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A Vision of Hope

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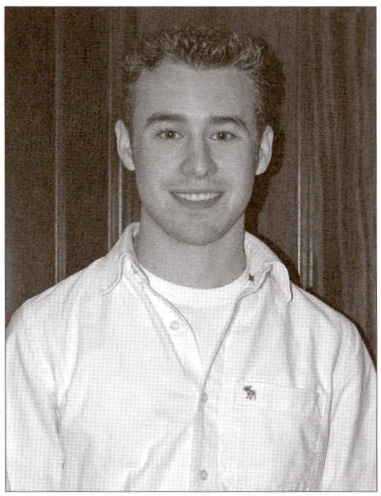
Introduction

With the ever increasing medical research developing in West Michigan, a professor and two students from Grand Valley State University collaborated on the Food and Drug Administration (FDA) approval process. The three authors concluded that this paper would benefit both students and business persons. As research facilities in Grand Rapids grow, so will the many attending businesses that are needed to make the devices and drugs that result from such discoveries. The persons who work for these companies will need to know the basics of the FDA process, and this paper may serve as a basic primer of the process.



Michael McCarthy

The authors thought the paper would be more interesting with a specific example to explain the FDA process. They researched the eye disease of one of the authors of this paper, Michael McCarthy, and a potential cure. Mike is a senior in the Seidman College of Business and has Choroideremia (CHM). The disease is slowly causing him to go blind. CHM is called an orphan disease because very few people have the disease. In this paper Mike will discuss his disease and a new product that offers true potential for slowing the progression of the disease. The paper will also explain how the Food and Drug Administration (FDA) regulates research developments through clinical trials. Finally, the paper will explain how business profits play a major role in determining which medical products make it to the commercial market, especially in regard to orphan diseases like CHM where the profits are less than those for non-orphan diseases.

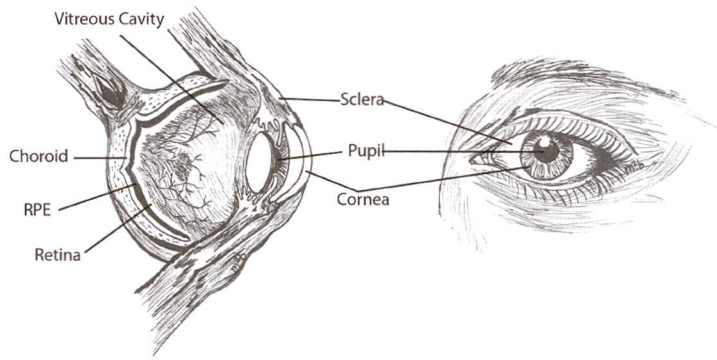
What is CHM?

The actual vision loss is caused by the degeneration of several layers of cells that are essential to sight. These layers that line the inside of the back of the eye are called the choroid, the retinal pigment epithelium (RPE), and the retina. (Refer to Figure 1.)

Cure?

There is now a new surgical procedure that offers hope to persons with CHM. The procedure involves placing a

Figure 1 Diagram of the Eye



synthetic membrane capsule into the eye that will produce proteins which may halt degradation. The platform is called ECT (Encapsulated Cellular Technology). These engineered membrane capsules contain cells that have been genetically altered to produce a desirable protein called CNTF (Ciliary Neurotrophic Factor). CNTF mimics the naturally occurring proteins (REP-1) that are typically found in a healthy eye but are missing in CHMers. The membrane is the size of a single grain of rice. The engineered cells inside the membrane continuously produce new proteins (CNTF) which flow out of the implant to the damaged area of the eye. It is hoped that the insertion of these synthetic membranes will provide the safe and effective delivery of proteins for the treatment of CHM.

The ECT implant is 6 mm (under a ¼ inch) in length. The capsule has a suture clip at one end and is stitched into the vitreous cavity of the eye. (See Figures 2 & 3) It contains

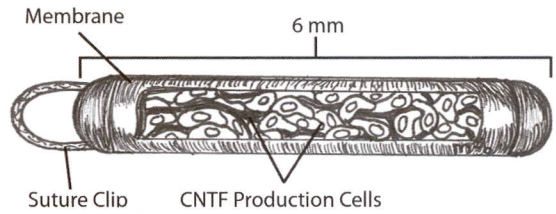


Figure 2 ECT implant capsule

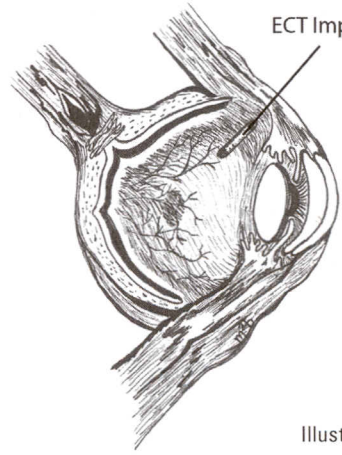
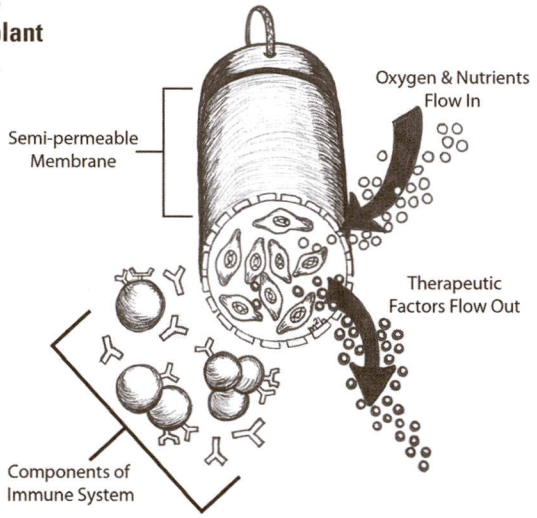


Figure 3 Implanted Capsule

Illustrations by Melissa Bobowski

Figure 4
ECT implant capsule



genetically-altered human cells in a semi-permeable fiber membrane. The membrane has specific hole diameters that allow the smaller CNTF proteins, but not the larger CNTF production cells, to flow out of the capsule and into the eye. The implant is attached in a way that allows for its removal when desired, providing an added level of safety as well as the ability to reverse or adjust the treatment. The surgery is performed as an out-patient procedure in about 20 minutes. For more information on ECT and animations of how the implant works visit Neurotechusa.com.

A patient named Larry Hall was one of the first people to participate in ECT clinical trials. While reading the Foundation Fighting Blindness newsletter in 2003, Mr. Hall read that the National Eye Institute (NEI) was seeking volunteers for a Phase I clinical (safety) trial for the implant. After about a year of decision-making, rigorous testing, and paperwork, Larry was checked into the hospital. In a speech about his clinical trial experience Larry said:

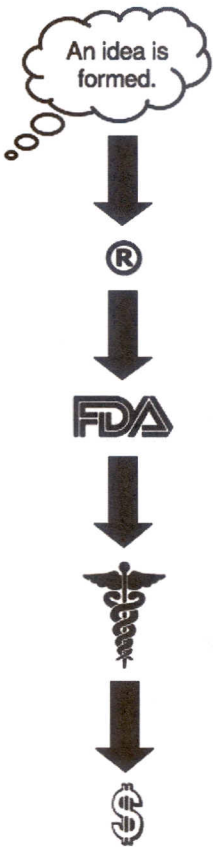
> *Every month (after the surgery), I went back for examinations and testing. Not much happened for the first two months. In the third and fifth months, my visual acuity improved. At six months, the device was taken out and returned to the company that made the device for examination. During the six month period the device was implanted in my left eye, my visual acuity improved from 20/120 to 20/50. A year later, my visual acuity was still 20/50.*

This hopeful new technology is unfortunately not yet commercially available. It remains in the regulatory processes of the FDA. Although Mike would gladly volunteer or pay to have the surgery to halt his impending blindness, there is no way to do that at this time. Mike was not chosen to participate in the clinical trials. It is now a waiting game for the FDA approval process to advance before he loses even more sight.

FDA Clinical Trials

So what is a clinical trial? And what role does the FDA play? A clinical trial is generally considered to be a biomedical or health-related research study of humans that follows a specified set of federal guidelines. Work is done by a team of researchers, scientists, nurses, social workers and other health professionals. In this case, trials are deemed interventional because a surgical procedure is being developed and evaluated.

Figure 5
ECT implant capsule



Applicants are considered in accordance with a set of inclusion/exclusion criteria before being chosen for participation. Some examples of factors that define participation eligibility are age, gender, the type and stage of a disease, previous treatment history, and other medical conditions.

There are benefits as well as risks that come with clinical trials in the medical field. Participants have the chance to take an active role in their own health care, gain access to new research before it is commercially available, and the have the opportunity to help others by contributing to medical research.

FDA Approval Process

The Food and Drug Administration is part of the U.S. Department of Health and Human Services. "The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of drugs, biological devices, and medical devices, and responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safe and more affordable." (FDA.gov)

Getting a new drug, device or procedure approved by the FDA is a complex process. No two trials are alike because of the numerous variables that pertain to each disease and new technology. As previously stated, the purpose of the rigorous FDA trials is to protect the public. Consequently, there is an intricate set of steps that must be completed before a drug, a device, or a procedure can be made commercially available.

Below is a basic outline of the research path and FDA process:

1. The idea for treatment is conceived by a scientist.
2. The idea (drug/device/procedure) is filed with the U.S. Patent Office to protect the intellectual property rights of the inventor (or corporate owner).
3. Research begins: pre-clinical trials.
   - Initial research is typically done in labs with animals.
   - The length of time for investigation is dependent upon the complexity and type of research.

- The funding for research is also imperative for progress. It may come from private and/or public sources, but research and production cannot be completed without money.

4. IDA—Investigational New Drug Application
   Many times the researchers hire a consultant group familiar with the FDA approval process to help them file the necessary paperwork and navigate the FDA application process.

If approved...

5. Clinical Trials: Human Testing Begins

Phase I (Toxicity)
Initial human testing begins here. Investigators look at the safety and risks of the device. Twenty to eighty participants are studied. Participants are screened for both medical and psychological stability. Potentially severe consequences, including death, must be acknowledged as recognized risks. Participants must release the researchers from all liabilities.

Phase II (Safety)
Multi-purpose research is conducted here. Prior safety research continues and new effectiveness research begins. One hundred to three hundred participants are studied. Samples of participants are selected from across the country. The trial may have ten to thirty different medical centers participating.

Phase III (Efficacy; this is the current standing of ECT trial)
The effectiveness of the trials is determined in the third phase. One thousand to three thousand people are studied. If the trials are successful, the FDA may approve the drug, device, and/or procedure for commercial use.

Phase IV (Post-Market Approval)
After the device is marketed, researchers collect information on long-term effects and potential "off-label" uses to aid in medical conditions other than the original intended application.

CHM in Clinical Trials

The purpose of this trial research was to look at the safety and effectiveness of the ECT implant in humans. This research was conducted because there are currently no cures for people with CHM, or other major eye diseases such as Macular Degeneration. The only reason CHMers were included in Phase II trials is because Larry Hall was diagnosed with CHM after Phase I. (He was originally misdiagnosed with another more prevalent eye disease.) Choroideremia Research Foundation members and friends wrote many, many letters to their Congressional representatives to plead their case for CHM to be studied in the trials. This advocacy effort was successful and CHM was included.

In the ECT implant studies, two different protein dose levels were used: a high dose or a low dose in one eye for half the patients. The other half of the patients (referred to as the control group), receives a placebo, or a non-medicinal surgery. These studies involved the following:

1. Multiple visits over one to three years for specific tests of the participant's vision and health. The visits included visual exams, blood draws for laboratory testing, family medical history, and exams. As stated previously, there were multiple research centers participating in the study with people enrolled from across the country.
2. The primary tool used to measure outcomes for this study was a visual field score one year after the implant surgery. At the start of the study, participants underwent a variety of visual field tests in order to map out their vision, including the EVR (Electronic Visual Acuity). One year after the trials, participants were retested and then given a score called their BCVA (Best Corrected Visual Acuity).
3. Other data collected in the study were: (A) average BCVA across all participants, (B) changes in the thickness of the rear of the eye, (C) atrophy within the eye and (D) a subjective assessment in changes in quality of life.

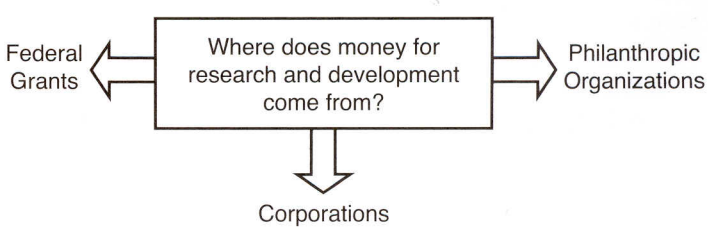
Researchers are currently collecting and analyzing the data from the most recent trials. The approval process waiting game is now in its final stages and will determine when, how, and in which direction the ECT implant research develops.

Profits versus Cure

The most difficult issue for many to accept is the chance that even though the ECT implants may show success in CHMers, funding is the bottom line for taking it to a commercial level. Medical manufacturing companies target a return of 6–7% profit. Most major corporations are focused on curing more "high-volume" (profitable) diseases such as Macular Degeneration (MD). About 1.75 million Americans have MD, and that number is expected to grow substantially with the increasing aging population. CHM affects only 1 in 58,000 people. Without hopes of a solid profit, companies tend not to pursue research and cures for most orphan diseases such as CHM. They typically receive little, if any, money from public/governmental sources. As a consequence, CHM research is mostly funded by parents, other loved ones, and umbrella organizations like the Foundation Fighting Blindness - Blindness.org and the Choroideremia Research Foundation - Choroideremia.org.

Figure 6 graphically describes the funding sources that are necessary to bring a cure to market. Those who conduct medical research and the companies that produce medical cures are like any other business. They must conduct research and make products that are going to provide for reasonable profits. Orphan diseases rarely offer such possibilities.

Figure 6
Funding Investment



Conclusion

Hopefully in the future the FDA process will be accelerated, new funding will be found for orphan diseases, and we will all benefit from the miraculous findings of upcoming scientific research. When we look at the numerous research facilities sprouting wings in West Michigan, there is good reason for hope. ■

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Real Estate Forecast *continued from page 8.*

there is a noticeable level of risk appetite returning to the market, and we anticipate increasing transaction volume in 2010. Obtaining financing will remain a challenge, and investors and sellers must continue a trend of exploring creative ways to complete transactions, such as assumption of debt, land contracts, and seller financing.

As anticipated there was an increase in the percentage of transactions that were completed by local investors. Investors are seeking opportunities to purchase distressed assets and are taking advantage of the price drops in the West Michigan market. Buyer activity can be expected to increase throughout 2010, as the national economy continues an improvement trend. There are distressed assets that well-capitalized investors with risk tolerance have begun to take advantage of. Local investors who understand the market will have increasing opportunity in 2010.

Cap Rates for properties that traded in 2009 have averaged 150 to 250 basis points higher than comparable sales in 2007. This equated to a 16 to 24 percent drop in value. While property values declined in 2009, it remained less than the national average of 40.6 percent. The primary reason for that disparity is that the local market did not hit the cap rate lows of the primary markets that generate much of the data. Additionally, this measurement did not include distressed assets, which have seen even greater price reductions. ■