Precompetitive Collaborations: Enabling Technologies for the Pharmaceutical Industry

Philadelphia, Pennsylvania • June 12 - 13, 2013

Chaired by:

Christopher Welch (Merck)
Joel Hawkins (Pfizer)
Jean Tom (Bristol-Myers Squibb)

Council for Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

Welcome!

Introductions

Wednesday, June 12, 2013

9:00 **Welcome**

9:05 **The Case for Change: A New Paradigm for Precompetitive Collaborations**
Christopher Welch (Merck Research Laboratories), Jean Tom (Bristol-Myers Squibb), Joel Hawkins (Pfizer)

10:00 **Break**

10:15 **Panel Discussion 1: Cross-Pharma Collaborations** Margaret Faul (Amgen), Chris Hill (Merck Research Laboratories), Steve King (AbbVie R&D), Chris Senanayake (Boehringer-Ingelheim), Robert Waltemire (Bristol-Myers Squibb), Gerry Tabor (Pfizer)

12:00 **Lunch & Networking**

1:00 **Case Studies in Funded External Collaborations** Nick Thomson (Pfizer)

1:30 **Academic Collaborations with Pharma: Past, Present, and Future**
Gary Molander (University of Pennsylvania)

2:00 **Panel Discussion 2: Vendor and Supplier Collaboration with Pharma**
Henry Dubina (Mettler-Toledo), Diane Diehl (Waters), Russell Gant (Sigma-Aldrich)

3:00 **Break**

3:15 **The Role of Government Labs in Facilitating Multi-Party Collaborations**
Mike Tarlov (National Institute of Standards and Technology)

3:45 **Role of Academic Science and Technology Centers in Developing Enabling Technologies** Huw Davies (Emory University)

4:15 **The Mission of CCR: Facilitating Collaboration in Chemistry & Chemical Engineering**
Marc Donohue (Johns Hopkins University, 2013 CCR Chair), Paul Mendez (CCR)

4:45 **Preview of Thursday's Breakouts**

6:00 **Networking Reception**

Thursday, June 13, 2013

8:00 Continental Breakfast

8:30 **Benefits of Cross-Pharma Collaboration on Enabling Technologies**
Jacquelyn Gervay-Hague (University of California-Davis, Director, Division of Chemistry at the National Science Foundation effective July 2013)

9:00 **Successful Negotiations of Research Collaboration Agreements**
Kim Folander (Merck Research Laboratories), Trude Amick (University of Pennsylvania)

9:30 **Parallel Break-Out Sessions**

Session A – Streamlining Agreements for External Research Collaborations
Session B – Preferred Mechanisms for Precompetitive Collaborations
Session C – Defining the "Edges" of Precompetitive Collaboration

10:15 **Break**

10:30 **Report Out from Breakout Sessions**

12:00 **Workshop Summary & Next Steps**

12:30 **Adjourn & Box Lunch**

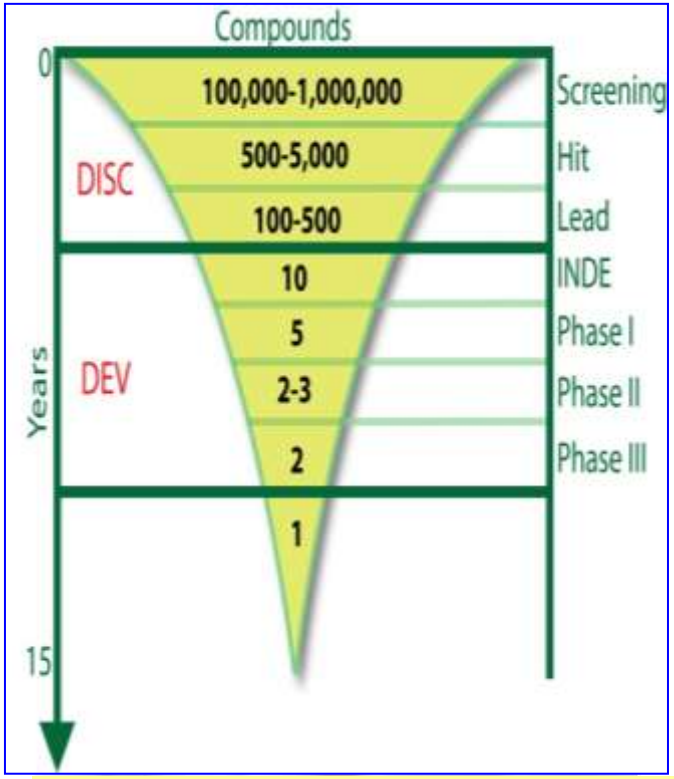
The Case for Change: Precompetitive Collaborations on Enabling Chemical and Chemical Engineering Technologies for Pharma

Jean Tom (Bristol-Myers Squibb)
Joel Hawkins (Pfizer)
Christopher Welch (Merck)

21st Century Challenges for the Pharmaceutical Industry

Increasing:

- Discovery and development costs
- Time to bring new discoveries to market
- Regulatory hurdles
- Market segmentation requiring 'customized' products
- Market share to low cost generics
- Focus on global customers – price sensitivity



Decreasing:

- Probability of success
- Customer appetite for high cost solutions
- Blockbusters
- Percentage of commercialized medicines that 'break even' paying for costs of discovery and development
- Availability of low hanging fruit – Easy targets gone

It can take 10-15 years and many hurdles to bring a new medicine to market

Pharma Spending on R&D

Pharma R&D Spend (2011)

Novartis	$9.6 Billion
Roche	9.4
Pfizer	9.1
Merck	8.5
J&J	7.5
Sanofi-Aventis	6.7
GSK	6.3
Astra-Zeneca	5.5
Lilly	5.0
Abbott	4.1
BMS	3.8
Amgen	3.2

Top 12 Pharma $78.7 Billion

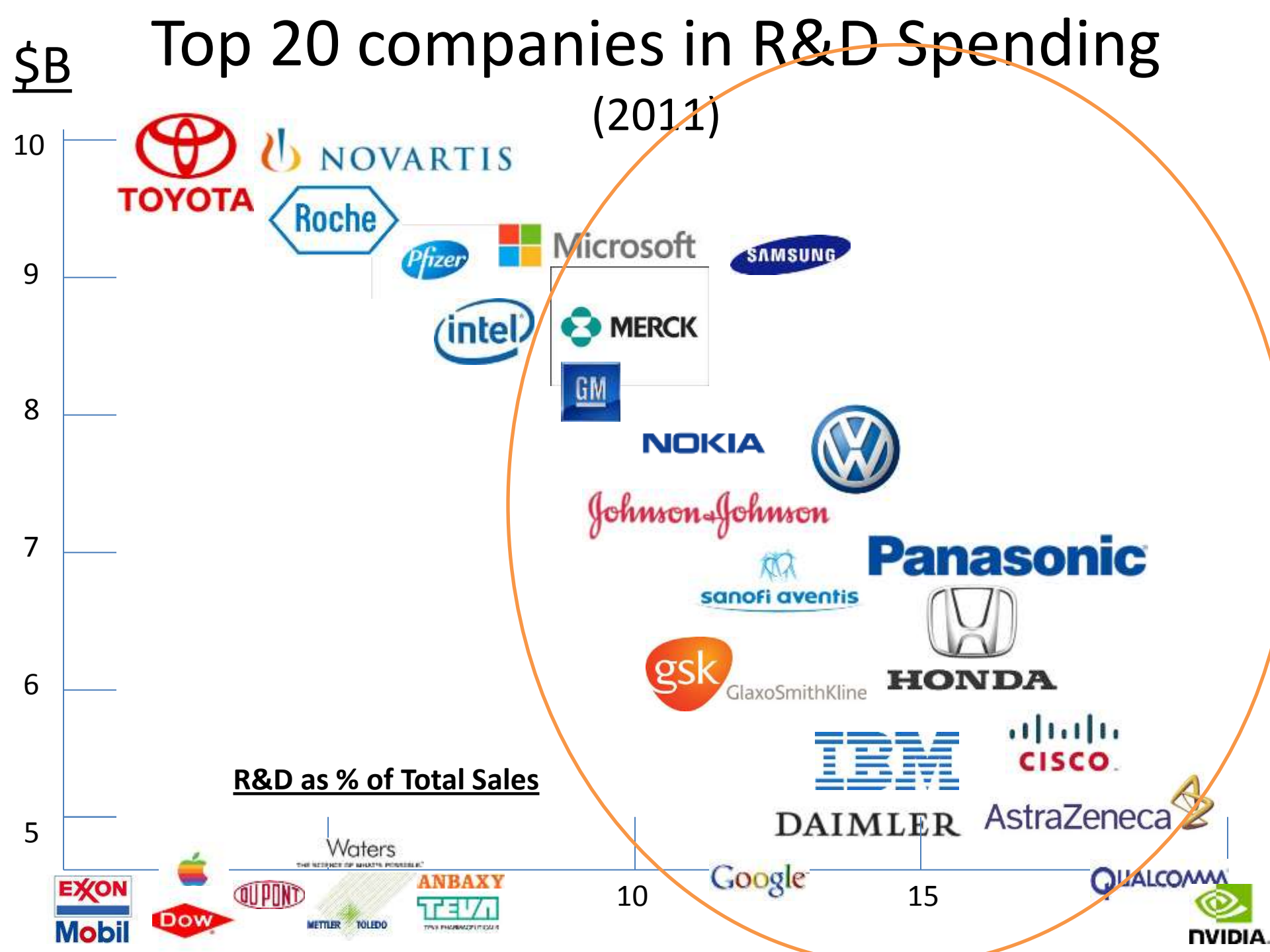
For comparison …

NSF	$8 Billion
NIH	$30 Billion

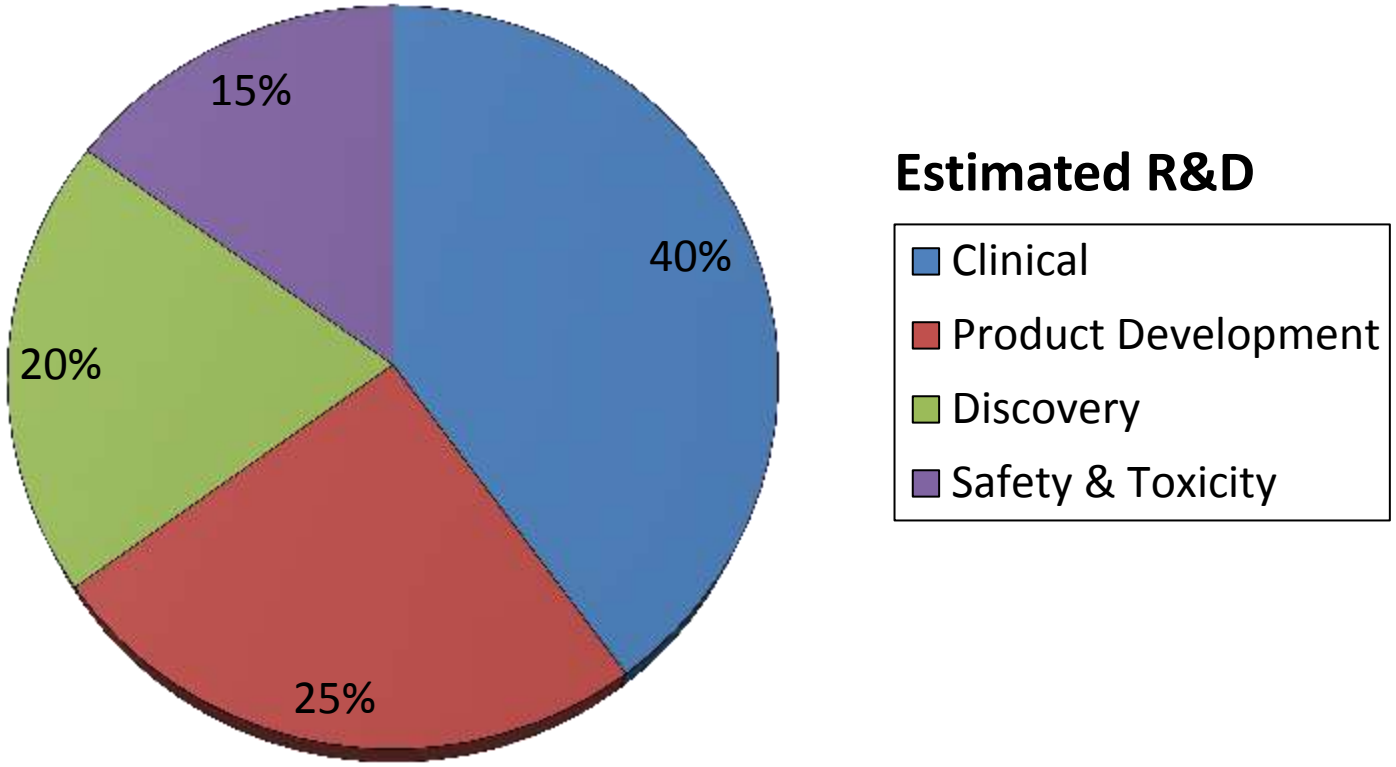
Top 20 companies in R&D Spending

(2011)

Top 20 companies in R&D Spending (2011)



Where Pharma R&D Spending Goes



Clinical Costs Dominate R&D Spending

Product Development is Significant R&D Spending

Progression of Technology Development and Collaborations

'the old days'

Independent Pharma

- Complete self contained companies
- Discovery to manufacturing, all in house
- Extensive internal infrastructure, even for glass blowers and machine shops

90s

Push for technology for greater speed

- One month sooner to market can be worth $millions

Greater acceptance of collaborations

- Growth of outsourcing to meet peak demands, staff for troughs and outsource for peaks
- Outsourcing peripheral infrastructure

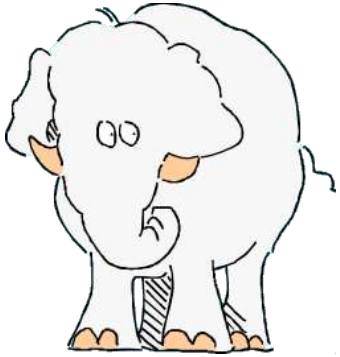
00s

Continual push to drive down cost

- Growth of outsourcing to low cost locations
- Contracting laboratory footprints for a shrinking internal core
- Everyone gets lean in response to the recession
- What Next?
- Need to be lean, flexible, and extremely efficient

Develop the technology in house and keep it internal?

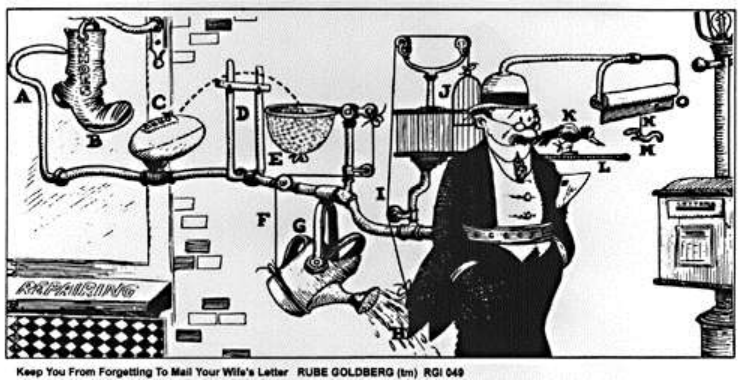
Great idea, but …



- Risk of creating a white elephant without input from outsiders, e.g. ending up with an unbalanced workflow

- Risk of obsolescence if not further developed and maintained (which is expensive to do alone)
- Risk of not having access to the technology at outsourcing partners if not known to and desired by the broader market
- Risk of insufficient exposure to regulators for regulatory acceptance if not broadly applied

Develop the technology via large *uncoordinated* consortia?



Great idea, but …

- Risk that the end result will be too complex, too big, too expensive …

$$\sum (\text{It has to do this})_n$$

1→n, n=number of partners

- Risk of "design by committee"

AVE(It has to do this)

Develop technology via *balanced* collaborations

- Share cost between pharma (and vendors where appropriate)
- Share risk, i.e. to develop a proof of concept
- Collective input from *likeminded* people with *different* perspectives

- Size it right, enough collaborators to bring value but not too many to manage
- Have a clear understanding of everyone's goals
- Choose partners carefully
- Develop trust within appropriate guidelines

Precompetitive Collaborations for the Pharmaceutical Industry

Precompetitive | Pharma | Competitive

Work together precompetitively …

… so that we can compete all the better competitively ...

Precompetitive Collaborations for the Pharmaceutical Industry

Precompetitive | Pharma | Competitive

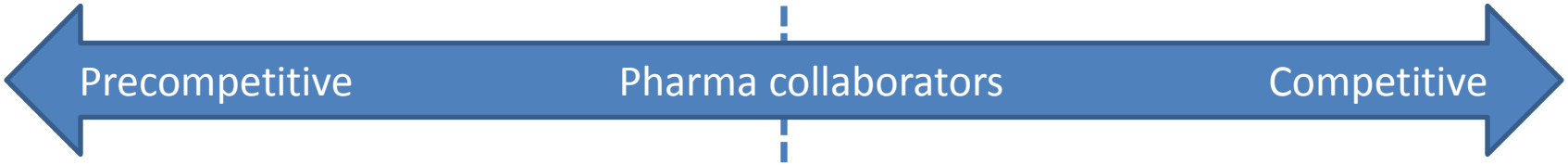
Work together precompetitively …

… so that we can compete all the better competitively … with ourselves, and ...

… with the common challenges of

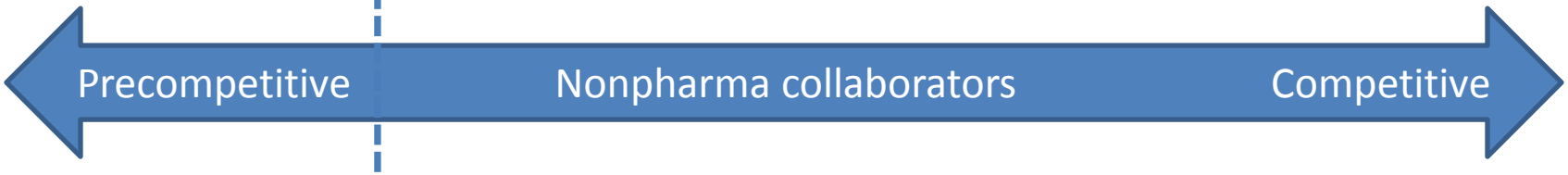
- patent expiries
- cost pressures
- more complex targets
- global economic crises

Precompetitive Collaborations for the Pharmaceutical Industry



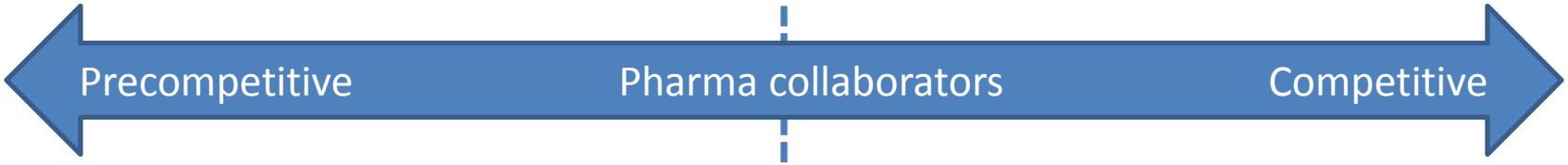
Pharma needs Freedom to Operate
- Publish the technology
- Make broadly available

Pharma needs exclusivity
- Patent the technology



(a) Nonpharma collaborator needs exclusivity
- Patent the technology
- Commercialize the technology
- Potential issues with sole sources and unknown future IP costs
  - E.g. catalyst exclusively licensed to one vendor
  - “Boutique” instrument vendor goes out of business

Precompetitive Collaborations for the Pharmaceutical Industry



Pharma needs Freedom to Operate
- Publish the technology
- Make broadly available

Pharma needs exclusivity
- Patent the technology

(b) Nonpharma collaborator does not need exclusivity
- Publish the technology
- Make broadly available
- Can increase the use of synthetic methodology*

Asymmetric catalysis in the pharmaceutical industry*, Hawkins, Joel M; Watson, Timothy J N *Angewandte Chemie (Int. ed. In English)* **2004, *43*, 3224.

‘Precompetitive’ Collaboration

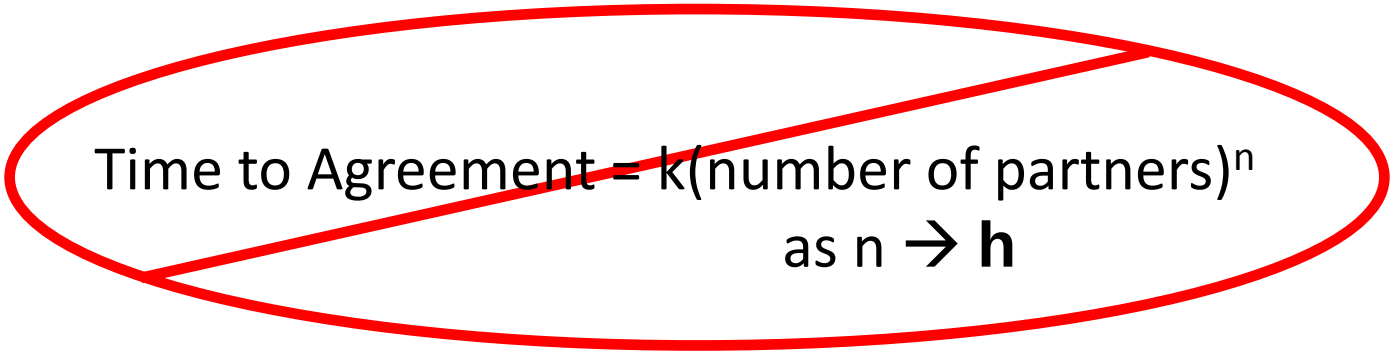
- Some area of our business are off limits for collaboration with our competitors – top secret, strategically important, differentiating capabilities
- While other areas may potentially be in scope for ‘precompetitive’ collaborations … general areas of science or business that are not closely linked to a key differentiating strategy.

Survey Results

A 4Q 12 cross pharma survey revealed:

- Strong interest in precompetitive collaborations
- Frustration with speed and difficulty of executing external collaboration agreements
- Wariness about potential involvement in consortia
- Out of scope for precompetitive collaboration: Lead ID, Lead Op, Manufacturing Route
- In scope: General laboratory tools including software, instrumentation, reactions and reagents
- Maybe in scope: Sharing of samples and reagents, predictive and modeling software tools, crystallization screening, new automation tools, new target discovery

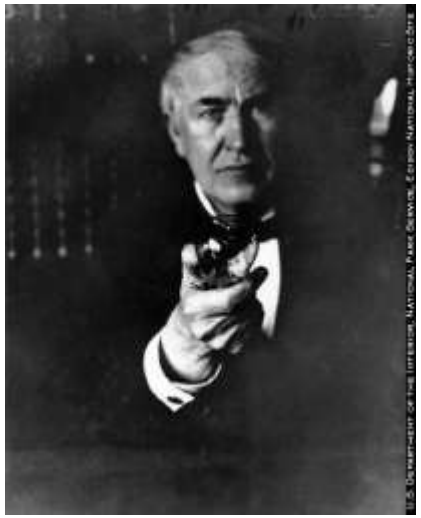
Collaborative Research Agreements



A wish list from the scientist's perspective (for discussion)

- Agree on a timeline for completion of the Agreement at the onset
- Assign accountable points of contact to progress this timeline
- Understand everyone's goals and expectations from the beginning

Merck's New Technologies Review & Licensing Committee



T.A. Edison

• Coordinate the identification, acquisition and evaluation of 'first into Merck' technologies with potential for positive crossfunctional impact

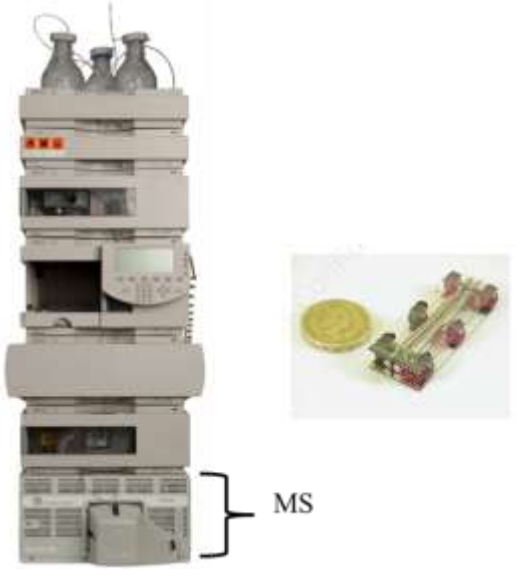
• Network of subject matter experts (Chemistry Synthesis, Modeling, Purification, Analytical Technologies, Drug Delivery & Formulation, Biological Production, Informatics, Analysis, Modeling & Simulation, Translational Models & *in vivo* Pharmacology, Screening & *in vitro* Pharmacology, Experimental Medicine & Biomarkers)

• ~ 30 projects funded each year – hardware, software, services, capabilities

• Typically 1:1 deals with vendors, academia… occasional multiparty deals

• Projects: 'buy it and try it', 'Beta test then acquire', 'long term development', 'establish proof of principle'

Case History: Disadvantages of going it alone on the development of new technologies



Inexpensive (<$50K)
miniature mass spec

high throughput analysis HPLC platform
~ 1h ‘plate time’ (96 samples)

Both projects…

-major vendors uninterested, contracted with small startup companies

- more than 5 years development

- similar requests ~ 1 year prior to launch…”can we discuss with other potential customers in pharma to make sure product features are suitable for successful commercialization?”

Dilemma: Exclusivity *vs* desire to create a viable product that will thrive in the marketplace

Why not collaborate from the outset?

Potential advantages:

- cost sharing/savings

- standardize on requirements, broader customer input into new product design specifications

- Access ‘pieces of the solution’ coming from all parties

- greater ability to influence potential solution providers to address needs

Potential disadvantages:

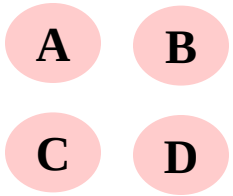
- unwieldy management of consortia or large collaborations
    - difficulty to steer to desired outcome
    - average (or sum) of group’s desires may not fit anyone’s requirements
    - ‘death by a thousand cuts’- multiple consortium membership fees

- reaching legal agreement between two parties is difficult enough…

- slippery slope leading to loss of proprietary information/inadvertent disclosure of key differentiating strategies?

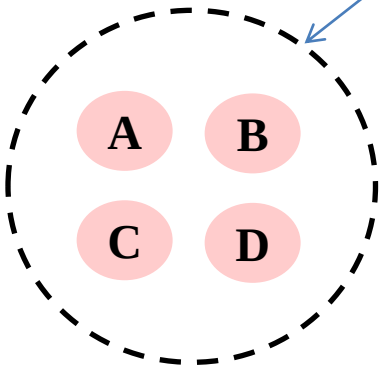
Many different models for multiparty collaboration…

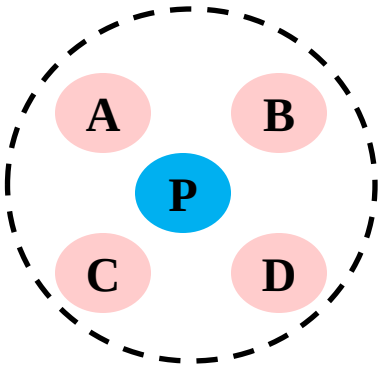
‘just do it’:
- research carried out jointly in the labs of participants
- no $ transferred
- for duration of single project
- no legal agreements
- …if only life in pharma were this simple…



Formation of collaboration agreement required

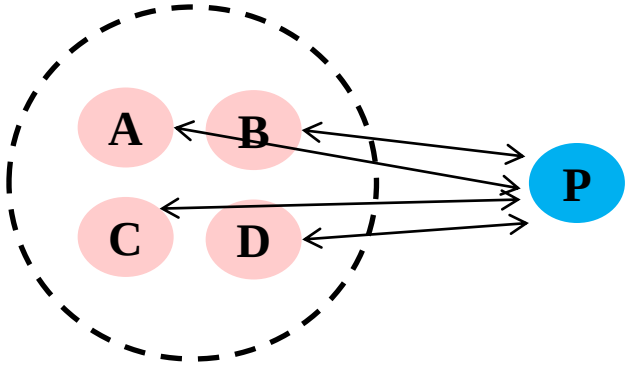
‘formalized collaboration’:
- research carried out jointly in the labs of participants
- no $ transferred
- for duration of single project
- collaboration agreements

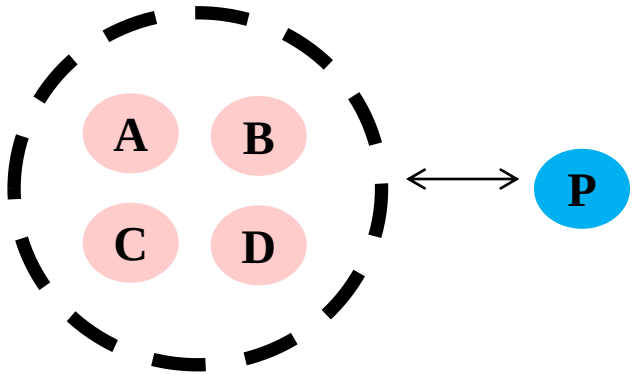




new product advisory group

Funded Projects at External Provider





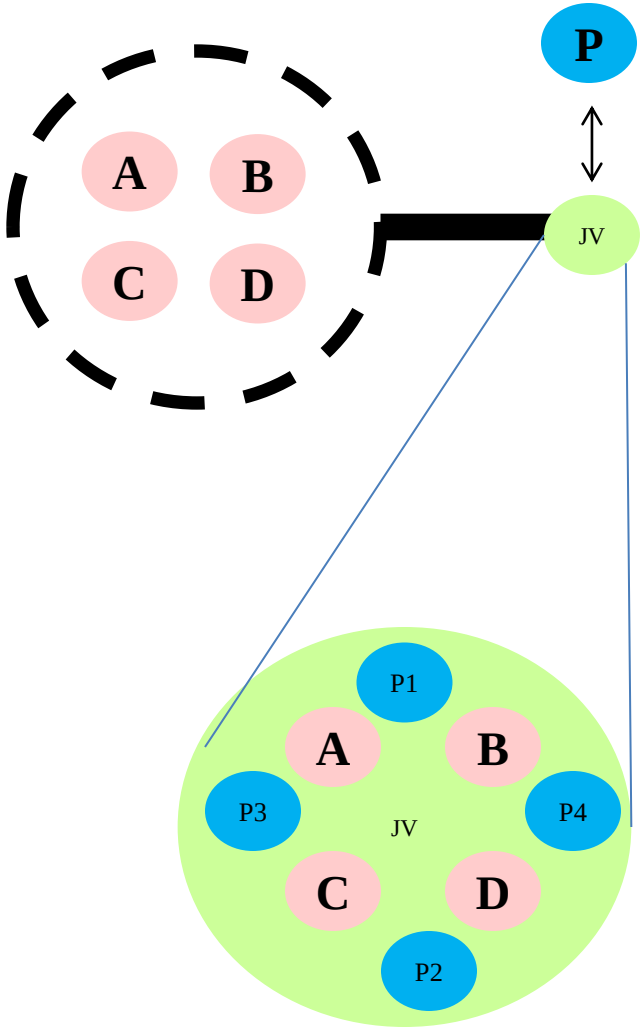
P = vendor, academia, govt
- Independent $ to P
- Independent contracts
- *complicated!*

Honest Broker: Formal entity created to act on behalf of members …consortium, joint venture, not for profit etc.

Advantage: once formed additional projects are possible under blanket agreement

Incoming technologies often acquired by each member, to allow parallel evaluation

Shared Lab in the Middle



including providers also possible

Honest Broker with…

Lab space staffed by postdocs, rotating scientists provided by member companies

Simplified rules of engagement for interaction with external parties

Economy of scale for joint evaluations at JV labs

Vendors, academics, government laboratories can participate

Transfer of $between members or to external parties

Decreases need for creating external agreements for each new project

Precompetitive Collaboration in Other Industries

Transportation

Banking TWIST

Geospatial OGC® Open Geospatial Consortium, Inc.

CDISC

Retail ARTS Association for Retail Technology Standards of the National Retail Federation

Clinical HL7

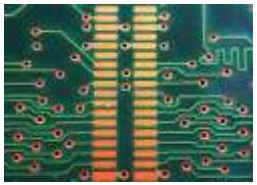
Automotive STAR Technology Dedicated to Business Efficiency

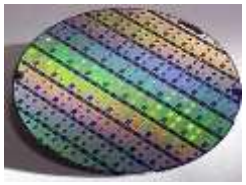
Healthcare HITSP

Precompetitive Collaboration in Microchip Industry

SEMATECH

Accelerating the next technology revolution.





imec

[link]

- R&D to advance chip manufacturing
- not-for-profit consortium, formed 1987
- funded by member dues (initial startup subsidized by DARPA - $500 MM)
- chipmakers, equipment and material suppliers, universities, research institutes, and government partners
- patent pooling, agreement on standardization

GLOBALFOUNDRIES, IBM, intel, Micron, SAMSUNG, Texas Instruments, tsmc, College of Nanoscale Science & Engineering, University at Albany, FRMC

[Link]

(Interuniversity Microelectronics Center)

- Micro- and nanoelectronics research center headquartered Leuven, BE, with offices worldwide

- >600 industrial residents and guest researchers
- €300 MM revenue

- Intel, Samsung, Panasonic, NVIDIA, STMicroelectronics, NXP Semiconductors, GLOBALFOUNDRIES, TSMC, Hynix, ASML, Xilinx, Altera, Cadence Design Systems, Qualcomm, Renesas, Siltronic, *etc*

Both involve ‘shared laboratories in the middle’

Precompetitive Collaboration in Pharma

Pistoia Alliance

link

The Pistoia Alliance is a global, not-for-profit, precompetitive alliance of life science companies, vendors, publishers, and academic groups that aims to lower barriers to innovation by improving the interoperability of R&D business processes.

- Focus primarily data, information technologies
- Founders AZ, GSK, Novartis, Pfizer
- now, ~ all pharma

IQ INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

Link

not-for-profit organization of pharmaceutical and biotechnology companies with the mission of advancing science-based and scientifically-driven standards and regulations for pharmaceutical and biotechnology products worldwide

- Focus primarily on building consensus and influence on regulatory issues.
- Founded 2011
- Steve King is Vice Chair

Structured Organic Particulate Systems

...an Engineering Research Center

(C-SOPS)

- World's largest academically-based research organization dedicated to modernizing pharmaceutical manufacturing and dosage forms
- NSF Engineering Research Center – 5 year - $15MM, started in 2007
- Rutgers University, NJIT, University of PR – Mayaguez, Purdue University
- Industrial Consortium- 8 pharma companies, 32 vendor/solution providers, FDA
- Development of the science and engineering methods for designing, scaling, optimizing and controlling dosage form design and relevant manufacturing processes

Solid State Pharmaceutical Cluster

- Science Foundation Ireland (SFI)
- Funding of €6.97 million, established 2007
- The cluster is a collaboration between Universities Researchers and Pharmaceutical companies in Ireland. The academic contributors are University of Limerick, National University of Ireland, Galway, Trinity College Dublin, University College Dublin and University College Cork. The Pharmaceutical Company members are Janssen, Schering Plough, GSK, Merck, Roche, Pfizer, Eli Lilly, Clarochem, Hovione and BMS

Centers for Multiparty Collaboration in Chemistry, Chemical Engineering

Center for Stereoselective C–H Functionalization

NSF

Advancing C-H functionalization to impact broadly the logic of organic synthesis.

Penn | P.R.S.S.C

Parallel Reaction Screening Service Center

Parallel Reaction Screening Service Center

General facilitators of collaboration in chemistry and Chem Engineering

Mission
"Improving Chemical Innovation through Collaboration and Advocacy"
CCR accomplishes its mission by linking R&D leadership across discipline, institution, and sector boundaries. (Industry, Academia, Government)

Vision
CCR will profoundly influence the success of chemistry-related science and engineering research in serving society.

Goals
Advance Research Collaboration
Advocate Research Investment
Enrich Graduate Education

What if…

- Pharma companies, solution providers jointly discuss public needs
- Priority areas for investment are identified
- Projects swiftly initiated, streamlined agreements
- Shared input leads to faster development of robust products and services.
- Rapid evaluation to determine value leads to reliable recommendations for deployment/retirement
- Overall cost savings and improved outcome relative to current approaches

Questions?

- Coffee is served

- Cross Pharma Panel Discussion in this room at 10:15 sharp!

10:15 - 12:00

Panel Discussion: Cross-Pharma Collaborations

- Margaret Faul — Executive Director of Process Chemistry R&D, Amgen
- Chris Hill — Head of Global Chemistry, Merck Research Laboratories
- Steve King — Vice President of Development Sciences in Research Development, AbbVie
- Chris Senanayake — Vice President, Chemical Development US, Boehringer-Ingelheim
- Gerry Taber — Global Technology Lead, Chemical R&D, Pfizer
- Rob Waltermire — Executive Director of Late Phase Chemical Development, Bristol-Myers Squibb

Joel Hawkins, Moderator

Council for Chemical Research

Panel Format

- Each speaker will present a brief ~7 min introduction, making key points.
- Limited discussion following each presentation, intended for clarification.
- Questions from the audience and lively discussion encouraged after all of the introductory presentations are completed.
- In the spirit of a workshop we want to hear everyone's ideas.

AMGEN
Pioneering science delivers vital medicines™

Precompetitive Collaborations:

Round Table on Cross Pharma Collaborations

Margaret Faul

Executive Director Chemical Process R&D

Amgen, Inc

Precompetitive Collaborations: Definition and Value Statement

Precompetitive Collaborations are a subset of translational research that is focused on improving the tools and techniques needed for successful translation, and not on the development of a specific product

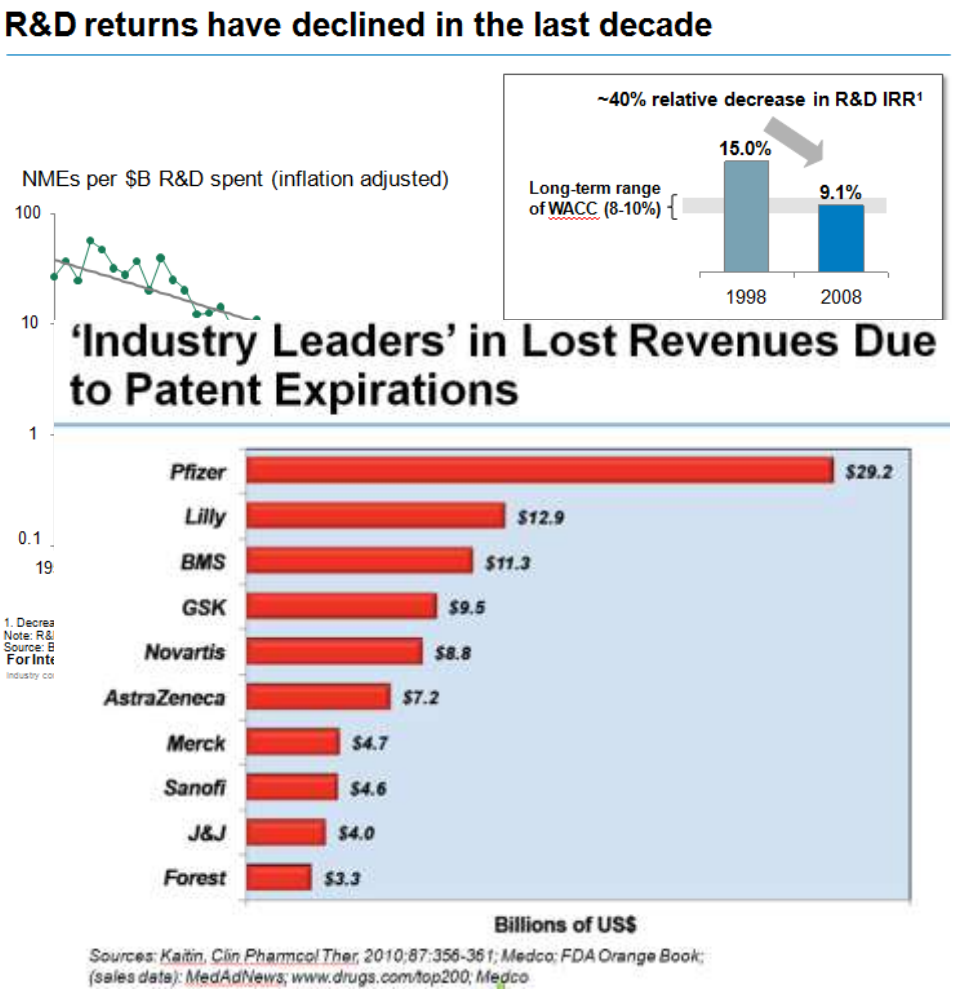
Janet Woodcock, Clinical Pharm & Therapeutics, 817 (5), ***2010*** *521-523*

Value Statement

- A Precompetitive Collaboration will provide a positive benefit to each party (impact to $$, IP, time, expertise) that exceeds what might be achieved by proceeding independently

Rationale for Engaging in Precompetitive Collaborations

- Internal R&D under pressure to deliver new therapeutics more efficiently
- Patents on many top-selling products are expiring
- Marketplace is highly competitive and reimbursement environment is increasingly restrictive
- Cost to meet safety and efficacy is rising due to increased regulatory hurdles are increasing
- Growing need to get new drugs to treat rare diseases and diseases in developing countries
- Pharmaceutical R&D remains a long, risky, and expensive process



What opportunities lie in the Precompetitive Space?

Current Amgen Investment in Precompetitive Collaborations

Consortia	Area of Focus	Consortium Objectives
IQ Consortium	Clinical & CMC	Innovation and Quality in Drug Dev
Zenith	CMC	To predict chemical degradation & mechanistic pathways
Innocentive	CMC	Forum for Problem Solving in Precompetitive Environment
Allotrope Foundation	IS	Develop a common laboratory open information framework
Rx360	Manufacturing	Management of integrity & quality of the supply chain
Biomarkers Consortium	Clinical	Develop Biomarkers for disease & Drug Dev
Predictive Safety Testing Consortium	Toxicology	Identify Preclinical & Translational Markers

An Assessment of Precompetitive Collaborations

Advantages	Challenges
Shared risk across Industry, Academics & Govn't to address key problems	Controlling the direction of research due to different business drivers
"Disruptive Innovation" and opportunity to move field forward	Timeline to implement & deliver misaligned with current industry model
Introduces efficiency avoids duplication	Logistical & managerial complexity
Shared costs structure	Define & agree on financial expectations for different contributors
Opportunity to leverage broad SME pool to collaborate & develop best practices that support Drug Dev.	Management of IP. Output is open source, business model to maintain needs to be defined.
Standardization of methods/data	Alignment on what to standardize, and metrics to measure outcomes
Communication and recognition of collaboration enhances public support	Timing of communication

Opportunities for Precompetitive Collaboration in CMC Drug Development

Precompetitive	Competitive
• Lab Standards • LOTF • Analytical and Purification Instrumentation • GTI Predictive data & analytical methods • Novel Excipients • Enabling Technologies • Quality and Mfg • Continuous Process Reactor Design • Synthetic Route Design • Lab Notebooks & Information Management • Automation for Chemical Research • *Experimental Design Software Tools* • *Process Modeling Software*	• IP for Mfg Ds/DP • Eng technologies in miniaturization e.g. nanotech & nanoformulation • Target delivery approaches • Particle engineering equipment/methodologies • Crystallization screening technologies

To add value we need to identify opportunities to differentiate where the investment is high, creation of IP is minimized but there is a tangible benefit to Drug Development

Precompetitive Collaborations: Enabling Technologies for the Pharmaceutical Industry

Chris Hill
Head of Chemistry
Merck Research Laboratories

MERCK
Research Laboratories

AMGEN

Needed Technologies at Merck

- Annual assessment of technology needs across the company
- A subset of these needs are communicated externally
- www.merck.com/licensing
- Areas where Merck is willing to collaborate
- Several of these areas may be suitable for precompetitive collaboration

AMGEN

Which areas best suited for precompetitive collaboration?

- Common industry need, not part of key differentiating strategies
- Faster, Better, Cheaper, Greener

'technology driven'

Greener:
- flash chromatography
- solvent free reactions
- solvent recovery
- oxidation

Cryogen-free NMR
(…also, benchtop, < $100k…)

'Palladium Chemistry'…

…with inexpensive metals

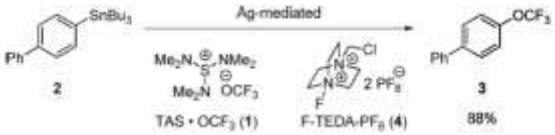
Generally enabling laboratory tools:
- reagents and reactions
- general labware and equipment
- intelligent analytical equipment
- electronic notebooks, structure drawing software, predictive tools, *etc*

AMGEN

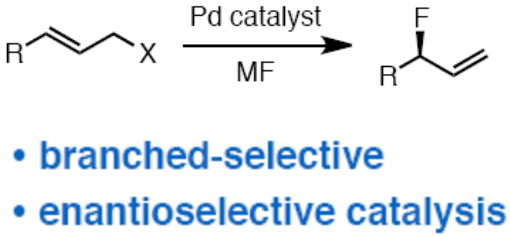
Collaborating with Academia to create needed capabilities: Fluorination Platforms

- Platform fluorination reactions identified as critical need for Merck Chemistry
- Funded collaborations with ‘rising stars’ in chemistry are delivering results
- Reactions beginning to be implemented in Merck Chemistry

Professor Tobias Ritter



Professor Abigail Doyle



- branched-selective
- enantioselective catalysis

“Fluorine newcomer John F. Hartwig of the University of California, Berkeley, thinks the spark that ignited the flurry of fluorine activity came from pharmaceutical companies better articulating their unmet needs”

Chemical & Engineering News, Feb 27, 2012 p 10-17

Taking Precompetitive Collaboration to the Next Level

Steve King
VP, Development Sciences
AbbVie

2014 Chair, IQ Consortium

Taking pre-competitive collaboration in pharma to the next level

- Today, most pre-competitive collaboration among pharma companies is focused on regulatory influence

- As a next step, collaboration intended to proactively:
  - Have a direct impact on companies' ability to efficiently discovery and develop drugs
  - Provide deliverables that member companies cannot achieve alone
  - **Bring important new medications to patients faster and more efficiently**

- Positive impact to industry, regulators, payers and the patient

What the Pathway Might Look Like

- A group of company representatives assembled by any mechanism develops a proposal to work together to answer address a specific topic
- Each representative then gains agreement of his/her management that collaboration on that topic improves company's prospects
- The first round of collaborations is successful and shows real business outcomes
- Cross-industry collaboration becomes more facile
  - Note that this is the current state in many technology fields
- Initial steps in pharma today have been taken by IQ and TransCelerate

Examples: Broad potential scope

- Collection of retrospective data across all companies providing more decision power than individual companies can achieve
  - e.g. translation of animal toxicology outcomes to human studies
- Generation of new approaches to solve existing bottlenecks in drug discovery and development
  - e.g. Allotrope Foundation for standardization of digital laboratory data
- Creation of standard practices that lead to industry-wide economies of scale
  - e.g. best-in-class automation platforms
- Collective evaluation of tools and technologies with broad validation of design principles and cut-points
  - e.g. formulation approaches for highly lipophilic molecules

Some potential challenges of this approach

- Individual companies may choose not to participate in certain projects
  - Impinges on internal strategic/tactical space
  - Perceive advantages/lead positions in specific areas they may not want to share
  - Will disclose (give away) more than they will gain in return for collaboration
- Perception that some companies will contribute more to outcomes than others
- Substantial effort is required to achieve successful outcomes

Advancing Science in Chemical Process R&D via External Collaborations in Pre-Competitive Space

June 12, 2013, Philadelphia, PA

Boehringer Ingelheim

Types of External Collaborations

Boehringer Ingelheim

BI with Academic

BI with other Industry Leaders

- ❑ Advance new science
- ❑ Economics
- ❑ Freedom to operate
- ❑ Training and Recruiting

- ✓ UCONN MS and PhD Program
- ✓ With individual professors
- ✓ Joint Seminar Speakers
- ✓ Consultants
- ✓ Interns

- ✓ BI-GSK-Pfizer consortium
- ✓ Green Chemistry Roundtable
- ✓ Pharma IQ consortium
- ✓ API Forum

Collaboration with UCONN on Education

Boehringer Ingelheim

BI-UCONN MS and PhD Programs

- The program was designed to train highly skilled MS and PhD chemists for pharma industry.
- BI provides funding to support 6 MS students from 2007-2010 and 3 PhD students from 2013-2016.
- A tailored curriculum was created through discussion between UCONN and BI.
  - As part of the curriculum, BI scientists teach a course “BI Lecture Series”.
  - Program capped with a 6-month internship at BI for MS students and a12-month internship for PhD candidates (in both Med Chem and Chem Dev)
- Intern research at BI has led to high-quality publications, e.g. in JACS and ACIEE.
- The program attracts highly qualified candidates by providing financial aids and

Funding Types for Academic Labs

Boehringer Ingelheim

New Investigator Awards:

- Established since1998
- Jump-start careers of new professors.

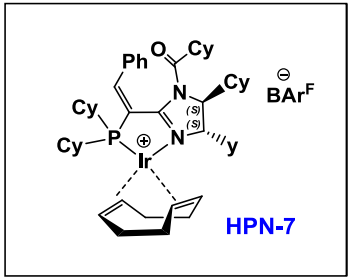
Unrestricted Grants:

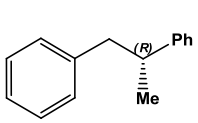
- Provided supports for labs at MIT, Harvard, Yale, Columbia etc.
- Intended to seed high risk, ground-breaking research

Contract Research:

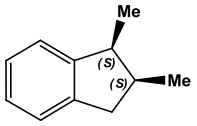
- Collaboration on specific topics related to the need from portfolio.
- Publish results together.
- Recent Example: With Prof. Peter Wipf at the U of Pittsburgh.

BI-Pitt Collaboration on Hydrophosphination and New Ligand Design





95% ee



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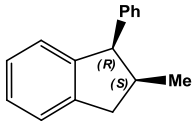


91% ee

Joint publications: Org. Lett. **2013**, *15*, 1132 and 1136.

BI-Pfizer-GSK Consortium

BI-Pfizer-GSK Consortium

- A 3-company consortium was formed to pool resources to drive innovation in critical areas.
- Advancements from this collaboration will be disclosed in a manner to ensure freedom to operate for all.
- Opportunities for future GOALI Grant and Research Center with academic collaborators

Computer-Aided Synthetic Design

Cross Couplings
Using Fe, Ni and Cu

Flow Hydrogenation

Other Industry Wide Consortia

International Consortium for Innovation and Quality in Pharmaceutical Dev.

- To advance science-based and scientifically-driven standards and regulations for pharma and biotech products
- >25 members from industry
- Strong representation from BI on the Board of Managing Directors

ACS Green Chemistry Pharmaceutical Roundtable

- Partnership between the ACS and pharma to integrate the principles of green chemistry and engineering into drug discovery and production.
- >15 members
- BI actively engaged in RoundTable Initiatives

API GMP Forum

- Purpose of the forum is to benchmark the best GMP practices
- Started in 1998
- Major pharmaceutical companies and several contract manufacturing companies

Summary

- Several models for collaboration with academics and other companies.
- Focus on innovation that impacts economics and green chemistry.
- Directly engaged in education/training of next generation of workforce.
- Actively participated in and provided leadership in various consortia.

Pre Competitive Collaboration on Chemical and Chemical Engineering Technology

Geraldine Taber, Pfizer

NIChE Workshop, June 12-13th 2013

A few thoughts from Pfe perspective..

1. **We need to keep telling the "Business Case for Action" story with regard to pre-competitive collaborations in Pharma, both internally and externally**

2. **Pre-competitive collaborations in Pharma will "live or die" by our ability to figure out a mutually successful IP strategy**

3. **There is a strong appetite in Pfe to build on current momentum, remove obstacles and "just do it"**

4. **Keep our "Eye on the Prize" – the "why" for pre-competitive collaborations**

We need to keep telling the story of pre-competitive collaborations…

It takes time to engrain a new way of approaching collaborative science – both internally and externally

What is “obviously a good thing” to some, may not appear so to others

Share the successes/quantify the impact
$, time and scientific impact
What was learned from the failures

Build trust that this approach works, and is worth the effort

Pfe Perspective – The IP factor…

- **Learn to speak the same language –what is pre-competitive space versus competitive space**
  - **This may be defined differently depending on the stakeholders frame of reference**

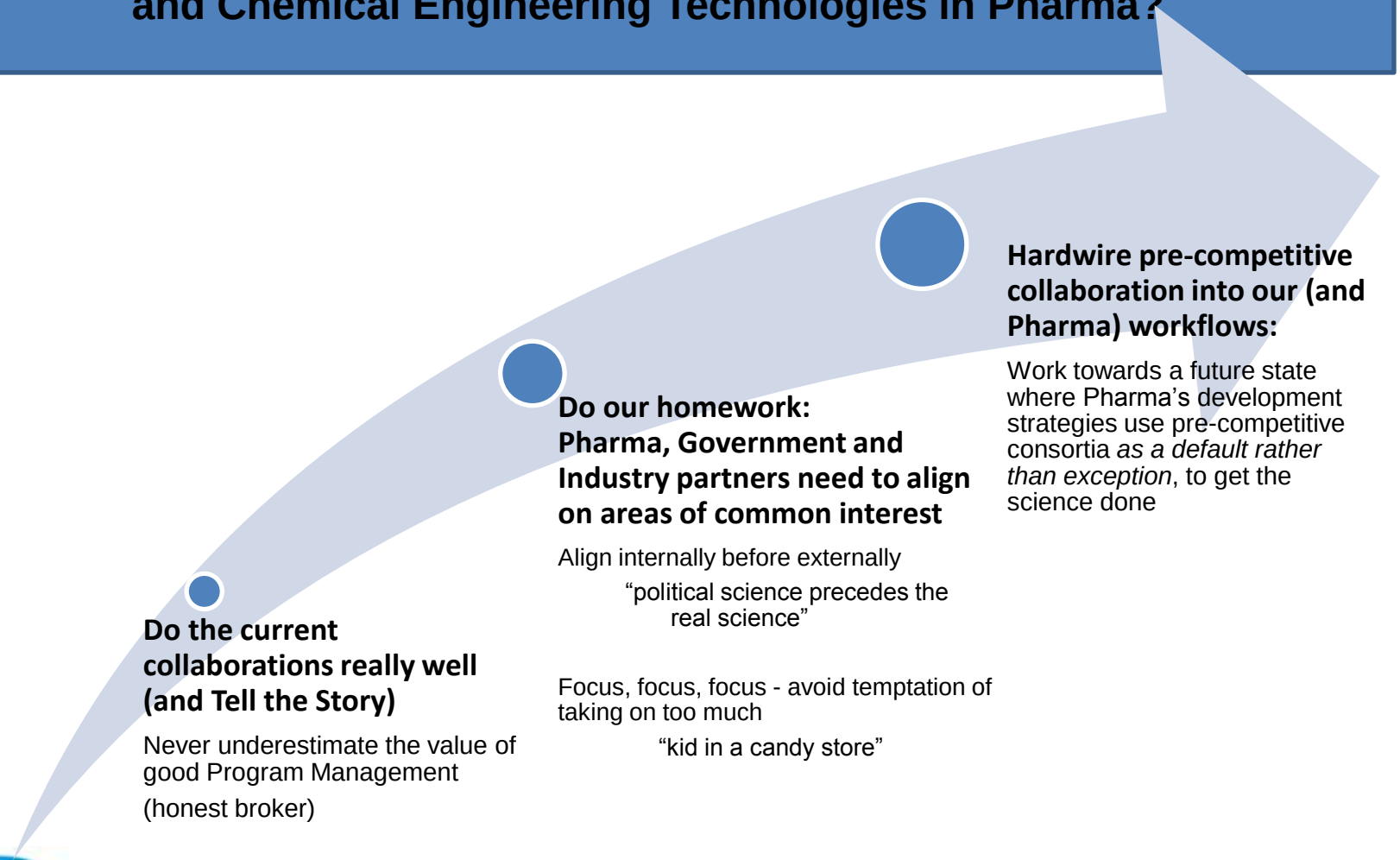
- **In the Chemical and Chemical Engineering space, often our primary interest is to have Freedom to Operate**
  - **There can be unique exceptions**

- **It can be done! We have successful collaborations in many areas**
  - **laboratory automation, enabling reactions, biocatalytic enzymatic screening panels**

- **Focus on establishing suitable templates for Agreements (CDAs, Guiding Principal Documents) that establish IP boundaries and processes**
  - **Clearly establish antitrust transparency**
  - **Avoid the cycle of complete "Agreement re-do" for every new technology**
  - **Keep it "simple" – smaller number of partners gives us a better chance to reach a suitable Agreement**

Appetite in Pfe to build on momentum…

What would enable more pre-competitive collaboration for Chemical and Chemical Engineering Technologies in Pharma?



Do the current collaborations really well (and Tell the Story)

Never underestimate the value of good Program Management

(honest broker)

Do our homework: Pharma, Government and Industry partners need to align on areas of common interest

Align internally before externally

"political science precedes the real science"

Focus, focus, focus - avoid temptation of taking on too much

"kid in a candy store"

Hardwire pre-competitive collaboration into our (and Pharma) workflows:

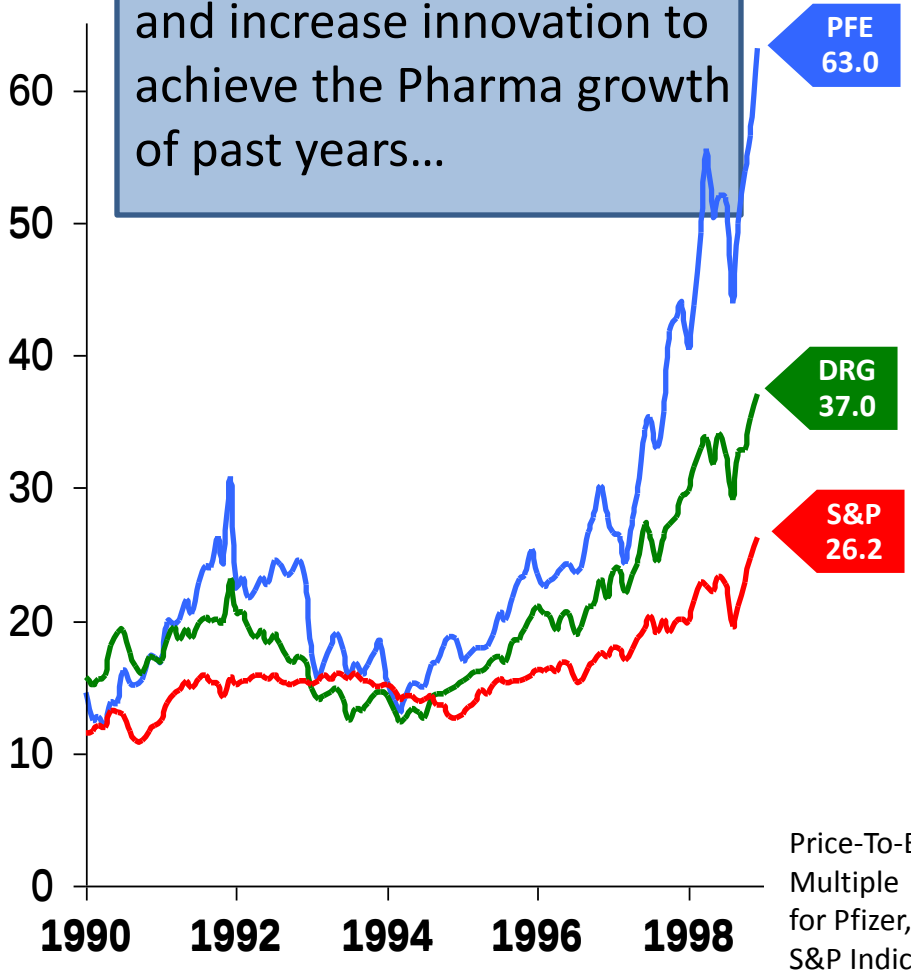
Work towards a future state where Pharma's development strategies use pre-competitive consortia *as a default rather than exception*, to get the science done

Pfe Perspective – Need to Remove Obstacles

- Historical perception of "slow, bloated projects“ that have poor relevance to industry, and/or low quality of results from one-off consortia
  - not true for recent consortia, which are very aligned to our Tech Strategy
- Long set-up time to create consortia
  - Metrics: average=18 mths to get a collaborative project up and running
  - Better structures now in place to enable quicker consortia start up, but its still not fast enough
- Lack of internal FTE time committed to collaboration management and follow through (especially application of the science)
- Consortia funding requirements do not always align with Pfizer's budget planning processes
  - Budget planning process can be lengthy and inconsistent yr on yr

"Eye on the Prize"

We need to control costs and increase innovation to achieve the Pharma growth of past years…



Price-To-Earnings Multiple for Pfizer, Sector and S&P Indices

One of our patients…
http://www.wset.com/story/18616416/3-year-old-cancer-free-on-clinical-trial

But even more importantly… so that vital medicines can be rapidly brought to our patients

Pre-competitive collaborations helped enable crizotinib (Xalkori) to advance from POC to registration in 2 yrs

Precompetitive Collaborations *Enabling Technologies for the Pharmaceutical Industry*

Robert Waltermire, Ph.D.
Executive Director
Chemical Development

Bristol-Myers Squibb

A View on the Value*

- Companies would like to invest less themselves per technology and see the technology come to market faster. General consensus that turnaround time for key technologies has to come down in time
- Companies' experience with trying to develop technology in-house reinforced belief that tool development is not their core business. If they tried to do it on their own they would have failed and stopped
- Hard pressed to identify instrumentation that is a competitive advantage to the pharma company.
- By not collaborating we are inherently never going to converge on technology
- Agreement that getting into instrumentation development together would further above goals

**Round-Table Discussion: 'Productivity Improvements Using Technologies', Nov 2012*

BMS Examples

Chemical Process Development

- Dynochem Resource Center (Scale-up, Inc)
  - Scale up models
- Process Systems Engineering Consortium
  - Automated Crystallization Platform (Prof. Richard Braatz)
  - Lilly, Merck
- Schuf Fetterolf
  - Modified bottom valves to accommodate FTIR probes
  - Improve safety and integrity

BMS Examples

Analytical Technologies

- Two-Square Science
  - Significantly enhanced automated micro-sampling dissolution system development
- Accelrys
  - Development of Lab Execution System (LES) to automate analytical method validation, reporting and approval
- Leap Technologies
  - Hardware and software optimization to improve robustness of UV Fiber Optics probe suitable for QC use

Current BMS Example of ongoing collaboration in pre-competitive space in Real Time Analytics

- **Novel PAT tool developed by Mettler Toledo**
  - Automated collection and preparation of reaction samples directly from process stream
  - Enables accurate analysis of reactive streams, high/low temp reactions, slow reactions, pressurized systems, etc.

- **BMS engaged in strategic consortium to drive product development and share risk**
  - Industry partners: Pfizer, Merck, J&J
  - Instrument prototype delivered to NB for testing May to August 2013

BMS Examples

Formulation/Materials

- Lipid Formulation Classification System
  - Improved understanding of lipid-based oral drug formulations
  - Development of classification system to match physicochemical properties to optimal lipid delivery system
- Engineering Research Center for Structured Organic Particulate Systems (C-SOPS)
  - Modeling and validation of material properites
  - Formation of Nano-Micro API composite powders

BMS Perspective

- See opportunity to streamline ability for and access to collaboration in pre-competitive space
  - Currently driven by functional areas within the organization
  - Many relevant centers and consortiums, but limited resources to join all
- Have strong interest in supporting new models for collaboration

Questions from the Panel

1. We are facing enormously tough problems in an increasingly difficult regulatory and commercial environment, and still have an old fashioned mind-set. This will change – it has to – but soon enough? Look at the car industry – they share motors. Samsung make a lot of parts for Apple….and so on. Why are we so special and how do we change our mind-set?

Questions from the Panel

2. Consortia take a very long time to set up legally and agree upon anything - so the question is whether there is any way we can cut through the red tape and get these collaborations running faster and more effectively?

Questions from the Panel

3. Provocatively, one could say that companies do not share their best science in consortia – since the weaker players benefit most ultimately bringing the entire effort down a notch. Unless this changes, consortia will only work for new unexplored science that nobody is any good at to start with – is there any way to change that or do we just accept it as it is?

Questions from the Panel

4. Does anyone know of an example of a consortium that delivered a top notch breakthrough science in pharma? Assuming the answer is likely no, is it fair to say that consortia are good for incremental optimization rather than breakthrough science? If the answer to the last question is no, are we happy with that and what needs to change to actually deliver a true innovation?

Questions from the Panel

5. For the correlation of Drug Substance powder properties to Drug Product performance does your company already have all the tools for measurement and modeling in place? If not, what do you see as the key gaps that a pre-competitive collaboration could address?

Questions from the Panel

6. At what levels in our organizations do these pre competitive agreements need endorsement, and what can we do to prepare our organizations to be receptive to them?

Questions from the Panel

7. How do we continue to build trust among the players in the Pharma/vendors/academia/ government space, so that precompetitive collaborations can be supported and flourish?

Questions from the Panel

8. Where does the line of pre competitive/competitive demarcation differ across each of the contributing partners businesses? Can we map out the common ground???

Questions from the Panel

9. Would an “Advisory Panel” with representation from the collaborating industries/academia/ government help steer us in this murky area – connect with IQ?

Questions from the Panel

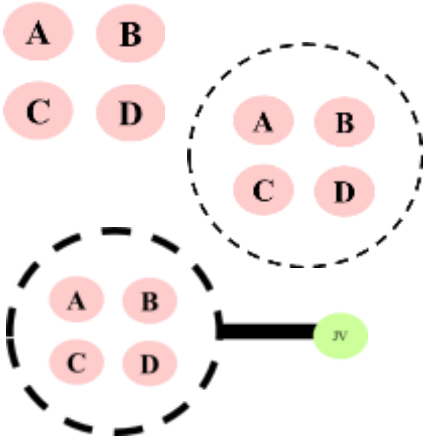
10. What does success look like in 5 years/10 years – are we all working towards the same vision?

Questions from the Panel

11. To impact the CMC development cycle a Precompetitive Collaboration must be disruptive. What opportunity do you consider will add the highest value in the CMC space and given the current economic climate how will you define the Value Proposition to convince your organization to invest?

Questions?

- Preferred collaboration model?:
  - just do it
  - formalized collaboration
  - shared lab in the middle



?

Questions?

- How to assure proper business practices?

- What can and can’t be done?

- How best to ensure openness and transparency of operations while allowing for confidentiality?

- Lunch is served

- Lectures resume at 1:00 pm sharp!

1:00 - 1:30

Case Studies in Funded External Collaborations

Nick Thomson (Pfizer)

Moderator: Chris Welch

Council for Chemical Research

Case Studies in Funded External Collaborations

Nick Thomson, Pfizer Inc.

NIChE Workshop, June 12th 2013

Outline

- Pfizer pre-competitive landscape
- The collaborative journey
  - Alignment, idea generation, partnerships, funding, execution
- A few examples of our journeys for laboratory and synthetic enabling technologies
- Some things we learnt along the way
- Thoughts on the future

Headline

- Pfizer Pharmaceutical Sciences wholeheartedly support pre-competitive collaborations that are aligned with our technology strategy
  - Aim to develop better solutions, faster, at lower cost, with less internal resource and with reduced risk

Partnership

“Bristol-Myers Squibb and Pfizer Announce U.S. FDA Approval of ELIQUIS® (apixaban)”

“Rival giants team on diabetes as Merck partners with Pfizer on SGLT2 combo”

“In the long history of humankind, those who learned to collaborate and improvise most effectively have prevailed.”

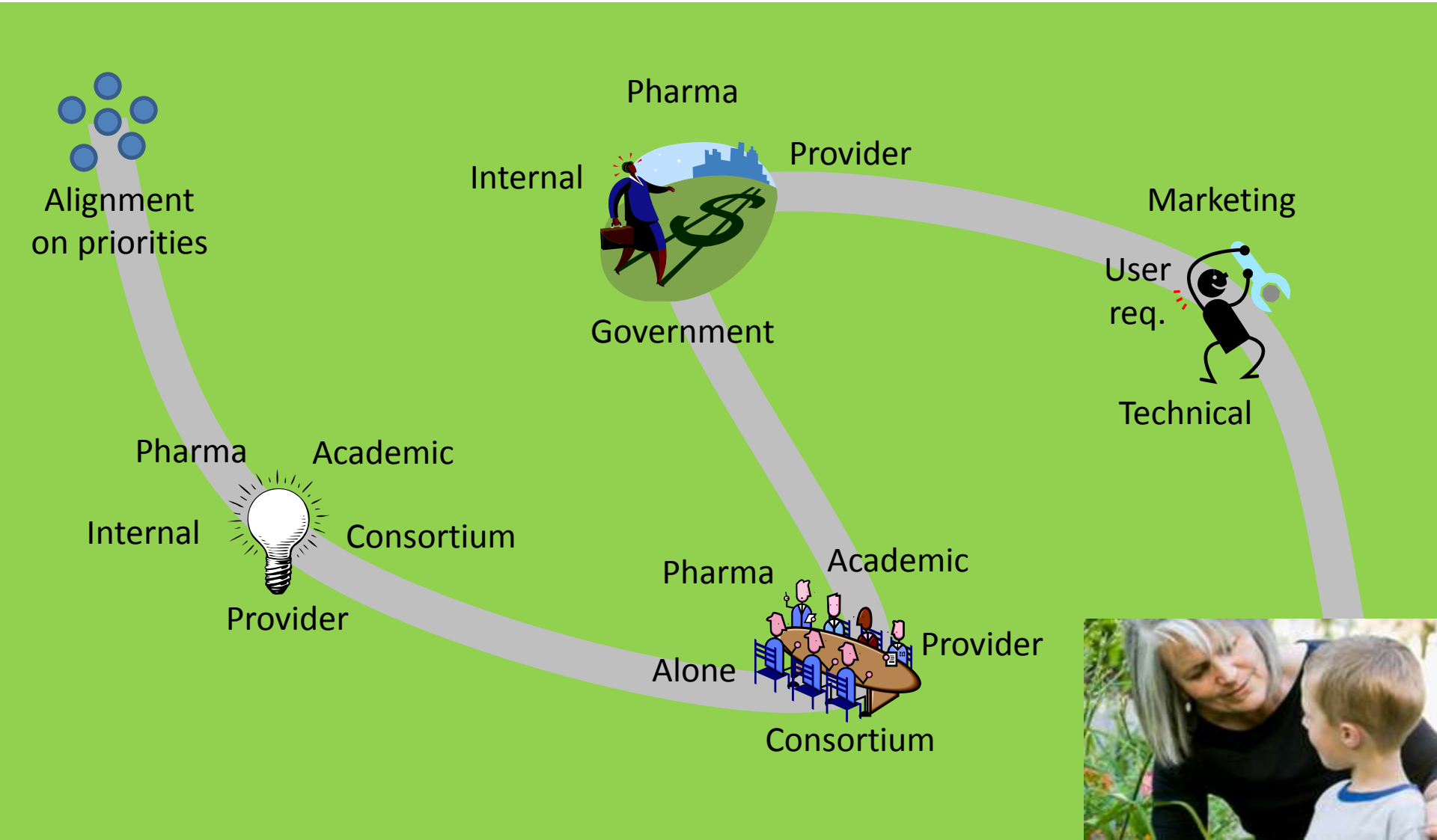
-Charles Darwin

Trust and Anti-Trust

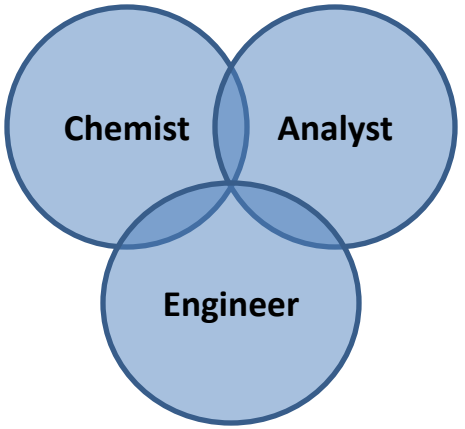
Diocletian, 301 AD

INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

The Collaborative Journey



Alignment



gsk GlaxoSmithKline

AMGEN

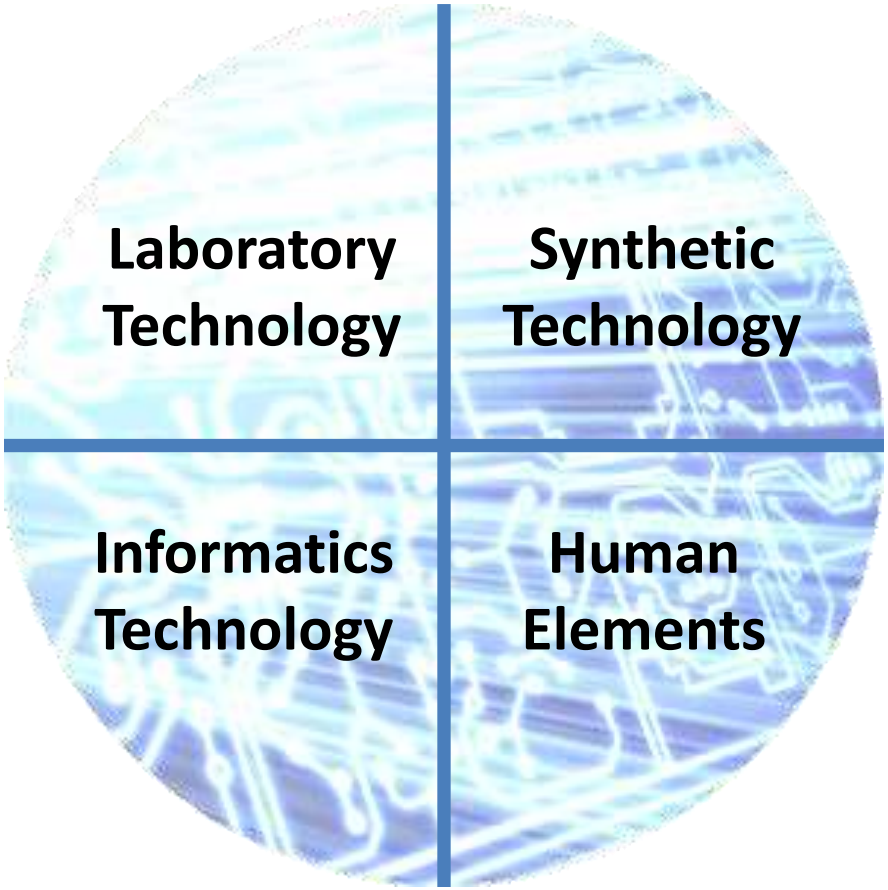
Pfizer

Boehringer Ingelheim

Bristol-Myers Squibb Company

janssen

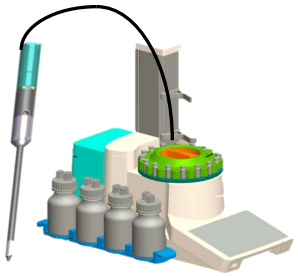
Alignment on Technology Strategy



Laboratory Technology

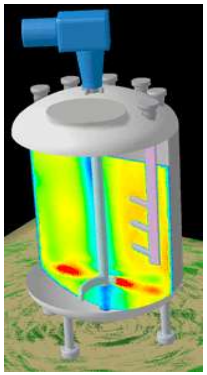






1998 → **Present**






Lab of the Future Investment

2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014

Development of Prototype Labs

Implementation Deployment of Ready Technologies

◆ Set up of new LOTF environment in US and UK facilities

- Multi-million dollar investment over 5 year period

METTLER TOLEDO

TELEDYNE ISCO

Waters THE SCIENCE OF WHAT'S POSSIBLE.™

SYSTAG automatically better

CHEMGLASS

HEL better chemistry - faster

Biotage

Optimization and Sustainability of LOTF

Continued Evolution of Technologies

Development of LotF Culture

Automated Parallel Lab Reactor Example

Argonaut AS 3400

Control experimental parameters

- Mimic scale up
- Minimize extraneous variables

Collect more **data**, e.g. calorimetry:

- "Rate meter"
- Safety data during route development

Shared back plane for **parallel** reactions

- a series for optimization
- or totally independent

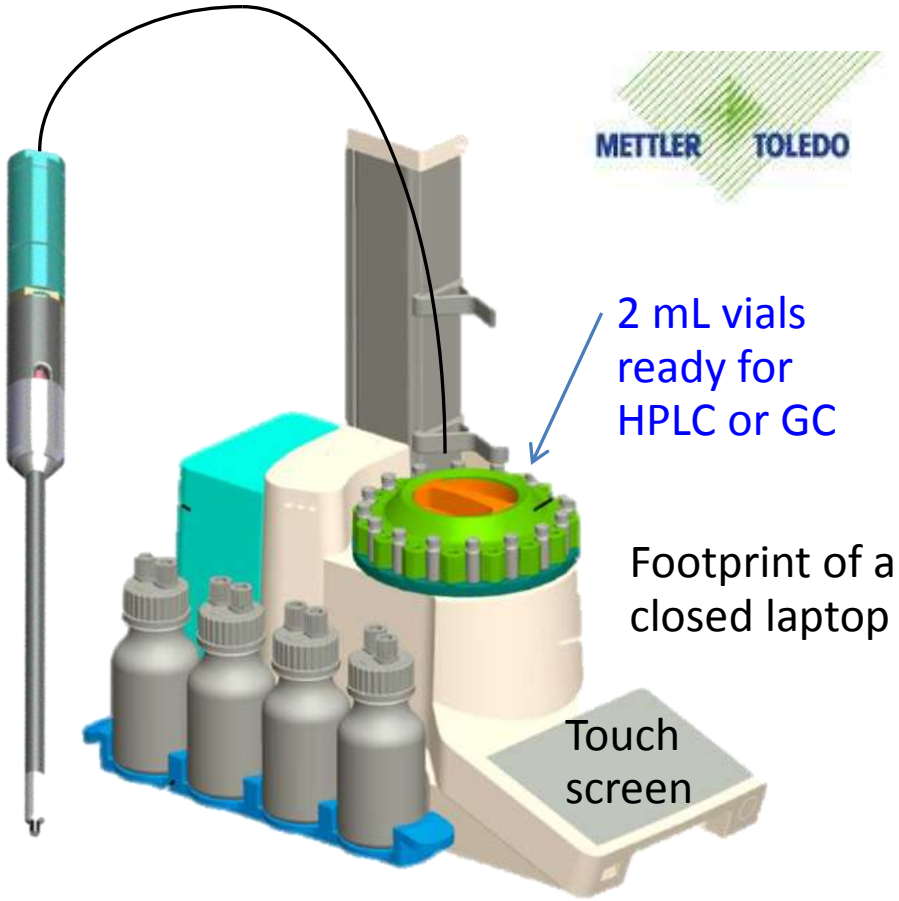
Greater Quantity and Quality of Data

The Collaborative Journey

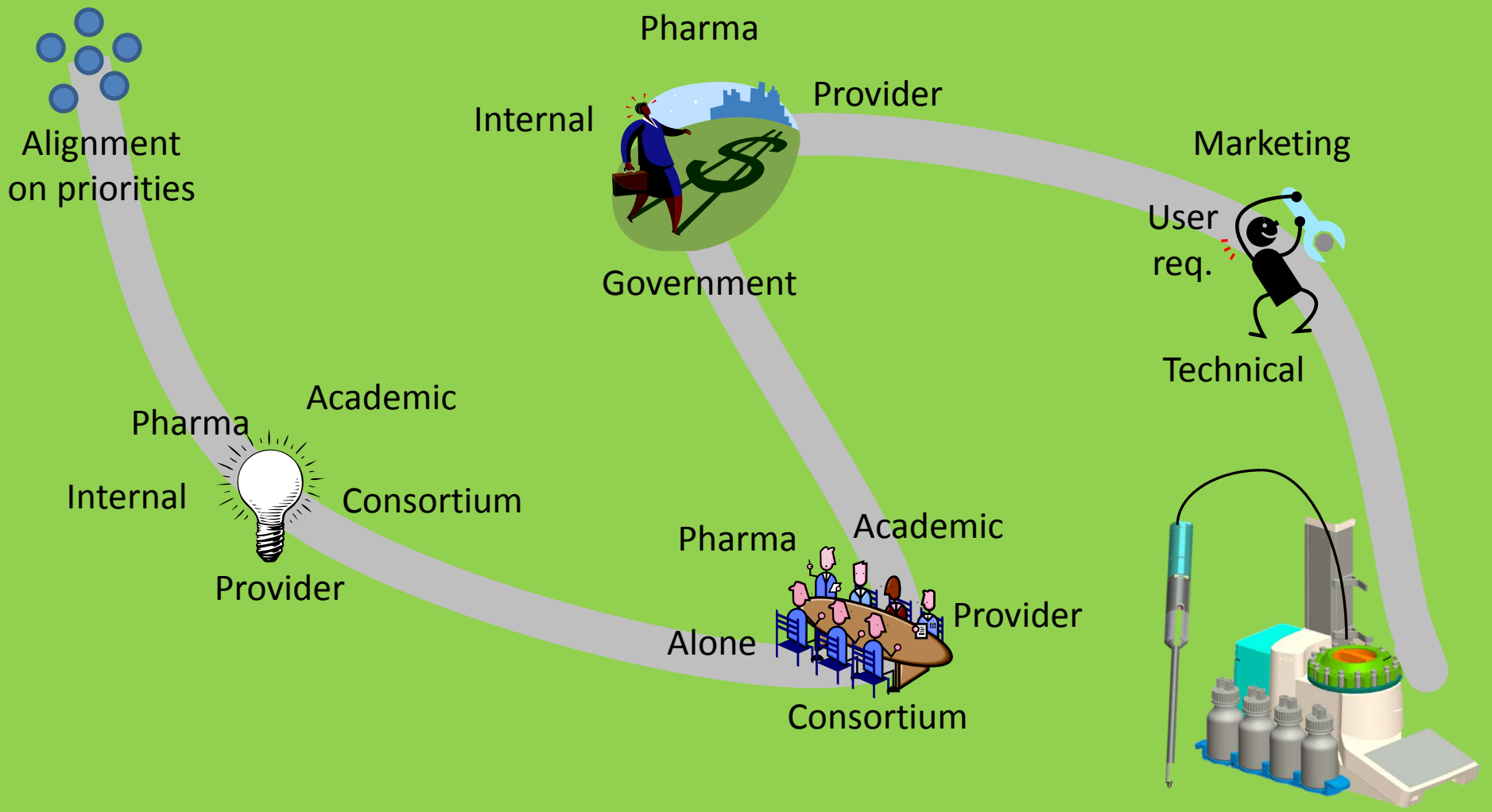
Automated Sampling Example

Goal to sample:

- Without air exposure
- From hot tanks without the need to cool first
- From cold systems with immediate quenching at the reaction temperature with proton or other electrophiles
- From slurries where the solids are sampled representatively
- With continuity of analytical method from lab to scale up
- Utilize the high dynamic range of HPLC to profile the main transformation and impurities



The Collaborative Journey



Continued Evolution

Technology Areas of Focus
Automated Parallel High Throughput Screening
Automated (parallel) lab reactors
Faster broader analytics - UPLC MS
In situ Monitoring and Characterization (Raman, FTIR and FBRM)
PAT Data Management
Computational Chemistry Algorithms
Predictive Tools for Chemical Properties
In-silico tools for Process Modeling (CFD, mixing, kinetics)
Crystallization Screening Technologies

Focus Areas

- Replacement of Endangered/Precious Metal Catalysts
- Catalytic Methods for Preparation of Chiral Amines
- Methods for “Direct” Amide or Peptide Formation
- “Direct” Substitution of Alcohols
- C-O and C-N Redox Interconversions

Gaining Knowledge

Horizon 1	Horizon 2	Horizon 3
Direct Portfolio Impact	**Targeted innovation for immediate portfolio**	**Broader funding of longer term innovations**
• Create internal technology champions • Establish best practices • Test against portfolio • Identify gaps • Opportunistically innovate new technology • Influence external environment	• Technology workflows in place (≥ 50% portfolio impact) • transferred to Pharma partners • Innovate solutions to targeted technology gaps	•Widespread value appreciation (private/public) • Broad uptake in academia and pharma
No external $ investment	**Focused Pharma $ investment**	**Selected Pharma $ investment**
Private Sector Pharma Consortium	Private Sector Pharma Consortium	Private Sector Pharma Consortium
	Private – Academic Alliances	Selective Private – Academic Alliances
		Government Funded Research Institute and GOALI grants

Non Precious Metal Catalysis

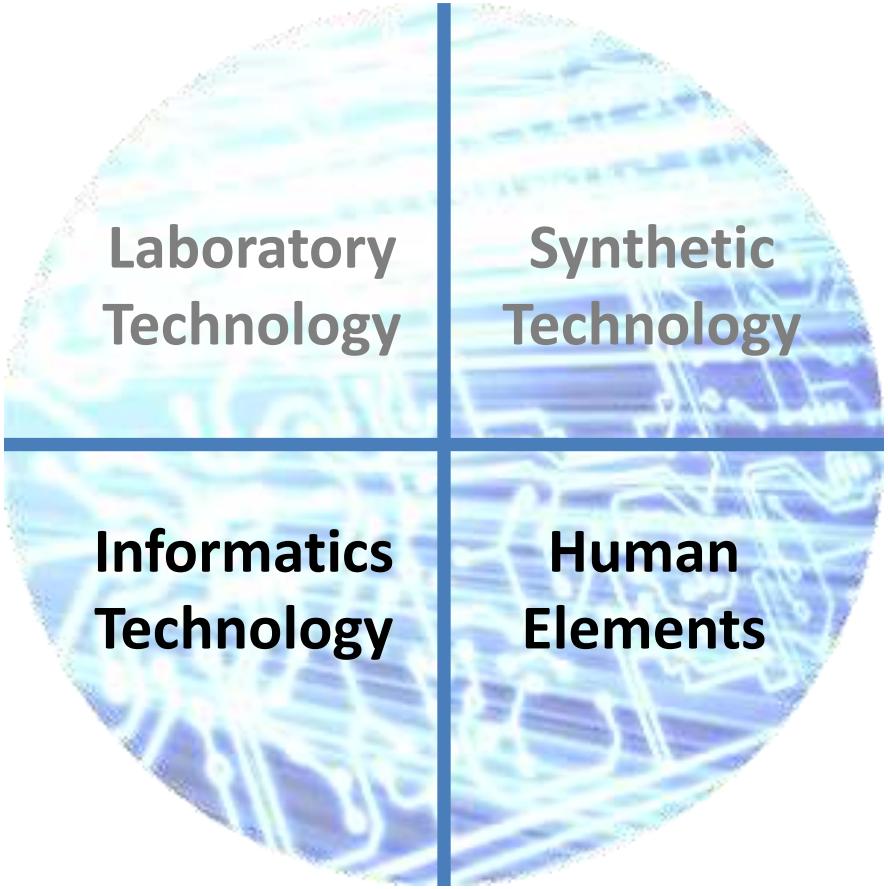
Boehringer Ingelheim

gsk GlaxoSmithKline

Academic Partners

Pfizer

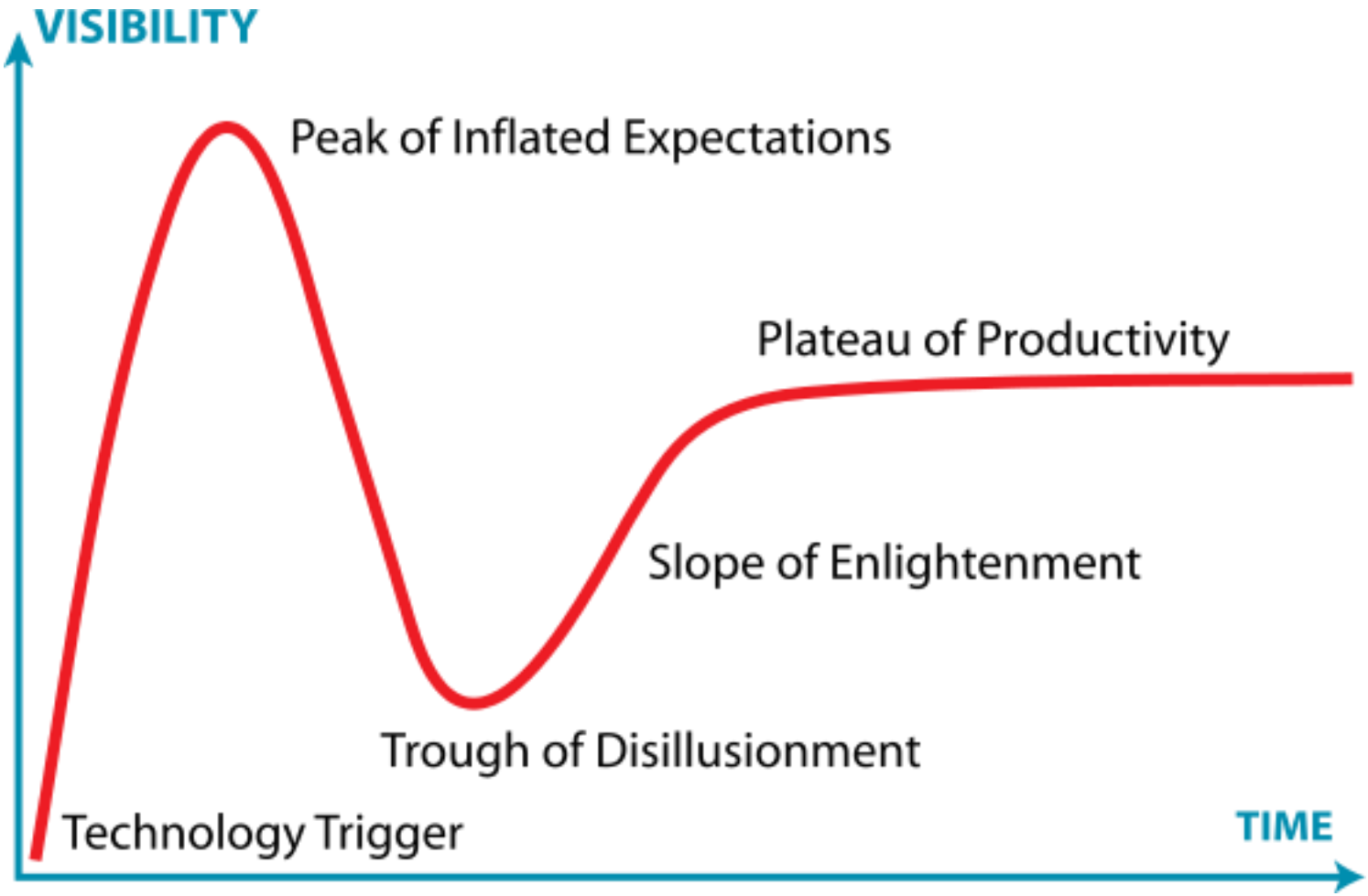
	Cost		Toxicity	Sustainability	
Metal	**Cost ($/oz)[1]**	**Annual Production (tonnes)**	**Oral Exposure limits (ppm)**	**Natural Abundance (ppm)**	**Supply Risk Index**
Pd	607	24	10	0.015	8.5
Ni	0.52	1,350,000	25	90	4.0
Cu	0.23	15,000,000	250	68	4.5
Fe	0.006	1,200,00,00	1300	56,300	3.5


Laboratory Technology
Synthetic Technology
Informatics Technology
Human Elements

Some Key Learning

- We should have gotten to this point through innovation rather than economic drivers
- Pet projects don't usually end well- align
- Appreciate the science outside your walls
- Work with others to disseminate an improved common platform/solution across the industry
  - Share cost, risk, ideas and enjoy the sustainability
- Find the right partners with complimentary skills and knowledge
  - Similar mindsets but different perspectives
- Pre-competitive collaboration is a bedrock of future technology strategy

Where are We?


VISIBILITY
Peak of Inflated Expectations
Plateau of Productivity
Slope of Enlightenment
Trough of Disillusionment
Technology Trigger
TIME


TRUST

Acknowledgments

- Gerry Taber
- Joel Hawkins
- Chris McWilliams
- Juan Colberg
- Many others!

1:30 - 2:00

Academic Collaborations with Pharma: Past, Present, and Future

Gary Molander (University of Pennsylvania)

Council for Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

FUNDING for INDUSTRY/ACADEMIC COLLABORATIONS

FORMS OF SUPPORT

- **INDUSTRIAL**
  - **Unrestricted/Gifts**
  - **Sponsored research projects**

- **FEDERAL GRANT SUPPORT**
  - **GOALI**
  - **Centers for Chemical Innovation**

Unrestricted Research Support/Gifts

- No IP Issues
- No Facilities & Administrative Costs
- Maximum Flexibility, but Minimum Accountability
  - No specific line of research
  - No conditions for reports/invoicing
  - No return of unexpended funds
- Young Investigator Programs

Sponsored Research Agreements

Sponsored Research Agreements

LAWYERS!!

Sponsored Research Agreements

- IP Issues
- Facilities & Administrative Costs – need approval to waive
- Specific line of research
- Specific reporting and invoicing requirements
- Dissemination of results – publication issues
- Relevance to educational mission
- Formal programs established

NSF GOALI

Grant Opportunities for Academic Liaison with Industry

Promotes University-Industry Partnerships

- Provides exposure of academic coworkers to industry
- Industrial scientists bring perspective to academia

Targets high-risk/high-gain, fundamental research

New approaches to solving generic problems

Development of innovative, collaborative educational programs

Direct transfer of knowledge

Funding of transformative research that lies beyond what industry would normally fund

NSF Centers for Chemical Innovation

Supports research focused on major, long term chemical research challenges – transformative, lead to innovation that attracts broad scientific and public interest

Translation or transfer of basic research results into social or economic benefit

PIs must insure that proposed project does not overlap with ongoing federally-funded research

Sustainable Chemistry, Engineering and Materials SusChEM

New emphasis related to synthesis, use and reuse of chemicals

Must advance science to inform societal actions aimed at environmental and economic sustainability

Specifically addresses interrelated challenges of sustainable supply chains, production, and environmentally benign use of chemicals by design

Fundamental research topics of interest include replacement of rare, expensive, and/or toxic chemicals

- Coffee is served

- Lectures resume at 3:15 sharp!

2:00 - 3:00

Panel Discussion: Vendor and Supplier Collaboration with Pharma

Moderator, Jean Tom

Panelists:
- Henry Dubina (Mettler-Toledo)
- Diane Diehl (Waters)
- Russell Gant (Sigma-Aldrich)

Council for Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

Panel Format

- Each speaker will present a 10-15 min introduction, making key points.
- Limited discussion following each presentation, intended for clarification.
- Questions from the audience and lively discussion encouraged after all of the introductory presentations are completed.
- In the spirit of a workshop we want to hear everyone's ideas.

Henry Dubina Deck Here

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Collaboration Facilitates a Keen Understanding

Diane M. Diehl, Ph.D.

Director, QC & Manufacturing

Pharmaceutical & Life Sciences Business Operations

Precompetitive Collaborations: Enabling Technologies for the Pharmaceutical Industry
June 12 & 13, 2013

Waters Corporation Origins

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

James L Waters

Waters Associates - 1958

GPC-200 - 1962

Waters Corporation Today

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Separations Science

Mass Spectrometry

Informatics

Chemistries

Standards & Reagents

Services

www.waters.com

TA Instruments

Microcalorimetry

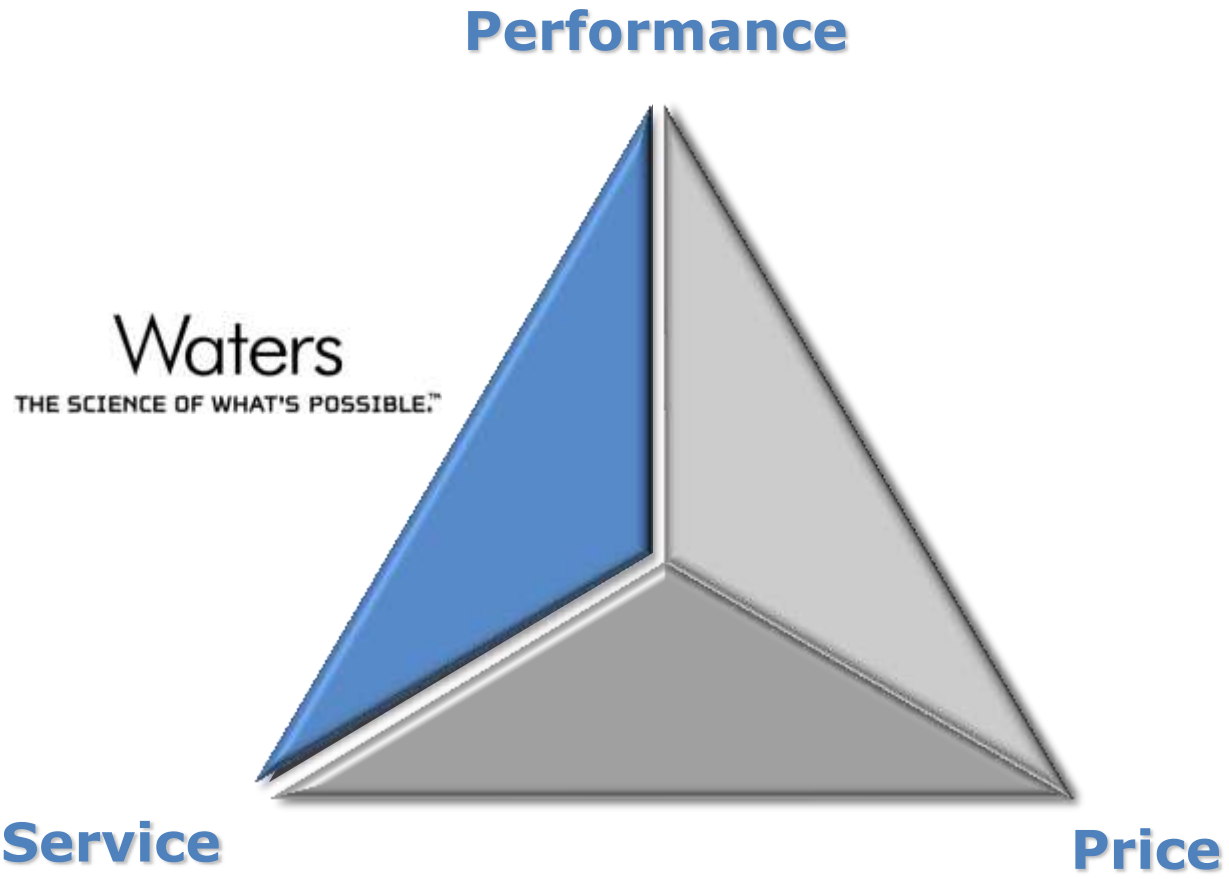
Thermal Analysis

Rheometry

www.tainstruments.com

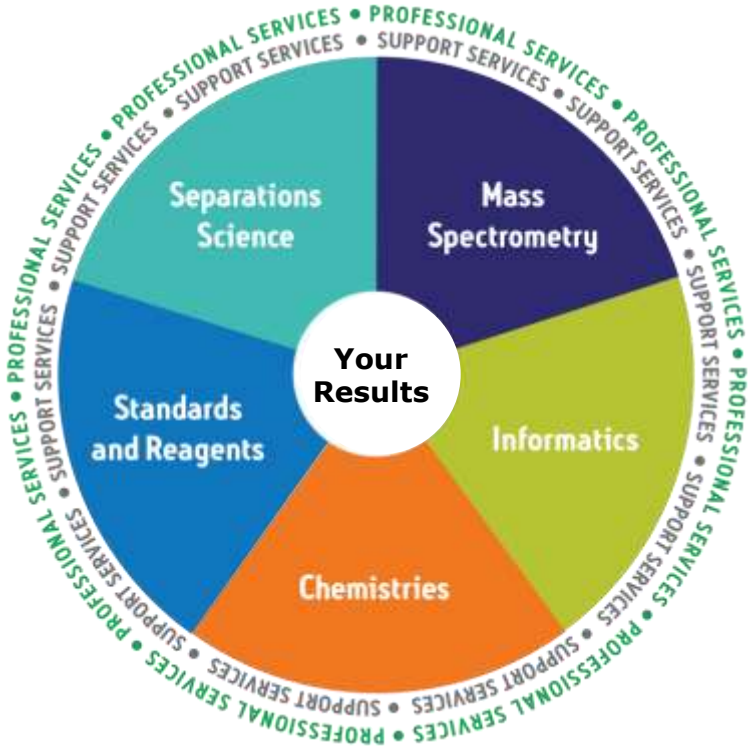
Our Business Strategy

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™



Our Differentiation Strategy

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™



Our strong core competencies are the foundations of fully integrated solutions

Our Mission

- Keen understanding of our customers
- Delivering innovative solutions
- Ability to make positive impact on customers' performance

Facilitating Keen Understanding

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

- Networking and open dialog
- Executive Technology Forums
  - Delegate speakers
  - Waters speakers
  - Roundtable discussions
- Centers of Innovation
  - 20+ Leading Analytical Chemists
- Research Collaborations
- Beta Programs

Points to Consider

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

- Clearly identified goals and objectives
  - Free flowing R&D?
  - Beta evaluation?
  - Application development?
  - Intent to purchase?
- Both parties engaged in the process
- IP ownership defined before collaboration starts
- NDA's when appropriate
- Mutually agreed upon timelines

Waters

THE SCIENCE OF WHAT'S POSSIBLE.™

Sigma-Aldrich Corporation

Enabling Science to Improve the Quality of Life

sigma-aldrich.com

Precompetitive Collaborations:

Enabling Technologies for the Pharmaceutical Industry

June, 12, 2013

SIGMA-ALDRICH®

“Lucky NASDAQ Winners…”

“Investors played a game of financial pile-on in 2000. Darlings…became household names, and individual investors jumped…Since then not one has paid off for investors.”

But several NASDAQ stocks that got little notice in 2000 turned out to be the real stars, including scientific gear maker ***Sigma-Aldrich…Sigma-Aldrich is up 600% since 2000, the best performance in the NASDAQ 100 after Apple.”***

THREE TOP NASDAQ PERFORMERS

1.

2. SIGMA-ALDRICH®

3.

Source: USATODAY.com – March 5, 2013

Sigma-Aldrich At-A-Glance

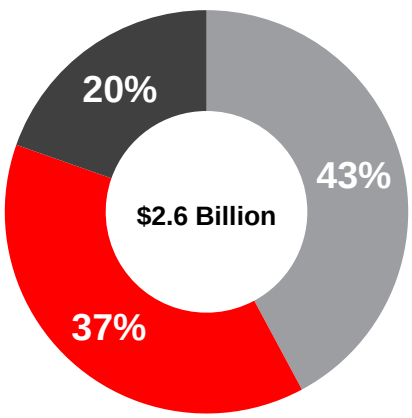
MISSION

Enabling Science to Improve the Quality of Life

VISION

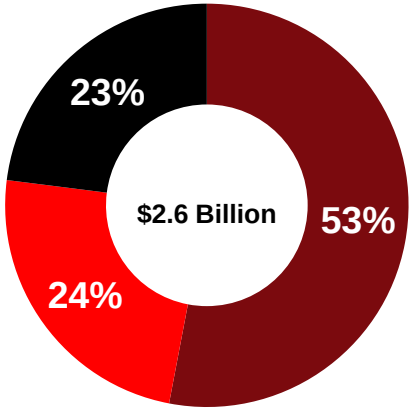
To be the trusted and preeminent global provider to the research laboratory and targeted applied and commercial markets

FACT AND FIGURES



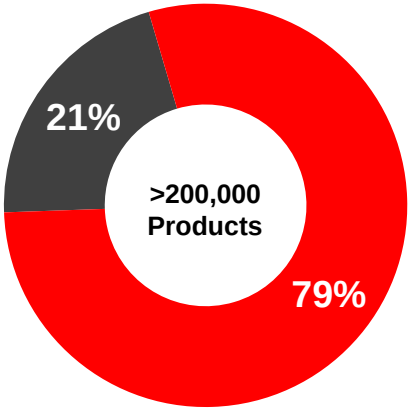
GLOBALLY BALANCED

- United States and Canada
- Europe, Middle East, Africa
- Asia Pacific and Latin America



DIVERSE END-MARKETS

- 53% Research
- 23% Applied
- 24% SAFC Commercial



QUALITY PRODUCTS

- >170,000 Reagents and Chemicals
- 45,000 Laboratory Equipment Items

Our People

~9,000

Employees Worldwide

Our Places

50+

Sales Offices

30+

Distribution Centers

40+

Production/Lab Facilities

SIGMA-ALDRICH®

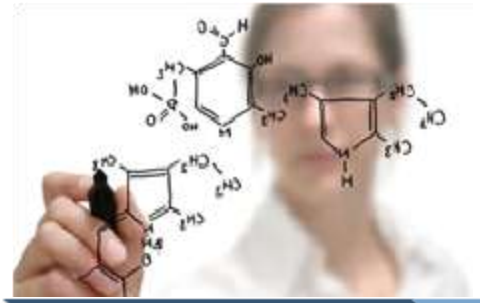
Chemical Synthesis Workflow

PIPELINE: Planning and Preparation → Synthesis and Manufacturing → Purification and Characterization

	Planning and Preparation	Synthesis and Manufacturing	Purification and Characterization
Products & Services for RESEARCH:	• Eight million unique chemicals on website • Compound management • Technical service & support	• Catalysts • Monomers • Specialty synthesis products	• LC and GC columns • Sample collection and preparation • Reference standards
Products & Services for COMMERCIAL:	• Customized packaging • Compound management • Technical service & support	• DNA/RNA amidites • Organometallics • High-potency API manufacturing	• Chiral offering • QA and Analytical Support

Essential Chemicals and Raw Materials

Life Science Workflow



PIPELINE: DNA & RNA → Proteins & Small Molecules → Cells & Organisms

	DNA & RNA	Proteins & Small Molecules	Cells & Organisms
Products & Services for RESEARCH:	• RNAi • ZFN gene editing • Whole genome amplification • Oligonucleotides • PCR reagents	• Protein depletion technology • SPME devices • LC and GC columns • LOPAC® small molecule library • Validated antibodies	• Reporter cell lines • Media • Expression systems
Products & Services for COMMERCIAL:	• Oligonucleotides • Industrial enzymes	• Vaccine development • Bioconjugation • LC and GC columns	• Media & supplements • CHOZN™ platform • Contract manufacturing • Single-use technology • Specialized assays

Essential Chemicals and Raw Materials

Analytical Workflow

PIPELINE: Sample Prep → Detection → Analysis

Products & Services Sigma-Aldrich Offers:

Sample Prep	Detection	Analysis
• Protein depletion technology • SPE, SPME….. • DNA/RNA extraction kits • Sampling devices • PCR reagents	• Oligonucleotides • Derivatization/detection reagents • Enzymes • Antibodies	• U/HPLC columns • GC columns

Standards & Reference Materials

High Purity Solvents

Essential Chemicals and Raw Materials

SIGMA-ALDRICH®

Innovation Process – From opportunity discovery to market capture

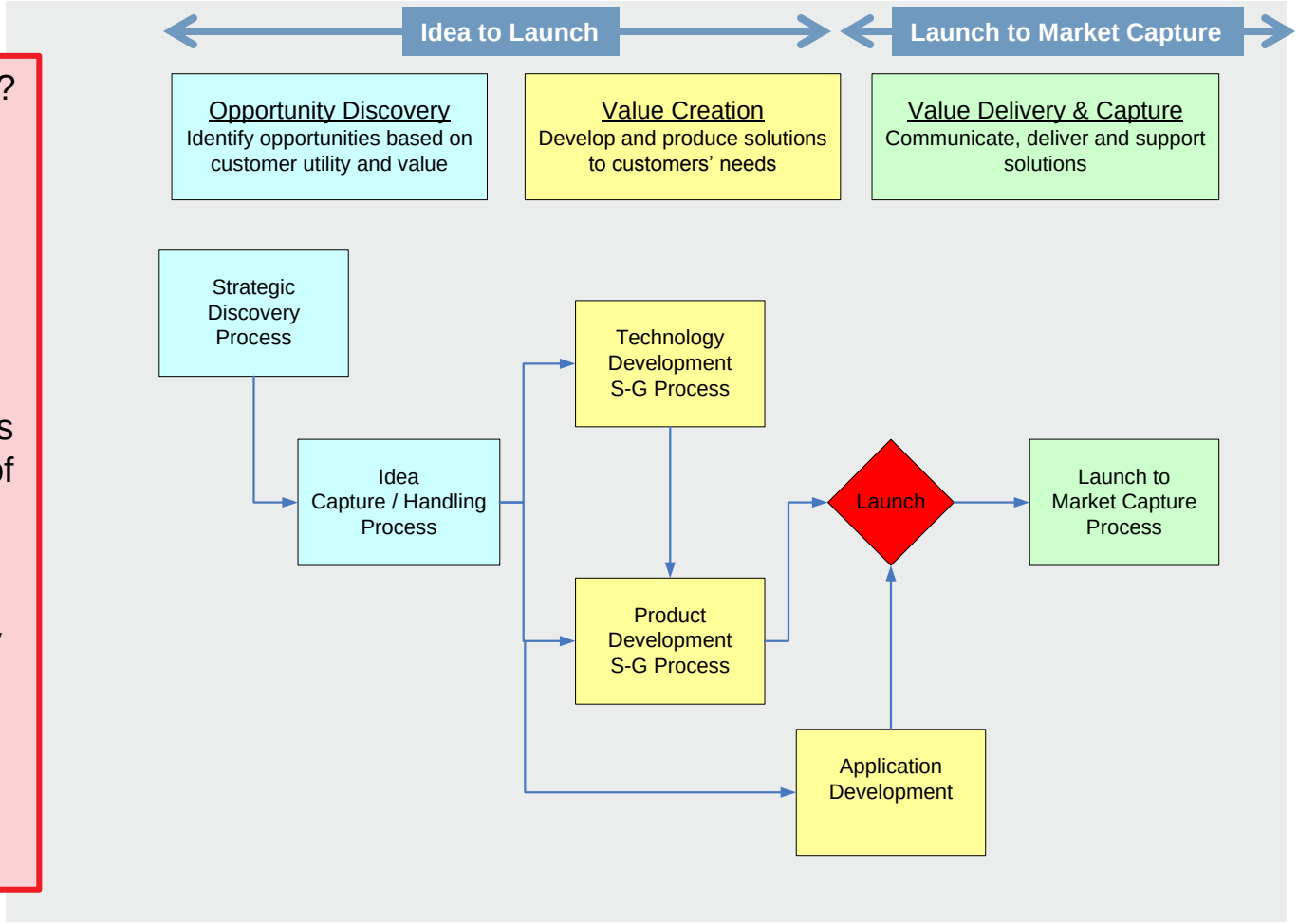
Where do ideas come from?

How do we turn ideas into products?

How can we improve?

Keys:

- Pharma customer needs
- Combined capabilities of academia, government and industry
- Common framework for turning ideas into reality
  - Scope
  - Scale
  - Speed
  - Effectiveness



Precompetitive collaboration: How can we work together to do a better job of identifying and solving important problems (faster)?

SIGMA-ALDRICH®

Thank You For Your Time…
Any Questions?

- Coffee

- Lectures resume at 3:00 pm

3:15- 3:45

The Role of Government Labs in Facilitating Multi-Party Collaboration

Mike Tarlov (National Institute of Standards and Technology, NIST)

Council for Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

The Role of Government Labs in Facilitating Multi-Party Collaboration

Michael J. Tarlov
Chief, Biomolecular Measurement Division
Coordinator of NIST Biomanufacturing Program
Material Measurement Laboratory

CCR Workshop on Precompetitive Collaborations: Enabling Technologies for the Pharmaceutical Industry

Philadelphia, PA
June 12, 2013

NIST
National Institute of Standards and Technology
U.S. Department of Commerce

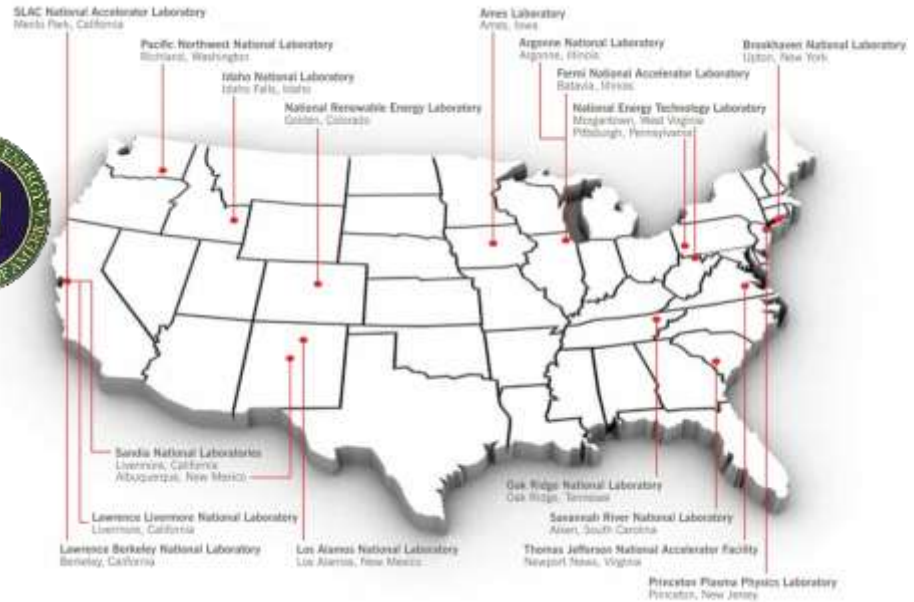
Talk Overview

- **The Federal Laboratory Landscape**
- **NIST Overview**
- **NIST Facilitating Multi-Party Collaborations: Examples from NIST Biomanufacturing Program**
- **Model for How Industry and Government Can Work Together on a Larger Scale: Sematech**
- **Future Opportunity: The National Network for Manufacturing Innovation (NNMI)**

*Some opinions expressed here are mine and may not represent the official view or positions of NIST

Federal Laboratory Ecosystem

Over 300 federal labs



17

13

>10

Intramural lab programs
NCATS

Air Force 34
Army 49
Navy 43

6
(JPL, Goddard, etc.)

>100

37

Collaborative mechanisms:

- Funding
- CRADAs
- Licensing of technology
- User facilities
- Regulatory

National Institute of Standards and Technology (NIST)

- Non-regulatory agency within U.S. Department of Commerce
- Founded in 1901 as National Bureau of Standards
- NIST responsible for US physical standards, test methods, & calibrations

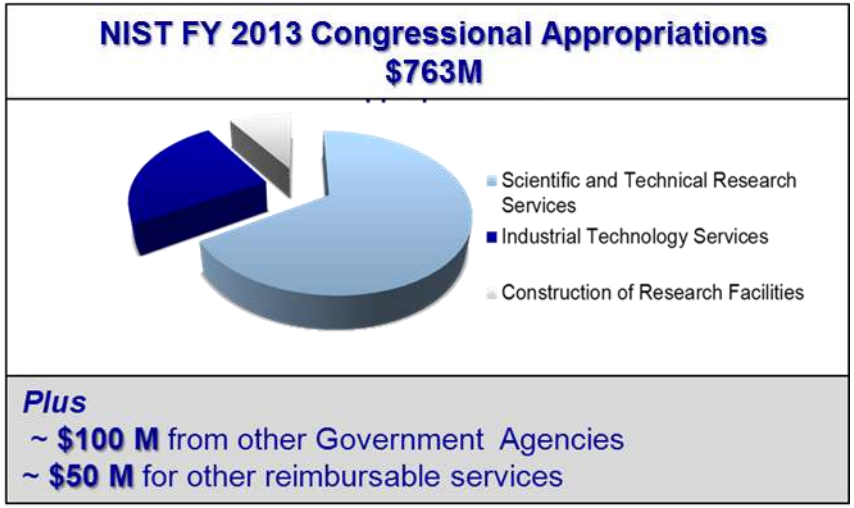
***Unique Mission within the Federal Government* ...**

to promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life

NIST-at-a-Glance

Major Assets

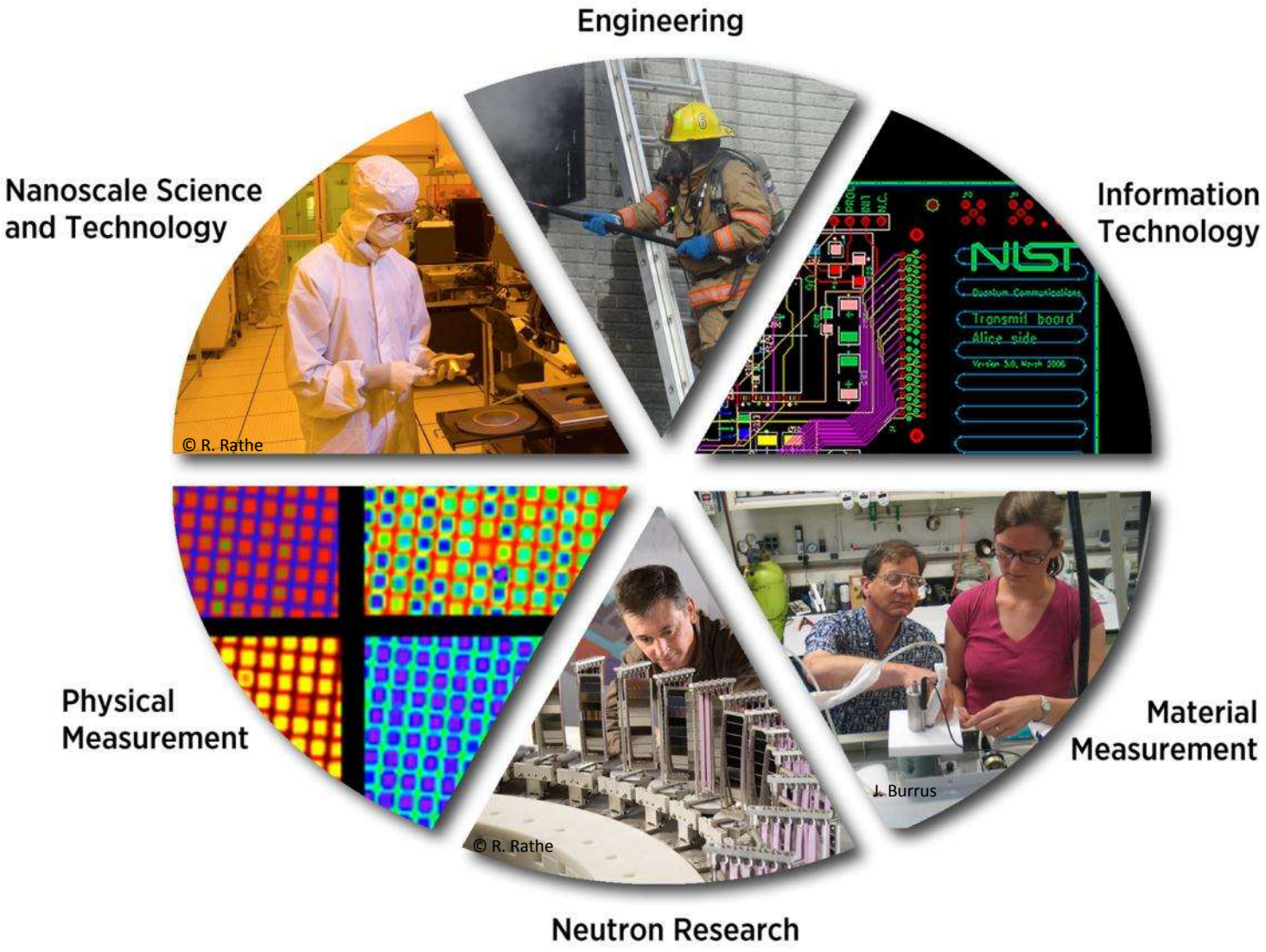
- ~ 3,000 Employees; 1,800 Scientists and Engineers (4 Nobel Laureates)
- ~ 2,800 Associates and Facilities Users
- Two main locations: Gaithersburg, Md., and Boulder, Colo.
- Four external collaborative institutes: biotech, basic physics, quantum, and marine science



Gaithersburg, MD
62 buildings; 578 acres

Boulder, CO
26 buildings; 208 acres

NIST Laboratories



NIST's Increasing Role in Addressing National Priorities

Healthcare

- Biomanufacturing
- Clinical Diagnostics

Advanced Manufacturing

- Nanomanufacturing
- Materials Genome Initiative
- The Advanced Manufacturing National Program Office

Cybersecurity

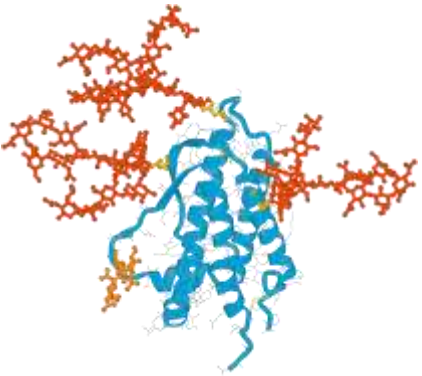
- National Cybersecurity Center of Excellence

Forensics

NIST Criteria for Priority Setting:

1. Magnitude/urgency of industrial need
2. Correspondence between need and NIST mission to develop infrastructural technologies
3. Can NIST participation make a major difference
4. Potential impact of NIST involvement
5. Can NIST respond with a timely, high quality product

NIST Program in Biomanufacturing



Measurement science, tools & standards to support development, manufacturing & regulatory approval of biologic drugs

Developed from Over 5 Years of Stakeholder Input:

AMGEN, Janssen, FDA, Genentech A Member of the Roche Group, biogen idec, MedImmune, Bristol-Myers Squibb, Pfizer, Lilly, MERCK, gsk, SANDOZ Biopharmaceuticals

Established the "NIST Biopharmaceutical Measurement Roundtable" in 2012:

- Purpose: identify current and future measurement needs in development, manufacturing, and regulatory approval of protein therapeutics; provide feedback on relevancy of NIST programs in biopharma
- Members: ~10 CMC subject matter experts from biopharma industry
- Convenes annually at the WCBP meeting in Washington, DC

NIST Biomanufacturing Program Areas

- ~$8.5M Total Funding: FY12 $4M + FY13 $2M + $2.5M base funds
- Supports ~25 staff, 3 Divisions

Protein Stability

- Predicting protein stability
- Protein particulates

Protein Structure

- Primary structure: sequence of amino acids
- Key modifications: sugars, i.e., glycosylation
- Higher order structure: complex folding of protein drugs

Tools for Understanding Production Cells

- Measurement science & tools for production cells to understand product variability & bioprocess-product quality relationships

Collaboration Through User Facilities: Neutrons for Protein Stability Measurements

PIs: Marc Cicerone, Ron Jones

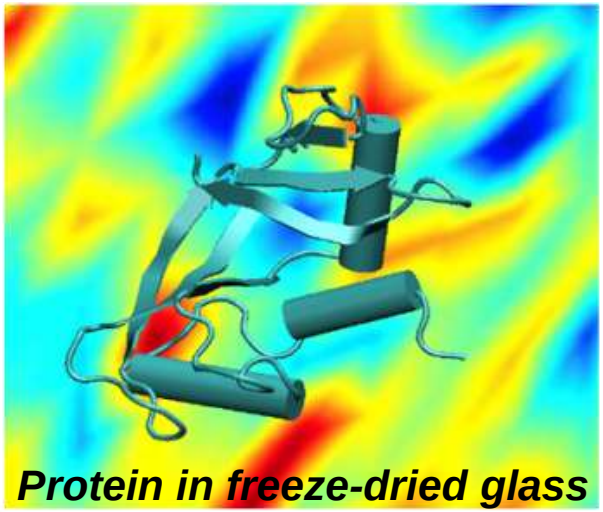
nSoft

- **New NIST-led industrial consortium established for access to neutron facilities for soft materials manufacturers including biopharmaceutical industry**
- **Current members: Dow Chemical, Rhodia, MedImmune, Genentech, Kimberly Clark, DuPont, ExxonMobil*, BristolMyersSquibb*, Chevron Phillips***

The NIST Center for Neutron Research

Protein Stability During Storage

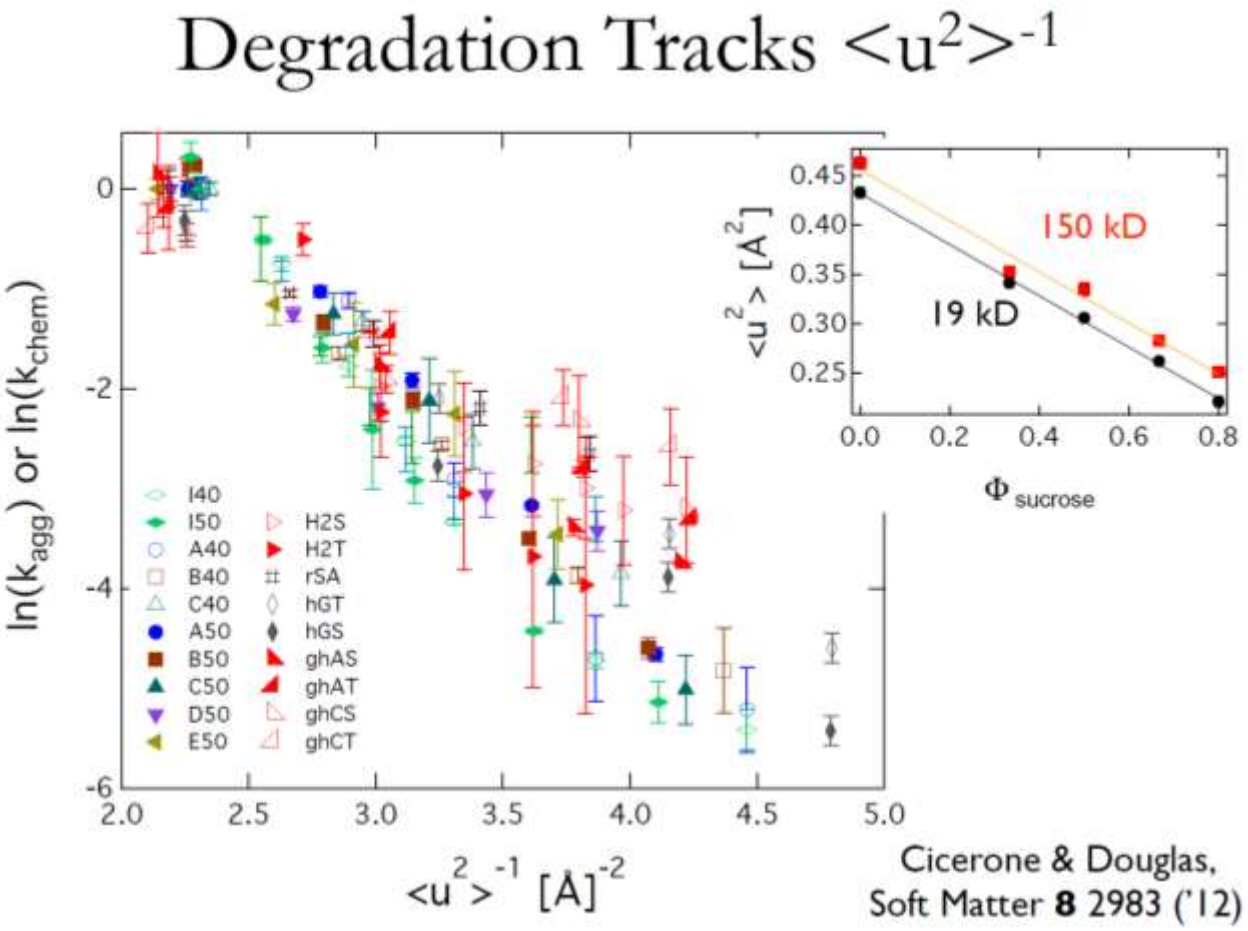
- **Half of therapeutic proteins are freeze-dried, but formulation for freeze-drying is empirical with 60% success rate**
- **Neutron scattering discovers new metric, fast β relaxation, correlating with long-term protein stability**



Protein in freeze-dried glass

AMGEN MedImmune NIBIB University of Connecticut MERCK Be well Lilly Pfizer WISCONSIN

Fast β Correlates with Degradation Rate



- **Bench-top fluorescence method currently being developed at NIST to measure β relaxation**

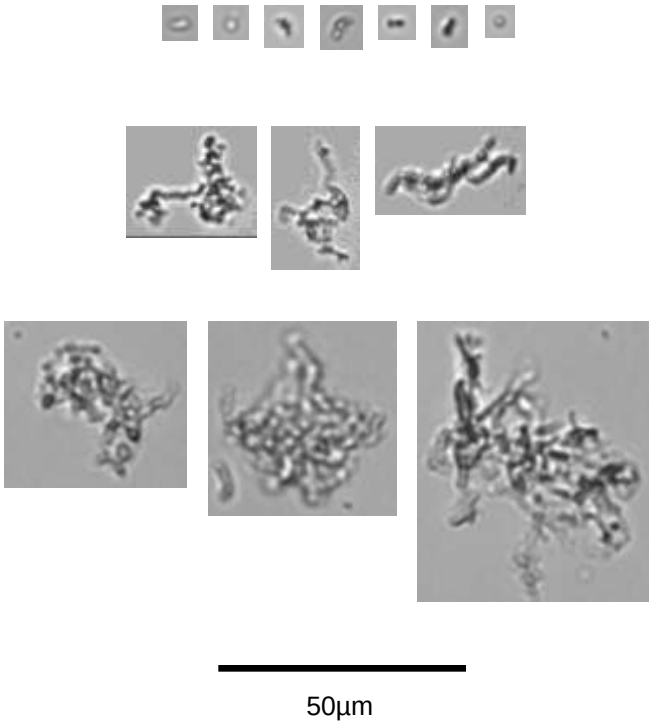
Collaboration Through A Common Shared Material: Protein Particles

PI: Dean Ripple

- Aggregates or particulates may cause adverse immune responses in patients
- Nearly all formulated protein therapeutics contain detectable particles
- Measurements of particles 1-100 µm with different optical methods can differ by 10X
- NIST requested to develop particle standards to reduce regulatory uncertainty

Particle characteristics:

- High hydration (≈ 95% water); low optical contrast can lead to large discrepancies between methods
- Irregular in shape & size, highly variable
- Existing bead standards do not mimic properties of actual particles



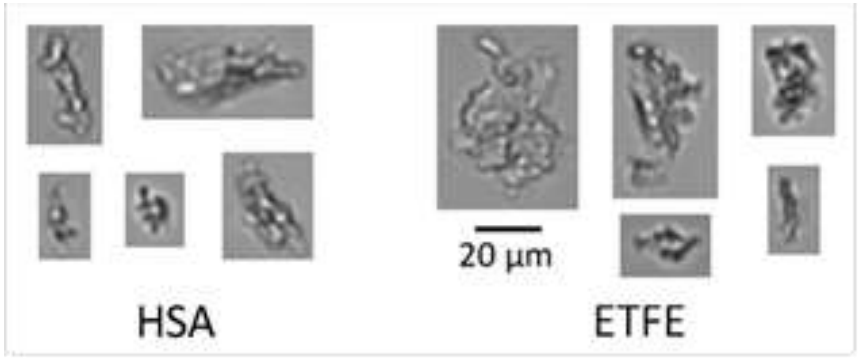
Three step approach:

1. Develop models for the instrument response
2. Characterize physical properties of protein particles relevant to physical basis of counting method, e.g., RI, density
3. Develop reference materials that mimic protein particles

Surrogate Protein Particles

Fluorocarbon (ETFE polymer) has desirable properties:

- Refractive index of 1.40—close to that of protein
- Durable & tough
- Mechanical abrasion process developed



NIST Round Robin on Sub-Visible Particles:

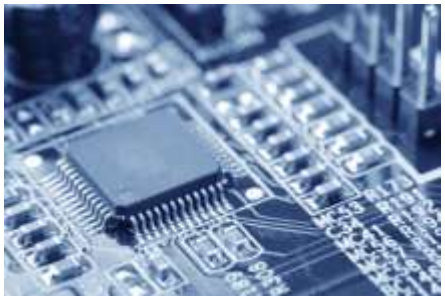
- NIST particles sent to industrial, academic, regulatory labs to assess stability of material and variability in particle sizing & counting
- Status: measurements complete, NIST analyzing data, preliminary results promising

Some Participants:

AbbVie
Amgen
Biogen Idec
Boehringer-Ingelheim
Bristol-Myers Squibb
Coriolis Pharmaceuticals
Eli Lilly
Genentech
GlaxoSmithKline
Human Genome Sciences-GSK
Johnson & Johnson
MedImmune
Novartis
Pfizer
Roche
Sandoz
FDA
Health Canada
Academia

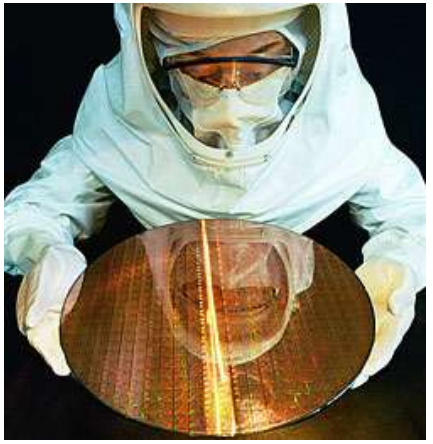
SEMATECH: Model for A Successful Public-Private Partnership (or how crisis breeds opportunity)

Consortium of semiconductor device, equipment, & materials manufacturers to advance semiconductor manufacturing, cooperatively build standards, & build infrastructure for next-generation technologies



History:

- Formed in 1987 in response to Japanese competition
- DoD-DARPA funded $100M/yr for 5 yrs, cost-matched by industry
- Goal: revitalize US semiconductor industry by speeding manufacturing development, reducing manufacturing costs & improving product quality



Successes:

- Catalyzed growth of strong equipment vendor base
- Enabled industry transitions (next-gen patterning, wafer size, novel materials and device structures)

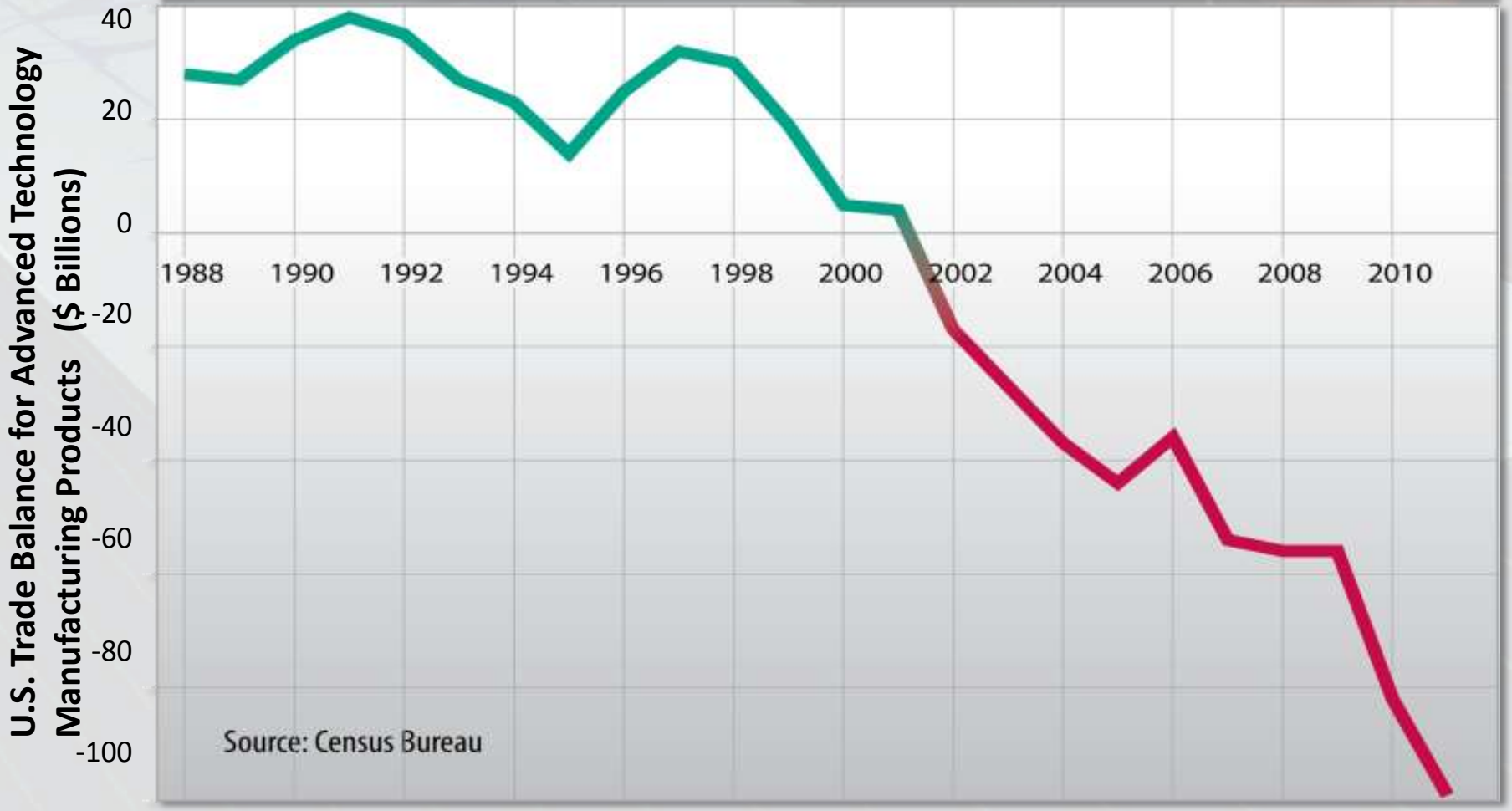
Organizational Features of Sematech

- **Commitment from senior executives & long term support**
  - Substantial member investments ensure activities are relevant & prioritized
- **Industry leadership**
  - Management led by industry so activities are aligned with industry priorities
- **Clear, pre-competitive mission**
  - Addresses common challenges articulated by an industry roadmap. Focus on building technology infrastructure and strengthening the manufacturing base
- **Broad representation of the industry**
  - Entire supply chain: manufacturers, equipment/materials vendors, universities, & national labs. Helps align and drive consensus across industry
- **Leveraging of government and industry funds**
  - Initially cost-shared, but eventually all industry funded. Leverages other government laboratory R&D programs (e.g. NIST)
- **Shared manufacturing development facility**
  - For manufacturing, testing equipment, materials, processes, developing products at scale to validate performance, reliability, and cost savings
- **Membership model**
  - Company personnel on 2-3 year rotations promoting tech transfer & manufacturing best practices

The Present Crisis: U.S. Trade Balance of Advanced Technology

- 11% of U.S. GDP
- 12 million U.S. jobs
- 60% of U.S. engineering and science jobs

- 57% of U.S. Exports
- Nearly 20% of the world's manufactured value added



National Network for Manufacturing Innovation

President Obama announces NNMI, March 9, 2012

"institutes of manufacturing excellence where some of our most advanced engineering schools and our most innovative manufacturers collaborate on new ideas, new technology, new methods, new processes."

- Up to 15 regional Institutes for Manufacturing Innovation (IMIs) across the country, each with a unique focus, to enable advanced manufacturing
- Partnership between industry members, federal labs, and universities
- Shared approaches to infrastructure, intellectual property, contract research, and performance metrics
- FY12 pilot institute on Additive Manufacturing
- $1B proposed for FY14 NNMI to be administered by Advanced Manufacturing National Program Office located at NIST

IMI Key Characteristics

- Institutes will be anchored by a shared use manufacturing R&D facility.
- Institutes will be partnerships between industry, academia, government. Collaboration and information sharing are critical.
- Each institute will have its own unique focus area, one of:
  - Manufacturing process
  - Advanced Materials
  - Enabling Technology
  - Industry Sector
- Focus areas will be defined by proposing teams.
- Cost sharing for 1st year & institutes expected to be self-sustaining after 7 years.

Suggested Technology Focus Areas from the RFI and Workshop

Flexible electronics, nano/micro, lightweight materials, personalized medicine, alternative energy, additive manufacturing, smart machining, pharmaceuticals, modeling and simulation, composite materials ,coatings, energy storage, sensors, metal casting, advanced forming , advanced joining, robotics, peening, machining, other surface finishing, coal compact internal burning, convert truck fleets to natural gas, thermoplastic recycling, sensors for harsh conditions, machining, forming, molding, casting, assembly, forgings, joining, surface engineering, electro-optics, nanomanufacturing, miniaturized electronics, design tools and informatics, nanoelectronics, autonomy, superalloys, precision machining, rapid prototyping, organic electronics, nanocomposites, sensors, embedded technologies, remote sensing, renewable energy, strategy development, printed electronics, sustainable manufacturing, bioprocessing, nanomedicine, nanomaterials, micromanufacturing, stoichiometry in thin films and bulk materials, photonic integrated circuits, electro-optic materials and devices, polymeric-based web converting manufacturing platforms, sensors for diagnosis and control of manufacturing, renewable energy, biofuels, nano/bio manufacturing, digital model-based manufacturing, advanced materials, medical technology manufacturing, additive manufacturing, smart manufacturing, advanced/intelligent machining and fabrication, advanced metrology, digital manufacturing, advanced joining, near-net shape technologies, forging, extrusion, rolling, casting, powder, molding, hydroforming, composites manufacturing, advanced nanomaterials, next generation semiconductor technologies, MEMS/NEMS and embedded sensors, energy efficient technologies, dynamic machine tool management, Big Data, robotics, automation technologies, advanced magnets, joining technologies, in-situ metrology, powder metallurgy, electron beam, cryogenic techniques, coatings, repair welding, composites, maritime technologies, photovoltaics, biomimetic engineering (related to solar), materials characterization, laser-based processing, non-destructive evaluation, wafer fab and equipment, ceramics, sustainable manufacturing, digital manufacturing, mechatronics and cyberphysical manufacturing, optics and imaging, electronics assembly, IT systems, metamaterials, rapid prototyping via flexible manufacturing, wide bandgap manufacturing, advanced batteries…

All ideas are viable! Make the technical and business case…

Conclusions

- **The federal laboratory ecosystem is vast and offers deep and broad expertise for collaboration with industry**
- **NIST has a unique mission, resources and mechanisms to facilitate cross-industry collaboration**
- **NNMI may be a unique opportunity for Pharma/Biopharma industry to develop a industry-wide collaborative Sematech-like effort on manufacturing breakthroughs**

Thank You!

Questions?

For questions about the Advanced Manufacturing National Program Office please contact:

amnpo@nist.gov

www.manufacturing.gov

301-975-2830

3:45 - 4:15

Role of Academic Science and Technology Centers in Developing Enabling Technologies

Huw Davies (Emory University)

Council for Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

Huw Davies slides here

4:15 - 4:45

The Mission of CCR: Facilitating Collaboration in Chemistry & Chemical Engineering

- Marc Donohue (Johns Hopkins Univ., 2013 CCR Chair)
- Paul Mendez (CCR)

Council for Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

Council for Chemical Research

Improving Chemical Innovation Through Collaboration and Advocacy

CCR – A Leadership Organization

Marc Donohue
2013 Chair

Paul Mendez
Executive Director

Seth Snyder
President

Council for
Chemical Research
Improving Chemical Innovation Through Collaboration and Advocacy

The Council for Chemical Research (CCR) was created in 1979 to improve trust and collaboration between the public and private research sectors.

CCR's Mission:

"Improving Chemical Innovation through Collaboration & Advocacy."

Council for Chemical Research

Improving Chemical Innovation Through Collaboration and Advocacy

Strengths & Benefits

- **Nexus of the three pillars of the chemical research enterprise**
  - *Unique platform for addressing "big picture" issues*
- **Membership composed of senior research leaders**
  - *Access to proven research leadership network*
- **Fosters collaboration**
  - *Enhanced collaboration opportunities*
- **Focus on graduate education issues for chemistry and chemical engineering**
  - *Access to world-class talent and employment opportunities*
- **United voice on research investment and the chemical enterprise**
  - *Impact in Washington on key science & technology issues*
- **Long range research focus**
  - *R&D Impact Studies*

Organizational Structure

- **Represents research leadership in 3 sectors**
  - Industry (13)
  - Academia (110 departments)
  - Government Labs (9 national labs)
- **Growing Membership!**
- **Institutional members,** represented by thought leaders who can influence policy and practice
- **Organized as a "not-for-profit" corporation**
  - Governing Board
  - Action Networks
  - Washington HQ Staff

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Action Networks

- **Research Collaboration**
  - *Collaboration Manual*
  - *IP Workshop*
- **Research Investment**
  - *Advocacy for federal R&D investment*
  - *Congressional and Agency Visits*
  - *Position Papers on policy and funding*
- **Graduate Education**
  - *Graduate curriculum*
  - *Department Chairs issues*
  - *Surveys on curriculum, postdocs, incentives, internships, etc.*

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Major Events

- **Annual Meetings** – distinguished speakers address a theme of current interest in the chemical enterprise
- **NIChE (New Industrial Chemistry and Engineering) Workshops** – experts focus on a specific emerging technology relevant to industry members
- **Chief Technology Officer Roundtables** – dialog on a significant policy issue
- **Webinars** – Showcase of capabilities and areas of potential collaboration between members

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2013 Annual Meeting

"Advancing Innovation: Breaking Boundaries, New Frontiers"

- *Innovation in Industry*
- *Frontiers of Research*
- *Lab Safety*
- *International Collaboration*
- *Role of the Scientific Socities*
- *Science Policy*

May 19-21, 2013
Arlington VA

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NIChE Workshops

Barrier Technologies

Arlington VA, September 19 & 20, 2012

Precompetitive Pharma Research Needs

University of Pennsylvania, PA, June 12&13, 2013

Nano Materials R&D

Pittsburgh PA, October 2&3, 2013

Shale Gas

Pittsburgh PA, October 2&3, 2013

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CCR-Organized Symposium at the AIChE Fall Meeting

Minneapolis MN on October 17, 2011

Larry Wendling
VP Corporate Research
3M, Inc.

Robert Brown
President
Boston University

Joe Miller
Chief Technology Officer
Corning, Inc.

Sangtaie Kim
Director
Morgridge Institute

Bill Banholzer
Chief Technology Officer
The Dow Chemical Company

John Anderson
President
Illinois Institute of Technology

Anthony Cuigini
Director
National Energy Technology Lab

Monty Alger
Chief Technology Officer
Air Products

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CCR-DOE Co-Sponsored Workshop

"Harnessing the Department of Energy's High-Performance Computing Expertise to Strengthen the U.S. Chemical Enterprise"

- March 10 &11, 2011 in Rockville MD
- 65 top researchers from industry, academia and government labs.
- 4 Breakouts:
  - * Biomass/Bioenergy
  - * Energy Storage
  - *Catalytic Materials
  - *Photovoltaics
- *Report Published by DOE and CCR.*

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Dow-University Safety Partnership

CCR Partners with Dow to Promote a Safety Mindset in the Future Workforce of the Chemical Community

DOW®

- *Exploiting CCR's Unique Nexus of industry/academia/government*
- *Leveraging Dow's Best-in-Class Safety Record*

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"Chemical Innovation: An Investment for the Ages"

McKinsey&Company

A Collaboration with McKinsey & Company

New Research finds Chemical Innovation:

- *Generates Financial Return*
- *Improves Society's Standard of Living*
- *Shapes our Future*
- *Grows GDP and Creates Jobs*

Publication date: May 2013

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Return on Investment Studies

- ***"Measuring Up: R&D Counts for the Chemical Industry"*** -- 2001

- ***"Measure for Measure: Chemical R&D Powers the U.S. Innovation Engine"*** -- 2005

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ROI Study Results

- **Chemical companies get $2 of operating income for every $1 of R&D invested - a 17% after-tax return**
- **U.S. economy gains roughly $40 dollars in GDP growth and $8 in increased tax revenues for every dollar of federal investment in chemical sciences research**
- **Chemical technology is highly dependent on publicly funded chemical science research**
- **Technology quality, innovation speed and strong scientific links deliver greater shareholder value**
- **All industries are significantly impacted by the chemical sciences. It is the most enabling science and technology**
- **The big opportunity is to reduce the 20-year innovation time lag from initial public research funding to commercialization**

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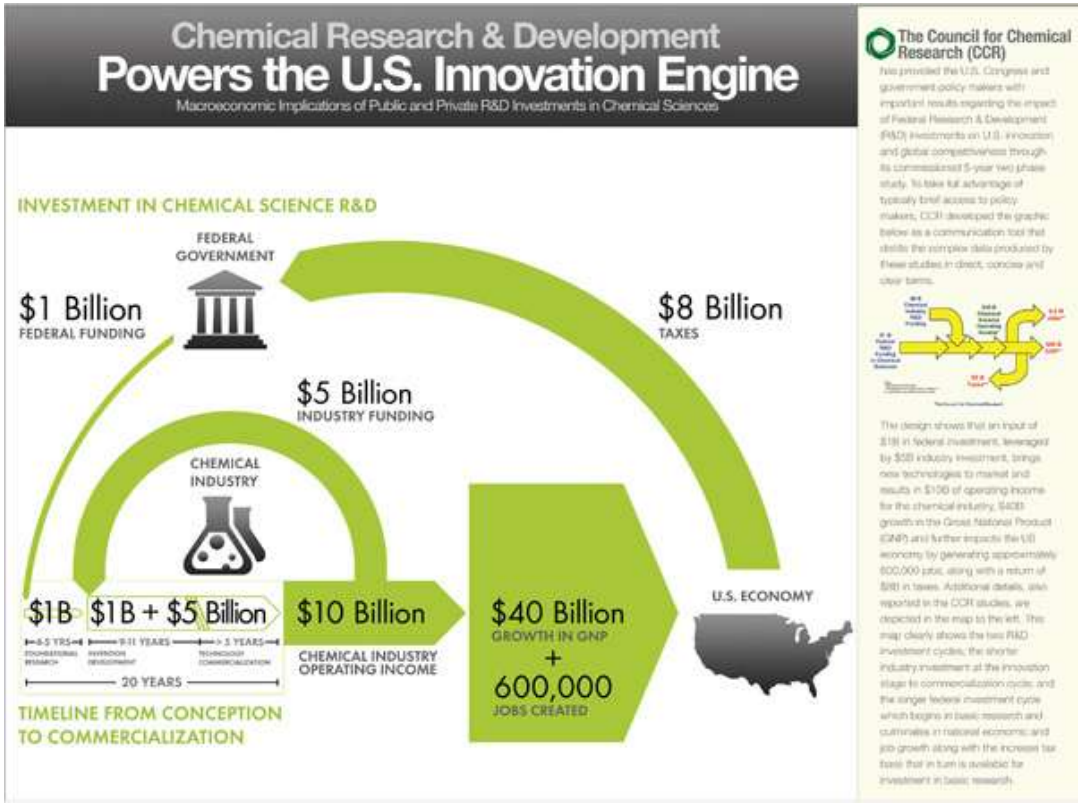
ROI Study Results



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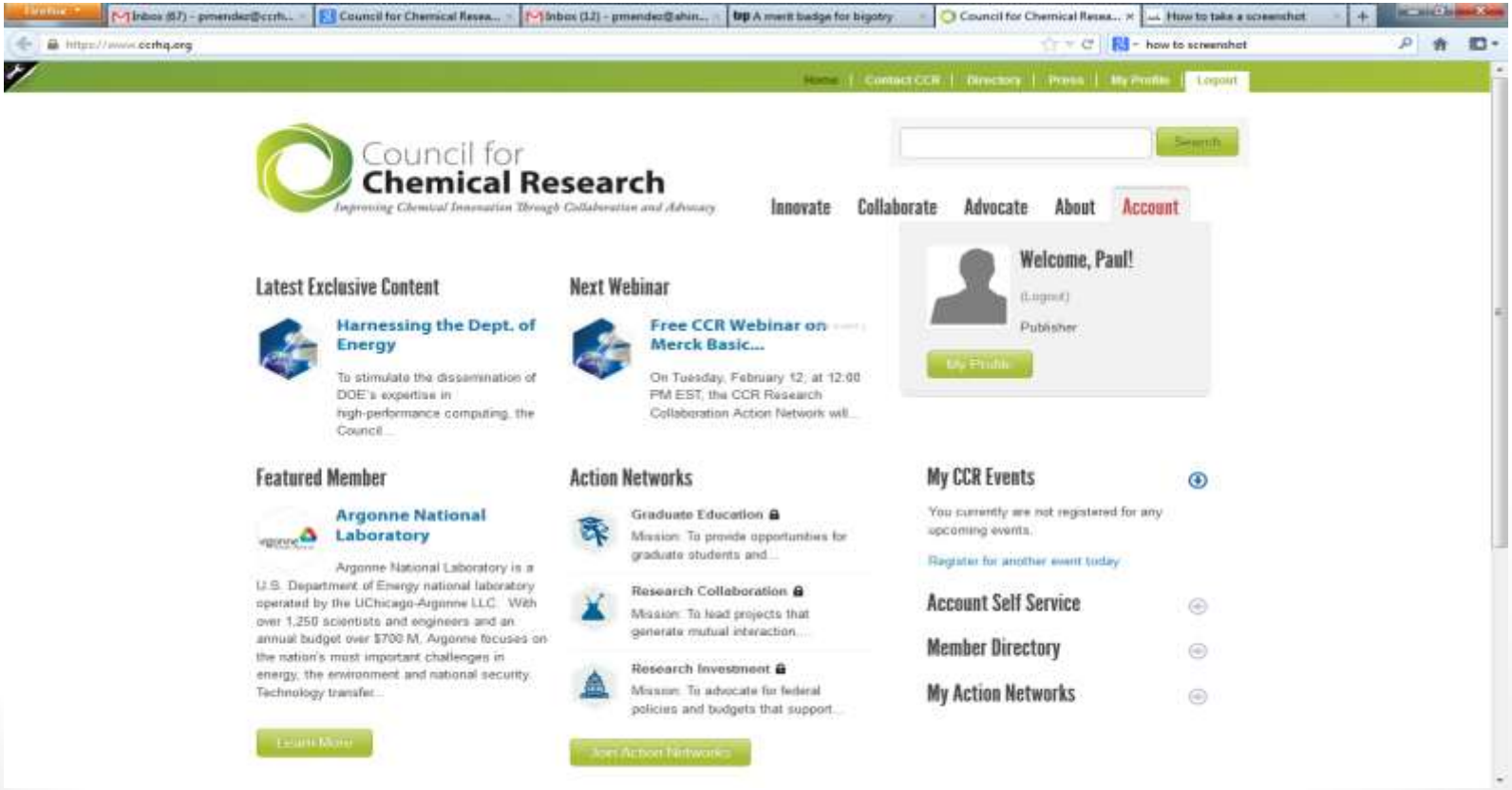
Interactive Website



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Awards

Malcolm E. Pruitt Award

Recognizing an individual with demonstrated outstanding contributions to the progress of chemistry-related sciences and engineering by promotion of mutually beneficial interaction among universities, industry and government.

Collaboration Award

Recognizing a collaborative team that has made outstanding contributions to the progress of chemistry-related science and/or engineering.

Diversity Award

Recognizing an individual who has directly impacted organizational ability to advance and promote diversity within and among the three CCR sectors.

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QUESTIONS?

4:45 - 5:00

Preview of Tomorrow's Breakout Topics

A – Streamlining Agreements for External Research Collaborations

B – Preferred Mechanisms for Pre-Competitive Collaborations

C – Defining the "Edges" of Precompetitive Collaboration

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4:45 - 5:00

Preview of Tomorrow's Breakout Topics

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8:30 - 9:00

Benefits of Cross-Pharma Collaboration on Enabling Technologies

Jacquelyn Gervay-Hague (University of California-Davis, Director, Division of Chemistry at National Science Foundation effective July 2013)

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Gervay Hague slides here

9:00 - 9:30

Successful Negotiations of Research Collaboration Agreements

- Kim Folander (Merck Research Laboratories)
- Trude Amick (University of Pennsylvania)

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Successful Negotiations of Research Collaboration Agreements

Precompetitive Collaborations:
Enabling Technologies for the Pharmaceutical Industry
June 12 & 13, 2013
on the campus of the University of Pennsylvania
in Philadelphia PA

Kimberly Folander, Merck & Co., Inc.
Trude Amick, University of Pennsylvania

This all works well when
both company and university understand
what the other party needs and wants
in a collaboration
and why it is important to them.

Primary Points of Negotiation

- **Scope of Work-Relationship during Collaboration**
  - Early Stage—Pre-competitive collaborations
  - Advanced Stage – reduction to practice, animal studies, preclinical and clinical data
- **Publication Rights**
- **Ownership and Use of Results**
- **Intellectual Property**
- **Patent Rights**

Glitches arise and things change:

This all works well when
both company and university understand
what the other party needs and wants
in a collaboration
and why it is important to them.

9:30 - 10:15 **Parallel Break-Out Sessions**

A – Streamlining Agreements for External Research Collaborations
B – Working with Government Laboratories
C – Defining the "Edges" of Precompetitive Collaboration

10:15 **Break**
10:30 **Report Out from Breakout Sessions**

Faciliators:
Group A: Jean Tom
Group B: Joel Hawkins
Group C: Chris Welch

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10:30 **Report Out from Breakout Sessions**

A – Streamlining Agreements for External Research Collaborations
B – Working with Government Laboratories
C – Defining the “Edges” of Precompetitive Collaboration

12:00 **Summary & Next Steps**
12:30 **Adjourn & Box Lunch**

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Thanks!

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