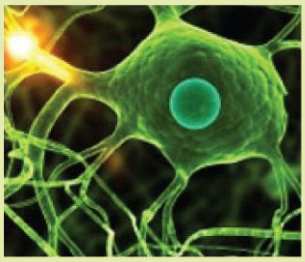
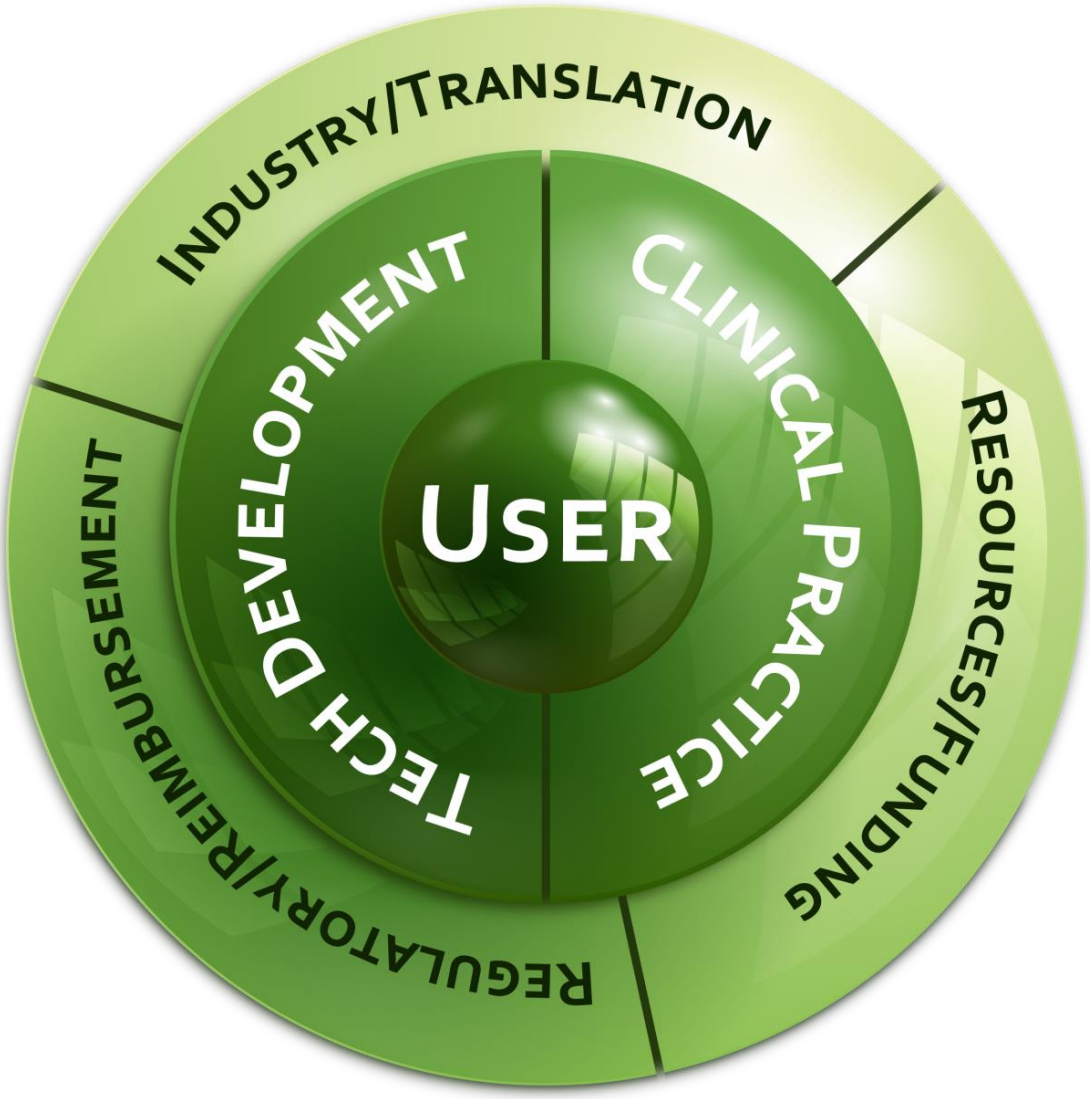


CLEVELAND NEW

NEURAL ENGINEERING WORKSHOP

June 24-26, 2015 www.ClevelandNEW.org

A ROADMAP FOR NEURAL ENGINEERING



EXECUTIVE SUMMARY

Innovation in medical technology for neural systems to address rehabilitation problems has made a significant impact on people's lives. The clinical applications that can benefit from neural technology are expanding rapidly beyond rehabilitation to domains traditionally considered amenable to pharmacological solutions only. The BRAIN initiative, interest from major pharma companies in bioelectronics medicine, optogenetics, and other major developments are fueling the growth of and need for advancements in neural engineering technology. The translation of innovative technology from concept to clinical care is a long and complex path that involves many entities including users, clinicians, innovators/developers, industry, regulatory bodies, reimbursement agencies, and funding sources. Further, it is an international endeavor. The timeline of innovation to clinic is currently very lengthy. The balance between ensuring user safety and rapidly implementing the most innovative and beneficial technology requires coordinated and optimized interactions between each of these stakeholders. As put by a meeting participant, "***It has taken too long to get where we are at!"*** It takes too long to deliver technological innovations to the user. There is significant need and opportunity to develop strategic plans, infrastructure, and practices to ensure that safe and effective technology is developed and delivered to users in a far more rapid and efficient manner. To this end, the NEW 2015 meeting developed a common vision statement for the community:

> *The Neural Engineering Community is dedicated to fostering an ecosystem that catalyzes consumer, academic, industry and government collaboration to develop and deploy the best solutions to reach consumers in the most efficient means possible to have a positive impact on human care and ability.*

In June 2015, the 3rd biennial Neural Engineering Workshop (NEW) was hosted by the Cleveland Advanced Platform for Technology National VA Center, Functional Electrical Stimulation National VA Center, and Case Western Reserve University in Cleveland, Ohio. It brought together thought leaders in the neural engineering community committed to providing neural technology-based solutions for individuals with neurological disorders. The meeting goal was to identify the opportunities, challenges, and directions for growth of the field. Specifically, this group looked to improve neural engineering-based clinical care, strengthen the neural engineering community, and build a common vision to affect change. The meeting was a continuation of strategic conversation initiated at the 2nd Cleveland NEW conference in 2013. Six Themes critical for success of the field were identified at ClevelandNEW 2013:

- Innovation
- Consumer
- Funding
- Commercialization
- Clinical
- Regulatory

The NEW 2013 meeting, however, did not develop a comprehensive guiding strategy for these themes, and therefore, did not advance them further following the 2013 meeting. NEW 2015 was organized around these themes with the explicit goal of developing a strategic plan to move the

efforts forward. The participants in NEW 2015 included leaders from industry, academic and translational investigators, clinicians, consumers, funders, and regulators.

The output of the workshop is captured within this Strategic Direction Roadmap to serve as a common consensus message such that stake holders can more effectively drive and coordinate strategic activities. For each theme, this Roadmap describes the

- **Vision**: What will the state of the field be in 20 years;
- **Goals**: The measurable five year milestones required to achieve the vision;
- **Deliverables**: The actions required within the next two years to achieve the goals.

By strengthening the larger community with a common consensus, strategic framework, and measurable actions, the impact on healthcare and its growth throughout organizations, funding agencies, and all aspects affecting success is greatly multiplied.

The output of the two days of highly-engaged workgroup discussions are provided in the table at the conclusion of this introduction. The rationale, identified key barriers to advancing the field, goals to overcome those barriers, milestones, and deliverables are detailed in the body of this document. It is notable, that there was one overriding theme, however, that was common among all the themes being discussed: communication and collaboration. A common exchange in all workgroup sessions would be as follows: one group of stakeholders saying, "We need more information and training about [*regulatory, industry, funding, etc.*]" followed by an expert in that area saying, "There is a resource for that at …" It was clear that information is available, but the communication; "ecosystem;" sharing of data, expertise, and know how; and sense of integrated community is underdeveloped. In nearly all theme's vision and goals, an effective forum for efficient and helpful exchange of information is identified as an important goal for achieving success moving forward.

In summary, a collection of the most influential and leading people in the neural technology community met in Cleveland for two days of intense discussions about a common strategy to advance our field for the next 20 years. This document captures a strategic direction resulting from these discussions. It should be distributed widely and serve as a common voice and vision for moving our field forward. It is intended to be a living document, as well. Feedback and ideas for improving can be directed to the dustin.tyler@case.edu. We will reconvene for ClevelandNEW 2017 on June 21-23, 2017 to assess progress towards this plan, adjust as necessary, and establish a continued vision and strategic direction.

VISION	2-5 YEAR GOALS
Theme: User/Consumer	
Consumers of neurotechnology will find accurate and credible information that is readily available and engaging. There will be an ecosystem where the consumer community engages in a co-creative process to the level of custom-creation and modification of self-optimized solutions.	1. Create a moderated neurotech forum 2. Engage users to collect data and information that will guide neurotech development.
Theme: Regulatory / Reimbursement	
All stakeholders work together within an expedient and smooth regulatory and reimbursement ecosystem to bring the best neurotechnology products to patients.	1. Create a training environment that addresses knowledge gaps. 2. Leverage community to improve regulatory science to fill gaps that affect the regulatory process. 3. Create a "feedback loop" – an ecosystem that learns through engaged communication with all parties.
Theme: Clinical Practice	
A "golden age" for neural engineering clinical research and consistently successful, life-changing neural engineering clinical interventions in 2030 by training more and better interdisciplinary clinical and scientific researchers through partnerships, emphasizing co-localization, enabling peer-to-peer and bidirectional communication, and market-responsive, higher standard of care treatment. We recognize the critical need for increased inclusion of clinicians in future NEW meetings.	1. Test the hypothesis that an interdisciplinary model for clinical research in neural engineering is more effective than traditional siloed engineering research. 2. Increase the footprint of engineers in the clinical world and clinicians in the engineering world through outreach. Merge these two segments into a single community by 2030. 3. Facilitate interdisciplinary training collaborations on every level, from predoctoral training to senior investigators/attending physicians
Theme: Technological Innovation	
We envision neural engineering playing a major role in alleviating and managing the leading causes of global morbidity.	1. Adopt an open platform for experimentation. 2. Create a global neural engineering forum. 3. Produce a state-of-art industry overview. 4. Develop a standards group for the neural engineering community.
Theme: Industry Translation	

VISION	2-5 YEAR GOALS
Our vision is to foster an innovation ecosystem that catalyzes academic, industry and government collaboration to enable successful commercial translation of maturing scientific research and technology within the constraints of global regulatory standards and business metrics.	1. Grease the skids – create an open source quality system and inventory of current research tools to assess risks, safety, and design controls. 2. Utilize translational coaching – create a venue for vetting and shaping commercial potential of ideas earlier in the pipeline.
Theme: Funding	
In 10-20 years, a comprehensive funding landscape that sustains research along the continuum from initial discovery to consumer-focused translation through to sustainable commercial dissemination will exist.	1. Create educational resources. 2. Establish routine planning meeting. 3. Identify and analyze gaps in the funding landscape.

CONTENTS

THEME: USER / CONSUMER

CURRENT STATE:

We cannot forget the consumer, who must remain the ultimate focus of the efforts in neural engineering. The success of the neural engineering community is directly tied to the active and productive engagement with the consumer. This theme discussed the related issues and opportunities to create a vision and set of goals to better integrate and include the consumer in development of neural technology.

The participants in the User theme at ClevelandNEW 2013 established and agreed on a definition for this stakeholder segment of the neural engineering community as follows:

> ***The consumer is an end user, that is, someone living with a condition and/or a clinical or lay individual caring for someone with a condition.***

In the preceding NEW 2013, participants identified the need for bi-directional communication, that is, to the user and from the user, along with the need to identify methods by which that communication might take place. Many challenges were identified such as the need for common, collective messaging and for better education of consumers.

One of the main drivers of this conclusion is the prevalence of easily accessible information on the internet for consumers and care-givers. It is no longer the case that the clinician is the only source of health information. Credible or not, health information is exponentially expanding on the web to reach the fingertips of internet searches. The antithesis is that inaccurate information is widely available, leading to misunderstandings, fears, and unmet expectations. Fielding, influencing and sourcing reliable information is an opportunity for the neural engineering field to build a dialogue with the consumer.

Since that meeting, the landscape has changed surrounding the neuroengineering sector. There have been several influential occurrences that will stand to impact the field ranging from clinical care to industry marketing to consumer acceptance. Some of these are highlighted here.

At the request of the Patient Safety Subcommittee, the American Academy of Neurology conducted a review of science and policy regarding the use of opioids given the increasing risk of opioid-related morbidity and mortality in the U.S. In September 2014, the Academy

published an article cautioning the use of opioids[1], further opening the door to the use of neuroengineered devices for pain management.

The Advanced Medical Technology Association (AdvaMed) launched its Life Changing Innovation Agenda in February 2015 to rebuild the innovation ecosystem to unleash the potential of medical technology to extend and improves lives with devices of the future, and maintain and enhance U.S. scientific and economic leadership. This initiative is highly likely to impact the field of neuroengineering.

As another example of the changing societal view of rehabilitation technology, there has been in influx of people living with limb loss; nearly 2 million in the United States according to the Amputee Coalition. The increased use of prostheses by amputees - and the trend to wear them visibly - has helped gain consumer acceptance of engineered devices.

While in the past, devices have been plagued with “last resort syndrome,” they have been moving up the decision tree. For example, the use of deep brain stimulation as an early intervention for Parkinson's Disease has gained acceptance among users and clinicians, particularly with the work from the EARLYSTIM study which was published in 2013. (Schuepbach WM, et al. Neurostimulation for Parkinson's disease with early motor complications.N Engl J Med. 2013 Feb 14;368(7):610-22. doi: 10.1056/NEJMoa1205158.)

Among the general consumer, external devices and the integration of body systems are gaining ground and becoming, in a sense, fashionable. This technology culture is exemplified by Fitbit®, the Apple Watch, and explosion of other “smart” and wearable technology. Neurotechnology devices are being marketed directly to the consumer. For instance, NeuroMetrix released the Quell, a wearable pain relief device, at the 2015 Consumer Electronics Show.

In another related cultural shift, the rise of the "Maker Movement," a contemporary **culture** or subculture representing a technology-based extension of DIY **culture.** Although not new, the Maker Movement is building momentum and has been labeled as the next Industrial Revolution. According to Atmel, there are 135 million adult "Makers" in the United States plus the millions of children influenced by the STEM and tinkering education forums. There are currently eight flagship Maker Faires, gatherings of hobbyists, engineers, entrepreneurs and innovators, around the country. This movement is likely to impact the device user's ability to take some control over the design and functionality of their device.

There are both significant opportunities and challenges with allowing users to “DIY” their neurotech. By engaging in the product, it becomes accessible and less scary to the user. This will enhance device adoption and combat the stigma of complexity in devices. However, a successful approach will also need to manage risks, patient safety, and FDA regulations.

Another form of user engagement becoming pervasive is the pseudo-real time feedback and big-data of the internet of things. In software, for example, usage patterns, failure modes, and preferences are constantly being streamed to the developers in order to develop more stable and wanted products. Wearable health monitors constantly track user data and integrate to other applications that can diagnose and analyze that data. Limited forms of this technology have long been part of cardiac devices. More recently, neurotech devices are beginning to incorporate more of these technologies for patient management, telemedicine, and device reliability. While companies are interested in expanding this capability to understanding user preferences, there was disagreement to this point during the session discussions. Continued dialog is necessary to determine the appropriate and desired level of user engagement.

The consumers of neuroengineered devices will be impacted by their ability to afford such devices. Financial considerations will be critical in the user's thought process. The impact of the Patient Protection and Affordable Care Act and general insurance industry acceptance of the neuroengineered device sector is a factor in any user theme discussion.

One premise that all workshop attendees could agree upon was that the consumer should be at the center of their efforts and the main reason they are engaged in the science and development of neural engineering technology.

In summary, for consumers and the broader community to accept neural engineered devices, the consumers must be included in the development of the technology. The sector cannot defer to an "if we build it, they will come" mentality. Further, communication with the consumer community must be ongoing and provide educational resources to maximize the consumer’s experience with the device after the decision to receive it. The neural engineering field must better understand the decision processes of the consumer; where and how consumers access information; and the roles that various stakeholders have to influence consumer’s decisions.

KEY FACTORS:

The group’s discussion was distilled to the identification of three key factors recognized as necessary in order to facilitate a shift toward a

greater consumer-centered focus in the neural engineering field. These include:

1. Responsible and Effective Communication and Engagement

The question of how to engage the user is a broad topic, impacted by the diversity of the user population Factors to consider include:

- The influence of internet search engines, social media and traditional media;
- The population diversity such as user versus caregiver, degenerative condition vs traumatic injury, or affluence versus underprivileged; and,
- The engagement of users in the development processes.

2. Decision Factors

An effective user communication strategy must include and support the factors that affect consumers' decisions. These include:

- The stakeholders and their impact on the consumers;
- The process that individuals go through when deciding to opt for or decline a device therapy solution; and
- The different communications needs in the testing/development phase versus commercial phase.

3. Cultural Perceptions

In many cultures, the increasing integration of technology into daily living provides an opportunity for the developers of neural engineering devices, as well as users. While these cultures welcome the "bionic" and actively engage technology, others cultures may technology as "less than human" and recognition of personal inadequacy. These differences may be between different social groups related to a common technology or between different technologies within a single social group. The field must identify, understand, and address the various perceptions within these diverse scenarios. It may be possible to maximize the cultural shift to further awareness of and increase the acceptance of biomedical devices and improve the acceptance of users into the mainstream.

VISION:

Consumers of neurotechnology will consistently and easily find accurate and credible information that is readily available and engaging. There will be an ecosystem where the consumer community engages in a co-creative process to the level of custom-creation and modification of self-optimized solutions.

Assumptions:

- Misinformation will remain available;
- “Snake oil salesmen” will not go away; and
- Wearable, personal technology and usage and personal data monitoring will continue to gain acceptance.

2-5 YEAR GOALS:

Goal 1: Create a moderated neurotechnology forum, clearinghouse, or society to enhance effective communication among a user-inclusive community.

Goal 2: Engage users of neurotechnology devices in dynamic data streams with a functional structure to collect and annotate data.

DELIVERABLES:

(2 Years)

Goal 1 deliverables:

- A “user-verse” working group with the following objectives:
  - Elaborate the expected gains to the consumer and neural engineering community through a user-centric communication strategy;
  - Identify true stakeholders expected to gain something meaningful;
  - Conduct a landscape search to understand what advocacy organizations currently exist and how to interact, collaborate, coalesce, leverage efforts;
  - Identify successful organization structures from other fields and capture best-practices (ex., International Society for Stem Cell Research);
  - Create a credible framework and strategy, including targeting communication channels, that will engage consumers and neural engineering stakeholders;
  - Survey existing information available to consumers regarding neural engineering devices.
- A business plan, including funding sources, to sustain this effort

Goal 2 deliverables:

- A strategic plan for data collection that will ultimately benefit consumers. The plan will include a risk-benefit analysis in engaging the consumer in big-data collection;
- Strategies for using data to inform stakeholders of elements such as therapy efficacy, diagnosing causality of outcomes, safety, reliability, and user preferences;
- Identified opportunities to interact with payer/reimbursement paradigms;
- Standard data structure and sharing definition. Sub-tasks include:

    - Research existing common data elements (ex., National Institute of Neurological Disorders and Strokes Common Data Elements)
    - Benchmark other existing device manufacturers that collect data (ex., Apple)
    - Determine what other data should be included for our community if areas are lacking (ex., Patient Reported Outcomes Measurement Information System)
    - Educate the neurological research community on the defined data structure
    - Create a prototype of the data structure that is common across all neuro-engineered devices
- A large data analytics set which can be made available to companies, clinicians, and consumers;

MILESTONES:

The first milestone is to form the working group that will develop and further elaborate the plan, including more detailed milestones. To be successful, this working group should be formed and begin engagement by end of January 2016. The group will report on its progress at the next NEW workshop to be held June, 2017.

THEME: REGULATORY / REIMBURSEMENT

CURRENT STATE:

In 2013, the ClevelandNEW participants characterized the current state for regulatory and reimbursement by its lack of a unified voice and the absence of a comprehensive roadmap for each stage along the regulatory and reimbursement translation path. Investigators and small companies, mostly disconnected from each other and operating, for the most part, within their own bubbles, find themselves having to navigate the basic regulatory requirements as if for the first time, unable to learn critical lessons from peers. Likewise, regulators observe common problems and obstacles with applications, and have only recently been able to do concerted outreach to this community to bring greater awareness of regulatory requirements. While there are many reasons why great neurotechnologies remain in the lab or in early clinical demonstrations, these inefficiencies around the regulatory environment certainly contribute.

This scenario would continue were it not for the enormous potential of neurotechnology and the momentum that is now building in this field.

At the 2015 ClevelandNEW workshop, participants agreed that the "current state" identified by the earlier workshop was largely unchanged. They asked what must be done to create a thriving ecosystem that advances both science and technology and provides medical solutions globally.

The Regulation and Reimbursement workshop group discussed regulations predominately designed for commercial interests to achieve marketing approval. Those requirements for testing are not optimal for early phase, academic research. In fact, some participants believe those regulations are becoming nearly prohibitive to academic clinical research and they voiced concerns about shifting attention away from pure scientific discovery for the sake of science.

Discussions also revolved around education. Solving knowledge gaps cannot be accomplished without establishing two-way relationships with the regulatory agencies. The agencies need to educate the community about their review processes and the community needs to educate the reviewers about their R&D processes. The need to engage as early as possible in their respective endeavors was acknowledged. What do reviewers need to know, and when? What do researchers and innovators need to know, and when? How can this knowledge transfer best be facilitated? Answers to those questions are, as yet, not definitive, nor are they documented and available to all stakeholders. In reality, strong linkages to other themes (commercialization, funding and reimbursement) call for a level of inclusivity - engaging all stakeholders

- that has not been reached to date, but which must be achieved to move forward in a less sporadic fashion.

Reimbursement was half of the dual theme for the 2015 workshop. Although regulatory issues drove most the conversations in both years, and the topic was barely touched upon in 2013, reimbursement is coming to the fore. In light of the passage of the Affordable Care Act, reimbursement policy changes are impacting Centers for Medicare Services and rippling throughout the insurance industry. Throughout the 2015 workshop, participants voiced concerns about changes in reimbursement policy that are impacting technologies not only coursing along the translation path today, but which are in the early stages of research and could be impacted down the line.

Several solutions to the current regulatory and reimbursement issues were offered and are described below as goals to accomplish.

KEY FACTORS:

Regulatory agencies are grappling with a rapidly-advancing neurotechnology industry that is pushing the bounds of regulatory precedents, driven by a wave of new researchers and small startups who lack key knowledge about the regulatory requirements. At the same time, the reimbursement picture is shifting dramatically, making it difficult to stay ahead of changing requirements. The neurotechnology community has not been speaking in a single, coherent voice to advocate for itself in these arenas. These factors have contributed to the numerous disconnects that exist among regulatory, reimbursement, research and commercial interests.

VISION:

All stakeholders work together within an expedient and smooth regulatory and reimbursement ecosystem to bring the best neurotechnology products to patients.

2-5 YEAR GOALS:

Goal 1: Create a Training Environment that addresses knowledge gaps

The intent here is to improve the capability of all sides to usher in neurotech solutions through science, engineering and clinical research and development. Workshop participants saw the need to change thinking and practices over time. Fine tuning the regulatory and reimbursement processes will take education that requires a needs assessment and appropriate training via *real world* examples.

Developing the curriculum begins with *defining* the curriculum. The input from all stakeholders is needed from research to reimbursement.

Goal 2: Leverage Community to Improve Regulatory Science to Fill Gaps that Affect the Regulatory Process

The consensus of the 2015 workshop participants is that the current regulatory requirements cause excessive drains on scarce funding resources and take too much time. The situation can discourage even the most stalwart innovators and researchers.

Participants discussed the importance of improving regulatory science in order to better predict success of different projects. For instance, identifying best practices (asking which are the best tests or tools to use) and building the case for what separates “good” from “bad” projects early on can be highly useful. Not only would these steps save time and money, but they also would elevate the levels of mutual understanding between stakeholders and spark new kinds of partnerships that serve to strengthen the fledgling field of neurotech.

The solutions to these problems are not insurmountable. Small steps taken today, such as building community through advocacy, and opening the channels of communication between innovators and regulatory agencies, will enable the growth of a viable ecosystem that ensures the sustainability of neurotechnology and improves the lives of many patients and users who stand to benefit.

Goal 3: “Feedback Loop” – An ecosystem that learns through two/three-way communication

To address concerns that too much “bad information” is being perpetuated by consultants and that no “one size fits all” solution exists, the consensus was to examine the interagency hand-offs for knowledge and process gaps, and to work out ways to bridge those gaps. In addition, the need to developed accurate instructions in plain English was emphasized.

Innovators need to understand how the FDA functions. It’s important to recognize that the agency has only recently been restructured to allow a deep and consolidated focus on neurological devices; before 2013, neurological devices were scattered among various divisions without cohesive leadership. When this issue was stated, the workshop participants considered ways to keep FDA updated, including establishing a liaison as a messenger to moderate communications. Another remedy consisted of creating a (monitored) online forum to

stimulate discussions and surface complicated hand-off issues in funding, review and other interagency relationships.

One of the most important ways to engage the FDA in two-way learning is to introduce them to early-stage technologies through their Pre-Submission program. The Pre-Submission program allows for an early conversation around requirements directly from the review team upholding those requirements - rather than from outside consultants who may not be apprised of recent policies - and it allows for early advocacy on the part of the investigator/company around their unique needs.

DELIVERABLES:

Goal 1: Create a Training Environment that addresses knowledge gaps

Holding regular working meeting to bring regulatory and reimbursement people togethe) will help nurture a healthy ecosystem where the each side comes to understand the training needs of the other. Making an inquiry with a carefully developed survey that can get at not just core issues, but the more subtle ones, can provide insight into which steps are causing confusion or creating roadblocks.

Meanwhile, the FDA has solicited comments for designing a customized computer-based curriculum and/or printed material that illuminates *that* agency's processes. In doing its own part to band together and to play a role as educator of all its constituents, the neurotechnology community can help the FDA become the most phenomenal consulting group supporting field. The Pre-Submission program was identified as the key method for engaging the FDA in this two-way educational system.

Goal 2: Leverage Community to Improve Regulatory Science to Fill Gaps that Affect the Regulatory Process

Using industry events, such as conferences, that are already established is an economical and efficient way to do outreach. Holding the first training workshop before NIC and holding the inaugural session *at* NIC to determine needs capitalizes on a target audience. This initiative can serve to identify key barriers and opportunities. A regular e-newsletter, such as the one NIH/NINDS neuroprosthesis program has been issuing, also can get information out to the community.

Funding for regulatory science has not been a priority, particularly not in the midst of economic recession. However, with the 2013 announcement of the BRAIN initiative, the priority is shifting. There needs to be a coordinated voice from this community continuing to advance the funding toward FDA regulatory science.

Goal 3: "Feedback Loop" – An ecosystem that learns through two/three-way communication

With goals in place and deliverables established, progress has to be measured. Putting metrics in place right from the start is important. The feedback loop is a good metric because asking "how are we doing?" is an integral part of it. A committee has to be established to define the parameters for measuring progress and identify the first test case to follow through the feedback loop design.

Because reimbursement is such a mystery to most of today's scattered community, raising awareness is key. The first step is to seek reimbursement "mentors" – those who have navigated the reimbursement system and are willing to share their knowledge. While great learning can come from mentors who have successfully navigated this space in the past, it is even more critical to identify mentors who are navigating this space in the new era of affordable care.

MILESTONES:

Goal 1: Create a Training Environment that addresses knowledge gaps

Work on the survey will begin in Q4, 2015. In the meantime, the FDA will have its first round of comments that were solicited in Summer 2015. The comments will guide the design of the agency's training curriculum and help structure its pre-submission program.

Goal 2: Leverage Community to Improve Regulatory Science to Fill Gaps that Affect the Regulatory Process

The first workshop organized to look at knowledge gaps will be held prior to the 2016 NIC. The outcome of the workshop will be presented at NIC.

Goal 3: "Feedback Loop" – An ecosystem that learns through two/three-way communication

By the end of 2015, a panel will be appointed to define progress metrics and a test case will be identified by January 2016.

Throughout 2015-2016, leaders will solicit comments and feedback from the community in response to requests for information by the FDA. Community members will be encouraged to respond to these requests, and Megan will share comments she receives and report out on this effort regularly.

A committee will be formed to call for reimbursement "mentors" who have navigated the new reimbursement system.

THEME: CLINICAL PRACTICE

CURRENT STATE:

There is a strong bond uniting neural engineering and clinical practice, but it is not well-enough articulated. A strong understanding of the synergies and balance of strengths between the two will further accelerate the conversations and development that must happen to advance the best options and technology to the consumer and the key stakeholders. The neural engineering community seeks to apply advanced technology to restore lost neurological function and/or improve quality of life while clinical practice is looking to apply the most advanced options available to address problems intractable to many of traditional medical approaches..

Positioned closely to the consumer of these technologies, the clinical community's specific objectives include maximizing the quality of life for neurotechnology consumers. This includes the success of the therapy, as well as the coordinated deliverly of the technology in the clinical care environment. Of course, both neural engineering and clinical care hold the consumer's safety paramount. A deep, bi-domain understanding leads to the most effective, reliable, deliverable, and safe technology.

Clinical practice should be understood to encompass the broad range of professionals that provide front line care, including primary care physicians, neurologists, neurosurgeons, physical medicine and rehabilitation professionals, physical therapists, occupational therapists, communication and swallowing disorders specialists, psychiatrists, neuropsychologists, social workers and others needed for the care of specific disorders. Ideally, these clinical research teams share a desire for interdisciplinary collaboration and a passion for research. They are professionals with academic incentives, appropriate facilities, institutional support/infrastructure, dedicated time and the necessary financial resources.

Key Barriers

The professionals gathered in the Clinical Practice theme felt that in its current state, research clinicians and neural engineers do not form a single community. Obstacles to the collaboration between clinical teams and neural device engineers were identified as:

- Demands on clinicians are substantial, including teaching, publishing, speaking, and participation in clinical research, alongside the translation of research to clinical application through the provision of design specifications for engineering projects;

- There may be economic, administrative, resource, and infrastructure issues that create impediments to collaboration in an interdisciplinary approach;
- Resistance to change within the clinical setting;
- Insufficient patient population for effective clinical research;
- Lack of optimal interdisciplinary clinical research collaborators and effective clinical research databases; and,
- The need for more "hybrid" professionals that combine approaches to the neurotechnology discipline such as clinician-scientists or clinician-engineers.

KEY FACTORS:

The Clinical Practice group examined key factors to determine how they should proceed to overcome obstacles to create a closer, more productive relationship between biomedical engineers and the clinical stakeholders practicing in the field.

Communication

There is a need to enhance communication between biomedical engineers and clinicians (especially clinical researchers). The communications should be bidirectional, meaning first, from the engineer to the clinician (for example, to help identify appropriate clinical research collaborators), and second from the clinician to the engineer to provide clinical input to assist in development of design specifications for neural engineering projects.

Best practices

The group identified the need to further best practices for successful clinical research in neurotechnology. How do we promote more clinical research, and how will we improve the quality of neural engineering clinical research that is being done? What is the formula for successful clinical research and how can we propagate that model?

- Most highly successful groups in both clinical care and neural engineering clinical research have exploited an ***interdisciplinary model with embedded engineers in clinical environments*** and embedded clinicians in engineering environments. There is a need to foster the development of interdisciplinary teams to eliminate silos between engineers and clinical researchers.
- In order to promote this model of a successful program, we need to model their methods and establish benchmarks.
- Most effective collaborations in this domain are with clinicians who are academicians with similar mandates to conduct impactful research that we have as engineers and have the need to be published.

- Best practices are needed to optimize the clinical care of patients with neural engineering devices in order to improve the outcomes of the clinical interventions.
- Once best practices for an interdisciplinary approach in the clinical care setting are established, these methods to improve the outcomes of neural engineering clinical interventions musts be promoted.
- The clinical team involved in the interdisciplinary approach encompass multiple disciplines - clinical team with a dedicated neurosurgeon, neurologist, neuropsychologist, psychiatrist, physical therapist, occupational therapist, communications and swallowing disorders specialist, social worker, and similar.

Future generations training

It was agreed that the greatest opportunity to create an interdisciplinary approach is to affect change in the current research education environment, that is, by creating a culture of collaboration in the next generation of neurotechnology professionals. Factors include:

- The need to improve training of the next generation of **biomedical engineers** to improve collaboration with clinicians. Incorporate mandatory clinical experience for biomedical engineering students.
- The need to improve training of the next generation of **clinical researchers** to improve collaboration with engineers/scientists.
- The desire to encourage engineering grads to become clinicians ("hybrid integrators")
- The need to incorporate collaboration with embedded engineers into the training of clinical trainees/fellows
- The drive to advocate for funding of interdisciplinary fellowship programs and post-doctoral engineering programs. Assert the value and advocate for research funding following this model.

VISION:

A “golden age” for neural engineering clinical research and consistently successful, life-changing neural engineering clinical interventions in 2030 by training **more and better interdisciplinary clinical and scientific researchers** through partnerships, emphasizing co-localization, enabling peer-to-peer and bidirectional communication, and market-responsive, higher standard of care treatment. We recognize the critical need for increased inclusion of clinicians in future NEW meetings.

2-5 YEAR GOALS:

Goal 1: Test the hypothesis that an interdisciplinary model for clinical research in neural engineering is more effective than traditional siloed engineering research.

Goal 2: Increase the footprint of engineers in the clinical world and clinicians in the engineering world through outreach. Merge these two segments into a single community by 2030.

Goal 3: Facilitate interdisciplinary training collaborations on every level, from predoctoral training to senior investigators/attending physicians

DELIVERABLES:

(2 Years)

Goal 1 Deliverables

- Conduct a study that evaluates the elements of successful clinical research in neural engineering;
- Develop metrics of success for clinical research
    - Number of publications
    - Quality of publications/impact
    - Grant funding
    - Patient-centric outcomes
    - Others to be defined
- Use these metrics to identify the most (and least) successful neural engineering clinical research programs;
- Compare the most and least successful programs to identify best practices;
- Identify commonalities among successful programs
    - How many investigators have interdisciplinary training backgrounds
    - Contrast to "controls" comparator programs of similar sized institutions
- Write a scientific paper that outlines the best practices for an interdisciplinary approach to clinical research. Assuming the paper concludes that the interdisciplinary approach is more favorable, show the results to key agencies, funders, etc. to gain support for what is needed to expand this approach .

Goal 2 Deliverables

- Increase the attendance of clinicians at NEW 2017 by to at least 20% of the attendees;
- Have research engineers run a session at a clinical conference;
- Include information about neural engineering technology in at least one clinical portal in order to increase visibility of neural engineering solutions to neurological conditions.

Goal 3 Deliverables

- Create a database (i.e. create collaboration.com) of physician scientists and translational engineers to establish potential collaborations;
- Advocate to increase funding for clinicians to participate in neural engineering research;
- Promote the incorporation of clinical training for neural engineers into NIH training grants.

MILESTONES:

Establish study group for scientific paper by end of 2015
Complete study in time to present results at NEW 2017.

THEME: TECHNOLOGICAL INNOVATION

CURRENT STATE:

Innovation is invention put to use. That's a deceivingly simple definition. It takes time, money and resources to move from a visionary idea to an implemented product or process. But innovation at all levels – from science to industry translation – is critical to advancing the neural engineering field.

Because innovation cuts across so many of the other themes discussed at Cleveland NEW, its related challenges are vast and diverse. They encompass core scientific ideas, such as gaining a better understanding of human physiology, to technological solutions, such as creating more effective means for interfacing with the nervous system.

Participants in the innovation session at the 2015 Cleveland NEW honed in on four primary challenges:

- Each human being is a dynamic system. Building a neural interface isn't as simple as creating a traditional gadget or tool. The critical factors of intended use and biology must always be considered.
- Our field struggles with resource issues. We need open access to resources to engage new participants and increase the impact of existing efforts.
- There is an inherent risk to innovation, but failure is not incentivized. Neural Engineering would benefit from a model where failure is accepted as a normal part of innovation and negative results are shared and published so others can learn from them.
- It is important to acknowledge the importance technological innovation and its distinction from the equally valuable role of more fundamental scientific innovation. An appreciation of these differences is necessary to address the challenges associated with secure funding for technological innovation.

KEY FACTORS:

Before determining key factors associated with innovation, participants in the 2015 ClevelandNEW session discussed central areas related to the theme. These include technical innovations, scientific innovations, translation of innovations, platforms for innovation and the culture of innovation. The group condensed its ideas to three key factors that, if addressed, would help further the neural engineering field:

1. Identify several grand challenges and their barriers.
2. Create common platforms that enable innovation. These platforms may be a device, collective knowledge, access to

patients and data, shared use of animal models, and other broadly applicable resources.

3. Create a culture of innovation that mitigates risk and allows us to learn from failures. That culture of innovation should extend to other themes, including industry, clinical, reimbursement, etc.

VISION:

In the next 20 years, chronic diseases and disabilities, including mental health diseases, neurodegenerative diseases, obesity, diabetes and heart disease, will become the leading causes of morbidity globally, as well as in the U.S.

We envision neural engineering playing a major role in alleviating and managing the leading causes of global morbidity.

Realization of this vision will require the development of easily used tools and devices that can safely, effectively, reliably and inexpensively stimulate and/or record from precisely identified neural systems. Stimulation systems must be programmable to meet the precision medicine needs of individual patients and must be adaptive to accommodate changing neurological states that develop over time and as a result of the treatment. To meet this requirement, we envision a small number of general platforms that clinicians and researchers can adapt to their specific needs.

2-5 YEAR GOALS:

Several things will be needed to realize this vision, including, but not limited to, an open source model for sharing resources and knowledge and enhanced communication from user to clinician to scientist. The following goals can help the neural engineering community achieve this vision:

- **Adopt open platform for experimentation** – Make available a suite of do-it-yourself neural engineering tools that lower the barrier for entry into this field, reduce replication of effort, and increase sharing of protocols and data. The tools and control processes should be sufficiently well defined that components can become interchangeable.

- **Create a global neural engineering forum** – The forum would connect neural engineering researchers and

clinicians and encourage sharing of data and best practices.

- **Produce a state-of-art industry overview** – This document would present the current state of science, clinical practice, and use of technology for addressing clinical issues in the realm of neural engineering.

- **Develop a standards group for the neural engineering community** – The group would facilitate the creation of generally accepted industry standards that provide a platform for excellence.

DELIVERABLES:

While there are many paths to achieve the four goals mentioned above, participants at the 2015 ClevelandNEW suggested a handful of deliverables that allow the neural engineering community to move toward those goals.

A solid first step in creating open source experimental tools that facilitate the sharing of protocols and data, and lower the barriers to entry in this field. Ideally, the system would be low-cost, and allow for neural stimulation and recording, as well as closed-loop operation. Two examples that may serve as models for development include the Open Ephys platform for electrophysiology, and the OpenOptogenetics Wiki.

The group suggested three potential components of a global neural engineering forum. The first was to develop a searchable laboratory website template that could be linked to a common interface for identifying experts in the domain of neural engineering and sharing best practices between them. A second was to create a forum for open lab meetings that facilitate communication between collaborators or other interested parties. Finally, the group envisioned community-generated documents for sharing knowledge that facilitates discovery and translation. One specific example was a library of FDA-approved materials suitable for implanted neuroprosthetic devices.

Creating a state-of-the-art overview document was inspired by Brain 2025, part of an NIH initiative aimed at unlocking the mysteries of the brain. The neural engineering equivalent would include grand challenges in clinical medicine, user surveys and

other metrics relevant to these challenges, current approaches and their limitations, and a map for how future advances may be applied.

Just as open platforms can facilitate discovery, standards can facilitate translation and deployment by liberating the developer from the multitude of design choices to be made and fostering compatibility between devices. Efforts towards this obejctive should begin by a discussion with standards groups, such as the IEEE, to establish a committee focused in the implanted device space, identify a site for the standard (such as Open Interconnect), and to begin development of the standard.

MILESTONES/PLAN:

This group's deliverables were acknowledged to be ambitious, but considered to be important. Rather than set milestones for a specific deliverable, the group proposed identifying leaders for each potential deliverable and providing them with the guidance and latitude necessary for development.

THEME: INDUSTRY TRANSLATION

CURRENT STATE:

Moving an innovative idea from research to clinical trials and ultimately to commercialization is a daunting task. During ClevelandNEW 2013, participants in the Industry Translation group identified several key barriers to translation. Many were related to the fact that many neural engineering technologies target injuries or diseases that affect small numbers of patients. Though the potential consumers may have severe disabilities that could benefit from neural technologies, the financial incentives may be too small for large-scale corporate investment. A related issue was understanding differing incentives for all possible stakeholders including companies, researchers, users, and payers. Those incentives may be at odds with one another. Finally, it can be challenging to understand which technologies are translatable.

Participants at ClevelandNEW 2015 acknowledged these barriers and expanded on potential solutions. They discussed the importance of continuing education for biomedical engineers so they better understand how commercialization works. The group considered the hand-off point in product development: When is an idea ready to move from researchers to companies? There's no simple answer, and both parties likely need to work together for some amount of time, emphasizing the importance of fluid and frequent communication between stakeholders. Another topic that generated lively discussion was the maturation cycle of technology: It's hard to know exactly when a process or product is ready to commercialize. When is an idea "good enough" for the first in-human system? Then, when does it make sense to replace first-generation devices with upgrades?

These big picture questions aren't easily answered – and most certainly don't have a "one-size-fits-all" solution. But they must be addressed for the neural engineering field to move forward and achieve the ultimate goal of improving the quality of life for end users.

KEY FACTORS:

Considering the challenges listed above, participants in the ClevelandNEW 2015 Industry Translation group agreed upon three key factors that, if addressed, could help facilitate commercialization:

1. Improve the efficiency of the translation process. The neural engineering community needs a mechanism for "early and often" feedback. The threshold to enter translation is the intent to study human subjects and it is market driven. To facilitate commercialization, it's imperative to have data on human studies available to researchers.
2. Improve the funding model throughout the translation process. This will help alleviate the business risk. In addition, funding

doesn't need to come from traditional sources: It's important to include alternative funding.

3. Create a method for educating both academia and industry that will lead to development of a common language and improved understanding of each segment's role in the neural engineering community. It's critical to understand the incentives of all parties. Plus, there needs to be pathways for translating technologies of varying complexities.

VISION:

Our vision is to foster an innovation ecosystem that catalyzes academic, industry and government collaboration to enable successful commercial translation of maturing scientific research and technology within the constraints of global regulatory standards and business metrics.

2-5 YEAR GOALS:

To begin moving toward an innovation ecosystem, participants in the ClevelandNEW 2015 Industry Innovation group set two primary goals:

1. **Grease the skids** – Help pave the way for commercialization by creating an open source quality system and inventory of current research tools that help the neural engineering community assess risks, safety, and design controls.

2. **Utilize translational coaching** – Our sector would benefit from a venue for vetting ideas. Translational coaching could take on many forms. One idea is to mimic the philosophy of the Walter H. Coulter Foundation, whose pioneering translational research programs use best practices of industry to accelerate academic innovations to market. Another component could be workshops and training sessions on topics related to commercialization and clinical trials.

DELIVERABLES:

The Industry Innovation group identified two to three deliverables for each of its aforementioned goals. To help “grease the skids,” the group suggests we identify and implement a template quality system. Ideally, the template will have gone through an FDA IDE process. This could drive uniform reviewing on the part of regulatory bodies. Next, the templates should be available via a website, and we should begin to promote the templates at various industry conferences.

While there are many steps to set up translational coaching, the group agreed the ideal way to start is by determining a key industry player to assemble a board. That person can lead creation of a group including industry representatives, end users, clinical implementers, foundation representatives and others. One of the first moves of the group will be to create a mission statement and explain what makes translational coaching different from business-based boot camps. Next, the group should establish a forum for submitting information (an application process) and reviewing written submissions. Those who submit ideas will be given initial and follow-up feedback, connected to funding and more.

MILESTONES / PLAN:

The Industry Translation group at the 2015 ClevelandNEW set milestones for its translational coaching goal. These were:

- Select someone to assemble the board (a goal champion) – End of 2015
- Establish a board, create a mission and distinguish translational coaching from business boot camps -- Within six months of selecting a goal champion
- Establish a forum for submitting ideas for review -- Within nine months of creating the board

In contrast, the group chose not to set milestones for the "grease the skids" goal, acknowledging that these would best done after identifying a champion for this deliverable.

THEME: FUNDING

CURRENT STATE:

Participants at the 2013ClevelandNEW cited the lack of clear pathways between applicants and government agencies (and other funders). They called for developing some type of matchmaking mechanism that could guide all stakeholders at various stages of the translational journey.

The ClevelandNEW 2015 Funding group revisited this issue. What would a funding roadmap look like? Who would it serve? How could it be most useful to the various stakeholders and *what* would it help sustain? These questions provided the basis for teasing out key factors that should be considered in going forth.

Throughout the workshop, discussions arose about *what* funding should sustain. Some participants advocate focusing on sustaining *scientific discovery,* while others set their sights on the pathway(s) from science to ultimate commercialization.

Reimbursement was another topic that occurred with some frequency. A number of discussions centered on considering the influence of insurance payers, such as Centers for Medicare (CMS) and private companies. Workshop participants voiced concerns about funding technologies today that ultimately could reach the market, but then face reimbursement barriers.

Discussions about public/private partnerships clarified the striking differences between entities serving the public interest versus serving investors. These differences impact funding seekers. Intertwined in these discussions was the issue of risk (safety vs. efficacy) and the way in which it underpins the types of research that get funded along with the numerous challenges it presents.

KEY FACTORS:

In light of such concerns and the natural fact that nothing happens without money, the 2015 workshop participants looked at components of a roadmap that can increase the number of successfully funded projects. Key factors and goals are described below.

Three key factors were listed as areas that must be strengthened in order for neurotechnology to forge ahead in a more organized fashion so that it makes a positive impact on the lives of patients, users, and consumers who can benefit:

1. Educational resources
2. Communication and coordination

3. Community with “one voice”

VISION:

In 10-20 years, a comprehensive funding landscape that sustains research along the continuum from initial discovery to consumer-focused translation through to sustainable commercial dissemination will exist.

2-5 YEAR GOALS:

Goal 1: Create Educational Resources

Creating educational resources was identified at the Cleveland NEW 2015 workshop as a way to provide a comprehensive roadmap for funding. The 'who, what, where and how' for all funding sources on the path - from basic science concept to pivotal trial and insurance reimbursement – need to be defined. All of those related stakeholders should provide input to develop these resources. Online international forums and digital newsletters were among the initial types of resources suggested by participants, but other forms (including those being developed by the FDA) would include computer-based training and print materials.

Goal 2: Establish Routine Meetings

Strengthening communication and coordination is crucial. Gaps between funding sources were identified as impediments to moving projects forward. These “black holes” in the funding landscape have been contributing to confusion, not to mention the loss of valuable work and ideas, career changes, and the discontinuity of technology transfer, translation and resulting advancement. The ultimate loser is the consumer when the system is broken.

Goal 3: Identify and Analyze Gaps in the Funding Landscape

This goal engenders advocacy for the community of individuals and institutions that work hard to make new biomedical solutions a reality, as much as it supports maximizing investment of funds. To correct the current “fits and starts” scenario that occurs with funding, communication and coordination between funding entities needs to be improved. Facilitating these two areas is crucial. Clearly defining data needed as output from each step on the translational path for funding from the next step appears to be a solution to minimizing the casualties and ensuring more successes.

The primary rationale behind this goal is developing “one voice / community advocacy” to promote inclusiveness and unity while at the same time, not impeding competition in any way.

The secondary rationale, the need for creating a feedback loop, helps to ensure understanding of new funding programs and the scientific review / management of those programs. A feedback loop can help reveal and close any gaps not currently addressed by existing programs.

DELIVERABLES:

The deliverables are to be completed by 2017. The first step is to immediately determine leadership and the committee personnel who will take up the tasks of accomplishing the three goals of creating educational resources, establishing routine meetings and forming an advocacy group.

Goal 1: Create Educational Resources:

The first order of business will be to perform a needs assessment and then define the appropriate forms and formats for the educational resources, as well as the metrics for evaluating and measuring the effectiveness of those resources.

An funding education committee should be established. It should be inclusive, representing those organizations and people who can provide a broad range of inputs and be capable of determining the audiences, venues and the technologies used to deliver training.

Goal 2: Establish Routine Meetings:

Between 2015 and 2017, set up a schedule of planning meetings. First priority will be to identify various funding entities and individuals to contact about serving on the funding panel for the NIC workshop. Based on the information that is captured at the meetings and any further analysis, a funding whitepaper will be commissioned.

Goal 3: Identify and Analyze Gaps in the Funding Landscape:

Form an advocacy group that acts to document and analyze knowledge gaps that exist in the funding landscape. Individuals who can bring the most value to the table will be identified and contacted.

One important role of the advocacy group will be to determine the mechanism for submitting advocacy requests. To evaluate the effectiveness of this measure, a test case has been suggested: the first official response to an NIH RFI.

MILESTONES:

Goal 1: Educational Resources

By end of 2015 the leadership and at least one committee will be formed. The needs assessment will be formulated and conducted within the first year. In two years, once the "who," “what, where and how” elements have been determined by the needs assessment, the education committee should be well on the way to developing at least one resource and putting into place a feedback loop.

Goal 2: Routine Meetings

By the end of 2015, a meeting committee will be formed. Within two months the committee will have in place a value proposition to submit to the funding agencies. By the end of Q1, 2016, the committee will have made selections for the funding panel at an neural engineering workshop.

Goal 3: Identify and Analyze Gaps in the Funding Landscape

Before the end of 2015, a committee to achieve this goal will be formed. By early 2016, potential advocates will be identified and contacted. The advocacy group, once formed, will determine the mechanism to submit advocacy requests. Between 2015-2017, the advocacy group will monitor a test case, the first official response to NIH RFI.

APPENDIX A – KEY TERMS & DEFINITIONS LISTING

- **Field/Sector**: Neural Engineering, as in the group, industry, academic disciplines involved in Neural Engineering Field.
- **Theme**: The primary areas involved in the field that have to work together for the field to succeed. 6 Themes arose from NEW 2013 (Innovation, Consumer, Funding, Commercialization, Clinical, Regulatory).
- **Key Factors**: The primary factors involved within each theme. The 2013 factors serve as an illustrative starting point.
- **Current State of Theme**: A brief summary descriptive overview of the current theme status: a synopsis with relevant factors.
- **Vision** (at the overall Field level): the Desired State for the overall field (what we intend to become or achieve) in the next 20 years. Encompasses the identified Visions of the individual themes and where they fit within the field during the next 10-20 years and/or how the overall Field is improved by the achievements within each Theme. This is not a wordsmithing exercise and an appropriate framing sentence for the Vision will be developed later.
- **Vision** (at the Theme level): Desired state of the specific Theme in 10 to 20 years time (within the context of the field) . This is not a wordsmithing exercise and an appropriate framing sentence for the Vision will be developed later.
- **Goals**: The goals are the next level down under Theme Vision and must be achievable within 2 to 5 years. A goal defines the direction and destination. Also they must directly support the theme vision. These goals should be necessary and assessable. The goals will serve as “progressive milestones” and be reviewed at NEW 2017 and 2019. Each Theme Group may commit to up to three Goals seen as necessary in order to achieve the Vision of the Theme.
- **Deliverables**: The Deliverables fall under theTheme Goals and are the action items that directly lead to each goal. Deliverables are the ways you will achieve each of your objectives; they are all about specific tactics, tasks and actions that must occur. A goal defines the direction and destination, and then the road to get there is accomplished by a series of deliverables. The deliverables should be consistent with what a small group of individuals can achieve in 12 to 18 months.
- **Strategic Direction for the field**: harnesses Strategic Thinking (as defined in the Vision) with Strategic Actions (as identified in the Goals and the Deliverables). Includes the set of Themes (and associated V G D) identified to impact the Field and also forms the road map for the field. This will be used for stakeholders to self-identify and also to recruit expertise and resources to each theme, including funding agencies.

REVISION HISTORY

Rev	Description/Comments	Author(s)	Date
1.0	First Release of the output from the 2015 ClevelandNEW meeting.	NEWExecCom, Susan Flynn, Patricia Alyward, Sandra Woodthrope	10/15
2.0	Updated Executive summary, footers, and appendices list.	Dustin Tyler	6/15