U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy

Agile BioFoundry Session Overview

March 8, 2021

Jay Fitzgerald

Chief Scientist

Program Manager Data, Modeling & Analysis

ABF Federal Team

Kevin Craig
Program Manager
Conversion

Jay Fitzgerald
Chief Scientist
Previously Technology Manager for ABF

Marykate O'Brien
Project Monitor

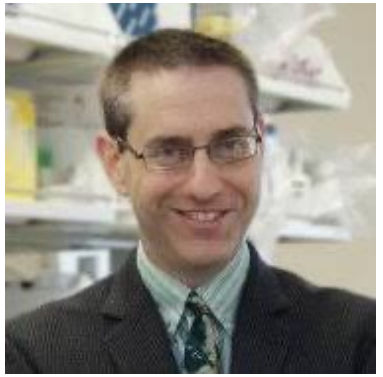
Gayle Bentley – will be taking over as Technology Manager for ABF

Introductions – Peer Review Panel

Name	Affiliation
Pamela Peralta-Yahya	Georgia Institute of Technology
Lily Fitzgerald	Ginkgo Bioworks
Fuzhong Zhang	University of Washington in St. Louis
Ben Gordon	MIT Broad Syn Bio Foundry
Patrick Rose	Office of Navel Research Global, London
Kirsten Benjamin	Amyris
Gale Wichmann*	Amyris

*Tuesday/Thursday only

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Where Does ABF Fit within BETO

BETOFY2020 Enacted Budget Authority = $259.5M

FY2021 = $255M, allocated similarly

Feedstock Technologies

FY2020:
$40,000,000

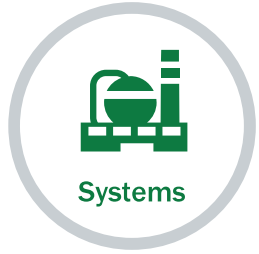
Advanced Algal Systems

FY2020:
$40,000,000

Conversion Technologies

FY2020:
$110,000,000

Systems Development and Integration



FY2020:
$60,000,000

Data, Modeling, and Analysis

FY2020:
$9,500,000

Agile BioFoundry

FY2020 BA:
$15M National Laboratory Core
$5M Directed Funding Opportunity

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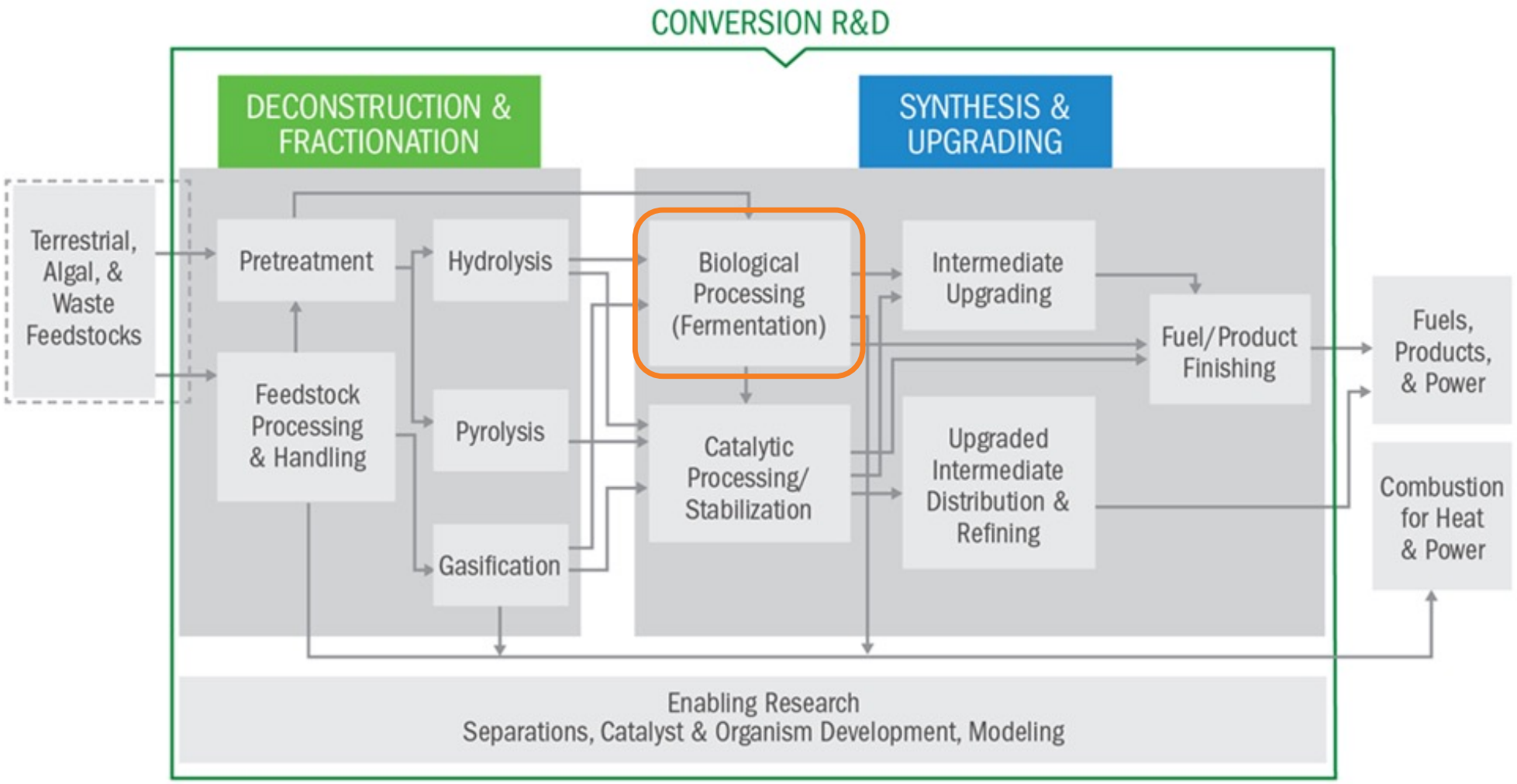
Program Structure

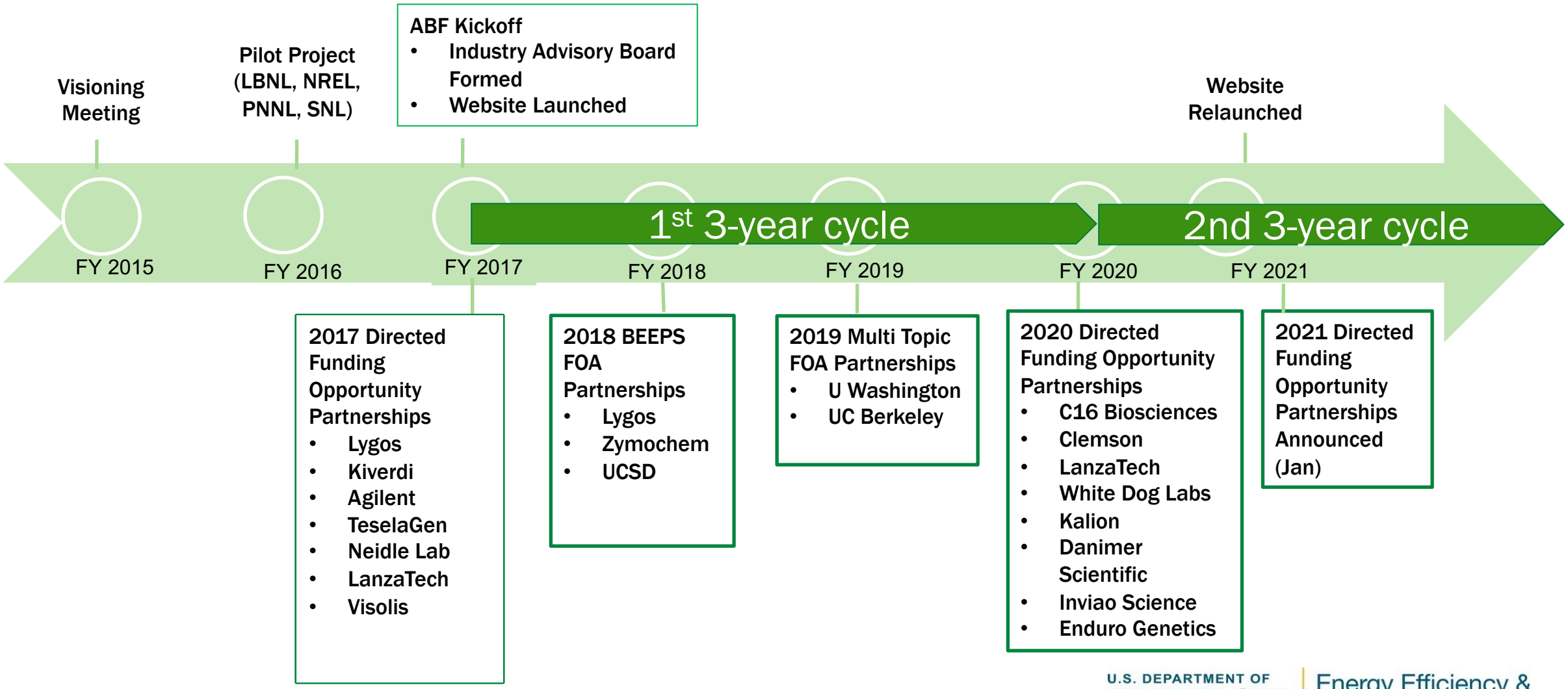


ABF Focus:

- Sugar feedstocks
- Collaboration for Upgrading/DSP with other BETO projects
- DOE-relevant products and fuels
- Forming industry & academic partnerships
- Internal TEA/LCA to guide R&D

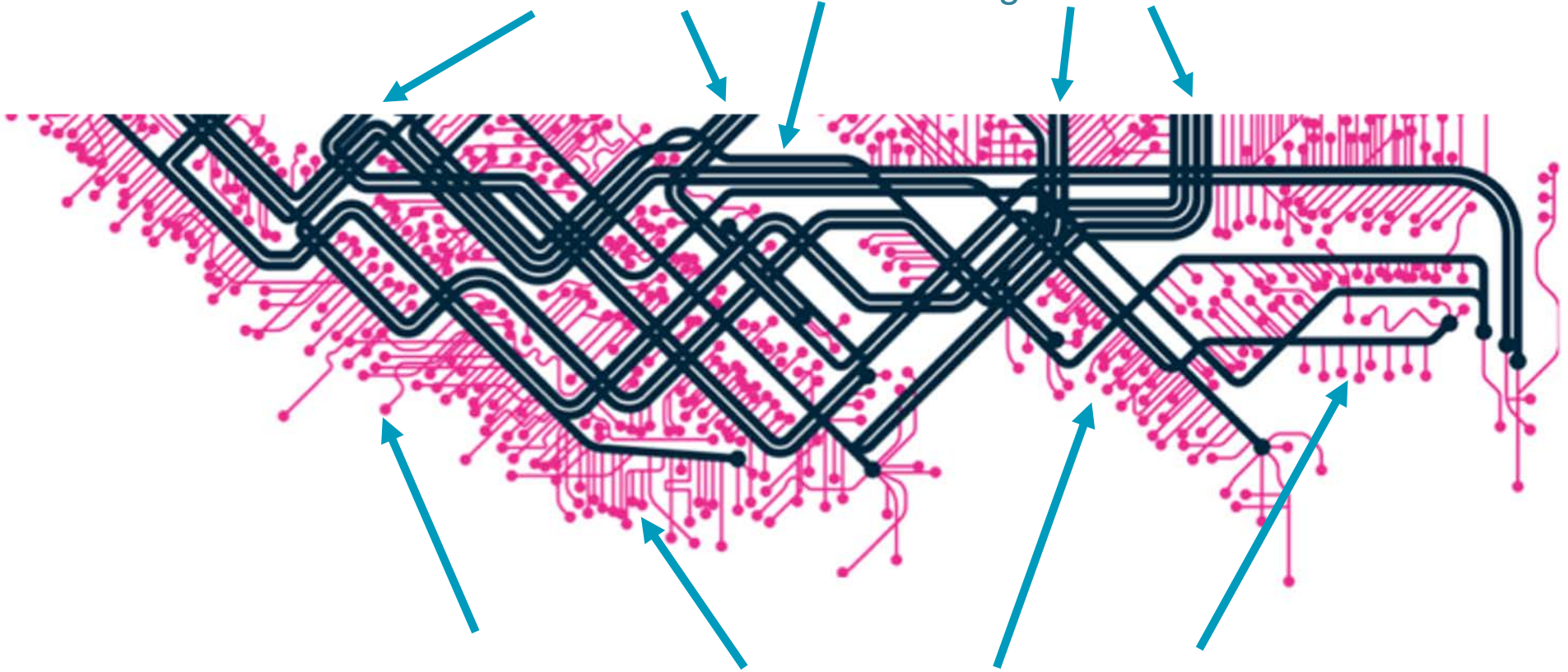
Note: Other biochemical processing work is funded as a part of the BETO State of Technology Projects & FOAs

ABF Timeline and History



Public Infrastructure Investment Enables Private Industry

Public investment in biomanufacturing infrastructure



Private investment in product development, scaling, and tailoring to unique pathways and products

Adapted from Lyft

ABF Goals, Outcomes, Relevance, Risks

- **Goal**: Enable biorefineries to achieve 50% reductions in time to bioprocess scale-up as compared to the current average of around 10 years by establishing a distributed Agile BioFoundry to productionize synthetic biology

- **Outcomes**: Development and deployment of technologies enabling commercially relevant biomanufacturing of a wide range of bioproducts by both new and established industrial hosts

- **Relevance**: $20M/year public infrastructure investment that increases U.S. industrial competitiveness and enables opportunities for private sector growth and jobs

- **Risks**: Past learnings do not transfer well across target molecules and microbial hosts. Experiment data sets are of insufficient quality/quantity/consistency to learn from

2019 Peer Review

- Reviewed in the context of the entire biochemical conversion portfolio
- No partner projects reviewed

Day 4: THURSDAY, MARCH 7, 2019

START TIME	END TIME	AGILE BIOFOUNDRY		
		Presentation	Organization	Presenter
8:30 a.m.	8:40 a.m.	Agile BioFoundry: Session Introduction	*BETO*	*Jay Fitzgerald*
8:40 a.m.	9:30 a.m.	Agile BioFoundry Overview	*LBNL*	*Nathan Hillson*
9:30 a.m.	10:00 a.m.	BREAK		
10:00 a.m.	10:40 a.m.	Pseudomonas putida	*NREL*	*Gregg Beckham*
10:40 a.m.	11:20 a.m.	Rhodosporidium toruloides	*SNL*	*John Gladden*
11:20 a.m.	12:00 a.m.	Aspergillus pseudoterreus	*PNNL*	*Jon Magnuson*
12:00 p.m.	1:00 p.m.	LUNCH		
1:00 p.m.	1:50 p.m.	Design-Build-Test-Learn Infrastructure	*LBNL*	*Nathan Hillson*
1:50 p.m.	2:20 p.m.	Integrated Analysis	*NREL*	*Mary Biddy*
2:20 p.m.	2:50 p.m.	Host Onboarding	*ORNL*	*Adam Guss*
2:50 p.m.	3:15 p.m.	BREAK		
3:15 p.m.	3:45 p.m.	Process Integration and Scale-Up	*LBNL*	*Deepti Tanjore*
3:45 p.m.	4:15 p.m.	Industry Outreach	*ANL*	*Phil Laible*
4:15 p.m.	4:45 p.m.	Directed Funding Opportunities and Partnerships	*LBNL*	*Blake Simmons*
4:45 p.m.	5:15 p.m.	REVIEWER/LEAD REVIEWER DEBRIEFING		

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2019 Peer Review

IMPACT The ABF appears to be on course to fill a critical need not currently addressed by industry or academia—facilitating the growth of the bioeconomy by lowering technical and economic barriers to commercialization of bioproduction, particularly from DOE-relevant feedstocks.

INNOVATION The ABF is demonstrating impressive innovation in three different spheres: (1) within the core DBTL technologies, (2) in areas extending beyond DBTL, and (3) in technology integration and program management.

SYNERGIES Perhaps uniquely within the BETO portfolio, the ABF is explicitly predicated on cultivating synergies across the national labs. The effort is predicated on the assumption that careful coordination of a portfolio of diverse technologies can bring about a paradigm shift in biotechnology R&D.

FOCUS The panel was satisfied with the focuses across DBTL, integration, and industry engagement. We note, however, that a comprehensive review of all individual component technical thrusts of DBTL itself was not provided in the peer review due to time constraints.

TECHNOLOGY DEVELOPMENT PIPELINE In general, the panel felt that the technologies pursued were very appropriate for the current stage of technology. The panel did note that the current testbed projects may be too early stage to realize (and test) the full potential of ABF's DBTL approach.

2019 Peer Review

RECOMMENDATIONS:

First, the panel recommends placing an even greater emphasis on production-oriented research; specifically, TEA/LCA and process development. The work products from these thrusts were very well received, but there is a critical need for even more innovation from both. Similarly, where possible, projects should transition from sugars to feedstocks as early as possible. Some of this is happening already. The recommendation in the previous section regarding application of ABF workflow to more mature projects also falls into this category.

2019 Peer Review

RECOMMENDATIONS:

Second, the panel has made a number of technology-specific recommendations in the individual project reviews. Overall, these recommendations provide guidance to ensure both that the areas of technical weakness are appropriately remedied, and that outcomes are appropriately benchmarked. As an example area of weakness, the panel noted that although DBTL cycle times are improving over time, they are still slow. One emergent bottleneck was "Test," indicating an area that ABF should focus efforts to increase efficiency. Similarly, regarding benchmarking, the panel noted that novelty in "Learn" algorithms may not be a firm requirement for ABF success as described above. At the program level, there needs to be clearer, direct connections made between project-level aims and milestones and the overall 10-times efficiency improvement goal.

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2019 Peer Review

RECOMMENDATIONS:

Third, as the ABF matures, the panel felt strongly that its program management, governance structures, and business model will also need to mature. First, as mentioned above, concerns from the 2017 Peer Review regarding distributed operations have so far been successfully addressed via a number of mechanisms to facilitate collaboration. In the present review, however, the panel is concerned that these mechanisms will not scale as ABF's purview and portfolio of projects grows. It will therefore become important to institute tools and additional layers of technical project management and coordination, both in terms of personnel and in terms of additional formal mechanisms for technical tracking and communication that, for example, may go beyond DIVA and the Office of Energy Efficiency and Renewable Energy annual operating plan (AOP)system. Regarding governance, the industry advisory board (IAB) would be strengthened and its perspective expanded by adding companies outside of bioconversion and representing more of the country.

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Agenda by Day

Day 2 – TUESDAY, MARCH 9, 2021

START TIME	END TIME	AGILE BIOFOUNDRY CONSORTIUM		
		Presentation	**Organization**	**Presenter**
9:45 AM	10:15 AM	GATHER, TECH CHECK, NETWORKING QUESTIONS		
10:15 AM	4:45 PM	**Agile BioFoundry Consortium**	***Conversion Program***	***Jay Fitzgerald***
10:15 AM	10:45 AM	Agile BioFoundry - Session Overview	*BETO*	*Jay Fitzgerald*
10:45 AM	12:15 PM	Agile BioFoundry - Overview & Infrastructure	*ABF*	*Nathan Hillson*
12:15 PM	12:45 PM	LUNCH (REVIEWER LUNCH TOGETHER, PUBLIC ON THEIR OWN)		
12:45 PM	3:15 PM	Agile BioFoundry - Target and Host Engineering	*ABF*	*Gregg Beckham* *Jon Magnuson* *John Gladden* *Ryan Davis* *Thatiana Benavides*
3:15 PM	3:30 PM	BREAK		
3:30 PM	4:15 PM	Agile BioFoundry - Host Onboarding and Development	*ABF*	*Taraka Dale* *Adam Guss*
4:15 PM	4:45 PM	Agile BioFoundry - Industry Outreach	*ABF*	*Phil Laible* *Chris Johnson* *Amanda Barry*
4:45 PM	5:15 PM	**Reviewer Wrap Up and Debrief**	***Reviewers***	

Agenda by Day

Day 3 – WEDNESDAY, MARCH 10, 2021				
9:45 AM	10:15 AM	GATHER, TECH CHECK, NETWORKING QUESTIONS		
10:15 AM	3:15 PM	**Agile BioFoundry Consortium**	***Conversion Program***	***Jay Fitzgerald***
10:15 AM	10:30 AM	Intro to partnerships	*BETO*	*Jay Fitzgerald*
10:30 AM	11:00 AM	Intro to Directed Funding Opportunities	*ABF*	*James Gardner*
11:00 AM	11:30 AM	ABF Industry Engagement Lab Call - Lygos	*Lygos*	*Andrew Conley*
11:30 AM	11:45 AM	BREAK		
11:45 AM	12:15 PM	ABF Industry Engagement Lab Call - Kiverdi	*Kiverdi*	*Dan Robertson*
12:15 PM	12:45 PM	ABF Industry Engagement Lab Call - Agilent	*Agilent*	*Alex Apffel*
12:45 PM	1:15 PM	ABF Industry Engagement Lab Call - TeselaGen	*TeselaGen*	*Mike Fero*
1:15 PM	1:45 PM	LUNCH (REVIEWER LUNCH TOGETHER, PUBLIC ON THEIR OWN)		
1:45 PM	2:15 PM	ABF Industry Engagement Lab Call - Neidle Lab	*University of Georgia*	*Ellen Neidle*
2:15 PM	2:45 PM	ABF Industry Engagement Lab Call - LanzaTech	*LanzaTech, Inc.*	*Wayne Mitchell*
2:45 PM	3:15 PM	ABF Industry Engagement Lab Call - Visolis	*Visolis*	*Deepak Dugar*
3:15 PM	3:45 PM	**Reviewer Wrap Up and Debrief**	***Reviewers***	

Agenda by Day

Day 4 – THURSDAY, MARCH 11, 2021				
10:00 AM	10:15 AM	GATHER, TECH CHECK, NETWORKING QUESTIONS		
10:15 AM	3:00 PM	**Agile BioFoundry Consortium**	***Conversion Program***	***Jay Fitzgerald***
10:15 AM	10:30 AM	Introduction to ABF FOA Projects	*BETO*	*Jay Fitzgerald*
10:30 AM	11:15 AM	Accelerating engineered microbe optimization through machine learning and multiomics datasets	*Lygos*	*Mark Held*
11:15 AM	12:00 PM	Development of Bacillus as an industrial host for the microbial production of biopolymers	*Zymochem*	*Harshal Chokhawala*
12:00 PM	12:30 PM	BREAK		
12:30 PM	1:15 PM	Advanced Algal Biofoundries for the Production of Polyurethane Precursors	*University of California San Diego*	*Stephen Mayfield*
1:15 PM	2:00 PM	Accelerating polyketide synthase engineering for high TRY production of biofuels and bioproducts	*UC Berkeley*	*Jay Keasling*
2:00 PM	2:45 PM	Developing multi-gene CRISPRa/i programs to accelerate DBTL cycles in ABF hosts engineered for chemical production	*University of Washington*	*James Carothers*
2:45 PM	3:00 PM	Wrap Up and Thank You	*BETO*	*Jay Fitzgerald*
3:00 PM	3:15 PM	BREAK		
3:15 PM	4:15 PM	**Reviewer Wrap Up and Debrief**	***Reviewers***	

Thank you!

Thank you to all the reviewers and presenters!

Contact: jay.fitzgerald@ee.doe.gov