

# Making the Six Million Dollar Man:

## The Federal Government's Role in the Commercialization of Neural Prostheses

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## **About the Author**

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## **About Washington Internships for Students of Engineering (WISE)**

The WISE annually chooses 14-16 engineering students to participate in a ten-week public policy internship program in Washington, DC. Students must be either rising seniors or recent graduates. Interns are expected to learn about the development of public policy and the engineer's role in influencing technology decisions. Through attending meetings with representatives from different organizations and agencies, students are to complete a research report and presentation on their specific technology policy topic. For further information, please refer to <http://www.wise-intern.org>.

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## **Introduction: What is Neural Prosthesis?**

More than 30 years ago, the National Institutes of Health (NIH) started its Neural Prosthesis Program to focus on creating regenerative technologies for disabled people. Whether researchers at the time could predict or not, the technology has since made astounding progress, leading to many new discoveries about the plasticity of the brain and even the development of several devices. Yet, one thing that researchers did not fully anticipate was the difficulty in commercializing these products. Aimed towards the severely disabled, neural prostheses serve a very small segment of society, making the technology less economically attractive to corporations.

Neural prosthetics fall under a newly coined area of research called neuroengineering. Broadly defined, a neural prosthesis is any type of mechanical or electrical device that can stimulate or replace nerve functions. The premise behind this concept is that scientists will be able to use microchips and electrodes to repair damaged neural areas in the human body. Today's research is mostly in the basic or pre-clinical stages, with a wide variety of applications being investigated. At present, these devices are intended to assist and improve the quality of life for people with severe to moderate disabilities. In addition, there are several efforts to broaden the technology beyond helping the disabled and into the realm of creating human mechanical enhancements.

Despite wide research interest in this subject matter, neural prostheses have had relatively little success in the commercial arena. The lack of incentives for high-risk technology transfer have impeded development past the prototyping stage. Also, the limited size of the market segment has made companies hesitant to invest in providing social goods with low profit margins. With most of the innovation being created at small, entrepreneurial businesses, the Food and Drug Administration (FDA) approval charges can be a significant burden, while waiting for adequate Medicare reimbursement reduces the opportunity to invest in further research and development.

In order to understand the present situation, this paper will attempt to create an overview of the impacts of neural prostheses, and analyze existing mechanisms for technology transfer and difficulties with the FDA approval and Medicare reimbursement processes. From this analysis, the following course of action is recommended to facilitate the commercialization of neural prostheses:

1. Provide incentives for companies to adopt high-risk technologies through mechanisms such as: development subsidies, tax breaks and exclusive licensing agreements.
2. Federally support clinical trials of neural prosthetics for FDA approval.
3. Shorten the length of time required to gain adequate Medicare reimbursement rates.

## **The Scope of the Technology**

Research efforts in neural prosthesis are being spearheaded by two government organizations, the National Institutes of Health (NIH) and the Defense Advanced Research Projects Agency (DARPA). NIH is currently sponsoring an extramural

program called the Neural Prostheses Program (NPP), while DARPA is maintaining a series of research endeavors that fall under their Brain Machine Interface (BMI) program. Both these groups provide funding and support for university research and publication. NPP is focusing on regenerative devices to aid the severe to moderately handicapped population. DARPA's initiative is similarly focused in the short term, but the program hopes to extend into military enhancement in the far future. Other organizations, such as the Veterans Administration and the National Science Foundation (NSF), have also taken an interest in this field, providing their own funding for various related research.

In present research and development, neural prosthesis is focused primarily on the deaf, paralyzed and blind communities (see Figure 1). The number of potential beneficiaries is quite significant, including not only the handicapped and their families, but also other third parties. According to the Johns Hopkins School of Medicine, approximately 28 million<sup>1</sup> people in the United States are identified as "hard of hearing" and 30-35% of people aged 65-75 suffer from age-related hearing loss. In 1994, 900,000 of the 28

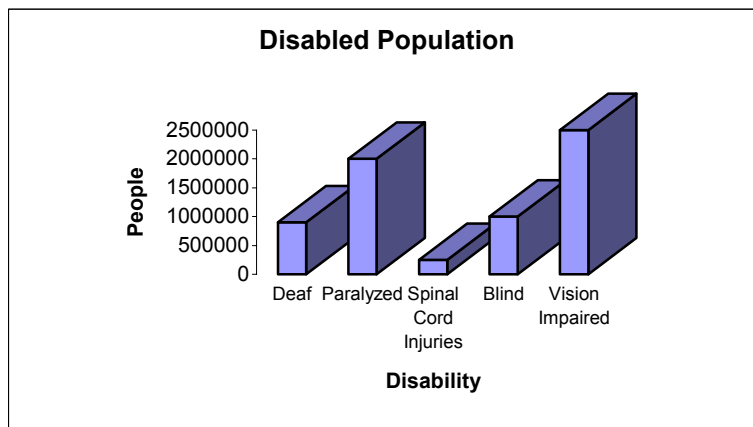


Figure 1: Disabled Population by Type of Disability

million were "completely unable to hear what was said in normal conversation<sup>2</sup>." In addition, based on statistical data from the Christopher Reeves Foundation, 2 million<sup>3</sup> people are paralyzed in the extremities and 250,000 people have sustained spinal cord injuries. The Department of Veterans Affairs has also identified

40,000<sup>4</sup> former service men who fall under this category. Furthermore, over one million people over the age of 40 are completely blind<sup>5</sup> and an additional 2.5 million<sup>6</sup> have severe vision impairments. In total, there are approximately 4 million<sup>7</sup> Americans who could potentially benefit from neural prosthesis at the early stages of its technical development and another 30 million once the technology has been refined. Worldwide statistics for these disabilities are significantly larger, ranging in the hundreds of millions. The numbers of people who may profit from the technology could also continue to grow as the expertise and knowledge in this area matures.

<sup>1</sup> <http://www.hopkinsmedicine.org/hearing.html>, accessed June 2003

<sup>2</sup> Bureau of the Census, *Statistical Brief: Americans with Disabilities*, [http://www.census.gov/aprd/www/statbrief/sb94\\_1.pdf](http://www.census.gov/aprd/www/statbrief/sb94_1.pdf), accessed July 2003

<sup>3</sup> <http://www.christopherreeve.org/hopenetwork/hopenetwork.cfm?ID=527&c=68>, accessed August 2003

<sup>4</sup> Department of Veterans Affairs, *Factsheet: VA and Spinal Cord Injury*, <http://www.va.gov/pressrel/spinalcfs.htm>, accessed July 2003

<sup>5</sup> <http://www.nei.nih.gov/eyedata/tables/BLINDFinal.xls>, accessed August 2003

<sup>6</sup> <http://www.nei.nih.gov/eyedata/tables/ALLVisionImpairedFinal.xls>, accessed August 2003

<sup>7</sup> Approximately 1 million blind, 2 million paralyzed and 1 million deaf as stated previously.

In aggregate, the cost of disability in the United States is over \$300 billion<sup>8</sup> annually, which includes funding for programs that provide health insurance, disabilities benefits, compensation payments, etc. The expected lifetime costs associated with a person with quadriplegia alone is \$1.5 million<sup>9</sup>, amounting to a possible \$188 billion<sup>10</sup> over the course of several decades. In 2002, the federal government paid over \$65 billion<sup>11</sup> in disability insurance benefits. Less than half of people with severe disabilities have private insurance, with 36% relying upon government insurance<sup>12</sup>. Total, there are over 7 million<sup>13</sup> disabled workers and dependents in the U.S. and over 2 million<sup>14</sup> disabled veterans who qualify for payments. In fact, the Veterans Administrations pays \$2,163 per month, or approximately \$26,000 annually, in spinal cord injury compensation to veterans with 100% disability<sup>15</sup>. In addition to healthcare and compensation costs, disabled people represent an opportunity cost in the American workforce. Only 26% of people with severe disabilities were employed in the age range of 21-64 years old<sup>16</sup>.

Given these statistics, the use of neural prostheses could become a huge potential benefit, both socially and economically. The technology could substantially improve the quality of life for handicapped people, allowing them the ability to perform day-to-day activities with little to no assistance. It could even provide enough support to enter the workforce. Additionally, these devices could present a long-term savings in the cost of healthcare and other benefits.

## The Emerging Technologies

Currently, there are three major areas of interest being pursued: cochlear implants for the deaf and hard of hearing, sensorimotor control for the paralyzed and retinal implants for the blind.

### Cochlear Implants

The first, and most successful, has been in the field of hearing loss and deafness. These studies have led to the manufacture and marketing of a device called the cochlear implant (see Figure 2). It was approved by the FDA in the late 1980's to provide some degree of hearing to the completely deaf and has, more recently, been approved to help the "hard of hearing"<sup>17</sup>.

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<sup>8</sup> <http://www.frrs.org/other/ADASPTXT.htm>, accessed August 2003

<sup>9</sup> <http://www.cwru.edu/menu/research/prosthesis.htm>, accessed July 2003

<sup>10</sup> \$1.5 million x y people = \$188 billion

<sup>11</sup> Social Security Administration, Disability Insurance Benefits Payments, <http://www.ssa.gov/OACT/STATS/table4a6.html>, accessed August 2003

<sup>12</sup> Bureau of the Census, *Statistical Brief: Americans with Disabilities*, [http://www.census.gov/apsd/www/statbrief/sb94\\_1.pdf](http://www.census.gov/apsd/www/statbrief/sb94_1.pdf), accessed July 2003

<sup>13</sup> <http://www.ssa.gov/OACT/STATS/DIbenies.html>, accessed August 2003

<sup>14</sup> [http://www.va.gov/vetdata/ProgramStatics/stat\\_app99/table\\_13.xls](http://www.va.gov/vetdata/ProgramStatics/stat_app99/table_13.xls), accessed August 2003

<sup>15</sup> Department of Veterans Affairs, *Factsheet: VA and Spinal Cord Injury*, <http://www.va.gov/pressrel/spinalcfs.htm>, accessed July 2003

<sup>16</sup> Census Brief, <http://www.census.gov/prod/3/97pubs/cenbr975.pdf>, accessed July 2003

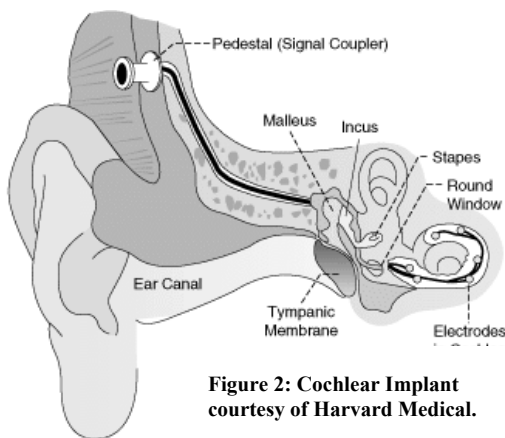
<sup>17</sup> [http://www.med.harvard.edu/publications/On\\_The\\_Brain/Volume3/Number4/Cochlear.html](http://www.med.harvard.edu/publications/On_The_Brain/Volume3/Number4/Cochlear.html), accessed July 2003

Deafness usually occurs when the cells in the inner ear, or cochlea, cease to vibrate. The nerves in the area require signals from the vibrating cells in order to transmit electrical impulses to the brain, which are then recognized as sound. Cochlear implants bypass the damaged cells and directly stimulate the nerves to send impulses.

The implants have three components: the headpiece, receiver and speech processor<sup>18</sup>. The receiver is a small array of electrodes and microcircuits that is implanted in the area behind the ear. A headpiece with a microphone and transmitter is also worn behind the ear to pick up sounds. The sounds are then transmitted to the speech processor, which converts the noise into signals to be sent to the receiver. From there, the receiver stimulates the nerve area, initializing electrical signals in the brain.

The surgical process requires approximately 2 hours<sup>19</sup>, after which implantees are taught how to use the device. Moderate to substantial rehabilitation is often required, involving working with an audiologist or speech pathologist.

According to the NIDCD<sup>20</sup>, currently, an approximate 13,000 adults have received this device, as well as almost 10,000 children<sup>21</sup>. However, the Centers for Medicare and Medicaid Services report that only 16% of the eligible beneficiaries under Medicare coverage have undertaken the implantation<sup>22</sup>.



The average cost of the procedure ranges from \$30,000-\$50,000<sup>23</sup>, which includes the costs of surgery, testing and limited rehabilitation services. Three companies are currently manufacturing and marketing cochlear implants: Advanced Bionics, headquartered in California; Cochlear Corporation, based in Australia; and Med-El, located in Austria<sup>24</sup>.

The benefits gained from a cochlear implant vary from person to person. Most people regain the ability to distinguish speech, even to the point of being able to have a conversation over the phone<sup>25</sup>. This promises great improvements in the quality of life among those individuals who may now be able to communicate more effectively. It is hoped that with further development of this product, it will be able to restore degrees of hearing to those with only partial hearing loss.

<sup>18</sup> <http://www.cici.org/whatis.html>, accessed June 2003

<sup>19</sup> <http://www.listen-up.org/ci/implant3.htm>, accessed July 2003

<sup>20</sup> National Institute on Deafness and other Communication Disorders

<sup>21</sup> <http://www.nidcd.nih.gov/health/hearing/coch.asp>, accessed July 2003

<sup>22</sup> Centers for Medicare and Medicaid Services, *Healthcare Industry Market Update*, [http://www.cms.hhs.gov/reports/hcimu/hcimu\\_10102002.pdf](http://www.cms.hhs.gov/reports/hcimu/hcimu_10102002.pdf), accessed July 2003

<sup>23</sup> <http://www.nidcd.nih.gov/health/hearing/coch.asp>, accessed June 2003

<sup>24</sup> <http://www.listen-up.org/ci/implant3.htm>, accessed July 2003

<sup>25</sup> Personal interview with Arlene Romoff.

## Sensorimotor Control

The second most prominent area of interest is in sensorimotor control for the paralyzed. These studies are mostly in the pre-clinical phases of research, with the exception of a preliminary device named the Freehand System.

The Freehand System, a “hand-grasp neuroprosthesis,” was pioneered by Dr. Hunter Peckham at Case Western University<sup>26</sup>. The device utilizes a technology called functional electrical stimulation (FES) to control upper and lower arm movement (see Figure 3). Electrodes are attached to the arms and hands, while a stimulator is implanted in the chest area. Small movements of the shoulder are monitored by external sensors which then transmit electrical signals to the arm, causing the muscles to contract. Implantees are able to cup their hands, a grasp called palmar prehension, in order to hold a cup, or pinch the fingers, known as lateral prehension, to hold pens or utensils<sup>27</sup>.

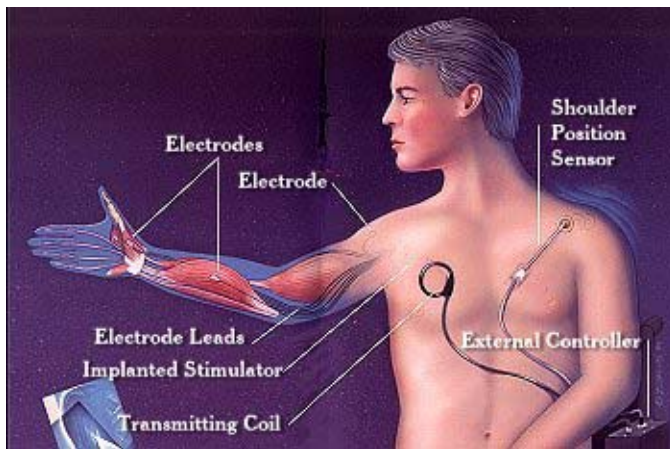


Figure 3: Freehand System courtesy of NeuroControl Corp.

In 1997, the FDA approved the use of the Freehand System for quadriplegics. The surgery is estimated to take 5-7 hours and rehabilitation can last up to 12 weeks. The Freehand System is estimated to cost around \$50,000<sup>28</sup>. The device was initially manufactured and distributed by NeuroControl Corporation, based in Cleveland, Ohio, and the surgery was performed at such hospitals as the Mount Sinai Medical Center in New York City and the James A.

Haley Veterans' Hospital in Tampa<sup>29</sup>. However, in 2001, NeuroControl decided to discontinue its production due to low sales and the high cost of rehabilitation. At present, no other company has made any plans to continue developing and producing the Freehand System<sup>30</sup>.

Other research has continued focusing on the feasibility of enhanced motor control. The two most notable researchers in this area are Miguel Nicolelis at Duke University and John Donoghue at Brown University. Both researchers are concentrating on mechanisms to directly use electrical impulses in the motor cortex of the brain to control robots. In 2002, Nicolelis published an article in *Scientific American* describing the

<sup>26</sup> <http://www.cwru.edu/pubs/cwrumag/fall1998/features/anniversary/sections/e/index.shtml>, accessed July 2003

<sup>27</sup> <http://remote-ability.com/unique/freehand.htm>, accessed July 2003

<sup>28</sup> <http://www.cwru.edu/menu/research/prosthesis.htm>, accessed July 2003

<sup>29</sup> <http://www.clarkmemorial.org/neurocontrol.asp>, accessed July 2003

<sup>30</sup> Based on personal interview with NeuroControl Corp. representative.

procedure<sup>31</sup>. An array of microwires was implanted in the cortex of an owl monkey named Belle at the Duke University labs (see Figure 4). The monkey was trained to use a joystick to follow a series of lights displayed on a computer monitor. From monitoring the impulses in Belle's brain, researchers were able to construct a mathematical model for



Figure 4: Experiment courtesy of Scientific American.

movement using a limited number of neurons. They then temporarily paralyzed Belle's physical arm and wired a robotic arm to the electrodes in her brain. As the monkey learned to think through movements, the robot mimicked her thoughts and was able to control the joystick. Further tests include implanting a similar array in a macaque monkey, which has a more complex brain, and implanting a wireless microchip. Such investigations have proven the success of these techniques; however, a large amount of research and

development is needed before human trials may be approved.

### Visual Prosthesis

The final significant area of study is visual prosthesis. Blindness or visual impairment typically occurs when the rods and cones in the eye stop functioning. Rods and cones are the photoreceptors in the retina of the eye, which translate the light received into electrical impulses. Impulses are sent through ganglion cells to the optic nerve at the back of the eye, connecting to the cortex of the brain<sup>32</sup>. Visual prostheses address two types of vision loss: macular degeneration and retinitis pigmentosa. Macular degeneration is an age-related condition which causes the degradation of photoreceptors in the eyes, while retinitis pigmentosa is a genetic disease that causes the same effect<sup>33</sup>.

There are two main schools of thought on design and implementation for visual

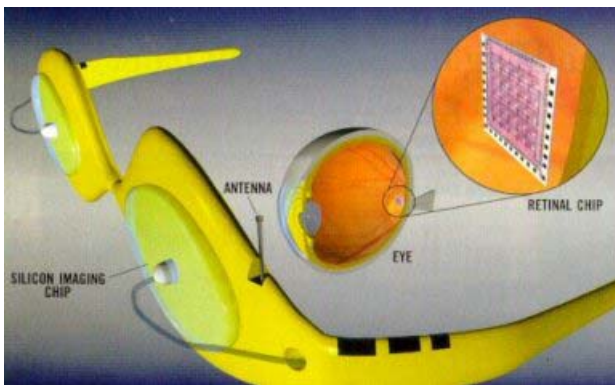


Figure 5: Artist's concept courtesy of University of Southern California, USC News.

prostheses. The first is the use of the subretinal implants, a technology pioneered by Drs. Alan and Vincent Chow, cofounders of OptoBionics. Optobionics' leading product, the Artificial Silicon Retina, is a microchip composed of small electrodes powered by 3500 solar cells and is implanted in the back of the eye. Light entering the eye hits the solar cells, powering the chips, which process the light into electrical signals. The electrical signals are then fed through the electrodes to stimulate the ganglion cells at the back

<sup>31</sup> [Scientific American, Controlling Robots with the Mind: Belle's 600-Mile Reach](http://www.sciam.com/article.cfm?articleID=0008F8E1-DEAB-1D80-90FB809EC5880000) by Miguel Nicolelis <http://www.sciam.com/article.cfm?articleID=0008F8E1-DEAB-1D80-90FB809EC5880000>, accessed July 2003

<sup>32</sup> <http://www.uweb.ucsb.edu/~mdaines/Introduction.htm>, accessed July 2003

<sup>33</sup> <http://www.optobionics.com/retinaldisease.htm>, accessed July 2003

of the eye, transmitting the signals to the optic nerve and eventually to the cortex of the brain. The device is designed to mimic the function of the rod and cone photoreceptors. In January of 2000, the FDA approved the Optobionics device for a two-year clinical study on safety and feasibility. Results from the study are currently unavailable to the public, but the company has released information stating that the device did not cause any infection or damage to the eye<sup>34</sup>.

The second major design approach is the epiretinal prosthesis (see Figure 5), which lies near the optic nerve and the ganglion cells. This design is currently under study by researchers at both the Johns Hopkins University and at the Massachusetts Institute of Technology (MIT). Epiretinal prostheses communicate directly with the cells and nerves at the back of the eye, bypassing the photoreceptors. The device has several components, including a camera, a transmitter, microchips and electrodes. The small eyeglass mounted camera is used for image acquisition. These images are then processed through a transmitter and are sent via laser rays to implantable chips at the back of the eye. The chip receives the coded information and translates it to series of electrical impulses, which are fed directly to the ganglion cells<sup>35</sup>.

Very little clinical data is available for either device and further development processes are being pursued to create viable chips for clinical testing. It is expected that as the technology matures, visual prosthetics will be available for those with minor visual impairments, as well as those with complete blindness.

### Future Applications

While DARPA has been funding research on neural interfaces which may have significant humanitarian applications, the agency's main focus has been to initiate work in areas of defense. While most research is still at the basic stages, DARPA has envisioned an entirely new role for technology and the soldier.

Using Nicolelis and Donoghue's work as reference, DARPA is exploring the idea that technology could allow soldiers to control weapons systems by thought alone. By monitoring and transmitting the electrical impulses in the brain, neural prostheses may be able to control small components, such as a joystick, to large systems, such as an unmanned vehicle. Through this type of technology, the military may be able to create a network of armed and unarmed systems on the battlefield, which can be remotely controlled<sup>36</sup>.

Not only could thoughts control robots, but the workings of the mind may be improved as well. Theodore Berger at the University of Southern California is leading a team investigating the formation of short-term memory. The hippocampus is the region of the brain responsible for learning and creating memories. Using information from implanted electrodes, Berger has created mathematical models of the signal processing occurring in the hippocampus. His group then programmed this information onto a microchip. The

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<sup>34</sup> <http://www.optobionics.com/index.htm>, accessed July 2003

<sup>35</sup> <http://www.rle.mit.edu/retinaweb/>, accessed July 2003

<sup>36</sup> Based on personal interview with Dr. Eric Eisenstadt, DARPA.

idea is that the chip will be able to mimic the processing done by the brain, replacing or even augmenting memory. However, it has yet to be tested and there are still many challenges in understanding how the brain works<sup>37</sup>.

To help unravel the inner workings of the brain, researchers are also looking into non-invasive ways to read signals from the brain. With this type of understanding, scientists hope to be able to augment the way information is transmitted and interpreted by the brain through the use of computers. Such work could enhance awareness and even lead to wireless communication between people<sup>38</sup>.

Much of this research is still in the early stages and most of the applications are purely speculative at this point.

### **What is the Federal Government's Role in Commercialization?**

The subject of neural prosthesis has been one of great interest to research and university groups, however it has been slow to enter the commercial market or to garner significant industry attention. For the most part, any attempts to develop this technology for the private sector have been done by small, entrepreneurial start-ups, especially those created or solicited by the researchers themselves. There are three main limitations in the commercialization of neural prostheses: the inefficiency in technology transfer of federally funded research, the cost of FDA approval to small companies, and the length of time before adequate Medicare reimbursement rates are reached.

#### **Facilitating Technology Transfer**

Currently, technology transfer happens in a limited variety of ways. One method that NIH employs is displaying the feasibility of the technology. Typically, intramural projects are highlighted in a workshop as a proof-of-principle. Various manufacturers and vendors are invited to attend these workshops to learn about new discoveries or technologies. It is, then, up to the discretion of the companies to decide whether they want to develop the product further and market it<sup>39</sup>.

Extramural projects through the NIH are primarily university funded. Thus, in accordance with the Bayh-Dole Act, the universities retain the patents and the rights to licenses. It was through this mechanism that Dr. Hunter Peckham solicited NeuroControl Corporation to manufacture and distribute the Freehand System. Dr. Peckham estimated the cost of the basic research and product development to be around \$60 million<sup>40</sup>. Unfortunately, despite his efforts, the technology did not earn a large enough profit margin to warrant continued production, leading NeuroControl to discontinue the product line in 2001. Since then, no other company has expressed interest in continuing the development of the system<sup>41</sup>.

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<sup>37</sup> *Technology Review, Mind-Machine Merger* by Gregory T. Huang, <http://www.technologyreview.com/articles/huang0503.asp>, accessed June 2003

<sup>38</sup> Based on personal interview with Dr. Eric Eisenstadt, DARPA.

<sup>39</sup> Based on personal interview with Drs. William Heetderks and Daofen Chen, NIH.

<sup>40</sup> [http://feswww.fes.cwru.edu/news/mar\\_00.php](http://feswww.fes.cwru.edu/news/mar_00.php), accessed July 2003

<sup>41</sup> Based on personal interview with NeuroControl Corp. representative.

DARPA's method of technology transfer is slightly different from either the NIH or university model. In a manner similar to NIH, DARPA funds research at both their federal labs and at university labs. However, since most of their basic research goes into laying the groundwork for future defense applications, their targeted audience is various sectors of the DOD and the armed forces, rather than the private sector<sup>42</sup>. Domestic technology transfer occurs primarily through encouraging one or more branches of the armed forces to pursue further development into a research area. Licenses are credited to the program manager who initiated the project at DARPA. Unfortunately, program managers only have a tenure of four years at the agency, making it difficult for them to establish continuity with a specific project once it leaves the agency. Most civilian applications are left to the researchers themselves, creating further difficulties in transitioning to the private sector<sup>43</sup>.

Both organizations have Small Business Innovation Research (SBIR) departments. Approximately 2-5% of the annual budget of each agencies is allocated to the small business areas. These groups facilitate and coordinate the technology transfer process described above<sup>44</sup>.

The difficulty with these proscribed methods of technology transfer lies in the lack of incentives for the private sector to take on high-risk, low profit projects. The basic research and proof-of-principle is essentially handed to the private market, yet they are reluctant to invest in developing products with questionable yield given the present state of the economy. Most of this type of development could require several years of heavy investment before any prototype would be ready to send into the market. Furthermore, with such large R&D efforts, it will require several additional years before a reasonable rate of return will be achieved. Knowing that such endeavors would require upwards of 10 years to become profitable, investors and venture capitalists are extremely hesitant to enter this field of research<sup>45</sup>.

Furthermore, the small size of the market segment for current neural prostheses creates an even greater barrier for technology transfer. The number of people who qualify for neural prosthetics at its current stage in development number approximately four million, which represents only 1.4% of the U.S. population<sup>46</sup>. Most medical device manufacturers anticipate an 18% rate of return on investment<sup>47</sup>. However, the low sales volume and high costs associated with this technology make it difficult for companies to turn the expected profit margin. In addition, corporations, such as Advanced Bionics, are

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<sup>42</sup> Based on personal interview with Dr. Eric Eisenstadt, DARPA.

<sup>43</sup> Based on personal interview with Connie Jacobs, DARPA SBIR.

<sup>44</sup> Based on personal interview with Dr. Eric Eisenstadt, DARPA.

<sup>45</sup> Based on personal interview with Blair Childs, Advamed.

<sup>46</sup> Calculations based on population statistics from: <http://www.census.gov/main/www/popclock.html>, accessed July 2003

<sup>47</sup> Centers for Medicare and Medicaid Services, *Healthcare Industry Market Update*, [http://www.cms.hhs.gov/reports/hcimu/hcimu\\_10102002.pdf](http://www.cms.hhs.gov/reports/hcimu/hcimu_10102002.pdf), accessed July 2003

continually reinvesting a large portion of their revenues into further R&D efforts in order to improve their products for a wider audience<sup>48</sup>.

In the past, the federal government has provided some incentives for this type of work. However, the magnitude of the legislation has not been enough to drive cutting edge medical devices. For example, the Orphan Drug Act<sup>49</sup> was passed by Congress in 1983 and signed into effect by President Reagan. The Act recognizes the limitations in development of drugs for rare diseases and tries to provide enticements for pharmaceutical companies to research treatment alternatives. Rare diseases are classified as those which affect “less than 200,000 persons in the United States or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug<sup>50</sup>.” The provisions of the act grant a seven-year exclusive license to manufacture a developed drug, as well as tax breaks and subsidies to defray the cost of clinical trials<sup>51</sup>. As of 1992, 469 drugs<sup>52</sup> had received the orphan designation and there are over 200 products in the market to date<sup>53</sup>. Although the act does mention the need to invest in orphan medical devices, the terminology is vague and only mandates that the Secretary of Health and Human Services conduct a study on what may be needed in the future<sup>54</sup>.

Currently, the Office of Orphan Product Development (OOPD) within the FDA sponsors a grant program for clinical development. The annual budget of the department is 12 million dollars and it typically funds projects up to three years at a cost of \$100,000-\$200,000 each per year<sup>55</sup>. However, of the 29 OOPD funded projects that received market approval, only three were devices. Of those three, one was an enhancement of the cochlear implant made by Cochlear Corp. and the other was a version of the Freehand System made by Dr. Peckham at Case Western University<sup>56</sup>. In comparison to the amount of funding priority that drugs receive, medical devices clearly fall far behind.

In order to rectify this situation, the category of Humanitarian Use Devices (HUD) was created as part of the Safe Medical Devices Act of 1990<sup>57</sup>. A device can be designated as a HUD if it benefits patients who have a disease or condition that affects fewer than 4,000 people in the United States. Under HUD, a company can file a Humanitarian Device Exemption (HDE) application to the FDA, which allows it to bypass the effectiveness requirement of a typical Pre-Market Approval (PMA) application. It also exempts companies from having to provide valid clinical data, although they must prove

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<sup>48</sup> Based on personal interview with Advanced Bionics representative.

<sup>49</sup> Public Law Number 97-414, 96 Stat. 2049

<sup>50</sup> Section 526 (360bb)

<sup>51</sup> Refer to text of Orphan Drug Act for further details: <http://www.fda.gov/orphan/oda.htm>

<sup>52</sup> <http://thomas.loc.gov/cgi-bin/query/C?r102.:/temp/~r10275j4dS>

<sup>53</sup> <http://www.fda.gov/orphan/>, accessed July 2003

<sup>54</sup> See text of Act for further details: <http://www.fda.gov/orphan/oda.htm>

<sup>55</sup> <http://www.fda.gov/orphan/grants/faq.htm>, accessed July 2003

<sup>56</sup> <http://www.fda.gov/orphan/grants/magrants.htm>, accessed July 2003

<sup>57</sup> Public Law 101-629

that a reliable, alternative device is not already available in the market<sup>58</sup>. So far, there have been 30 different medical devices that have been approved under the HDE, none of which include any type of neural prosthesis<sup>59</sup>.

Although both the Orphan Drug Act and the Safe Medical Devices Act attempt to provide provisions for market development, their scope is too small to create a definite, positive impact on those people with paralysis and profound deafness or blindness. In fact, the Orphan Drug Act does not even provide specific incentives for the clinical and market development of medical devices. All three of these disabled populations number over the cap specified in HUD. Although HUD has made several beneficial devices possible, the population condition of the Act is still too small to make a significant difference in the healthcare arena. This creates a gap in which people with uncommon, though not extremely rare, conditions are being underserved by the government. Yet, their numbers are not significant enough to draw sufficient market attention or development through pure private sector mechanisms.

The solution is that the federal government should provide the same incentives for “orphan” medical devices as it did for orphan drugs. Congress passed the Orphan Drug Act because it recognized a need to provide remedies for people with rare conditions and that without the aid of the federal government, such remedies would never be made possible. It states, “there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and it is in the public interest to provide such changes and incentives for the development of orphan drugs<sup>60</sup>.” This same reasoning can be applied to medical devices, such as neural prostheses. The cost of development for neural prostheses is large and the resulting profits are low in comparison, sometimes resulting in a financial loss. The expectation that such prosthetics may not be developed without federal assistance is made evident by the failure of the Freehand System to remain in the market. Yet, the benefit garnered by these technologies is substantial, both socially and in a broader economic sense. As such, there is a strong public interest in supporting the development of these devices.

Thus, the federal government should adopt a piece of legislation similar to the Orphan Drug Act, which would specifically provide the same added benefits and incentives to the medical devices industry to promote the use of neural prostheses. With subsidies, tax breaks and exclusive licensing agreements, manufacturers will be able to achieve appropriate rates of return. They can, then, funnel revenues back into the R&D process, refining the technology to incorporate applications for a wider public market.

### Lowering the Cost of FDA Approval

The second barrier to entry is the cost of the FDA approval process. The FDA has three different classes for types of devices that undergo the approval process. Class I devices are those with relatively low health risk, such as bandages. Through the FDA

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<sup>58</sup> <http://www.fda.gov/cdrh/ode/hdeinfo.html>, accessed July 2003

<sup>59</sup> <http://www.fda.gov/cdrh/ode/hdeinfo.html#2>, accessed July 2003

<sup>60</sup> <http://www.fda.gov/orphan/oda.htm>, accessed July 2003

Modernization Act<sup>61</sup>, these types of devices no longer have to go through the lengthy pre-market approval applications. Class II devices are those with medium risk and need to meet specific performance criteria before approval is granted. Class III devices are those with the potential for high health risks to patients and must meet rigorous design controls. Neural prostheses fall under the Class III designation of devices. FDA Pre-Market Approval (PMA) is required if any incremental changes are made to any medical device, as well as for entirely new devices. Through the PMA, new devices must demonstrate a substantial improvement in life through their use or have the ability to sustain life. They must also “establish substantial equivalence” with respect to safety and efficacy as existing treatments do. Details of the manufacturing process, design, pre-clinical and clinical trials are carefully scrutinized<sup>62</sup>.

Both pre-clinical and clinical trials are paid for at the expense of the company requesting approval, regardless of size or effect. Before clinical trials on a new device can begin, the company must also file an Investigational Device Exemption (IDE). This application focuses on the safety of the tests and has a 30-day turnaround period<sup>63</sup>. There are two types of classifications for the IDE: A or B. Devices designated as A are new to the market while B devices feature incremental improvements. Medicare subsidies are available for B applications, but not for A<sup>64</sup>. If the FDA fails to respond within 30 days, the company is free to begin the testing.

From the time a PMA is filed, the FDA has 180 days to act upon the application. During this time, they can request further information if they find “major deficiencies” in the data. This request effectively resets the deadline to 180 days from when appeal was made.

Companies must also generate annual reports on the progress of the device and any innovations and changes that have occurred. Any adverse affects from the device must be reported to the FDA within 10 days of discovery. Any incremental changes to the device must also be approved through a supplemental PMA, which has a six-month timeline associated with it. These changes include different manufacturing processes and any alterations in design. For relatively minor modifications, a company can request a real time review, which will be completed in a span of 5 days. An example of such a change would be a difference in labeling<sup>65</sup>.

In order to expedite the data review for the approval process, the Medical Device User Fee and Modernization Act (MDUFMA)<sup>66</sup> was passed in 2002. This piece of legislation allows the FDA to charge incremental fees to companies. The fees pay for the hire of new staff to handle the additional workload, creating a quicker turnaround period<sup>67</sup>. Fees

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<sup>61</sup> Public Law 105-115

<sup>62</sup> Based on personal interview with Eric Mann, FDA.

<sup>63</sup> Based on personal interview with Eric Mann, FDA.

<sup>64</sup> Centers for Medicare and Medicaid Services, *Healthcare Industry Market Update*, [http://www.cms.hhs.gov/reports/hcimu/hcimu\\_10102002.pdf](http://www.cms.hhs.gov/reports/hcimu/hcimu_10102002.pdf), accessed July 2003

<sup>65</sup> Based on personal interview with Eric Mann, FDA.

<sup>66</sup> Public Law 107-250

<sup>67</sup> Based on personal interview with Eric Mann, FDA.

are based on the type of application to be processed and the size of the company. Firms who qualify for the small business designation are charged a lesser fee. In 2003, those businesses that earned less than \$30 million in gross sales and revenue fall under this category<sup>68</sup>. Below is a table listing some of the various fees collected by the FDA through the MDUFMA:

<b>Table 1 - FY 2003 Device Review User Fees</b>		
<b>Application</b>	<b>Standard Fee</b>	<b>Small Business</b>
Premarket application (PMA, PDP, BLA)	\$154,000	\$58,520
Premarket report (premarket approval application for a reprocessed device)	\$154,000	\$58,520
Panel-track supplement	\$154,000	\$58,520
Efficacy supplement	\$154,000	\$58,520
180-day supplement	\$33,110	\$12,582
Real-time supplement	\$11,088	\$4,213
510(k)	\$2,187	\$2,187 *

It is important to note that the fees charged to small businesses are substantially smaller than those typically charged, making it more affordable to those companies. According to the Advanced Medical Technology Association (Advamed), the typical cost of developing a device is approximately \$25 million. Given this, the user fees should be within a reasonable range for most manufacturers, even smaller start-ups<sup>69</sup>.

The FDA has recognized the difficulty small businesses face in obtaining device approval and its use of staggered user fees is an important example of the prior efforts to accommodate the needs and financial capabilities of small companies. This legislation has created significant assistance to small businesses, however, one area that the FDA neglects is in defraying the cost of clinical testing. Even those companies whose devices fall under HUD are required to conduct and finance their own trials, although they are exempt from any user fees. At first glance, this may not seem like an unreasonable request, but testing may cost several millions of dollars, especially if it involves prolonged studies.

For small companies with products targeted at small market segments, the cost of carrying out full clinical trials is burdensome and often a barrier to entry. The FDA does not consider the size and income of manufacturers with regards to testing and the IDE. In fact, the Freehand System's FDA approval was largely due to the funding of clinical trials by Department of Veterans Affairs. Without such financial support, Dr. Peckham's group would not have been able to run comprehensive tests which involved implanting

<sup>68</sup> <http://www.fda.gov/cdrh/devadvice/pma/userfees.html>, accessed July 2003

<sup>69</sup> Based on personal interview with Blair Childs, Advamed.

61 subjects at a price tag of \$50,000 each. As Peckham states, “The FDA approval is important because it makes the hand grasp prosthesis much more widely available<sup>70</sup>.”

Thus, in order to improve commercialization efforts, the FDA should provide subsidies for clinical testing to HUD manufacturers and expand their population cap on HUD requirements. Providing subsidies will allow companies to focus on the technical development of the product, rather than on the lengthy approval process. That way, they can better guarantee an effective, safe device from the start of the prototyping stages. Such assistance will give a cost saving incentive to organizations creating devices such as neural prostheses. Furthermore, by placing the cap on the HUD designation at 4,000 people, the FDA is ignoring a key group whose healthcare needs are not being met by the private sector. In expanding the cap, small device manufacturers will have the opportunity serve those needs by taking advantage of the cost effective opportunities afforded through the legislation.

### Medicare/Medicaid Reimbursements

The slow process of reaching adequate Medicare/Medicaid reimbursement levels is the final main barrier to entry for medical device companies in neural prosthetics. The Medicare reimbursement process is a lengthy ordeal that is composed of several steps. First, the Centers for Medicare and Medicaid Services (CMS) must determine coverage of a device. There are two types of coverage: national and local. Local coverage determination is at the discretion of the state, which usually investigates the effectiveness of the device on a case-by-case basis. At a national level, the Department of Health and Human Services calls upon a Medicare Coverage Advisory Committee (MCAC) to review the literature and clinical data to make a recommendation as to whether or not a technology is viable. However, the committee is purely advisory and it rests upon CMS to make the final decision on coverage. The National Coverage Determination (NCD) is usually triggered by the interests of an outside party<sup>71</sup>.

Once coverage is obtained, a device is given a tracking code and put into a Diagnostic Related Group (DRG). A DRG is a bundle of related illnesses, which the device is supposed to address. The device is given an initial reimbursement rate based on the cost of the previously existing technology in its DRG. The code is then tracked as it is used in various hospitals and the rate of reimbursement is adjusted to the appropriate level as the technology becomes more widespread. It is important to point out that CMS does not directly reimburse manufacturers for the cost of their product. Hospitals buy devices from companies at the market rate and it is the hospitals that receive the reimbursement from CMS. According to the Advanced Medical Technology Association, adequate reimbursement rates are typically not reached until 3 years after a device is approved<sup>72</sup>.

The length of time it takes CMS to reach an appropriate level of reimbursement creates a large disincentive for hospitals to continue purchasing such devices as cochlear implants and Freehand Systems. For at least the first three years of use, each hospital will be

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<sup>70</sup> <http://www.cwru.edu/menu/research/prosthesis.htm>, accessed July 2003

<sup>71</sup> <http://www.cms.hhs.gov/coverage/default.asp>, accessed July 2003

<sup>72</sup> Based on personal interview with Blair Childs, Advamed.

effectively losing money for each patient they support. As a result, hospitals tend to use fewer advanced medical devices, defaulting to the cheaper, less effective devices which were previously used. This directly correlates to a slow sales growth for manufacturers of neural prostheses, who face a small market segment as it is. Eventually, this lack of sales volume can lead them to entirely discontinue their line of products. Similar events are what led to the termination of NeuroControl Corporation's production of the Freehand System. Even those companies who have been market leaders in the field of neural prosthetics are facing reimbursement difficulties. Advanced Bionics' cochlear implant was approved by the FDA in 1996. Currently, the reimbursement rate for their device is at \$19,000, which is less than half the average hospital borne cost of \$40,000<sup>73</sup>.

Given these difficulties, CMS should change its reimbursement policy for cutting-edge medical devices with humanitarian applications. Instead of lumping neural prostheses in an outdated DRG, CMS should create a new classification for these devices that will provide compensation which more closely reflects the market cost. This will increase the rate of hospital repayments, eliminating the disincentives they face to support neuroprostheses. With better rates, hospitals can choose to carry the most advanced medical devices, providing the best quality care to their patients. With a steadier initial income and growing customer base, small manufacturers will be able to achieve suitable profit margins. Such margins will allow them to continue to invest in further R&D efforts, refining the technology to widen their market and continuing to sustain their level of production and development.

### Opposing Viewpoints

However, recommendations that the federal government play any type of role in the private sector do not come without opposition. The key stakeholders in these proposals are patients, device manufacturers, hospitals and, of course, taxpayers. Most patients and hospitals favor a more active government role in promoting medical devices, allowing each the access to the most effective procedures and treatments. Patients and hospitals are primarily concerned with promoting quality healthcare, a goal that could be well advanced through the use of cutting-edge medical technologies. In turn, by providing access to such technologies, manufacturers are seeking financial profits and growth, a process that the federal government can facilitate in the area of neural prostheses. In the end, it is up to the average taxpayer to decide whether this is a course that the federal government must or should assist in, a decision that often leads to several debates.

The main argument opponents would pose is that it is not within the scope and jurisdiction of the federal government to direct industry. They claim that in meddling with the capitalist mechanisms of the economy, the government is upsetting the efficacy of the open market and going beyond its proscribed duties<sup>74</sup>. Although these assertions are not without merit, neural prostheses are devices that are important to social welfare. Although the disabled would use these devices, the benefits of the technology would affect more than just those handicapped. The federal government would be able to spend less money on welfare programs and insurance costs. Disabled people would be able to

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<sup>73</sup> Based on personal interview with Advanced Bionics representative.

<sup>74</sup> Based on presentation given by Marc Stanley, NIST.

return to the workforce, becoming productive members in society. The average quality of life for those disabled and their families would increase. Given these advantages, neural prostheses is a product that is in the interest of the public to develop. And, as previously shown, these technologies might not be developed at all without some sort of government assistance. So, although government intervention may not be necessary in the commercialization process, it is necessary in the production of neural prosthetics for humanitarian purposes.

The second argument made is that with the growing federal deficit, the government does not have sufficient funds to support these types of incentives. In 2003, only 19% of the federal budget was allocated towards non-defense discretionary spending, while 64% of the budget went to paying entitlements and interest (see Figure 6). In future years, the amount of entitlements is expected to increase, leaving diminishing levels of funding for other programs (see Figure 7)<sup>75</sup>.

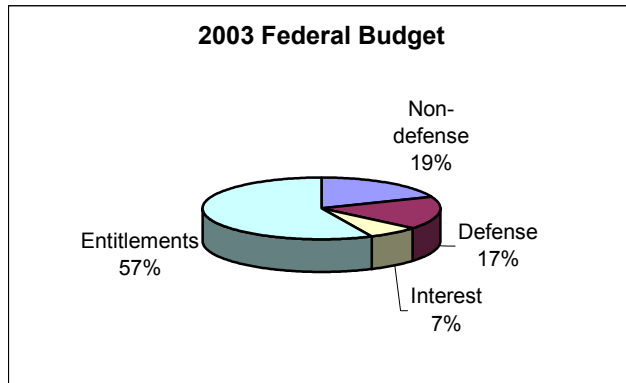


Figure 7: Chart courtesy of Sen. Dianne Feinstein’s office.

While this is a major economic concern to the taxpayer, in providing business incentives, the government is investing in long-term commercial growth. Neural prosthesis is only the beginning of a stream of innovations from a potentially lucrative biomedical industry, which is just starting to emerge. The market challenges that these devices face today may well be ones that other products will have to contend with in the future. In addition, the European Union (EU) is investing heavily in advanced technology, such as biotech, and has devoted over 400 million euros to the venture capital market<sup>76</sup>. Already, 2 out of the 3 cochlear implant manufacturers are based in Europe, with branches in the U.S.<sup>77</sup>. Therefore, it is in the interest of global economic competitiveness for the federal government to provide incentives for high-risk technology commercialization, such as neural prostheses.

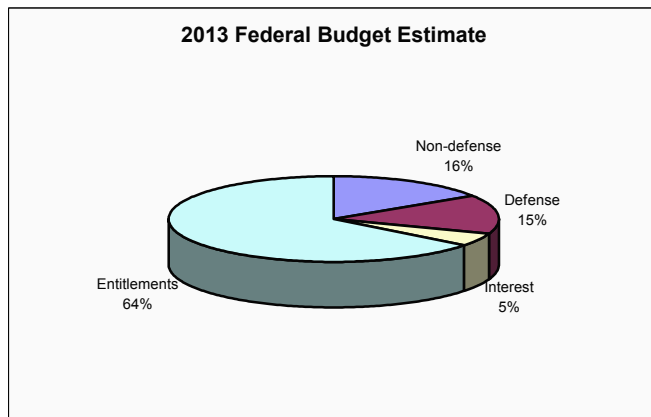


Figure 6: Chart courtesy of Sen. Dianne Feinstein’s office.

Therefore, it is in the interest of global economic competitiveness for the federal government to provide incentives for high-risk technology commercialization, such as neural prostheses.

<sup>75</sup> Based on presentation by Kei Koizumi, AAAS.

<sup>76</sup> [http://fei.eu.int/news/press/pr2003\\_01.htm](http://fei.eu.int/news/press/pr2003_01.htm), accessed August 2003

<sup>77</sup> <http://www.hopkinsmedicine.org/hearing.html>, accessed July 2003

## **Recommendations and Concluding Remarks**

The research and development of neural prostheses has led to many remarkable applications in both humanitarian and defense areas. Work on the cochlear implant has enabled tens of thousands of deaf and hard of hearing people to regain their hearing. Continuing progress on motor control prosthetics and retinal implants will hopefully lead to similar success in the paralyzed and blind/vision impaired communities. These devices will allow disabled individuals to more fully participate in society, improving their quality of life.

However, the companies trying to commercialize these devices face serious barriers. First, there is a lack of incentives to promote market development for high-risk technologies. Basic research in the biomedical arena has garnered significant federal funding over the past several years, yet the technology transfer has been discouraged as the private sector faces rising costs in development. In order to ameliorate this situation, the federal government should create legislation for the development of medical devices that provides exclusive licensing agreements, subsidies of research and tax breaks. With this type of encouragement, manufacturers will be able to produce neural prosthetics with reasonable economic costs, providing improvements in medical technology to help the disabled. These companies will also be able to, then, funnel revenues back into R&D to refine the technology, allowing them to reach a larger customer base.

Additionally, the current FDA approval process favors large corporations, making it difficult for smaller, less established companies to gain access to markets. Most clinical testing that is submitted to the FDA is paid for at the expense of the company filing the approval application. Since most innovation occurs in small revenue firms, these manufacturers are less capable of funding extensive trials for high-risk medical devices. As a result, such businesses must look for outside funding or discontinue their development. To alleviate this situation, it is suggested that the FDA create mechanisms to subsidize companies whose devices have humanitarian impacts and applications. Through subsidies, organizations can better afford to test their products for approval, providing needed devices for the handicapped and underserved sectors.

Lastly, the lag time until adequate Medicare reimbursement is received is too long to sustain production of medical devices such as neural prostheses. Medical devices are purchased by hospitals, which then are reimbursed by Medicare. Typically, a hospital will have to wait more than 3 years until they receive sufficient rates to defray their costs. This type of payment system discourages hospitals from carrying advanced medical devices to provide quality care. This results in lower sales among manufacturers, inevitably causing them to cease production. One solution to this problem is to implement new payment systems for cutting-edge medical devices, which would reimburse at the market rate of the device. Then, hospitals would be able to purchase the technologies they wish to provide and companies would have a steadier source of income to continue production.

While the biomedical industry is still in its infancy, the U.S. economy faces strong competition from other global manufacturers, such as those in Europe and Japan. The

European Union, especially, has increased its R&D funding and efforts to finance venture capital firms. However, with much of the technology is still emerging, there are no clear winners.

Still, future applications for neural prostheses are creating a large window of opportunity for creativity, investments and benefits. Growing innovations may lead to more refined devices, which can perfectly mimic the natural processes of the senses. Such innovation could even lead to the possibility for human enhancement. Yet, with the market success of neural prostheses still left to be determined, the focus of all involved is in the present developments, with a vision for the future looming decades away.