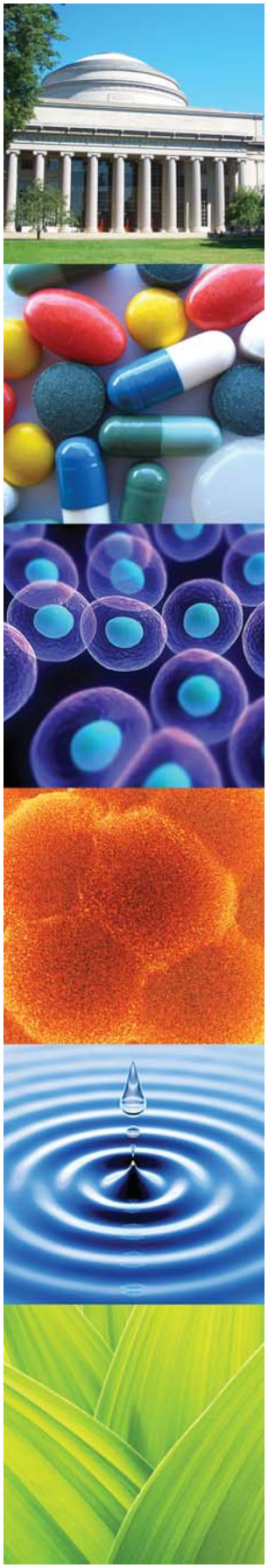

2013 Biotechnology & Standards Conference

The Prospects for a Life Sciences Standards Revolution

Conference Summary

October 1, 2013
The MIT Media Lab
Cambridge, MA

MIT CBI
Center for Biomedical Innovation

GBSI®
Global Biological Standards Institute®

HOSTS

Stacy Springs – Director, Biomanufacturing Research Program; Executive Director, MIT Consortium on Adventitious Agent Contamination in Biomanufacturing; Director, MIT-Sanofi Alliance, Center for Biomedical Innovation, MIT

Leonard P. Freedman – President, Global Biological Standards Institute

Scott Stern – David Sarnoff Professor of Management of Technology, MIT

Anthony J. Sinskey – Faculty Director, Center for Biomedical Innovation; Professor of Microbiology and Engineering Systems; Professor of health Sciences & Technology, Harvard-MIT Health Division of Health Sciences, MIT

INTRODUCTION – SCOTT STERN

Scott Stern (*David Sarnoff Professor of Management of Technology, MIT*), one of the conference organizers, set the stage for the 2013 Biotechnology and Standards Conference by pointing out the novel mix of presenters at the meeting. Of course the group included life science and biomedical researchers who are leading the standards effort. But also present were economists and social scientists who have been assessing the "standards issues" through entirely different lenses. Many of these participants have been researching the roles standards play in other disciplines, most notably in information and communication technologies.

To introduce the topic of standards in the life sciences, Stern noted that he has become a fan of synthetic biology. He is guessing that synthetic biology will make a significant impact in the life sciences – and in scientific research in general – in the near future and for decades to come. Precisely because synthetic biology involves building new products from predefined components, it lends itself to standardization, which would, in turn foster extensive interchangeability.

Stern thus wonders what sorts of standards systems might develop: Will they be consensus rules or open standards? Or, will products be protected by intellectual property rules? Or, will every lab or company proceed down its own path with no imposed standards?

Stern noted that many of the practitioners of synthetic biology are looking for guidance not from the life sciences but areas of IT, where standards setting organizations and governance have been essential for "shaping the productivity of that field." Thus, synthetic biology may be an experiment to help us think about some of the issues in standards development and implementation.

Stern posed a set of questions for the audience to keep in mind as they listened to the day's presentation; issues to

consider in developing and implementing new and better standards for life science and biomedical research. (**See Box 1. Rules of the road for developing and implementing standards in life science and biomedical research.**)

Box 1. Rules of the road for developing and implementing standards in life science and biomedical research.

- What is feasible?
- What sort of governance will work? And how can it be set up?
- What resources need to be in place?
- How much should be public and how much private?
- Will people play by the rules?
- What will it take to define, shape and facilitate productive transactions along this path?

He concluded by reminding the group that they are the people who may lead the decision-making about standards in life and biomedical sciences. Therefore, they will need to decide where the efforts should go, given the limitations of time and resources. (**See Box 2. Decisions for leaders in life science and biomedical standards-setting.**)

Box 2. Decisions for leaders in life science and biomedical standards-setting.

- What should the product /effort look like?
- What are the benefits and what are the challenges?
- How to govern life science standards?
- What can we do as a community to facilitate effective life science standards going forward?

PANEL 1. STANDARDS IN THE LIFE SCIENCES: PROSPECTS AND CHALLENGES

In biomedical research, a major reason for retraction of peer-reviewed papers is the authors' inability to reproduce the findings. Retraction itself is just one tip of an iceberg of problems in 21st Century biomedical research. **Pierre Azoulay** (*Associate Professor of Technological Innovation, Entrepreneurship, Sloan School of Management, MIT*), moderator of the first panel, offered a window into these problems. He studies the consequences of retracted papers, and his recent work shows that retractions can have downstream effects, diminishing the citation rate of papers in the immediate area of the retracted papers. This notion that irreproducibility in research has many repercussions, both immediate and indirect, became a key theme for the first panel.

A need for standards

Panelist **Leonard P. Freedman** (*President, Global Biological Standards Institute*) picked up the topic of irreproducibility in biomedical research, giving three examples of problematic areas:

(1) DNA sequence data – here is a vast amount of it, and the quantity of data is growing rapidly. The two major problems with existing databases of DNA sequences are the errors they contain and the limit to which two or more such databases can be used together – i.e. are interoperable – including for the purpose of cross-checking independent analyses of the same DNA material.

(2) Antibodies – biological reagents that are widely used in research, clinical diagnostics and therapeutics. At least in the research realm, antibody quality varies considerably, both from commercial and private sources, and currently there are no mechanisms for standardization and product validation.

(3) Clinical trials – many fail because of problems introduced early in the research that go unrecognized until this late stage of the process.

The overall effect of these problems can be devastating in terms of the time, money and human resources wasted. In addition, as Freedman noted, problems stemming from such irreproducibility erode public trust in the biomedical research enterprise and diminish opportunities to enhance global health.

Recognizing the extent of these problems is prompting the formation of organizations such as GBSI and existing organizations such as MIT CBI to consider the development and implementation of enterprise-wide standards as a means of improving the quality of biomedical research and its applications.

But what is meant by *standards*? As Freedman said, in the biomedical sciences, there need to be both material standards and written (aka process) standards. (**See Box 3. Life science standards.**)

Box 3. Life science standards.

- Material standards
  - > Well characterized, purified biological reagents
    - Examples: Reference cultures of microorganisms and cells as well as material derived from these living organisms – e.g. RNA, DNA, proteins
  - > Synthetic biological materials
    - Example: Synthetic macromolecule that mimics a naturally occurring one such as viral RNA
- Written standards
  - > Consensus-based documents on specifications, procedures, or processes involving biological materials

And who are the stakeholders who might benefit from developing and implementing standards? Freedman mentioned several:

(1) academic laboratory researchers and their parent institutions;

(2) for-profit industries and investors;

(3) funding agencies, both public and private; and

(4) journals and professional societies.

GBSI, as Freedman explained, aims to advance the effort toward standards development and implementation through policy, thought leadership and educational initiatives. It will do so through advocacy of harmonized, consensus-based standards, which can facilitate future innovations.

Biomarkers – A case in point

Biomarkers – biological/biochemical indicators of the physiological state of an organism – hold the potential to help researchers and physicians in myriad ways; in drug discovery and development as well as in determining patients' disease risk and response to therapy. In the last decade or so, researchers have put major efforts, and funding sources have put major resources, into the identification of useful biomarkers. Unfortunately, the reality in the biomarker field lags severely behind the potential.

As the panel's next speaker, **Carolyn Compton** (*CMO, National Biomarkers Development Alliance, and Professor of Life Sciences, Arizona State University*), noted, while more than 1200 potential biomarkers have been described in a literature amounting to over 150,000 papers, currently only about 100 validated biomarkers are in use. (G. Poste, *Nature* 469, 156-157, 2011.)

All this comes at a time when clinical laboratories need to cope with increasingly sophisticated testing. (**See Box 4. Technology is changing the way clinical data are collected.**)

Box 4. Technology is changing the way clinical data are collected.

"Point-of-care testing, high-resolution ultrasound at home or a patient's bedside, miniaturization and convergence of technologies are all changing how clinical and pathological data are collected and analyzed, directly from patients in real time with continuous feed. Lab-on-chip, lab always on, lab-on-me."

Carolyn Compton

Drug discovery and medical treatment alike could benefit from a robust biomarker enterprise. But, as Compton noted, the biomarker field is plagued by numerous problems. (**See Box 5. Current problems in biomarker development.**)

Box 5. Current problems in biomarker development.

- Poor access to well-annotated, fit-for-purpose biospecimens from well-phenotyped sources ("garbage in-garbage out" syndrome)
- Insufficient control of pre-analysis material and procedures
- Idiosyncratic lab-specific protocols
- Small sample sizes lacking statistical power
- Chaotic data-reporting format and poor database interoperability
- Poor compliance with journal policies. "Requirements for publishing from industry are virtually unknown in the academic arena."
- Nonexistent quality management systems

Some of the hurdles standing in the way of an effective biomarker enterprise are starting to be dealt with. For example, "the FDA has announced that they will require data standards by 2017. This is likely to incentivize people to use standards across the board," says Compton. Also, the academic lack of compliance with journal policies is now being addressed at National Biomarkers Development Alliance (NBDA) at ASU. (See comments below from *Nature* editor Véronique Kiermer about what that publisher is doing in standards implementation.)

The problems in biomarker development involve more than just implementation of standards in one or two areas; standards are needed all along the process. That, she notes, is why NBDA has formed a public-private partnership, working with the academic community, industry and the FDA to develop standards across the pipeline for biomarker development.

Process standards for clinical assays

Whereas problems in biomedicine stemming from lack of standards abound in the developed world, they cannot begin to compare with those in the developing – and therefore resource-limited – countries, as **Mary Lou Gantzer** (*President, Clinical and Laboratory Standards Institute*) discussed. CLSI has as its mission the development of clinical laboratory best practices, meaning that it focuses on process standards, not product (material) standards.

To identify and tackle challenges facing clinical labs worldwide, Gantzer helped to found the International Consortium for Harmonization of Clinical Laboratory Results. Clinical labs in underdeveloped countries have problems beyond those in developed countries including issues stemming from limited resources. Gantzer gave as an example that when resources are limited, reagents and medicines sometimes get diluted to make them go further. But dilution can invalidate assay results and also make drugs ineffective.

As an example of the sort of standards developed by CLSI, Gantzer mentioned antimicrobial susceptibility testing. The need for such a process standard stems from the considerable mistreatment of microbial infections that occurs. The mistreatment can take the form of either under- or over-treatment, or treatment for the wrong disease. Problems in interpreting antimicrobial testing results can arise because of inter-lab procedural differences. Even small differences in the pH at which a test is done can affect the outcome. Therefore, standards are needed so that a given test uses the same conditions everywhere.

How can this sort of process standard be enforced? Gantzer said that if regulatory agencies such as the FDA, the Centers for Medicare and Medicaid Services or the healthcare accrediting/certifying Joint Commission come to rely on standards, that will be a critical motivator for their implementation. “It doesn’t matter what the regulatory body is; if there is one, standards are much more likely to be used.”

PANEL 2: BIOMATERIALS STANDARDS: CHALLENGES AND OPPORTUNITIES

Ron Weiss (*Associate Professor of Biological Engineering and Electrical Engineering and Computer Science; Director, Synthetic Biology Center, School of Engineering, MIT*) chaired the Biomaterials panel. He charged the panel with covering a range of issues, such as: governance (top-down, bottom-up, or some hybrid model); bringing together different communities of researchers, each siloed with a different model organism; seeking a balance between perfection and pragmatism; ways in which standards can keep pace with technological development; and the roles of various regulators and funding sources.

Tissue engineering for drug discovery and body-part repair

In the field of biomaterials – tissues-on-a-chip and mini-organs – prototypes abound. As **William E. Bentley** (*Robert E. Fischell Distinguished Professor; Chair of Bioengineering, University of Maryland*) explained, researchers are creating these miniaturized living systems largely for use in drug screening. NIH and DARPA (*Defense Advanced Research Projects Agency*) have funded programs in this area with a goal of replacing animal testing with these *in vitro* systems.

For example, researchers at UMD are creating a gastrointestinal tract-on-a-chip to learn how ingested bacteria evade the immune system. Humans have immune responses to just a subset of bacteria that we consume; otherwise our food would poison us far more often than it does. The device under development mimics the layer of epithelium that lines the gut, which is responsible for this discriminatory function. The challenge of engineering such *living devices* is huge since the devices must be reproducible both in starting material and in biomarkers of system behavior and response to manipulation, according to Bentley.

To move this type of research forward, NIH and DARPA co-host workshops that enable academic researchers to discuss their ideas with host representatives as well as representatives from FDA and NIST. The complexity of the academic works-in-progress keeps growing, Bentley explained. (**See, for example, Box 6. Organs- and organ-systems-on-chips.**) In addition, workshop participants are starting to discuss ways to incorporate living-system-on-a-chip into personalized medicine.

Box 6. Organs- and organ-systems-on-chips.

- **Liver-connected-to-kidney-on-chips** are being developed at places such as Cornell University and Harvard's Wyss Institute to learn what effect a drug that goes first to the liver might have on the kidney. Such devices pose unique challenges. For example, how long does it take for a drug to go from liver to kidney in the intact organism, and does the in vitro system mimic that time.
- **Human-body-on-a-chip** is being developed at MIT. The project involves creating a suite of up to 10 different **micro-organs** to mimic different physiological systems together on a tiny scale. This too will be accurately predicting drug and vaccine efficacy, toxicity, and pharmacokinetics in preclinical testing.

Along with developing these living devices for use in drug development, an effort is underway in tissue engineering, which is the *in vitro* development of new tissues that can be used to replace damaged or malfunctioning ones in the human body. This category of new materials often includes synthetic scaffolds on which living cells will be grown to form new tissue or mini-organs, which will then be implanted into a person. (**See Box 7. Printing the building blocks of bone.**)

Box 7. Printing the building blocks of bone.

UMD researchers are seeking new ways to help people who have suffered major traumatic bone loss. To stimulate new bone growth, the researchers first make 3D-printed polymeric scaffolding containing bone cells. This living scaffold can then be implanted and serve as a site of bone regrowth, with the polymeric scaffolding eventually dissolving and being replaced by bone mineral and extracellular matrix. For the device to be successful, researchers must be able to predict its therapeutic benefit and monitor its state, all of which requires have standardized materials and conditions.

Depending upon the condition to be corrected, the cultured cells may themselves receive genetic alteration (to help correct the medical defect) before being developed into new devices. Each step of the way creates a need (and an opportunity) for both material and process standards.

But how will those standards be decided upon and then implemented?

As Bentley noted, the FDA recognizes that it must play a key role in solving this problem. Agency scientists and administrators also see that their agency needs to develop a better understanding of the 21st Century experimental and analytical techniques that industry and academic researchers want to include in their new drug and device applications. To this end, the FDA has, over the past few years, begun to partner with experts who can instruct them in such matters. UMD is one such partnering institution, and Bentley is the Co-Principal Investigator of the Center of Excellence in Regulatory Science & Innovation (http://www.cersi.umd.edu/). Another is MIT, which has a long history of collaboration with the FDA. The Center for Biomedical Innovation, co-host of this conference, will be launching a Working Group on Biotechnology and Standards in 2014, and has significant collaborations with the FDA through its Biomanufacturing and NEWDIGS programs (http://cbi.mit.edu/).

Genome sequence data

The Human Genome Project generated massive amounts of data. Now that the project is complete, much of the new human genome sequence data being gathered aims to uncover DNA variants that underlie disease, or that can give information about disease risk or likelihood of response to one or another therapy. Currently, a great deal of the DNA sequencing is being done in clinical labs, frequently ones that keep their findings siloed.

The concern that **Brad A. Margus** (*CEO, Genome Bridge*) expressed is that many of the questions people want to address – such as figuring out which rare genetic variants play key roles in specific diseases – require huge datasets. Such datasets of both genome sequences and of the associated information about patients and tissues in question could be amassed from smaller datasets if the latter can be made interoperable. Importantly, such efforts need to both maintain necessary patient confidentiality and be of high-quality, containing accurate information.

Margus, who previously headed Perlegen, the first biotechnology company to amass whole genome sequences from individual patients, is now a leader in the Global Alliance (http://www.broadinstitute.org/files/news/pdfs/GAWhitePaperJune3.pdf), an international consortium established "to enable responsible sharing of genomic and clinical data." As Margus explained, the Alliance aims to "create and maintain the interoperability of technical standards for managing and sharing sequence data in clinical samples. Its plan will "encourage responsible and voluntary sharing of data and methods" while maintaining patient privacy. Begun in early 2013, the Alliance has over 110 participants, including leading genomics researchers and health care administrators from academic medical centers and non-profit organizations. The group is expanding to include providers of technology and equipment as well. Looking at other massive-scale IT-based projects, Margus notes that the Alliance aims to emulate the successes of the World Wide Web, and avoid the failures encountered in the development of electronic health records (EHRs) in the US.

Separate from the new Global Alliance, which will set standards, Margus also launched Genome Bridge to help biomedical researchers make effective use of the available data about genomic sequences and patient information. This non-profit organization aims to create "a cloud-based technology platform for aggregating and analyzing genomic and clinical data." The start-up is currently being incubated at The Broad Institute.

Cell line imposters and what to do about them

John R. Masters (*Professor of Experimental Pathology; Director, Prostate Cancer Research Centre, University College, London*) returned to the problem of cell line misidentification in biomedical research. According to Masters, approximately 20% of human cell lines are in actuality derived from a different individual or are otherwise misidentified. Geneticist Stanley Gartler first brought the problem to light in the mid-1960s. Gartler discovered that cell lines he was studying, coming from many different sources and presumably all different, were indeed, all the same cells – HeLa cells, from the now famous rapidly growing cells derived from the cervical tumor removed from a Baltimore woman named Henrietta Lacks. Now there are more than 400 misidentified cell lines.

The problem continues because there is limited validation. But the situation is rectifiable if investigators act proactively. Cell line authentication can be done using a molecular biology technique called short tandem repeat (STR) profiling. (STR was first used by forensic pathologists to determine paternity and to identify crime suspects.) American Type Culture Collection (ATCC) now routinely subjects all cell lines it handles to STR analysis, employing the method established by Promega.

The recent founding of the International Cell Line Authentication Committee has raised awareness that cell misidentification is a common, global problem. The committee has produced guidelines (http://standards.atcc.org/kwspub/home/the_international_cell_line_authentication_committee-iclac_/Authentication_SOP_9-6-2013.pdf) to help investigators assess the cell lines they are using, either by sending a DNA sample from the cells to a commercial STR profiling analyst or doing STR analysis in-house.

According to Masters, the publication of the ANSI/ATCC standard for human cell line authentication (ASN-0002-2011) by ATCC achieved more in 1 year than was accomplished by individual scientists trying to tackle the authentication problem over the past 50 years.

Still, authentication is largely a voluntary act. Biomedical journals are beginning to require authors to authenticate the cells they are reporting on, and cell authentication is a requirement for funding from some governmental or private sources. As a result of the ATCC American Standard, authentication of cell lines is becoming increasingly common. (See below for the current approach taken by *Nature Publishing Group*, as explained by speaker Véronique Kiermer.)

Challenges posed by cell-based therapies

Leslie E. Silberstein (*Director, Joint Program in Transfusion Medicine, Children's Hospital, Boston*) spoke about his effort to promote cell-based therapies. The Center for Human Cell Therapy, which he directs, grew out of the program in transfusion medicine because both use living cells.

As Silberstein explained, blood transfusion products are regulated by the FDA, with regulations focusing mainly on safety. Such classical standards are insufficient for cell therapy products and procedures. For cell-based therapies, Silberstein argues, standards are needed for both *product manufacturing and assay characterization*. (**See Box 8. Standards for cell-based therapies.**)

Box 8. Standards for cell-based therapies.

- **Material standards** – includes equipment used for collecting and processing the cells, cells type and number, and also the nature of the non-cellular material in the product
- **Assay characterization (process) standards** – includes procedures used to monitor the cells, both during their preparation and after they are given to the patient

Given the wide range of different types of cell therapies here and on the horizon, Silberstein argues that standards should be developed that are relevant to the particular treatment at hand.

As examples of two cell therapies that would require different types of standards, Silberstein gave the following:

(1) treatment for severe combined immunodeficiency (SCID) using genetically-modified bone marrow cells; and

(2) treatment for a limbal stem cell (LSC) deficiency, a unilateral eye disease that can be treated with stem cells harvested from the affected eye.

Among the standards needed for treating SCID but not LSC would be those involving DNA expression vector construction and expression levels, whereas the standards needed for LSC but not SCID would be ones involving expanding the *in vitro* culturing conditions to obtain sufficient numbers of stem cells in a matrix before implantation in the diseased eye. These examples make it readily apparent why at least some standards need to be treatment-specific in cell-based therapies.

PANEL 3: LESSONS FROM OTHER INDUSTRIES – THE ECONOMISTS' PANEL

Panel Moderator **Fiona E. Murray** (*Associate Dean for Innovation; Alvin J. Siteman (1948) Professor of Entrepreneurship; Associate Professor of Technological Innovation, Entrepreneurship, and Strategic Management; Faculty Director, Martin Trust Center for MIT Entrepreneurship*) opened the session by noting that biomedical researchers now collaborate with engineers much more than in previous decades. Whereas life scientists have a paucity of standards in their research culture, engineers bring to the collaborations a history of developing and using standards to deal with big ideas in their profession. Murray suggested that this interaction with engineers might help lead biomedicine to solutions to some of the current problems.

Also changing is that in the past, standardization issues were discussed behind the scenes. There is increasing openness about discussing problems of reproducibility, and that means that patients too are learning about these problems. Murray suggested that this growing awareness by the population at large stimulates increased expectations for healthcare standards. She used the analogy of the expectation that people had about being able to seamlessly move documents between Macs and PC, an expectation that took some time to meet.

She posed three questions for panelists: When do standards emerge and when do they fail? What is the process? And what are the consequences?

What biomedicine can learn about standards from the technology sector

Timothy Simcoe (*Associate Professor of Strategy and Innovation, Boston University School of Management; Faculty Research Fellow, National Bureau of Economic Research*) spoke about standards and standard setting in the technology sector in general and IT in particular. In IT a major motivator for developing standards has been is the issue of compatibility.

Professor Simcoe began by noting that there are multiple ways of creating a new standard:

(1) *Standards wars* (think BetaMax versus VHS);

(2) *Converters*, i.e. patching things together after the fact, without formal standards (e.g. the adaptor that plugs into American electrical devices so that they can run in the EU; or

(3) *A follow-the-leader* approach, where the leader may be a government, a platform leader (e.g. Apple or Android), or a major customer (Walmart/K-Mart); and

(4) *Consensus standard setting*, typically through membership organizations such the Institute for Electrical and Electronics Engineers (IEEE) or World Wide Web Consortium (W3C).

Economic perspective of standards development – Barcoding as a case study

To illustrate the long-term economic impacts of standards, Professor Simcoe discussed the development of bar code standards. Barcodes and the scanners that read them came about in the 1970s, introduced first in the grocery industry. The implementation of barcodes had a range of challenges, starting with the incentive, chicken/egg, problem – to set standards first or to get grocers to put on labels first? There were also organizational problems – who should give out labels? And technological problems – e.g. how to deal with codes the got obliterated when boxes got crushed or labels drenched? And then there were the institutional problems such as item-pricing laws. But the system did get launched, initially as the Universal Grocery Products Identification Code (UGPIC), with a pack of Wrigley's chewing gum being the first product to be bar-coded and scanned in 1974. Adoption of barcodes took time, first by the food industry and then by the apparel industry, etc. Broad-range acceptance of standards took off when the big customers – Walmart and KMart – adopted them.

Looking at barcoding today, we see myriad economic benefits in many sectors and in the way the codes are used. Many industries use barcodes, there are several new types of scanning devices, and information gathered from barcode scanners gets used in a range of ways. Think about a factory today run by Amazon. Not only do boxes get scanned, but product location is barcoded and robots can locate products via barcodes. Thus, complementary innovations have emerged that build on the barcode concept.

Measuring the impact of standards

Measuring the long-term economic impacts of specific standards is challenging, Simcoe said. As one means of gathering some quantitative information, he looked at patents across industry sectors. For that project, he worked with a colleague surveying >20,000 inventors. He found that the frequency with which inventors used standards varied across industries. In telecommunications ~40% of surveyed inventors said they referred to standards. By contrast, biotechnology had the lowest user rate overall at 7.6%.

Simcoe sees this limited use of standards by biotech inventors as an opportunity. He suggested that there is a need to define the goals and then consider ways achieve the goals. For goals, he identified three,

(1) shared platform governance,
(2) certification of quality, and
(3) information sharing.

How to design the institution to achieve the goals? While there may be some challenges specific to biomedicine, Simcoe suggested some general approaches, starting with identifying the challenges and then determining the organizational design parameters.

Be aware of potential problems in standard-setting

One problem Simcoe mentioned is the "tragedy of the commons" issue, where a few individual who don't adopt the standards can harm the whole system. This can be avoided by implementing certification processes and enforcement rules, so that "everyone is in the tent." Another concern is the need to balance participation in setting the standards with paying the cost for their creation; incentives may be needed for designing and implementing the standards whereas different incentives may be required for using standards created by others.

Standards organizational design parameters to consider – Scope

How broad should the new organization be and how much activity should it take on? For example, should it develop specifications? Should it promote and market the specifications to end-users? Will the organization establish certification and monitor compliance? If so, is there underlying intellectual property (IP) that needs licensed, and how will that be done?

Membership and governance issues

The IT world uses at least two approaches:

(1) Developing **accredited standards development organizations (SDOs)**, which consider

(a) balance of interests,

(b) the process used to reach consensus, and

(c) how to deal with objections; and

(2) **Consortia**, which are similar to clubs and open the outcome so that all can use the standards they produce. *SDOs are good for process standards whereas consortia are useful for product standards.*

Intellectual property issues

Many standards implicate IP owned by firms involved in the standards developing process. (Think about the smart-phone patent wars!) Therefore, there should be an up-front consideration as to whether the standards setters will sort out pricing issues while the standards are being set. Alternatively, the standards-setters could decide to get promises from participants about the reasonableness of using their IP.

Standards reduce friction

Shane Greenstein (*Kellogg Chair in Information Technology and Professor of Management and Strategy, Kellogg School of Management, Northwestern University*) opened with the reminder that some standards are government-mandated and some are voluntarily. Pointing to a fire alarm on the wall, he said that it carried a mix of governmental and private standards whereas the Wi-Fi box next to it was completely a private, voluntary effort. His talk focused on private, voluntary standards.

Greenstein then posed the question: Why do people/organizations get involved in setting standards voluntarily? He offered two reasons: a shared mutual interest in cooperation and/or the value in coordinating product designs.

He offered several possible (and largely beneficial) consequences of having voluntary standards, including the coordination of independent efforts, reduced design costs and modification costs, reduced labeling/information costs, reduced entry costs for specialists, and provision of a forward-thinking roadmap. (**See Box 9. Possible consequences of voluntary standards, with examples.**)

Box 9. Possible consequences of voluntary standards, with examples.

- **Coordination of independent efforts**: The grocery scanner allows group of parties who would otherwise have difficult time communicating with one another coordinate their efforts.
- **Reduction in design cost**: With the cable modem, cable companies saw that they just needed to work on a specific part of the device and didn't need to redesign it all. With this modular system, they could redesign a single component and the rest of the Internet would work fine.
- **Reduce labeling/information costs**: Language shorthand such as Wi-Fi often develop. One doesn't need to understand how Wi-Fi works; you just see that some things (e.g. laptops) are sold to be Wi-Fi-compliant and you know it will work with Wi-Fi.
- **Reduction in modification costs**: The 56K modem was designed to send information at high speeds over telephone lines. The standard for this modem, once created, was accessible to anyone. Fax machine equipment providers took it, and with no additional cost, all fax machines became faster worldwide.
- **Reduction in entry costs for specialist**: USB (Universal Serial Bus), an industry standard that defines connectors, has been used by thousands of firms to run their devices by simply plugging into a computer.
- **Provides predictability**: For Wi-Fi standards, designers needed to say in what context they anticipated the standard would be used. That revealed assumptions about possible costs and other issues going forward. This collective thinking forward in standards organizations can generate a single roadmap to be used by all.

On patents and standards

Stuart Graham (*Senior Advisor on Economic Policy, U.S. Patent & Trademark Office Assistant Professor of Business Strategy, Scheller College of Business, Georgia Institute of Technology*) spoke about issues of patents in the context of SDOs. Having a patenting system, according to Graham, means that in the short-term, society gives up some efficiency but in the long-term gains a supply of inventions and disclosure of those inventions.

A key concern that Graham, among other speakers, mentioned is the *ex ante/ex post* conundrum, which refers to the difference of negotiating about patent rights before large investments are made in the technology (*ex ante*) versus the opportunity for claiming on technologies and industries created after sunk investments have been made (*ex post*). Patenting inside SDOs raises such concerns about ex ante negotiation versus ex post claiming associated with patents. The accepted solution generally involves obligating parties who voluntarily join a standard to follow guidelines respecting their Standard Essential Patents (SEPs). A common set of obligations includes that such patents be licensed on FRAND terms – fair, reasonable, and non-discriminatory. That said, actions in this area vary considerably within SDOs: some SDOs have a committee to examine the patents and to determine whether they are essential to the operation of the standards. But more commonly, SDOs never ask that question, thereby leaving substantial uncertainty in the patent landscape for most standards.

Speaking about the IT and communications fields, Graham said that development and commercialization of devices in this sphere often involve complex technologies covered by many patents. For example, a smart phone may be the compilation of thousands or tens of thousands of patentable inventions. And the same may be true for standards; there may be thousands of individually patented technologies in a given standard for many electronics and telecommunications platforms. Such complexities can give rise to problems of coordination.

Biochemical products and medical drugs, by contrast, typically have many fewer patents associated with the technology. However, the extent of the utility of standards will be in the modularization and interchangeability of technology. Therefore, this complexity, in which there may be multiple patentable inventions, can be expected to be an issue in the emerging field.

The potential for conflict within the patent system will always exist because patenting offers exclusivity and it supports that exclusivity through the law. By contrast, a standard-setting process is best driven by inter-operability, common platforms and openness. So, conflicts between patenting and standards seem unavoidable.

Graham gave two different sorts of examples of this conflict. The first involved the inventor Jerome Lemelson. In the 1990s, he allowed his patent arguably covering barcoding technology to "pop out" of the patent office, where it had been working its way secretly through the system for almost 40 years. It is widely reported that Lemelson then sought royalties from companies in industries that had widely adopted barcoding technologies, including semiconductors and automobile manufacturing.

A second example involved the technology-licensing company Rambus. In the 1990s, representatives from Rambus participated in an SDO aiming to set standards around communications protocols of SDRAM (synchronous dynamic random access memory). Rambus team members took part in the standards-setting process, but ultimately withdrew from the committee. After the standard was set, Rambus, unbeknownst to others, obtained patents that included technology deployed in the standard. Some claimed that Rambus was mapping the claims of the patent onto what they were learning inside the standard development committee process. "Clearly, a patent that writes directly onto the standard can be very valuable," Graham said. And being on the standard-setting committee during the process of

developing the standard obviously gives one an advantage in the patenting arena, since patents have the potential to hold up companies that have made sunk investments.

Graham next discussed anti-trust issues. As generally viewed by the anti-trust authorities, standards bring enormous benefits to consumers, but involve the meeting by companies in an industry to set the conditions for competition. Recently, the anti-trust authorities in the US and EU have announced that a set of fair conditions for the use of patents in standards, the core of which is FRAND licensing, are expected if they are to not involve themselves in regulating such competition-setting by industry. The parameters are still developing, and a "dance" continues between industry and the regulators. Presently, the definitions are loose and have been problematical, in part due to ex ante versus ex post conflict; often language is unclear in the requirements set by the SDOs for their members, leading to a higher likelihood of ex post problems.

Graham closed by considering hurdles and benefits of patents in the context of biotechnology standards. Chief among the hurdles is that, as biotech becomes more modular, that such complex technologies, by their very nature, create additional opportunities for patent hold-up. On the positive side is the history of good practices in patenting in the biotechnology space. Unlike fields like software, biotechnology patents tend to give much clearer notice of what the parameters of the invention include, a fact largely driven by the well-accepted nomenclature in chemistry and biology. Graham also puts in the positive column the standards conference itself, which to him shows that the relevant community is starting to identify and discuss potential problems openly, early in the development of a standard-centered approach.

The upsides and downsides of standards

Iain M. Cockburn (*Richard C. Shipley Professor in Management, Boston University School of Management; Research Associate, National Bureau of Economic Research*) discussed the benefits and costs of implementing standards. Topping the list of benefits was gains in efficiency from coordination of effort, such as that seen with the Human Genome Project, which involved development of a common language and common set of data structures and was driven by the ability to access and share data. Other obvious benefits of having standards are reduced costs, through re-use and recycling of materials and methods, and better availability of complementary products and services.

Less obvious benefits include those derived from modularity and standardized interfaces. For example, the development of standardized PC data-transfer systems connecting data processors, disk drives, video cards and other components gave users the ability of to mix-and-match components, build customized configurations, and "add in" specialized peripherals. These interconnection standards also enabled rapid innovation within components. Finally, standards can reduce barriers to entry, stimulating completion. This can be a benefit to newcomers but, as Cockburn reminded us, can hurt existing big players.

Turning to the potential downside of standards, Cockburn asked, "What can go wrong?" He answered with several

possibilities: *lock-in* to inferior technology, such as what happened with early Microsoft Windows, where most users opted to stay with an inferior technology rather than switch; *standards wars* in which the winner-takes-all competition can burn up scarce resources with no clear benefit at the end of the day to users or producers; *whiplash*, where rapid displacement of one standard by another can increase uncertainty, and leave users holding "stranded" investments, as has happened with the Blackberry; *monoculture*, where economic incentives to comply with a standard can result in the stifling of competition, like Microsoft in the mid-1990s; and the *forking problem*, where a tweak in the standard can brings private value to the instigator but destroys a lot of social value associated with a common platform. His example is Linux, a robust, high-performing operating system hampered by the Linux community's struggles to reach consensus about ways to advance.

One of the most significant challenges of working in a standardized sector is *monetization*. In the IT world, companies have come up with very creative business models to capture value from sponsoring standards and ecosystems. A prime example has been Google, which gives away things like search services, Gmail, and Android for free, but is able to make money by using its control of these platforms to sell advertising. Very often the basis for monetization of a platform changes as the platform evolves. Google went from being a revenue-free technology developer, to licensing its technology, to engaging Apple in a standards- and compatibility-driven war for the smartphone market, discovering various ways to collect money throughout the process. In this context, Cockburn suspects that increased standardization of biomedicine will bring significant challenges concerning how to monetize genetic information.

He concluded by stressing that the governance model, and how the standards are assembled is critical. When standards become critical, winner-takes-all competition becomes more likely. People accustomed to gradual, performance-focused change, working with regular forms of competition can encounter some perverse market phenomena when standards are implemented. Finally, IP rules are critical and he sees much greater roles for IP in the future.

AFTERNOON PRESENTATIONS

KEYNOTE ADDRESS: Raymond H. Cypess (*Chairman and CEO, American Type Culture Collection*)

ATCC is well-known as the principal repository and source of reference cultured cells and a knowledge hub used by the life science and biomedical research communities. In addition, Cypess aims to expand ATCC's leadership role for the development of standards in the biomedical and life sciences.

To lead the charge for standards development, ATCC itself became an accredited standard's development organization. It did that in 2007, making ATCC the first biological resource organization to gain such accreditation by the American National Standards Institute (ANSI). Moreover, because ANSI operates as part of a global community, the standards that ATCC develops must harmonize with those of the International Organization for Standardization.

ATCC's first official consensus standards activities involved the development of two process standards, an assay for anthrax toxin (ASN-0001-2009) and a cell authentication assay that uses STR DNA profiling (ASN-0002-2011). More recently, ATCC has introduced a significant new materials standard, specifically a reference cell line for propagating and titering viral vector constructs for gene therapy.

Cypess enumerated reasons why standards matter and why the paucity of them in life and biomedical science has posed problems. For example, in the past few decades we have witnessed an explosion of technological advances that bring new tools and methods to life science researchers. Many of these tools and methods generate vast quantities of data, the analysis of which is typically complex. Moreover, studies employing these applications can be costly, making it prohibitive to conduct many independent replications before the work is submitted for publication. At the same time, many researchers have transitioned from siloed discipline-oriented work to interdisciplinary efforts. Taken together, these changes offer the potential for creative synergies leading to important breakthroughs. But, in reality, they have also have led to wasted human and material resources when published findings could not be independently replicated, much less built upon.

Some of that waste has come about, Cypess argues, because the technological advancements have not been accompanied by the development of either material or process standards. Compounding these problems is the increased competition among academic researchers for fewer federal grant dollars. And smaller grants can, for example, translate into smaller research sample sizes or cutting corners in other ways.

One area in which numbers have been recently gathered to document the problem is cell misidentification. In work supported in part by ATCC, studies found that fewer than 50% of researchers queried regularly verified their cell lines[1-4]. Consequently, many errors of misidentification go unrecognized. This problem has been confirmed by seeing that, of the cell lines submitted to ATCC, over 30% are misidentified.

Why is this lack of authentication so seemingly widespread? Cypess suggests that authentication, for example, is not

high on scientists' to-do lists. Also he suspects that young investigators don't have much training in cell culture techniques or quality control issues. The push to use pre-assembled reagent kits in research has eliminated much of the concern for understanding the details of each and every technique.

What does Cypess think is needed to rectify the problem? He had several suggestions. (**See Box 10. Recommendations for reducing irreproducibility in life and biomedical sciences.**)

Box 10. Recommendations for reducing irreproducibility in life and biomedical sciences.

Enhanced governance to optimize research reproducibility, including the following:

- Harmonized consensus-based life science standards
- More formal definitions of terms leading to a dictionary and a working language, to minimize confusion when working across disciplines
- Quality control at critical points in the research & development process
- Harmonization of regulatory agency policies and practices
- Supportive journal policies
- Education and training

And what plans does Cypess have for ATCC to address these problems? He intends for the organization to take on projects that will produce high impact (e.g. a cell authentication assay) for the most commonly used assays, tools, and reagents that are utilized in basic, translational, and clinical research. The organization will start with projects in both process (written) standards and material standards. (**See Box 11. New standards projects for ATCC.**)

Box 11. New standards projects for ATCC

- **Process (written) standards project: IT**
  Non-biomedical IT field already makes effective use of standards
- **Material standards project: Antibodies**
  Use of antibodies spans basic, translational, and clinical research
  Many commercially available antibodies perform poorly and quality control is lacking
- **Material standards project: Synthetic Biology (an emerging field)**
  Readily measurable.
  Already have implemented two – synthetic RNAs for West Nile and norovirus
- **Consent and procurement of tissues**
  Going on already throughout the country and globally but without formal harmonization

Commenting on antibody standards, Cypess said that problems with commercially available antibodies have arisen due to lack of product validation formally provided by culture collection. Since the 1980s, the tradition of depositing biomaterial by investigators cited in publications by authors have essentially stopped, primarily due to changes in intellectual property laws regarding biomaterials (Bayh-Dole). Recently, ATCC has pioneered new material transfer agreements that allow investigators at institutions to deposit materials without risk to their IP rights.

Cypess, among others, suggested that journals and funding sources both have potentially important gatekeeper roles in helping to implement and enforce standards. (See below for Véronique Kiermer's presentation on the program *Nature Publishing Group* has recently implemented.)

To implement changes going forward, Cypess proposed the ATCC create a non-profit arm whose mission includes thought leadership, policy, and training in standards. He got the go-ahead from the ATCC Board of Directors, and thus the Global Biological Standards Institute (a co-sponsor of this conference) was formed in 2012.

GBSI, with Leonard Freedman at the helm, aims to develop advocacy campaigns that will help stakeholders to understand why standards are important and what the outcome of their expanded development and use could be. (**See Box 12. The Mission of GBSI.**)

Box 12. The Mission of GBSI.

- Provide global leadership in advocating the development and use of life science standards
- Engage diverse stakeholders to catalyze actions and policies leading to expanded adoption and use of biological standards
- Ensure credible, replicable, and translatable results through standards-based frameworks, life science standards, and reference materials.

To gather background for such campaigns, GBSI has just released a white paper (*The Case for Standards in Life Science Research*; http://gbsi.org/sites/default/files/uploads/pdf/the_case_for_standards.pdf) based on interviews with 50 stakeholders, including leaders from academia, industry, scientific publishing and funding agencies. The white paper, along with ideas and information gathered at the current conference, will provide substance for moving forward in the advocacy of standards development in biomedical and life sciences.

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[1]Capes-Davis, A., et al., *Int J Cancer 2010*.

[2]Boonstra, J., et al., *J Natl Cancer Inst.* 2010.

[3]Korch, C., et al., *Gynecol Oncol.* 2012.

[4]Capes-Davis, A., et al., *Genes Chromosomes Cancer.* 2013.

A publisher sets new standards

Véronique Kiermer (*Executive Editor and Head of Researchers Services for Nature Publishing Group*)
It is an open secret that, whereas research done in industry typically employs formal accountability structures for data collection and reporting, such is not the case in academia. Moreover the two cultures have different incentive and reward systems, with creativity and novelty being honored more in academia, and reproducibility in industry. Now, the consequences of not incentivizing reproducibility in academia is wreaking havoc, largely down-stream, in industry[5,6].

Academic journals, as gatekeeper, are poised to help the life science and biomedical community improve the reproducibility of published findings, said speaker Véronique Kiermer. However, implementation of guidelines alone may not suffice; *Nature Publishing Group* (NPG) learned that through an experiment of its own. The experiment in questions drew on the fact that for several years NPG journals has asked its authors to deposit into designated repositories the datasets that were part of newly accepted manuscripts. In 2008, the editor of *Nature Genetics* (NG) recruited research teams to try to reproduce results from one microarray table or figure from each of 18 selected NG papers. For this test, the teams used data that had been reported in the paper and/or deposited in the MIAME (Minimal Information About Microarray Experiments) database[7]. Only 2 of the 18 tables or figures could be reproduced in full – 6 in part and 10 not at all. Kiermer said that the main problem was a lack of the full dataset in the deposition.

Therefore, NG and other NPG journals have increased their scrutiny of data deposition. In addition, NPG's newly implemented plan provides authors with new ways of making their data available even for smaller datasets – such as presenting numerical data underlying the graphical representations published in figures.

NPG has implemented other changes as well. Notably, they have introduced a checklist that authors must complete before their article goes out for review[8]. Checklist items range from questions such as whether the cell lines and antibodies used in the study had been authenticated, how many times a study was repeated in the laboratory, whether the assays were done in a blinded fashion, what statistical tests were used, and why those tests were selected. To help evaluate the statistical data, NPG now has professional academic statisticians serving advisory roles for each of their journals. Finally, the journals now give authors unlimited space online to report methods.

Commenting on the checklist, Kiermer stressed that authors cannot just check off each item; they must explain where in the text each item was covered. Thus, for example, if the researchers did not do the experiments in a blinded fashion, they need to say so. Then reviewers can decide the importance of that limitation and, if the paper is published, readers know that experimental limitation.

Is the system working? It is too early to tell. However, Kiermer did report that authors are now beginning to send in the filled-out checklist when they submit their papers for review.

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[5]Prinz, F., et al., *Nature Review Drug Discovery*, 2011.

[6]Begley, C.G., Ellis, L.M., *Nature*, 2012.

[7]Minimal Information About Microarray Experiments (MIAME http://www.mged.org/Workgroups/MIAME/miame_2.0.html

[8]Reporting Checklist for Life Sciences Articles http://www.nature.com/authors/policies/checklist.pdf.

New models in microbiology

Tom Dedeurwaerdere (*Professor, Université catholique de Louvain; Director, Biodiversity Governance Unit, Centre for the Philosophy of Law, Université catholique de Louvain*) brought a social science perspective to the discussion of standards in life sciences, based on an in-depth analysis of the use of standards in microbiology. He stressed that to succeed at standards-building, the stakeholders need to develop a shared understanding of the problems by confronting them together. That means there needs to be effort put into the community-building per se, which can be done through science federations or other intermediary organisations.

Dedeurwaerdere reported that, in terms of standards, the field of microbial sciences has what he called emerging community standards; different communities, each developing its own sets of standards but realizing the value of inter-community interactions. The community standards he referred to are

(1) materials standards,

(2) microbial taxonomies,

(3) genomics standards, and

(4) literature standards.

Dedeurwaerdere provided two examples of successful interconnection of the community standards in which the benefits are already being reaped.

The first example is a World Bank-funded consortium, a resource known as CGIAR (formerly Consultative Group on International Agricultural Research),[9] which deals with both crop plants and microorganisms that infect them. One of CGIAR's efforts concerns a major wheat disease caused by a fungus. A strain of the fungus had wreaked havoc on the US wheat crop in the 1960s. Now a related strain is having similar effects in the Middle East. CGIAR, through a global effort drawing on online digital resources in the public domain and preservation of purified microbial materials according to community standards in the network of public collections of the World Federation of Culture Collections, was able to determine that the new fungal strain came from Uganda. Using this information, it has been possible to develop wheat that resists the deadly fungal strain.

The second example was a local one with impact on private sector economic development, namely the development of a bacterial strain for making yogurt in the country of Georgia, based on global community standards both in the field of genomics and microbial cultures. To make the strain, Georgian scientists compared the results of their own collection efforts on farmers' markets with relevant bacterial strains in resource centers such as ATCC. They also compared DNA sequences of local strains with those in Genbank. Using these two public information sources, they were able to optimize the selection process of an industrial yoghurt strain. From that effort, a new yogurt-manufacturing business emerged that now has captured a sizeable fraction of the European market. Thus a well-built global infrastructure enabled individuals outside the standards' setting communities to benefit from the standards.

Next Dedeurwaerdere discussed current challenges of such infrastructures, specifically the challenges of improving both access to samples that satisfy the community standards and curation of data. In terms of sample access, he cited evidence from the European Culture Collections' Organisation10, which recently surveyed 8 microbiology journals, focusing on non-prokaryotic cultures. The survey found 1261 papers on non-prokaryotic cultures, involving 20,172 isolates. Less than 1% of these isolates have been deposited in public collections, demonstrating how limited the access to validated samples is, in spite of a clear guideline to deposit samples upon publication of the research results.

In terms of data curation, he cited the example of a DNA sequence listed in GenBank that carries an ATCC number for the strain associated with the sequence. In this case the ATCC number is wrong due to a misspelling. This type of error then gets propagated via citations in journal articles. Developing a mechanism for making systematic correction of these errors poses a huge challenge for the future.

With the view to tackle these challenges, Dedeurwaerdere and his team are currently running a project to identify the drivers for upscaling the standardization process. Surveying the microbial research community, the team identifed three categories of drivers: the need to

(1) formalize the informal system;

(2) build confidence via expertise with standards; and

(3) build on the sharing ethos of science.

(**See Box 13. Drivers for upscaling standardization in the microbiology research community.**)

Box 13. Drivers for upscaling standardization in the microbiology research community.

- **Formalize the informal system**. Worldwide, no single culture collection can do it all. Hence there is a need for having a standardized collection of collections.
- **Build confidence through expertise with standards**. Investing in well-curated standards can attract industry to the collection.
- **Build upon the sharing ethos of science**. Scientists who are contributing to the collection seek something in return; storage, technical services, information on project results, provision of education and training.

Dedeurwaerdere and his team are studying some of the new science initiatives, paying particular interest to the types of governance structures used. One such example is the EU's MicroB$_3$ (Biodiversity, Bioinformatics, Biotechnology) Project[11]. MicroB3 deals with sampling in the ocean, enabling information gathering on non-culturable organisms. (**See also Box 14. New microbiology efforts to watch for their approach to standards.**)

Box 14. New microbiology efforts to watch for their approach to standards.

- **The Human Microbiome Consortium** (http://www.human-microbiome.org/) - Of note is their pre-publication data-release standard, based on the Fort Lauderdale principles. It uses a joint governance mechanism involving scientists, journals, and funding sources.
- **Sloan Foundation Program in Microbiology of the Built Environment** (http://www.sloan.org/major-program-areas/basic-research/microbiology-of-the-built-environment/) – The project extends beyond DNA sequencing to include environmental standards in the annotations of the DNA sequences.
- **Micro B3** – Of note is the Micro B3 standard Material Transfer Agreement for acquisition and transfer of material in accordance with the Nagoya Protocol agreed upon by all the consortium members.
- **Systems Biology Knowledgebase (Kbase)** from Department of Energy (http://kbase.science.energy.gov/) – A long-term effort based on bottom-up scientific input.

In establishing Micro B3, its organizers needed to standardize procedures for activities, such as sampling of metagenomes in ocean water from aboard the boats and submission of the sequence data to a global data center. These procedures were developed and standardized as part of formal contractual agreements with the institutions that will store the organisms (Argonne National Laboratory) and the water containing the metagenomes (Smithsonian Institution). According to Dedeurwaerdere, the strength of project is the governance – all based on formal agreements amongst the institutions that put the formerly informal arrangements on a more solid institutional and organizational basis. He thinks this approach guarantees long-term sustainability.

Dedeurwaerdere concluded by identifying several questions that now need answers:

- What additional drivers are there for up-scaling standards?
- How can the learning curve about these drivers be speeded up?
- How to address issues of heterogeneity and uncertainty?
- Is the inclusion of academia and regulatory bodies in the standards-setting process feasible and advisable?

[9]http://www.cgiar.org/

[10]http://www.eccosite.org/

[11]http://www.microb3.eu/

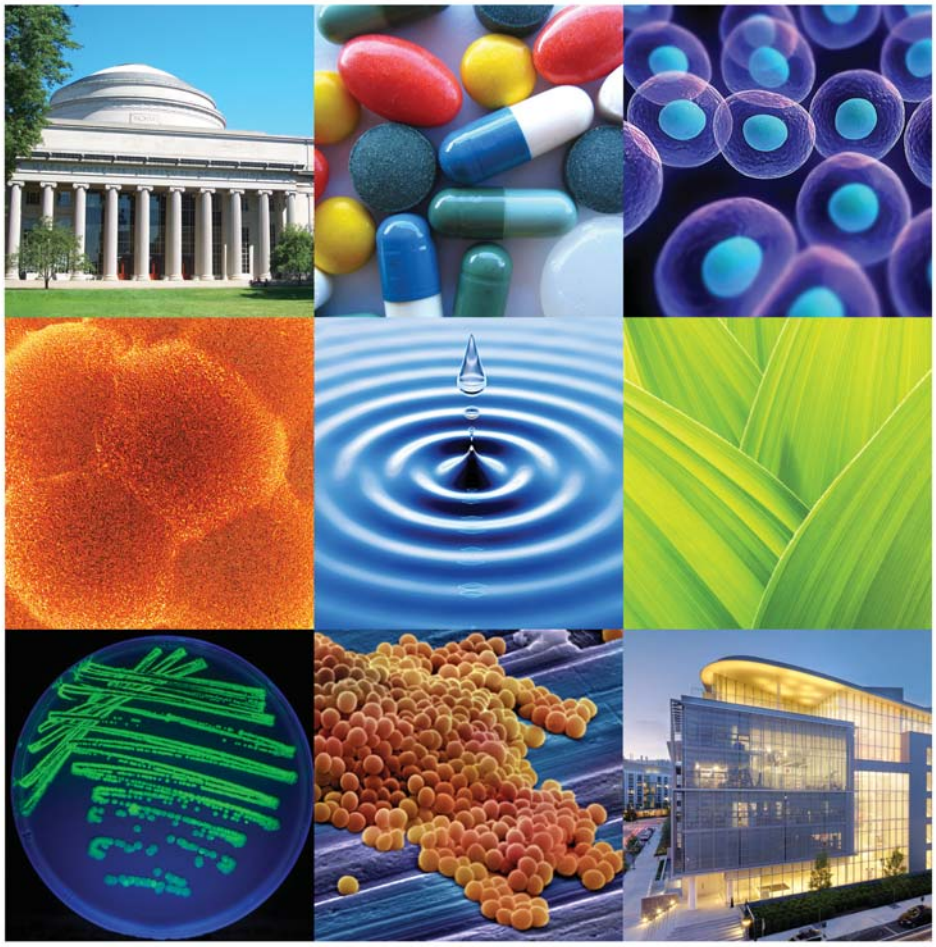
CONCLUDING REMARKS FROM SCOTT STERN

Stern started his wrap-up of the formal session by noting that across a wide range of domains – from biomedicine and microbiology to information and communications science – conference speakers told stories with many similarities. And, those similarities may not have been fully appreciated by the speakers until they got to hear each other.

He then reflected on the changing nature of life and biomedical science and science policy. These disciplines have enjoyed a several decade-long history of rapid growth and strong promise. But recently, public funding has stagnated, and expressions of frustration have been heard about insufficient payoff for all the past research investment. These challenges have prompted an effort to view the system more analytically and undertake some grass-roots efforts, both by individuals and institutions, to try to "redesign that system to enhance the cumulativeness of research process and the ability to translate research findings in a meaningful way." Pointing to the efforts in scientific publishing mentioned by Veronique Kiermer, Stern noted that "as you impose standards at the level of science reporting, that will force people at the top to change not just what goes into the manuscript (to comply with the checklist) but to change how the lab may be organized and what types of grants to apply for. The considerations apply both to scale and scope."

A key take-away from the conference was that biomedical researchers can look to IT for models of standards development. Standards-setting in the IT domain was not an easy process, but the payoff has been tremendous. Consequently, Stern sees a potential for similar developments in the biomedical and life science arenas. Figuring out the best strategies will be critical, and several ongoing efforts were described to translate concepts across disciplines. And, as Ray Cypess mentioned, setting goals that can be readily reached and are quantifiable will be particularly useful.

Stern concluded by expressing the hope that the conference marks the start of an ongoing conversation among those committed to determining how to use lessons about standards-setting as a mechanism for doing high-quality biomedical research that can be translated into heath benefits.



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