI
Cara Mazzarini	ARM
Jason Davis	RPI
Randy Yerden	BioSpherix
Branson Brockchmidt	Southwest Research Institute
Burak Ozdoganlar	ARM
Martin Jun	Purdue University
Jeff Baker	FDA
Matthew Verber	Univeristy of NC
Ali Ilhan	ProMechdys
Kaschif Ahmed	Biogen Inc.
Robert Soldner	Sartorius Stedim
Jonas Austerjost	Sartorius Stedim
Saly Romero-Torres	Biogen



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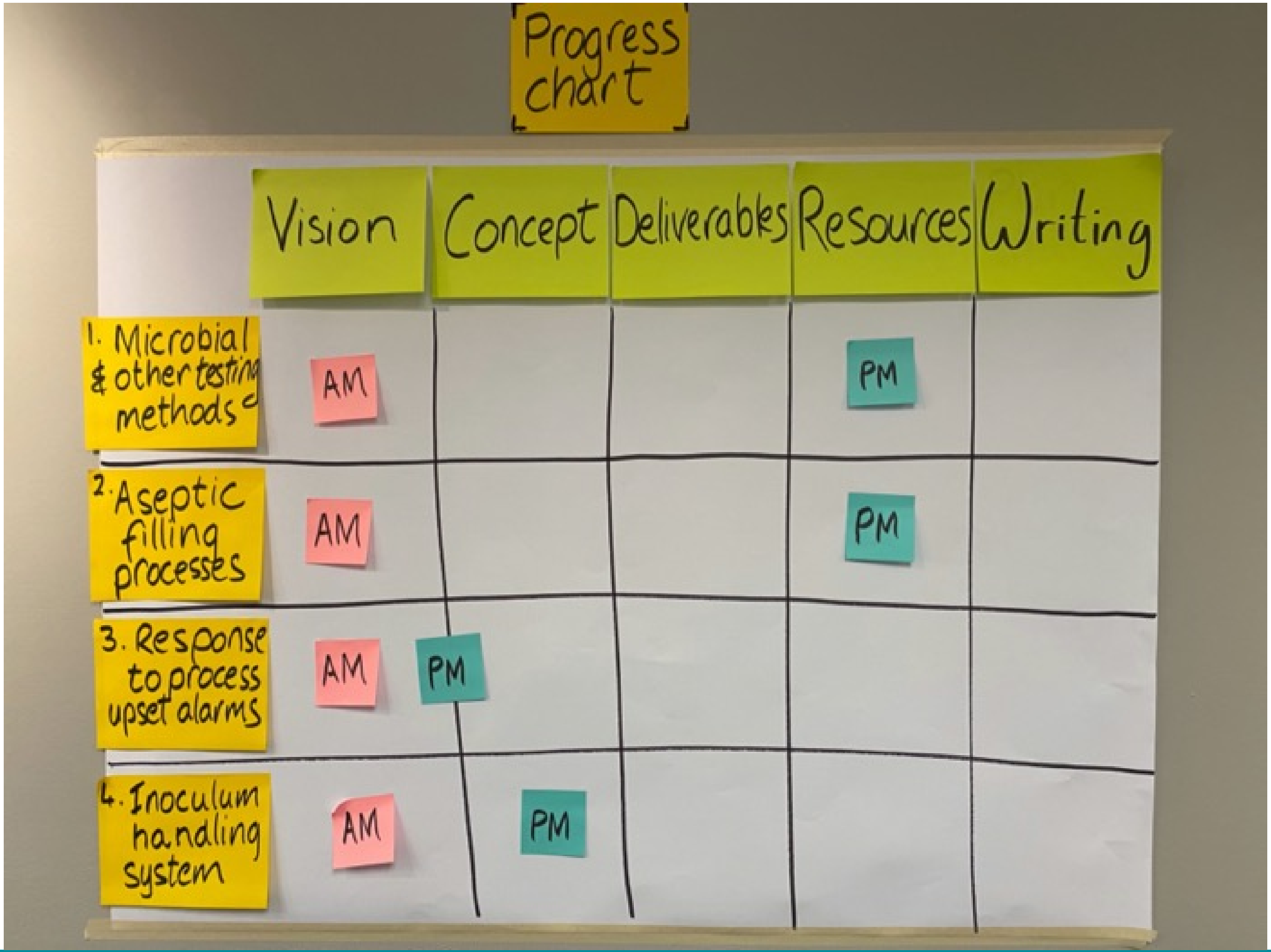
Robotics

– project development tracker showing status of each project in the morning (AM) and at the end of the workshop (PM)



Project concepts for Robotics / Automation in Bioprocesses

Robotic Sampling

Concept: To develop and adapt robots capable of precise and high-integrity sampling for, e.g., environmental monitoring, cleaning validation, (raw) materials sampling, and fill/finish processes. The functions of robotic sampling includes sample acquisition, data collection/documentation, sample preparation for testing, packaging, labeling, and handling/delivery of sample to the tests.

Robot Assistance for Fill/Finish

Concept : To develop and adapt robots that (minimize or) eliminate human intervention in fill/finish (FF) processes by taking corrective action (and to detect?) as a response to process fault events (such as a broken vial) and to perform instrument calibration and alignment. Such robots could support initial setup of the FF system and will be flexible to address different applications (e.g., volume, throughput).

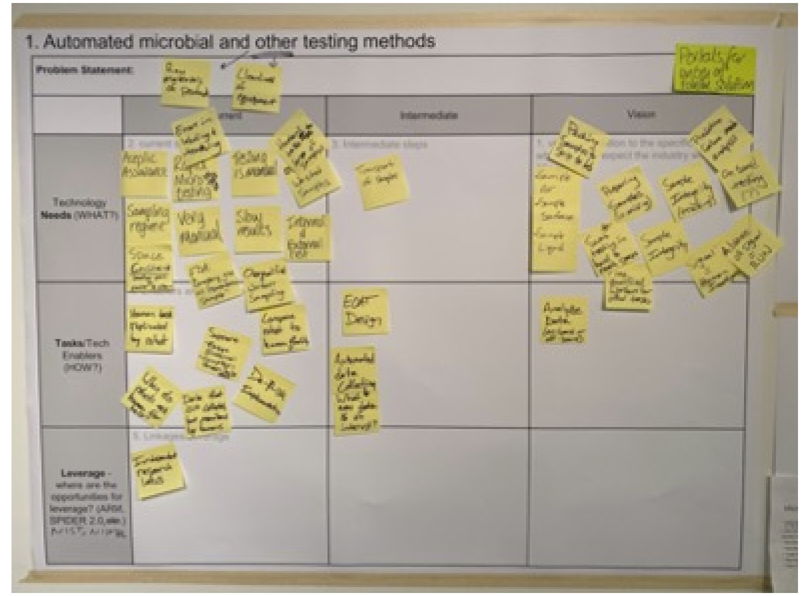
Robotic Inoculum Handling

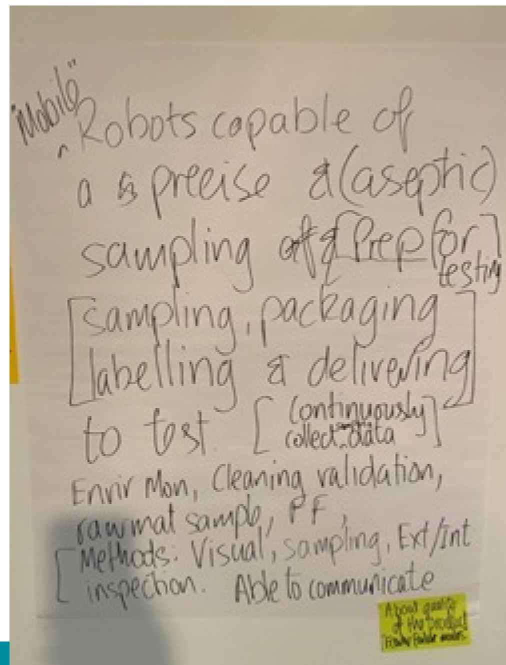
Concept : To develop and adapt robots that perform aseptic handling (e.g., liquid extraction, liquid injection, liquid transfer) between the expansion steps during the inoculum production for monoclonal antibodies.

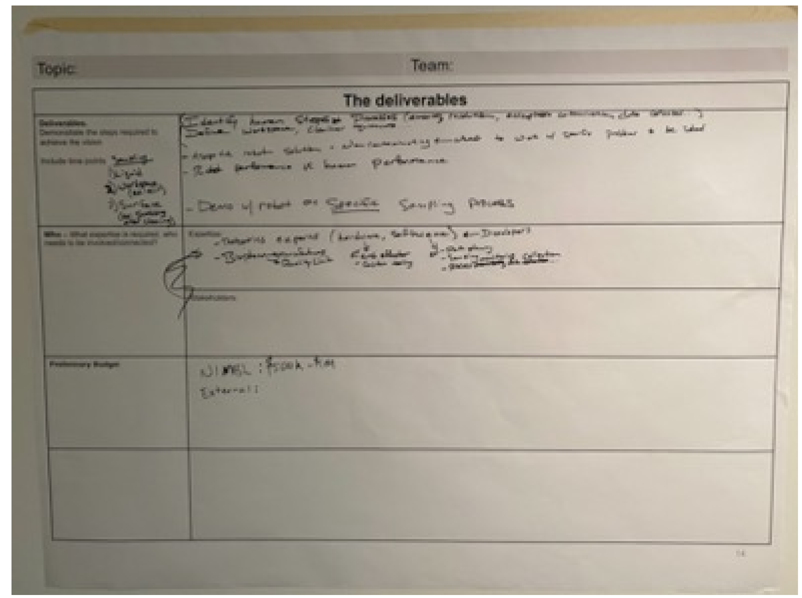
1. Robotic microbial and other (raw material, product and equipment cleanliness) testing

Contributors;

Burak Ozdoganlar	Carnegie Melon University
Branson Brockchmidt	South West Research Institute
Martin Jun	Purdue University
Matthew Verber	University of NC
Jeff Baker	FDA







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1. Robotic microbial and other (raw material, product and equipment cleanliness) testing

Problem Statement:			
	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	No aseptic assurance, variable sampling regime, very manual, slow results, overqualified workers sampling. Space constraints- smaller space easier to clean. Errors in labelling and tracking. Limited uptake of rapid micro testing. No aseptic assurance, variable sampling regime, very manual, slow results, overqualified workers sampling. FDA: “Company, give us representative sample”	Transport of samples	Sample air, surfaces and liquids. Swab testing in hard to reach spaces, sample integrity and tracking, predictive failure mode analysis, on board testing?, Signal/no signal = human interaction/run, prepare (and pack) samples for test- free up qualified workers for other tasks
Tasks/Tech Enablers (HOW?)	Human tasks replicated by robot. Compare robot to human quality. De-risk implementation. Define data that isn’t collected but monitored by humans. Define when robots ask humans for help. Support: Easy= internal, complex = vendor helpdesk	EOAT design, automated data collection (define data of interest)	
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)	Independent research labs Define portals for entry of robotic solutions		

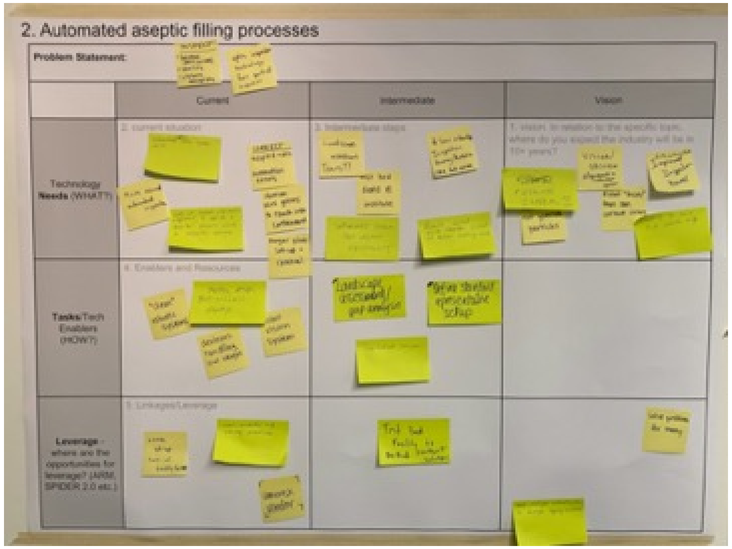
1. Robotic microbial and other (raw material, product and equipment cleanliness) testing

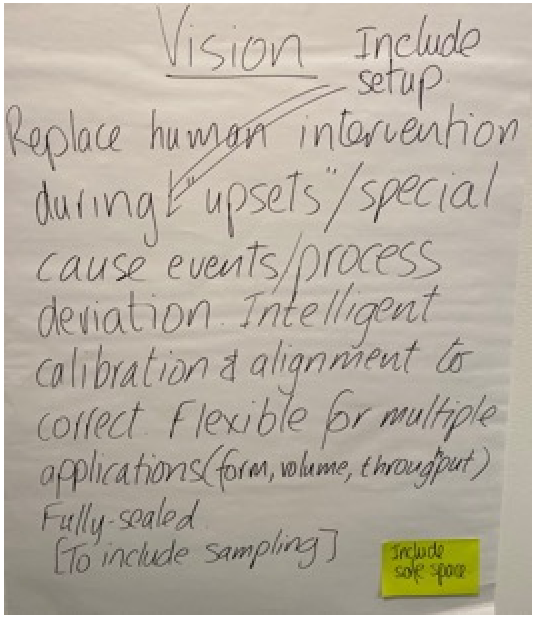
The deliverables		
Deliverables. Demonstrate the steps required to achieve the vision Include time points	Identify human steps and processes (amounts, resolution, acceptable contamination levels, what data to collect) Define workspace and cleanliness needs… Aseptic robotic solution and non-contaminating (to work with specific problems to be solved) Robot v human performance Demo with robot on specific sampling process	
Who – What expertise is required, who needs to be involved/connected?	Expertise: Robotics experts: hardware developers- eg. End effector, custom testing software developers- eg. Path planning, sensing, process monitoring and collection Biomanufacturers snd quality unit	
	Stakeholders:	
Preliminary Budget	NIIMBL: $500k-$1M External: tbc	

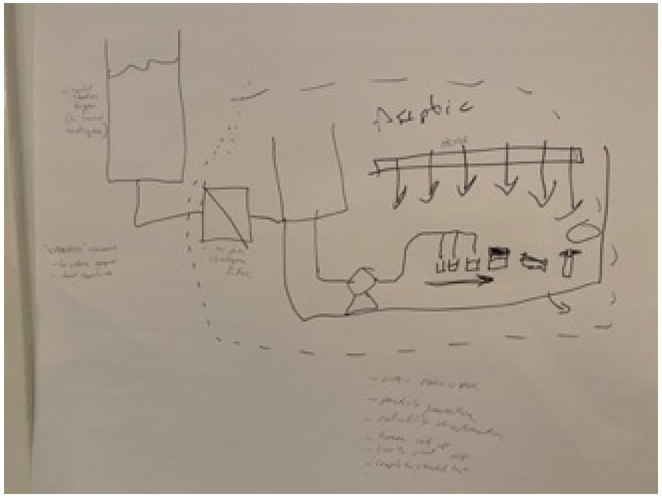
2. Automated aseptic filling processes

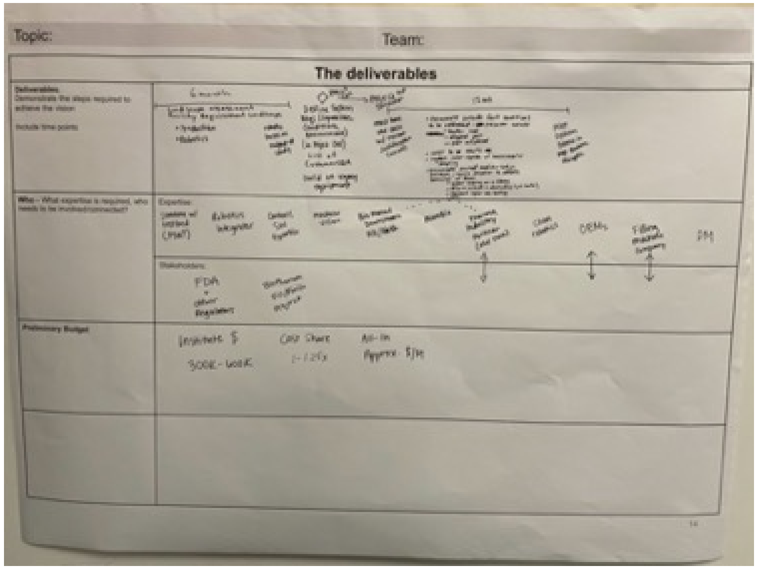
Contributors;

Glenn Saunders	RPI
Caraa Mazzarini	ARM
Jason Davis	RPI
Randy Yerden	Biospherix Ltd









2. Automated aseptic filling processes

Problem Statement: INSPECT: - spectral articulates - sterility - closure integrity. optic inspection technology for particle inspection			
	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	- automated aseptic filling systems exist - lots of human intervention required to set up + monitor process inside an aseptic volume - CORRECT. Toppled vials, automation errors - Human uses gloves to reach containment - angular plate setup & removal	- Landscape assessment tours?? - upgrade systems for legacy equipment - test bed demo @ institute - Semi automated inspection Human/Robotic like 2nd opinion - remote control inside chamber instead of human reaching inside	- absolute closer end to end - robot does not generate particles - vision driven alignment & calibration system - Robot "inside" that can correct issues - Fully automated Improved Inspection process - Flexibility for low + high volume mfg
Tasks/Tech Enablers (HOW?)	- "clean"; robotic systems - Model after best in class VanRx - dexterous handling low weight - robot vision system	- Landscape assessment gap analysis - standardized subsystems - define standard representative setup	
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)	- NIIMBL setup tours of facility for ARM - semi-conductor mfg industry practices - vanerex vendor	- Test bed facility to de risk intelligent solutions	- more intelligent automation/robotics to leverage legacy systems - solve problem for many

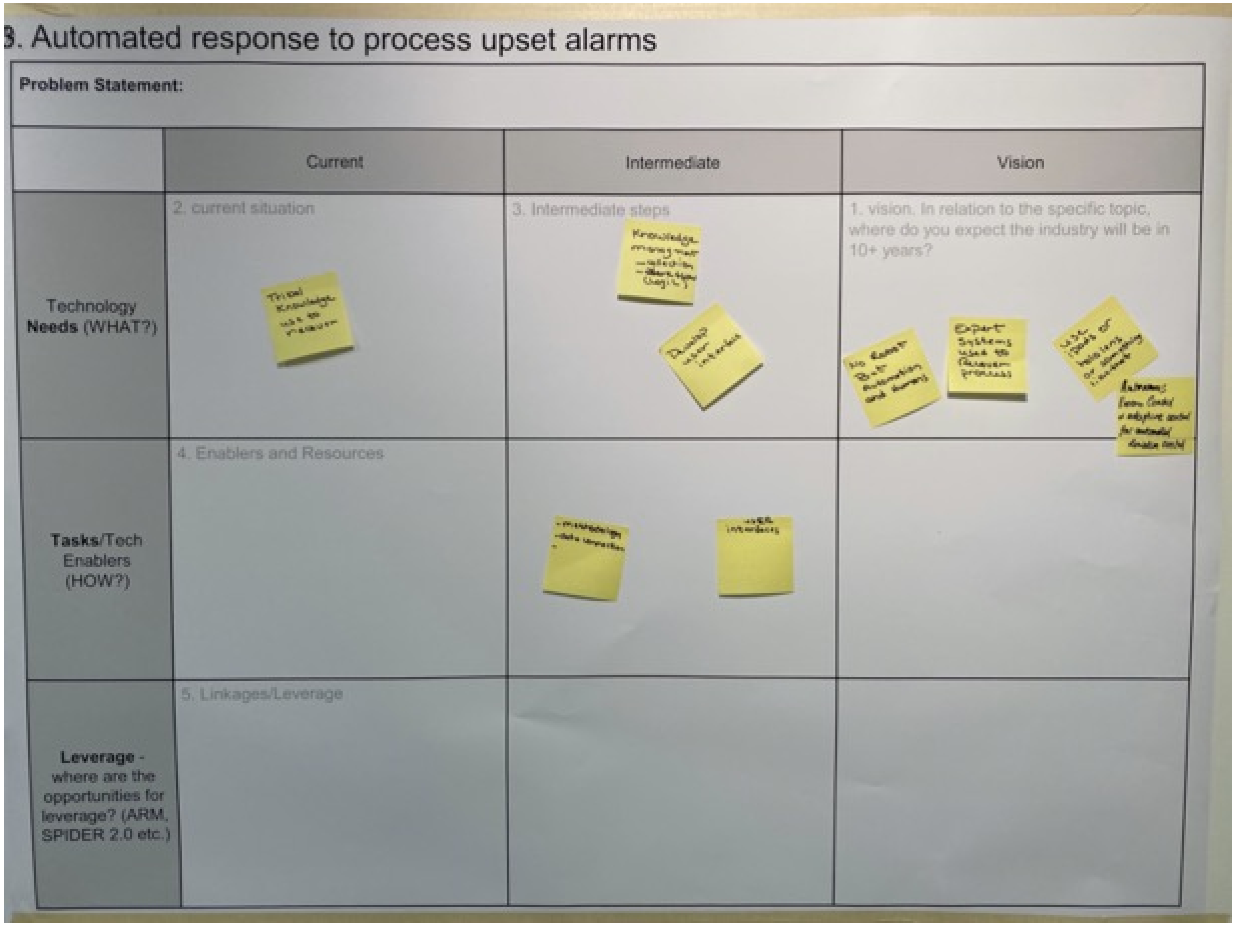
2. Automated aseptic filling processes

The deliverables			
	6 month	* Project Call ->>>>>> Project POP Execution	12 months
Deliverables. Demonstrate the steps required to achieve the vision Include time points	- Landscape assessment Facility Requirement Landscape. - Production - Robotics - Robotic tasksk as output of study	- Define Systems requirements (Capabilities, condition, environment) (in project call) list of CustomerCGW build on legacy equipment - Must hav use case w/market justification (Need)	- * enumerate possible fault conditions to be addressed , proposer selects; - broken vial, - dropped part,- part misplaced - * must be aseptic. - * requestrobot capable of environmental sampling - * enumerateseveral machine setup processes; require proposer to be addresses some/all of them; - install tubing on a fitting, - align & calibrate a device (e.g. liquid handler), - transport liquid w/o spillling, - etc. - Pilto system demo in rep.environ aseptic
Who – What expertise is required, who needs to be involved/connected ?	- Expertise: someone with testbed (PDA?) - Stakeholder: FDA + other regulators - Robotics Interrogator - Stakeholder: BioPhorum Fill/Finish project - Controls sw expertise	- Machine vision - Biomanuf downstream Fill/Finish - Microbio	- Pharma industry partner (use case) - Clean Robotics - OEMS - Filling machine company - PM
Preliminary Budget	- Institute $ 300k - 600k	- Cost Share 1 - 1.25x	- All-in Approx $1M

3. Automated response to process upset alarms

Contributors;

Saly Romero-Torres	Biogen Inc.
David Pollard	Sartorius Stedim



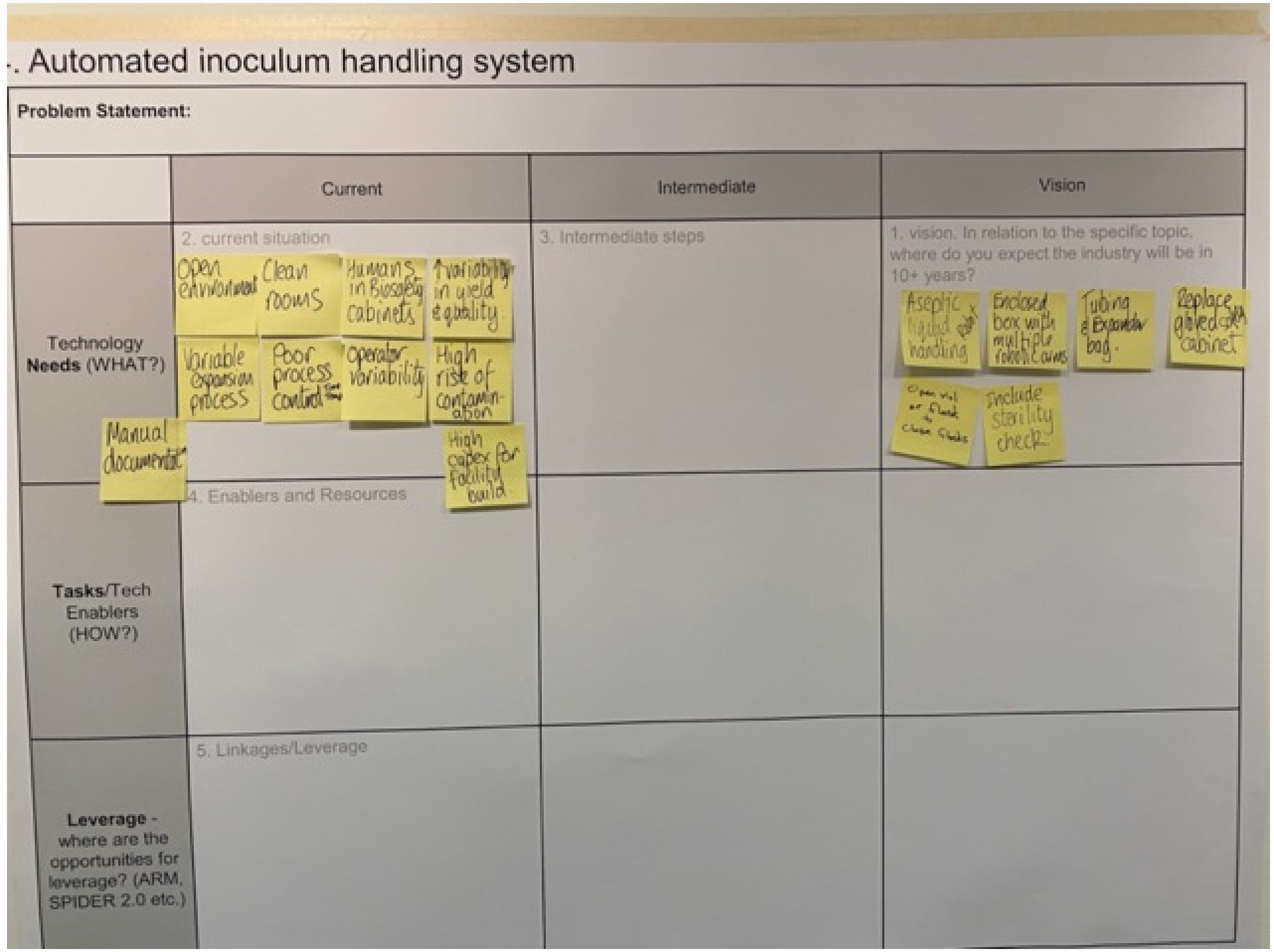
3. Automated responses to process upset alarms

Problem Statement:			
	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	- Tribal knowledge used to problem-solve and restore production line	- Knowledge management- collection, workflow (logic) - Develop user interface	- No robot but automation and humans - Expert systems used to recover process - Using e.g. iPads or hololens or similar - Autonomous process control – adaptive for deviation control
Tasks/Tech Enablers (HOW?)		- Methodology, data collection - User interface	
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)			

Project 4. Automated inoculum handling system

Contributors;

Saly Romero-Torres	Biogen Inc.
David Pollard	Sartorius Stedim



Project 4. Automated inoculum handling system

Problem Statement:			
	Current	Intermediate	Vision
Technology **Needs** (WHAT?)	- Open environment - Clean rooms - Humans in biosafety cabinets - Increased variability in yield quality - Variable expression process - Poor process control (time, temp) - Operator variability - High rise of contamination - High cap ex for facility build		- Aseptic liquid handling robot - Enclosed box with multiple robotic arms - Tubing and Expander bag - Replace gloved safety cabinet - Open vial or flask to close flasks - Include sterility check
Tasks/Tech Enablers (HOW?)			
Leverage - where are the opportunities for leverage? (ARM, SPIDER 2.0 etc.)			