July 2008

Development of an Informed Consent Multimedia Tool for Research

Denise Cifelli
University of Pennsylvania, cifelli@mail.med.upenn.edu

Follow this and additional works at: http://repository.upenn.edu/od_theses_msod

http://repository.upenn.edu/od_theses_msod/16

Submitted to the Program of Organizational Dynamics in the Graduate Division of the School of Arts and Sciences In Partial Fulfillment of the Requirements for the Degree of Master of Science in Organizational Dynamics at the University of Pennsylvania

Advisor: Larry Starr
This paper is posted at ScholarlyCommons. http://repository.upenn.edu/od_theses_msod/16
For more information, please contact libraryrepository@pobox.upenn.edu.
Development of an Informed Consent Multimedia Tool for Research

Abstract
Standard research practice has been to protect the rights of human subjects by providing an informed consent document that explains the study in clear and concise language. The problems inherent in writing this document are considerable and it is not known how effective these documents are in providing information and enhancing understanding about research participation. I have selected a clinical research trial involving older men to illustrate the challenge of providing sufficient information so that a person can make an informed choice. I describe the many human, educational and technological aspects that must be considered in developing an alternative method to the written informed consent process. I have developed a tutorial that can be tested within the clinical trial to compare the differences in informed consent methods. The research community is obligated to improve the informed consent process and these preliminary efforts are worthy of further development.

Comments
Submitted to the Program of Organizational Dynamics in the Graduate Division of the School of Arts and Sciences In Partial Fulfillment of the Requirements for the Degree of Master of Science in Organizational Dynamics at the University of Pennsylvania

Advisor: Larry Starr
DEVELOPMENT OF AN INFORMED CONSENT
MULTIMEDIA TOOL FOR RESEARCH

by

Denise Cifelli

Submitted to the Program of Organizational Dynamics in the Graduate Division of the School of Arts and Sciences in Partial Fulfillment of the Requirements for the Degree of Master of Science in Organizational Dynamics at the University of Pennsylvania

Philadelphia, Pennsylvania

2008
DEVELOPMENT OF AN INFORMED CONSENT

MULTIMEDIA TOOL FOR RESEARCH

Approved by:

_______________________________________________________
Larry M. Starr, Ph.D., Program Director
ABSTRACT

Standard research practice has been to protect the rights of human subjects by providing an informed consent document that explains the study in clear and concise language. The problems inherent in writing this document are considerable and it is not known how effective these documents are in providing information and enhancing understanding about research participation.

I have selected a clinical research trial involving older men to illustrate the challenge of providing sufficient information so that a person can make an informed choice. I describe the many human, educational and technological aspects that must be considered in developing an alternative method to the written informed consent process. I have developed a tutorial that can be tested within the clinical trial to compare the differences in informed consent methods. The research community is obligated to improve the informed consent process and these preliminary efforts are worthy of further development.
I would like to thank the many friends and family members who supported me during the development of this project, as well as the people who motivated me and made my experience in Organizational Dynamics at Penn so stimulating. They are: Andrew Cifelli, Gregg Fromell, M.D., Conley Heaberlin, Chris Helker, Rosemary Madigan, Sandra Smith, Peter Snyder, M.D., Samuel Vrooman, Jean-Marc Choukroun, Ph.D., Barry Dornfeld, Ph.D., and Larry Starr, Ph.D..
# LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Department of Health and Human Services 45 Code of Federal Regulations 46.116 Essential Elements of Informed Consent</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>Pilot Study Participant Demographic Characteristics</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>Testosterone Trial Tutorial Table of Contents</td>
<td>28</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>FIGURE</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Check Your Understanding About Testosterone Risks</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>Risks and Benefits Module: Prostate Cancer Risk</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>Risks and Benefits Module: Confidential Health Information</td>
<td>35</td>
</tr>
</tbody>
</table>
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>iii</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>iv</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>v</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>vi</td>
</tr>
<tr>
<td>CHAPTER</td>
<td></td>
</tr>
<tr>
<td>1 Introduction History of Human Subjects and Informed Consent for Clinical Research</td>
<td>1</td>
</tr>
<tr>
<td>2 Description of the Informed Consent Problem</td>
<td>10</td>
</tr>
<tr>
<td>3 Human Factors</td>
<td>16</td>
</tr>
<tr>
<td>4 Methodology</td>
<td>26</td>
</tr>
<tr>
<td>5 Conclusion</td>
<td>37</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>40</td>
</tr>
<tr>
<td>APPENDIX</td>
<td></td>
</tr>
<tr>
<td>A Research Informed Consent Multimedia Tutorial</td>
<td>44</td>
</tr>
<tr>
<td>B Testosterone Trial Informed Consent Document</td>
<td>72</td>
</tr>
<tr>
<td>C Multimedia Tool Development Proposal</td>
<td>89</td>
</tr>
<tr>
<td>D Informed Consent Evaluation Survey</td>
<td>92</td>
</tr>
<tr>
<td>E Informed Consent Evaluation Survey Results</td>
<td>95</td>
</tr>
</tbody>
</table>
CHAPTER 1

INTRODUCTION

History of Human Subjects and Informed Consent for Clinical Research

The history of human subject protection in clinical research in the United States has several important milestones. In 1906 the United States Congress passed the Food and Drug Act to address concerns about the quality and safety of food and medicines. The Nuremberg Code was written in 1947 in response to human experiments conducted during World War II. This code became the foundation of the Code of Federal Regulations, Title 45-Public Welfare, Part 46-Protection of Human Subjects (45 CFR 46). In 1962 Congress passed the Kefauver-Harris Amendments to ensure drug efficacy and greater drug safety, and in what was the initial acknowledgement of the rights and voices of consumers, the Consumer Bill of Rights. In 1973, the Consumer Product Safety Commission was established, followed by the Bioresearch Monitoring program in 1977, which focused on protection of human subjects. In 1981, 45 CFR 46 was revised to focus specifically on the elements of informed consent (Milestones in US Food and Drug Law History, 2005).

In parallel to these events, medical science was exploring new research methods. The clinical trial emerged in the late 1950’s as the valid and objective research method to test the safety and efficacy of medical treatment. A clinical trial is defined as an experiment testing medical treatments on human subjects. Medical science has relied on this standard for almost five decades (Piantadosi, 1997).
Federal standards established and refined over the last century to regulate drug and device development have generated enormous growth within the pharmaceutical industry. Standards of medical care have changed to integrate the information that is generated from clinical trials in the name of improved health care and patient safety. For example, mammography and colonoscopy, originally used as diagnostic tests, are now used as routine screening tests intended to detect early changes that could result in breast or colon cancer.

The process of conducting research to inform medical care, however, is dependent on people to participate as subjects. Without people to volunteer for clinical research, medical science would not know enough about the effects of drugs on humans and therefore would not have the essential information needed to advance medical knowledge and ultimately improve public health. Animal and laboratory studies can provide data but only human beings can provide subjective information about the signs and symptoms associated with how a drug or device makes them feel.

Throughout the history of medical research there have been several identified instances of misconduct wherein the rights of research participants were purposefully violated by those entrusted with their protection. One such instance occurred in Tuskegee, Alabama. Between 1932 and 1972, the United States Public Health Service (PHS) physicians and researchers conducted a study of African-American men with syphilis. Though it was discovered in 1940 that penicillin could cure syphilis, treatment was purposely withheld from these men so that the research study was allowed to continue in order to further
evaluate the impact of the untreated disease. Three hundred ninety-nine men were told they had “bad blood” and were continuously misled about their health and subjected to many unnecessary and often risky medical procedures. Because these men were poor and had limited access to healthcare, researchers at Tuskegee were able to exercise control over what happened to these subjects. Worse, when 250 of these men registered for the draft during World War II and were ordered to get treatment for syphilis, the PHS intervened and had them exempted from this requirement. The experiment came to an end only when it gained media attention in 1972. By then many of the wives, partners and children of these men had contracted the disease and almost half of the men had died from syphilis or its complications (Jones, 1981). One of the consequences of this tragedy was the strong mistrust of the medical establishment that developed and persists among many African-Americans (Braunstein, 2008).

Several other instances of unethical research were exposed by Dr. Henry K. Beecher, a professor of anesthesiology at Harvard Medical School. In 1966, Dr. Beecher published an article in the New England Journal of Medicine that gained attention outside of the medical community. He cited 22 examples of unethical research that violated the principle of voluntary consent in human subjects research. This article emphasized the thoughtless, as opposed to the willful disregard that researchers had toward some human subjects and heightened the awareness of researchers, the public and the press to the problem of unethical human subject research.
These disclosures coincided with professional and governmental action to curb unethical research practices. In 1964, the Declaration of Helsinki was developed by the World Medical Association (WMA) which established a set of ethical principles for the conduct of human research. In 1966 the American Medical Association (AMA) released Ethical Guidelines for Clinical Investigation, and the National Institutes of Health (NIH) published rules applicable to all federally funded human subject research. In 1981, additional laws and guidelines were specified to ensure the protection of human subjects in sections of the U.S. Code of Federal Regulations (CFR) and the International Committee on Harmonization (ICH) Guideline for Good Clinical Practice (NCI Guide to Understanding Informed Consent, 2001).

The ICH GCP Guidelines have been established as the ethical and scientific quality standard and have their origin in the Declaration of Helsinki (ICH Guidance for Industry, 1996). The underlying ethical principles in these guidelines are that research must be conducted with the well-being of subjects as the most important consideration and that the research goals must be scientifically sound and focused on improving clinical outcome. Embedded in these guidelines, which have been adopted by the United States, Canada, Japan and the European Union, is recognition of the obligation of researchers to fully disclose information about the potential risks and benefits of research, as well as respect for the autonomy of individuals to make informed decisions based on full disclosure of this information (Sharp, 2004). It is this obligation that has led to
additional oversight to the protection of human subjects and the informed consent process.

These codes and guidelines are based on the assumption that all involved parties are knowledgeable about research quality and ethics and are fully committed to their application, which is not necessarily the case. Academic medical centers have established Institutional Review Boards (IRB) composed of medical researchers and non-research members who are charged with protecting the rights and welfare of human subjects recruited into research studies. Because of the unique composition of this board, which includes physicians, nurses, researchers, and patient representatives, the IRB is well suited to evaluate each research study and the human subject informed consent documents that are written to accompany the research protocol. IRBs are granted the authority to disapprove or modify a research study based on human subject protections (45 Code of Federal Regulations 46, Subpart A, 2005). Though these ideal standards have been available to guide the conduct and review of medical research, the implementation of these research standards is often flawed at the organizational level.

In 1999, a young man who voluntarily participated in an experimental gene therapy study at the University of Pennsylvania (Penn) died, not from his underlying medical condition but as a direct result of administration of a gene transfer product. This prompted a thorough examination of the entire medical research arena at Penn and within the Department of Health and Human Services (DHHS). DHHS suspended all gene transfer research at Penn and
other academic institutions nationally and convened an advisory committee on Oversight of Clinical Gene Transfer Research. Their recommendations focused on establishing rigorous requirements for accountability, reporting and transparency in all aspects of the scientific conduct of gene transfer research (Enhancing the Protection of Human Subjects in Gene Transfer Research at NIH, 2000). Prior to this occurrence, the research administration at Penn functioned in an arena that had cursory oversight to the activities of individual researchers. It subsequently introduced more stringent standards and accountability for training, documentation, and inspection across the School of Medicine that had not previously existed.

As a result of increasing awareness about the need to ensure safety of research subjects, as well as to compel researchers to register research activities, and document compliance with established Federal guidelines, the School of Medicine established the Office of Human Research to provide education and training about all aspects of conducting sound, safe research. This office was charged with developing activities that ensure the protection of human subjects and was authorized to oversee the specific procedures and methods being used across the university. In establishing itself as the local government proxy, the University would be able to evaluate research practices before the U.S. Government had reason to do so. One of the benefits is the heightened awareness that investigators and their staff have about human subject safety and their increased attention to the process of obtaining informed consent.
Though U.S. federal regulations specify eight elements of information that must be disclosed to research participants, (see Table 1), ethically valid informed consent demands more than just disclosure and as such, presents several challenges to the researcher (Flory, 2004).

Table 1. Department of Health and Human Services (45 CFR 46.116)
Essential Elements of Informed Consent

Except as provided in paragraph (c) or (d) of this section, in seeking informed consent, the following information shall be provided to each subject:

| 1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; |
| 2. A description of any reasonably foreseeable risks or discomforts to the subject; |
| 3. A description of any benefits to the subject or to others which may reasonably be expected from the research; |
| 4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject; |
| 5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; |
| 6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained; |
| 7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and |
| 8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. |

Writing an informed consent document requires meeting at least four objectives. It must be (1) compliant with regulations and institutional legal requirements; (2) accurate; (3) informative; and (4) understandable (Sharp, 2006). To write this document at a level of readability (defined as the ease with
which printed material can be read) that is at or below the eighth-grade level, which is the NIH recommendation that has been adopted by most institutional review boards, can be difficult (NCI Simplification of Informed Consent Documents, 2006). In a review of informed consent documents of 18 cancer clinical trials, Sharp (2004) found that only 1.0% of the informed consent documents were written at the eighth-grade level and that over the last decade most consent forms have become longer and more difficult to read.

Researchers and bioethicists have recognized this problem of reading difficulty. Explaining a complicated research project in simple language in many pages of printed text does not ensure that it will be understood. There are many variables to consider including the educational level of the participant, differences in learning style; language used; and the medical urgency or level of illness (Jimison, 1998). If people do not understand what they are agreeing to, being informed is not assured.

**Purpose of Thesis**

I have selected a clinical trial that is being developed at the University of Pennsylvania, School of Medicine, to illustrate the challenge of providing sufficient information so that a person can make an informed choice about participating in a research study. I propose developing a multimedia tool to enhance the informed consent process by providing information in a familiar and accessible format instead of the standard paper document. In Chapter 2, I provide relevant information from medical literature that describes the problem of measuring the outcome of the informed consent process. There is little literature
on this topic and a confounding factor is the difficulty in discerning what is remembered versus what is understood. In Chapter 3, I explore the important human considerations that may be encountered in this complex clinical trial of older men. Chapter 4 describes the methods employed in developing the tutorial. Chapter 5 contains my conclusions about the final product, reflections on how it may enhance the informed consent process as well as the potential for acceptance as a useful tool in clinical research.
CHAPTER 2

DESCRIPTION OF THE INFORMED CONSENT PROBLEM

The informed consent document is the starting point for the dynamic process and exchange of information that occurs between the physician/research team and the potential participant over the course of the research experience (NCI Simplification of Informed Consent Documents, 2006). A review of the literature on the topic of informing patients for the purpose of obtaining consent (for medical treatment or research participation) indicates that there is not a great deal of quantitative research available.

Flory (2004) reported a meta-analysis of 12 studies that compared the understanding of participants who had undergone a standard informed consent process to participants who had received an intervention to improve their understanding. The samples included adult men and women of all ages who were parents of pediatric patients, oncology patients, psychiatric patients, IV drug users, pregnant women and healthy volunteers. The interventions (defined as information delivery methods) varied among the 12 studies and included PowerPoint presentations, video, text reformatting as a booklet, and readability reduced to the 7th grade reading level. The results showed a consistent demographic predictor: research participants with higher education or reading levels had significantly higher level of understanding of information presented in the informed consent process, based on a post consent assessment. The results also indicated that levels of satisfaction were highest among participants who perceived that they had extended discussion time about the consent form (Flory,
2004). This suggests that the experience of discussion or personal interaction plays an important role among subjects who are considering participating. This resonates with bioethicists and medical researchers who emphasize the importance of conducting informed consent as a process and not just a form that requires a signature (Lavori, 1999).

Agre (2003) analyzed eight studies of informed consent interventions that included modified print, computer and video consent formats and knowledge quizzes among adults. The mean age was 60 years; 57% were men. The findings were that better educated subjects scored better in the knowledge quizzes and that computer and video consent formats produced improvements in understanding over standard text media. These subjects also reported that the video clips of patients were the most useful part of the computer intervention.

Wirshing (2005) reported a study comparing 261 adult medical and psychiatric patients who viewed a videotape that explained the informed consent process and emphasized good decision making in considering research participation, with a control group of healthy volunteers. The videotape repeatedly emphasized the need for subjects to be assertive in seeking information, and included role-playing vignettes of doctors and patients that reinforced the subject’s right to know and the physician’s responsibilities in providing clear explanations of the research procedures during the informed consent process. Results showed larger gains in knowledge among those who viewed the video about informed consent when measured before and after the process, as compared to the control group.
Hitchcock-Bryan (2007) reported a study of 77 cancer research patients who participated in an evaluation of an informed consent video. A post consent analysis indicated that watching the video did not measurably improve the subjects’ understanding of cancer clinical trials. However, subjects reported that the video provided important information, helped them educate their families and improved communication with their provider (Hitchcock-Bryan, 2007). This suggests that subjects perceived increased value and meaning despite a lack of benefit on the measured assessment of knowledge.

Jimison (1998) designed a study that approached patients as consumers who demand a greater choice and involvement in their healthcare. A needs assessment was conducted around the topic of informed consent for medical treatment that included feedback from focus groups and individual interviews with medical and psychiatric patients. The primary findings indicated that most patients felt that the consent forms were too long, that the wording was too complex and that the level of detail was confusing. Patients reported that they preferred information presented to them in smaller segments and felt that the use of video made the information more understandable and the situation less stressful. Patients reported that one source of the stress occurred due to difficulty in concentrating on the printed text. The authors concluded that the use of a multimedia tool that offered the ability to proceed through the material at a self-selected pace made the material more interesting to the patient and reduced dependence on the patient’s ability to read. Such a tool may have the potential to enhance and standardize the quality of the informed consent process. Since so
little is understood about how to make the process effective, however, the authors recommended that the patients or volunteers needs must be understood before a multimedia approach could be designed to address them (Jimison, 1998).

Dunn (2001) conducted a meta-analysis of 34 heterogeneous medical studies of adult men and women who were cardiology, surgical, radiology, cancer, and psychology patients. Dunn recommended that a variety of educational interventions to improve understanding of informed consent should be used to enhance the process, including video, multi-media and web-based technologies. Dunn argued that further investigation is needed about interventions to improve understanding because although the problem has been well described, studies that actually test intervention methods have been limited.

Rosoff (1999) summarized the features of “prepackaged” informed consent education programs such as those presented on DVD or CD-ROM. The apparent benefits to the physician/researcher are that this method allows a low-transaction cost transmission of fixed information. If accurate, it would provide all of the relevant and necessary information with significantly less time and effort than other (written) methods, and could document electronically the subject’s comprehension. For the physician, the gains are in efficiency and standardized information delivery. The apparent subject benefits are the receipt of a thorough explanation with full details on risks and consequences. In addition, the subject is able to access the material at their own speed without the pressure of the clock, and discuss it with their family/spouse, but not the researchers, in the privacy of
their home, instead of the physician’s office. If the technology permits, they can self-test their comprehension and review topics that are not clear to them. However, this technology eliminates the human interaction between the patient/subject and physician/researcher and eliminates the opportunities for spontaneous knowledge exchange with a professional that is the foundation of a personal medical relationship. Rosoff (1999) acknowledged that the presentation of information (in any format) does not assure knowledge and that it is very difficult to objectively measure understanding when information is complex. Yet, he asserts that comprehension is so important to autonomy and self-determination that any approach that comes closer to assuring comprehension should be encouraged.

Current research on the informed consent process is slow in catching up with the available technology offerings. Research studies focused on genetics and proteomics, for example, have resulted in the creation of longer and more complex informed consent documents. Medical researchers, focused on innovative scientific methods, have not applied the parallel technological innovations that are available to improve the informed consent process, nor has there much effort spent in measuring the outcomes of varied informed consent methods.

The Testosterone Trial at the University of Pennsylvania, School of Medicine, is designed for men aged 65 and older. It has a complicated study design; six separate informed consent documents (five abbreviated and one comprehensive document); eligibility requirements in four separate areas;
potential health risks; and a significant time burden. A risk assessment of these factors served as an alert that the study may be difficult for potential subjects to understand, resulting in a low rate of recruitment and a weak study initiation phase. If this is the case, shortly after the study begins, the design and protocol will require revision, resulting in delays, inefficiencies and cost overruns. In an effort to mitigate this risk and the possible negative impact on the launch of the study, I have developed an informed consent multimedia tool for this study to serve as a supplement to the written form which I propose will add clarity to the issues described above. The Research Informed Consent Multimedia Tutorial (developed as a Powerpoint presentation) in Appendix A provides specific information about the Testosterone Trial as well as the essential elements of informed consent listed in Table 1.
CHAPTER 3
HUMAN FACTORS

This clinical trial, designed to test the efficacy of testosterone, is currently under review and is expected to begin in January 2009. Based on research by Jimison (1998), Dunn (2001) and Rosoff (1999), there are several important human factors to consider in developing the appropriate tool for use in this research study including cognitive characteristics of older adults; learning styles of individuals; knowledge assumptions; use of technology; and the physician-subject relationship.

It is important to note that the participants in the Testosterone Trial are research subjects who may or may not be patients of study investigators. As the clinical settings will vary among the 18 research sites, it is possible that the participants are not patients, and the investigators are researchers but not healthcare providers to the participants. The terms subject and participant can be used interchangeably; however, the term patient implies that a person is participating in a health care relationship with the investigator/physician.

Another feature of this clinical trial is that it will be conducted as a double-blind experiment. This means that participants are randomly assigned to the treatment or placebo group and that neither the subject nor the researchers will know which treatment a given subject is receiving. These methods are used to reduce the unconscious and deliberate human influence on treatment assignment and evaluation, and mimic the laboratory model of scientific experimentation (Piantadosi, 1997).
Cognitive Characteristics of Older Adults

Aging is associated with a gradual and progressive decline in many aspects of cognitive function. The terms age-associated memory impairment (AAMI) and late-life forgetfulness (LLF) are used to describe a condition that is characterized by temporary memory lapses in otherwise healthy individuals (Smith, 1991). The typical symptoms of AAMI include difficulty in recalling names and words, and in associating a name with a face. In a memory study of 527 adults ages 55 to 98, Smith and Ivnik (1991) reported that age-related memory changes vary depending on several factors including educational experience, activity level and motivation. It is a challenge for clinicians to distinguish normal age-related memory changes from early dementia, and there is lack of agreement regarding the criteria for detecting the difference. Larabee and Crook (1994) reported that the prevalence of AAMI among adults older than 50 ranges from 39 to 85% and increases with age.

Sugarman, McCrory and Hubal (1998) performed a meta-analysis of 99 published empirical research measures on informed consent with older adults. They found consistent evidence of impaired understanding of informed consent information in older subjects and those with less formal education. Their recommendations to improve the informed consent process included simplification of text, and novel formats and tools that promote interaction to enhance comprehension. Recognizing these natural, complex outcomes of aging, it is prudent to assume that many of the men who read the Testosterone
Trial informed consent document will have some difficulty remembering the details described in its 17 pages (see Appendix B).

Recall alone does not imply understanding; indeed, there is a lack of clarity in defining understanding. The complex cognitive processes involved in reading, attention and memory are called by several different terms such as understanding, knowledge, comprehension, and recall that do not mean quite the same thing but are often used interchangeably. Dunn (2001) reported a meta-analysis of 34 clinical studies which included people of all ages, in which problems with understanding the research consent form were widely reported. These included lack of awareness about being a subject in a research study, poor understanding of placebo and randomization, confusion about risks and benefits, lack of awareness of the ability to withdraw from the study without consequence, and therapeutic misconception which is the belief that treatment decisions are being made solely for the individual’s benefit. The problem of therapeutic misconception occurs more often when a subject’s only role is as a participant in a research study, compared to the subject who is also a patient in a healthcare relationship. There are studies that acknowledge the difficulty in measuring memory for presented information versus comprehension in assessing understanding of informed consent information, but the number of studies that test methods to improve the process has been limited.

Learning Styles of Individuals

Adults bring many years of learning experiences with them to any new learning situation, integrating new learning with prior learning. In order to meet
the learning needs of adults the content of any material must be relevant; if adults see the usefulness of the material presented, their motivation to learn increases. Adults also tend to prefer active learning that is related to their real-life situations as well as self-directed learning (Disabilities, Opportunities, Internetworking and Technology, Adult Learning, 2006).

This is relevant because participation in this research is voluntary; only those men who are eligible and motivated by the potential for improvement in the four research realms will reach this stage of the enrollment process. I believe that this multimedia tutorial will enhance the informed consent process for the adult learners in this study as it allows self-directed learning, in which the learner has some control over the pace and content of the program.

The men who volunteer to participate in the Testosterone Trial will be a diverse group of 1200 older men varying in race, level of education and geographic location. In developing a multimedia tool, it is important to acknowledge that they are also individuals who will have different learning styles. It has been reported that educational level is directly correlated to level of understanding of informed consent, which is one of the reasons that the readability of informed consent documents has been established at the eighth grade reading level. But this one parameter does not consider the many other aspects of taking in information that are relevant.

VARK (Visual, Aural, Read/Write, Kinesthetic), developed by Flemming (1987), is one of the many dimensions of learning preferences, and is focused on the way that an individual takes information in and puts information out in a
learning context. VARK is a mechanism for profiling individual learning preferences, but not necessarily strengths. There are some consistent reports of matches between VARK results and perceived preferences; however, statistical data are not yet available to prove the validity and reliability of VARK.

In order to reach every learner, media should be constructed to address the VARK preferences for obtaining knowledge of the audience. The VARK data indicate that men have more kinesthetic responses than women but overall learners are distributed across the four domains. There are limitations to the kinesthetic learning experiences that the multimedia tool can provide; however, the tutorial will include visual, aural, and read/write components to address those learning aspects. (See Appendix C, Multimedia Tool Development Proposal).

Knowledge Assumptions

Recruitment techniques in the Testosterone Trial will vary widely. One technique will use national media, local media and mass mailings targeted at older men who will be asked to contact the research center if they are interested in a testosterone research study. This subject generated contact implies only that respondents are willing to learn more information. No further assumptions should be made about what respondents know about research or testosterone. Holden (2005) reported a study of men aged 40-79, wherein 27% of respondents were not familiar with the term testosterone; more men (40% of respondents) in the older age group (60-79) indicated unfamiliarity with the term.
Pilot Study

I conducted a pilot study of structured individual interviews with eight men who appeared to be candidates for the Testosterone Trial study. The interview instrument is included in Appendix D. This group was a convenient sample of friends and family members; therefore, the results should be considered exploratory data only. The instrument and process warrant further evaluation and refinement. I recruited eight White/Caucasian men ranging in age from 65-85 years (Mean = 73.7 years). Educationally, 3 (37.5%) attended or graduated from college; 5 (62.5%) had a high school education or less (see Table 2). A complete summary is included in Appendix E.

Table 2. Pilot Study Participant Demographic Characteristics (n=8)

<table>
<thead>
<tr>
<th>Education</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7th to 12th grade, no high school diploma</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>High school graduate or equivalent (e.g. GED)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Some college education, but not completed degree</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>College graduate</td>
<td>2 (25%)</td>
</tr>
</tbody>
</table>

Subjects and Methodology

Each man read the consent form to himself after which I conducted an interview with him and collected information about his reaction to several sections of the consent form, including understanding the four trials, the Interactive Voice Response system, placebo, and risks, as well as willingness to discuss this study with his spouse/significant other/family member and physician, and capacity to use other media to explain the clinical trial. The interviews were conducted at the respondent’s homes between February 12 and March 10, 2008.
The respondents had many shared opinions. The comments that I recorded during the interviews provided much more information about the preconceived notions, knowledge and understanding that the interviewees had, than the dichotomous responses to the questions.

I had extensive discussions with five of eight men about use of a placebo. None of the men interviewed had ever participated in a research study. They stated that they understood the difference between the active and placebo medications used in the study, but they also said that they would not want to be in a study where they might use a placebo instead of testosterone gel. These men learned about testosterone primarily from sports news. They knew that it was available by prescription from a physician and felt that there would be no need to participate in a trial if they were inclined to use testosterone. (I explained that testosterone should only be used if the level of that hormone is significantly low. Also, I explained about the importance of monitoring adverse effects.) These discussions suggest that some men may have had trouble understanding and/or accepting the value in using a placebo in this study and that it is important to include a clear explanation of the placebo in the tutorial and to evaluate the level of understanding.

Addressing the ethical concerns of the placebo controlled trial has been controversial and debated in the medical literature for many years. Opponents claim that it is unethical in that it places scientific rigor over the needs of people. Proponents explain that regulatory oversight of research and the informed consent process ensure that its use is ethical, provided participants understand
the rationale and risks if assigned to the placebo condition (Emanuel, 2001). It is probably naive to assume that regulatory oversight in academic medical centers, local clinics, doctor’s offices and wherever research is conducted, can provide the needed rigor and standardization to protect research subjects. Bok (1978) warned that the use of placebos is not innocuous, that the safeguards against this practice are few or nonexistent both because it is secretive in nature and because it is condoned but rarely discussed in the medical literature and that it undermines the medical relationship.

The men in this sample had a wide range of accurate and inaccurate information about prostate cancer. Their comments suggest that the experiences of individual men they knew seemed to influence their perceptions more than information they heard from doctors. All of the men (100%) expressed concern about prostate cancer; 75% were not clear about the effect of testosterone on their risk of prostate cancer. I discussed “occult” prostate cancer with all of these men and found that half of the men understood the concept of occult prostate cancer but that the term “occult” in this context created confusion. This is the kind of practical information that helped me write the risk section of the tutorial, which I found to be the most difficult.

Use of Technology

It would be a mistake to assume that the men in the testosterone trial will be able to easily use a web-based tool or a DVD to view the tutorial at home. Three major studies conducted between 2003 and 2005 revealed that 25 - 41% of adults aged 65 and older use the Internet (Doing the Math, Older Adults...
Online, 2005). In this sample of eight men, five (63%) did not own a computer and 75% did not feel comfortable accessing the tutorial from a website. This is important information to know about potential participants. It suggests that the tutorial may be viewed primarily at the research clinic during the baseline visit, under the guidance of the research staff; however, it must also be portable so that men who are facile with technology can take the tutorial home to read and answer the questions. The method must be uncomplicated and reliable however subjects prefer to access the tutorial. A brief training or practice session should precede distribution of the DVD for home use to ensure that users have the ability to access the media and know how to use the features of the tool.

This also suggests that one of the potential benefits of the tutorial, the transmission of information with less time and effort by the research staff, may not be realized. A common research practice used to gain efficiency in the informed consent process is to distribute the document and other educational information, such as a study fact sheet, to the subject even before it has been determined that he is eligible. In this study, a man who has completed the screening visit could be given the informed consent document and tutorial to take home, even though his eligibility status has not yet been determined. When it is verified (by confirming lab data) that a man is eligible, he can be contacted and instructed to read the form and complete the tutorial at home, before the next research clinic visit. There are potentially negative consequences to this approach. If a man has questions, he has no one to ask and if he encounters technological trouble using the tutorial he may become frustrated and abandon
the tutorial. In addition, the introduction of technology into the informed consent process may dilute the compassionate, human exchange that forms the core of the medical relationship (Rosoff, 1999). Therefore, it could be risky to rely on technology to meet the needs of subjects during the informed consent process, unless the research team continues to invest the time and energy needed to thoroughly discuss the research and address all of an individual’s concerns. Ultimately it is the combination of the technology and the human elements that will determine how well the tutorial will be received.

**Physician-Subject Relationship**

The current practice of obtaining informed consent relies on the physician/subject relationship and is based on the assumption that this activity is worthwhile to the physician and the subject (Rosoff, 1999). In introducing technology to educate subjects about research, it is important to consider how it could diminish the important bonding process that takes place when a doctor and subject engage in a meaningful conversation about their health or quality of life. It is essential that human interaction is not reduced because a tutorial or other electronic aid is used. In obtaining informed consent, physicians must be committed to meeting a subject’s emotional needs in addition to their informational needs.
CHAPTER 4

METHODOLOGY

Three subject matter experts contributed to the development of materials for the tutorial. The design team included Peter J. Snyder, M.D., Principal Investigator of the Testosterone Trial. Dr. Snyder is an endocrinologist at the University of Pennsylvania, School of Medicine, and has conducted testosterone clinical research for over 30 years. Dr. Snyder was the subject matter expert for the medical content presented in the tutorial. Gregg Fromell, M.D., Director of the Office of Human Research (OHR), at the University of Pennsylvania, School of Medicine, provided expertise on research education, training and compliance. Dr. Fromell leads the initiative to develop standard tools, methods and teaching materials for the Penn OHR and has extensive experience in evaluating informed consent documents. He was the subject matter expert on the essential elements of informed consent, readability and format of the tutorial. Barry Dornfeld, Ph.D., is an Educational Media Consultant and co-leader of the Center for Applied Research (CFAR) Action Learning initiative. Dr. Dornfeld provided expertise in development of content and organization of biomedical knowledge and served as a reviewer of the entire multimedia tool.

The initial project to develop an informed consent video was modified to a multimedia tutorial to reduce delivery time and facilitate anticipated revisions to the project following review by the research network investigators. The design team focused on developing a multimedia tutorial that would enhance understanding of the information presented during the informed consent process.
for the subjects; meet established institutional guidelines for research; be appropriate to subjects; be interesting and attractive to users; be portable as well as accessible from the internet.

Print media is inexpensive, convenient and familiar; however, it is not interactive and often requires higher literacy levels of users. Advances in computer technology have enabled the construction of multimedia learning tools from online libraries of static and dynamic images, but it is difficult to know what changes for the learner when you add pictures to words (Elloumi, 2008). Mayer (2001) defined multimedia as the presentation of material using words (printed and spoken text) and pictures (static graphics and video). In proposing to use a multimedia tool in addition to text, there are several adjustments to consider.

The tutorial structure was based on the model designed by the National Library of Medicine (NLM) which provides a comprehensive program of authoritative health information tools (Medline Plus, 2008). The content is in alignment with but not identical to the informed consent document as the tutorial is meant to work in conjunction with the document. The pilot test results helped shape the content significantly in terms of emphasis on explaining the four trials, use of placebo, and risks. It also suggested that some words were confusing so we avoided terms that require specialized knowledge. The tutorial was developed in parallel with the interviews as well as continuous review by the design team. It was reviewed at regular intervals by Dr. Snyder, Dr. Fromell and my colleagues in the Clinical Research Computing Unit. Table 3 identifies the content of the tutorial modules.
The tutorial that accompanies the Testosterone Trial informed consent document was designed to enhance information in order to facilitate balanced decision-making. Based on data from Rosoff (1999), it seemed important to simplify the content, permit self-paced learning and support interactive learning. We wanted the users of this tutorial to make sense of what they see and hear. The output of responses to the “Check Your Understanding” questions is provided to guide the research team about the topics that should be reviewed or reinforced with the subject. Figure 1 presents two questions from the Risks and Benefits module.

**Figure 1. Check Your Understanding about Testosterone Risks**

<table>
<thead>
<tr>
<th>Check Your Understanding</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Using testosterone will cause you to have sleep apnea.</td>
<td>☐ True  ☐ False</td>
</tr>
<tr>
<td>You will have a prostate biopsy at the end of the study.</td>
<td>☐ True  ☐ False</td>
</tr>
</tbody>
</table>

I avoided focusing on the technology over the content and have included features that are functional without embellishments. The tutorial was developed to incorporate brief video streams to present information from men who resemble...
the subjects in the study, and from physicians who convey concern for the health and safety of participants in the study. It is important that these images are appropriate as well as interesting to attract the subject’s attention.

The tutorial will be implemented and accessed from a secure Internet website; it will also be portable to permit access from a stand-alone computer system, via DVD. It will be introduced with a brief explanation of its purpose which is to provide information about the study, not specific medical advice. It will explain that the video and pictures have been included to enhance the text. The ‘Check Your Understanding’ questions are asked to verify that the subjects understand the material as presented at that time. By documenting responses within the program, the tutorial will provide those administering the informed consent process the opportunity to review content that is not clear by examining the subject’s responses, thereby verifying understanding. This method of assessment does not address the problem of understanding versus recall, nor does this tutorial distinguish between short and long term recall. However, it has the potential to enhance satisfaction with the informed consent process, provide added value to potential subjects and may serve to reinforce learning by repeating information that is provided to them in the informed consent document in a media that is familiar, accessible and clear (Jimison, 1998).

The benefits of the tutorial are that it provides the same critical information to all subjects and documents the provision of it for legal purposes. In addition, if presented to subjects during the baseline visit, the tutorial is a prudent use of the subject’s waiting time, which is a concern in this study where this first research
visit can last up to four hours. This is also a risk as the use of this program has the potential to diminish an aspect of relationship building and trust that evolves before and during the informed consent process. Rosoff (1999) noted that the personal bond between the physician and subject/patient, which has been considered an essential element of the therapeutic relationship, may be weakened by the use of computerized information disclosure devices. As subjects/patients become better educated, the nature of the relationship becomes more collaborative; however, there is a tendency when a transaction is routinized and reduced to a ritual, for the ritual to stifle dynamic human interaction. It is important that this is not overlooked because a subject may begin, but may not continue to participate in a study that offers no direct benefit to him, unless there are some interpersonal and/or social reasons for doing so.

In trying to incorporate all of these elements into the tutorial, differences of opinion among the design team emerged. Dr. Dornfeld suggested that repetition is useful in conveying such specific information whereas Dr. Snyder expressed concern that the tutorial was too long and repetitive. Everyone was interested in selecting the photos and graphics. As the tutorial is graphics based, it was believed to be important to include the appropriate representation of men and health care providers in the pictures and video clips. This meant including men in the entire age range, of all races, professions and lifestyles. (The present photos are those that were freely available and will be replaced before the tutorial is produced.) The graphic elements could add impact by streaming video of a physician explaining the complex aspects of the study such as the study design,
placebo and risks. Providing a message from a familiar authority figure was believed to enhance the credibility of the content. The video clips could also include men as subjects demonstrating a procedure such as stair climbing, as subjects have reported that they find such clips useful (Agre, 2003). Ultimately the richness of the media will be balanced by the cost.

It is worth noting that not only will the subject matter experts have different reactions to the tutorial but that the users will also have diverse opinions about the content. The original objective was to develop a tutorial that would be more informative for participants than the traditional text method; as such, it will be important to include a step in the development process that incorporates the feedback of these stakeholders in the design process.

Dr. Dornfeld and I discussed the “Check Your Understanding” sections and how they can be most useful, given the static nature of the media and the 8th grade reading level requirement. The Flesch Kincaid Grade Level score of the tutorial is 7.6, which is equivalent to a reading level between 7th and 8th grade. The Flesch Kincaid Grade Level Score is a measure based on the number of words per sentence and the number of syllables per word (Flesch Kincaid Readability Score, 2008). Initially, the tutorial had two questions per module as I tried to avoid asking questions in which the responses were a simple return of facts just learned. Dr. Dornfeld urged me to examine what I was trying to achieve in asking these questions; is it important for subjects to answer them correctly or to serve as an indicator of level of understanding? As the long-term objective was to test this method for improving understanding of informed consent rather than
to rely on the paper document only, the responses should serve as an indicator of understanding associated with each module. He pointed out that many important aspects of the study were presented in each module and that this is the only opportunity in the process to evaluate what a subject knows at this point in time. He suggested that I develop additional questions for each module as they can serve, at a minimum, as a way to demonstrate that a subject has paid attention. Additional post-test questions could be developed and administered at a subsequent research visit, one or three months later, for example, that could serve as measures of information retention. Dr. Snyder was concerned about asking so many questions of subjects during the tutorial and thought that this could be an obstacle to some subjects. We agreed to include all of the questions and to conduct a formal pilot test and focus group to learn more about each subject’s reaction to the number and content of the questions. Dr. Dornfeld also recommended that the tutorial include guidelines with the output that would direct the person administering the informed consent process to review the topic areas that are not clear to the user. Early evaluation (during pilot testing of the tutorial) of the number and content of incorrect responses will help to revise the tutorial to meet the needs of the users.

As an endocrinologist, Dr. Snyder focused on presenting the medical content clearly and succinctly. He concentrated on the prostate cancer risks of the study as they are the most difficult to convey because they assume some knowledge about prostate cancer and its risk factors, non-specific symptoms, and the approaches to treatment that the medical community endorses (The
University of Texas, M.D. Anderson Cancer Center, 2008). The pilot data indicate that these issues are cloaked in some level of anxiety by men. The safety monitoring for prostate cancer that is included in the Testosterone Trial is more vigilant and conservative than is the standard medical practice, which is a fact that may not be apparent to subjects. To explain these distinctions may require providing additional information about prostate cancer; however, this may heighten fears about prostate cancer that may or may not be warranted. This is a complex issue that the investigators have been struggling with at every phase of the proposal and is under discussion with the sponsor and the scientific review committee. Yet, our obligation in the informed consent process is to fully disclose all risks to the subject and this may require providing supplemental information. Figure 2 depicts the prostate cancer risk section of the tutorial.
Prostate cancer

There could be small areas of cancer in the prostate that are not harmful and are not causing a health problem to you now. Using testosterone could change these small prostate cancers that are not harmful, into harmful ones.

Presently, there is not enough information to know for certain about the effects of taking testosterone on prostate cancer.

You will have rectal exams to check your prostate, and blood tests to learn your PSA result, which is the prostate cancer blood test. You will be asked questions about your prostate health and medical history.

Your prostate and the risk of developing prostate cancer will be monitored closely over the course of the study. Regular screening such as the kind you will receive in this study, helps detect prostate cancer in its early stages.

Dr. Fromell focused on the essential elements of the informed consent document as they are represented in the tutorial. Because of several recent instances of loss of research data in NIH and Veteran’s Administration studies, there is heightened interest by universities and sponsors about issues of data privacy and the disclosure of Protected Health Information (PHI), the individually identifiable health information such as name, address, medical history and medical record number (HIPAA Privacy Rule, 2007). All informed consent documents and any information provided to subjects as informed consent tools...
such as this tutorial, must describe how these data will be protected, how they may be used and to whom they may be disclosed. The institution must not use vague statements such as “every effort will be made to protect your personal information;” rather we must strive to be as specific as possible in describing how confidential data will be protected. This can be confusing and worrisome to subjects. Figure 3 depicts the section of the tutorial that describes protection of confidential information.

Figure 3. Risks and Benefits Module: Confidential Health Information

<table>
<thead>
<tr>
<th>Will confidential health information be collected as part of this study?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some private information about your health will be collected like your medical history, and your answers to questions about your physical function, sexual function, and other questionnaires. All information (including blood samples) collected in this study is kept strictly private by using study code numbers to collect information instead of names. This code number will be on the blood samples, questionnaires and in the computer that saves your responses. Your contact information will be locked securely in files at the research clinic and used only by the staff to contact you.</td>
</tr>
<tr>
<td>The information collected in the study is saved in a highly secure computer system. Only those people who are working to analyze the information will be able to view it. Authorized study representatives may review and copy data collected from this study and your medical records. Your name will never appear in any articles that are published of the results from this research.</td>
</tr>
</tbody>
</table>

In order to advance this tool to the implementation stage, Dr. Dornfeld recommended that I write a development proposal to accompany the tutorial that describes the scope of work for the production phase. This was completed and is presented in Appendix C, Multimedia Tool Development Proposal. It includes information about who will be responsible for the content, description and
expectations of the incorporated technology, and the review and approval process. He urged me that the production process should not begin until such information is written and clarified.

The content and format of the Testosterone Trial tutorial will remain stable for a brief time. The next phase will be review and revision by a larger group of physicians and researchers from among the 18 Testosterone Trial Research Network clinical sites who will evaluate it based on their institutional requirements and the needs of their local study populations. In order to evaluate this aspect of the tutorial it will be pilot tested in several research centers. This is an important step as the clinical sites differ widely, from an upper-middle class San Diego, California suburb to downtown Birmingham, Alabama. The tutorial will ultimately be reviewed by the Institutional Review Board of each participating medical center.
CHAPTER 5
CONCLUSION

The informed consent process is an imperfect one as it is dependent on many variable human factors. Yet, it is a pivotal element of clinical research; without human volunteers, advances in medicine would be very limited and much riskier. Research practitioners have a responsibility to ensure that participation in research is informed and voluntary. This implies that we should strive to improve the effectiveness of informed consent methods.

The scientific literature consistently reveals evidence of impaired understanding of informed consent information in older subjects and those with less formal education (Sugarman, McCrory, Hubal, 1998). This is an important consideration for the Testosterone Trial. The men in the trial will be 65 years and may have some health problems and age-associated memory impairment. The Testosterone Trial informed consent document is lengthy (17 pages), yet it still may not be adequately explaining important issues such as prostate cancer risk. It is difficult to reduce complex medical problems and research procedures to a few written paragraphs, while simultaneously acknowledging that there are still many aspects of testosterone use and risk that are unknown.

What can be expected of people to know about the Testosterone Trial in order to make an informed choice, and how should it be measured? For informed consent to be meaningful, research subjects deserve to have all of their informational needs regarding a proposed intervention met. A growing body of literature shows that decision aids such as multimedia tools can influence
subjects’ decisions and improve satisfaction with research participation, and it is almost certain that as technology weaves its way into all aspects of daily living that such tools are here to stay (Rosoff, 1999).

The next step to developing and implementing this tutorial is to present it to the research network investigators for final review and revision of content, pictures and graphics. After the final product is reviewed and approved by the Institutional Review Board at the University of Pennsylvania, it will likely be developed as a multimedia tool. During the pilot phase of the trial, I propose to conduct a pilot study of the informed consent process. The design will be a three-armed study to measure differences in subject reactions among those who read the paper informed consent document only; those who use the multimedia tool only; and those who use the paper document and multimedia tool. The study will include pre- and post-testing phases and follow-up testing at 3 and 12 months. The tests will aim to discern differences between the three groups in terms of ability to answer specific questions about the research purpose and risks as well to accurately describe the study. It may be feasible to conduct focus groups with subjects who complete the study to discuss the reality of study participation compared to the initial description presented during the informed consent process.

There is little research about the research process. As a result, established methods for conducting a study of this type are not available. I will examine the preliminary data and evaluate the process early during the pilot study to further develop and refine the methods. I will seek collaboration with the
Penn Office of Human Research, as they are the subject matter experts and thought leaders in the development of informed consent materials. I expect that this study will provide information about whether understanding of informed consent can be improved with educational interventions.

Future research in this area could assess the optimum length and content of multimedia tools; feasibility and acceptability of this media; and legal and ethical implications of using multimedia instead of written text for obtaining informed consent. The publication and presentation of the results will inform researchers about the utility and benefits of advanced technology approaches to the informed consent process. The organizational changes that would have to occur in order for this process to gain acceptance in the medical research community will be formidable. It will require an extensive communication plan to show that such a process change is advantageous to researchers as well as an improvement for subjects.

As clinical trials continue to evolve, becoming increasingly large, decentralized and global, it is important to maintain the fundamental human principals of autonomy and self-determination. As the shapers of medical care and public health, researchers are obligated to strive to improve the human aspects of the medical research process as well as the scientific ones, and to seek innovative and informative ways to benefit the citizens who participate. Gaining truly informed consent should be the objective of the process, not merely meeting the letter of the law.
REFERENCES


Flesch-Kincaid Readability Score.  


HIPAA Privacy Rule: What Health Information is Protected by the Privacy Rule? (2007).  


Introduction

This tutorial includes information about the Testosterone Trial, not specific medical advice. The pictures have been included to improve your understanding. If you have questions, please write them down and ask the doctor or someone from the research team.

NOTE: This slide will explain the functionality that is incorporated into the tutorial and will describe the features (using audio and video) that are included in the modules such as the table of contents, navigation buttons, mouse-over information and the Check Your Understanding sections.
Welcome to this education program about the Testosterone Trial Research Study.

The Testosterone Trial is sponsored by the National Institutes of Health and Solvay Pharmaceuticals.

This program will explain the Testosterone Trial to you so that you can decide if you are interested in taking part.

The Testosterone Trial is being conducted by doctors and nurses at your health center and around the United States to study how using testosterone affects men’s health.

The information in this program accompanies the consent form that you were given to read.

This education program was made to provide clear explanations of the study details to help you better understand the study and make an informed choice about participating.

Experienced doctors, nurses and members of their research teams will conduct this research study at 18 medical centers in the United States.
Audio - These are the 18 medical centers that are part of this research study.

This is a research study about men, age 65 and older, using testosterone. Your regular doctor will continue to work with you to manage your medical care.

As people age, they change in many ways which are part of the normal aging process. They may have difficulty walking, less interest in sex, difficulty remembering and less energy.

When men get older, the amount of testosterone, the main male hormone, gets lower. It is possible that low testosterone could be a cause of these changes.

The goal of this study is to find out if older men who take testosterone will have improvement in walking, be more interested in sex, improvement in memory and an improved energy level.
Slide 13

The 4 areas of research in this study are...

- Physical Function
- Sexual Function
- Memory
- Energy

Slide 14

Physical

...is focused on walking, climbing stairs, moving around safely and doing daily activities.

Slide 15

Sexual

...is focused on your interest in sex and your ability to have sex, as well as your thoughts and feelings about sex.

Slide 16

Memory

...is focused on your memory for information that you hear, information that you read to yourself, and other tests of your mental ability.
Slide 17

Energy

...is focused feelings of tiredness, energy level, moods and emotional states.

---

Slide 18

Check Your Understanding

The study will be conducted in men under age 65. [True False]

When men get older, their testosterone level decreases. [True False]

---

Check Your Understanding

A mouse-over feature will be used in the checkboxes to explain which answers are correct and incorrect, including a brief explanation.

Check Your Understanding Statement:
The study will be conducted in men under age 65.
True. Incorrect. The study will include men who are 65 and older.
False. Correct. The study will include men who are 65 and older.

Check Your Understanding Statement:
When men get older, their testosterone level decreases.
True. Correct. As men age their testosterone level decreases over time.
False. Incorrect. As men age their testosterone level decreases over time.

---

Slide 19

Check Your Understanding

This is a study of how testosterone affects your... (Choose one)

- a. Walking, sexual interest, reading ability, energy
- b. Walking, sexual interest, memory, relationships
- c. Walking, sexual interest, memory, energy

Check your answer here.

- a. Incorrect. The study will look at the effect of testosterone on walking, sexual interest, memory, energy
- b. Incorrect. The study will look at the effect of testosterone on walking, sexual interest, memory, energy
- c. Correct.
Slide 20

Participating in the Trial

Slide 21

What will happen in this study?

During this research study, men will take testosterone for 1 year. Men will participate in research visits by answering questionnaires and performing tests. When the study is over, doctors will know a great deal more about the effects of testosterone, and if it improves men’s health and well-being.

Slide 22

Voluntary Participation

Taking part in this research study is voluntary. You do not have to take part in it if you do not want to. If you do take part, you can leave at any time. If you decide not to take part, your medical care will not be affected in any way.

Slide 23

Qualifying to be in the study is based on ....

- Age - 65 years or older
- Testosterone level between 100 and 250
- Symptoms you report
- Your medical history
- Answers to questionnaires
Slide 24

Why are you being asked to take part in this study?
You are being asked to take part in this study because you are 65 or older and your testosterone level is low. This information was found when your blood was tested at the previous visits.
The questions that you answered show that you have some of the signs and symptoms of aging that low testosterone might cause.
You have been asked to read this consent form and consider being in the study because you seem to be a good match for the study.

Slide 25

What is the purpose of this research study?
Testosterone is a hormone produced by your body. The amount of this hormone decreases with age.
The main goal of this study is to find out if using testosterone improves walking, sexual interest and function, memory, and energy in men your age.

Slide 26

How long will you be in this research study?
If you decide to take part, you will be in the study for 2 years.
In the 1st year, you will take testosterone or a placebo.
In the 2nd year, you will not take testosterone, but will continue to be in the study.

Year 1
Testosterone Treatment Phase (12 months)
Year 2
Follow-up Phase (12 months)

Slide 27

During the 1st year, you will come to the research clinic for 7 visits and you will be called by the research team 6 times for information. The chart below shows when those visits will happen.

Year 1
Testosterone Treatment Phase (in Months)
0 1 2 3 4 5 6 7 8 9 10 11 12
C C C P P C P C P P C

This visit is called the Baseline Visit. 
C = Research Clinic visit in person; P = Phone contact
Slide 28

During the 2nd year, you will come to the research clinic once and answer questions by telephone once.

Check Your Understanding

If you take part in the study, you have to stay in it for 2 years.

True. Incorrect. If you start the study and do not want to finish it, you may stop when you want.

False. Correct. If you start the study and do not want to finish it, you may stop when you want.

Check Your Understanding Statement:
Accurately reporting your medical history is important to the study.

True. Correct. It is important to provide accurate information about your past and present health conditions.

False. Incorrect. It is important to provide accurate information about your past and present health conditions.

Check Your Understanding Statement:
Testosterone is a male hormone that decreases with age.

True. Correct. As men age it is normal for testosterone, the main male hormone, to decrease.

False. Incorrect. As men age it is normal for testosterone, the main male hormone, to decrease.

Check Your Understanding Statement:
You are being asked to participate in this study for 6 months. Incorrect. You will participate in the study for a total of 2 years.

1 year. Incorrect. You will take testosterone for 1 year but will participate in the study for a total of 2 years.

2 years. Correct.

Slide 29

Check Your Understanding

Testosterone is a male hormone that decreases with age.

Check Your Understanding Statement:
Testosterone is a male hormone that decreases with age.

True. Correct. As men age it is normal for testosterone, the main male hormone, to decrease.

False. Incorrect. As men age it is normal for testosterone, the main male hormone, to decrease.

Check Your Understanding Statement:
You are being asked to participate in this study for 6 months. Incorrect. You will participate in the study for a total of 2 years.

1 year. Incorrect. You will take testosterone for 1 year but will participate in the study for a total of 2 years.

2 years. Correct.
4 Testosterone Trials in 1

What is involved in this research study?

This study involves using testosterone or a placebo for one year in the form of a gel applied to the skin. The tests that you take and questions that you answer will show what changes, if any, happen.

The questionnaires that you answered were done to find out which of the 4 areas of study match what you reported about your health.

You could be in one or more of the 4 separate studies, called trials. For the trials in which you qualify, you will take part in those that you choose. The four trials are focused on:

- Physical Function
- Sexual Function
- Memory
- Energy

…is about how well you get around physically in terms of walking and moving around. This trial measures walking speed, stair climbing, and asks questions about physical activity.
Slide 35

Sexual Function

...is about your interest in sex and your ability to have sex. This trial asks for information about your sexual function and thoughts.

Slide 36

Memory

...measures memory of information you have heard, written information and several other tests of your mental ability such as your memory of designs and drawings.

Slide 37

Energy

...asks about your energy level, moods, depression and quality of life.

Slide 38

What does study assignment mean?

You will be in one of two groups. One group will be given testosterone gel. The other group will be given a matching placebo gel, which does not contain testosterone.

Study assignment means being put in one group or the other. A computer program will select the group that you are in.
Placebo
A placebo is a substance that is made without the active ingredient, but looks like the "real thing." The testosterone and placebo gels will be in identical pump bottles. The 2 gels will look, feel and smell exactly the same.
No one who is working on the study (the doctors, nurses, staff or you) will know which group you are in. This is done so that everyone is treated the same, without different expectations of how you might answer questions or perform in tests.

How do you take testosterone?
You will apply a specific amount of testosterone gel directly on your chest, stomach or upper arms once a day, every day for a year.
You will be shown how to do this so that you use the correct dose of gel.

The amount of gel that you get from the pump bottle will be prescribed. This is the dose of testosterone that you will be using.
You should not use more or less than this dose.

It is important to wash your hands after putting on the gel. You must then let the gel dry and cover up your chest with a shirt before having any physical contact.
Blood will be drawn to check your testosterone level each time you come to a research clinic visit.

If a dose change is needed, you will be told exactly what to do.

Check Your Understanding

Check Your Understanding Statement:
It does not matter how much gel is used when applying testosterone gel.
True. Incorrect. The amount of gel applied to the skin is the prescribed dose of testosterone that should be used.
False. Correct. The amount of gel applied to the skin is the prescribed dose of testosterone that should be used.

Check Your Understanding Statement:
Blood will be drawn at each research clinic visit to check the testosterone level.
True. Correct. Blood will be drawn at each visit to check testosterone level as well as several other tests.
False. Incorrect. Blood will be drawn at each visit to check testosterone level as well as several other tests.

Check Your Understanding Statement:
Study assignment means that....

a. Incorrect. Study assignment means that you will be put into one of two groups.
b. Correct.
c. Incorrect. Study assignment means that you will be put into one of two groups.
Slide 46

Check Your Understanding

The study doctors and nurses will choose which group you are assigned to.

True False

After applying the gel, you should wash your hands and cover the skin so that others do not touch the gel.

True False

Check Your Understanding Statement:
The study doctors and nurses will choose which group you are assigned to.

True. Incorrect. The group that you are in (testosterone or placebo) will not be chosen by anyone in the research study. A computer will make the study assignment.

False. Correct. The group that you are in (testosterone or placebo) will not be chosen by anyone in the research study. A computer will make the study assignment.

Check Your Understanding Statement:
After applying the gel, you should wash your hands and cover the skin so that others do not touch the gel.

True. Correct. Even after the gel dries on your skin, you must wash your hands and cover the skin so that others do not come into contact with the testosterone on your skin.

False. Incorrect. Even after the gel dries on your skin, you must wash your hands and cover the skin so that others do not come into contact with the testosterone on your skin.

Slide 47

Check Your Understanding

In this study, the placebo is...

(a) A pill
(b) A gel with a different medication than testosterone
(c) A gel that will seem identical to testosterone gel but will not have testosterone in it
(d) A device

Check your answer here.

a. □ b. □ c. □ d. □

Check Your Understanding Statement:
In this study, the placebo is...

a. Incorrect. In a different study of oral medication it could be a pill, but in this study testosterone is being given as a gel that is applied to the skin, not a pill taken by mouth.

b. Incorrect. In this study the placebo is a gel that will seem identical to testosterone gel but will not have testosterone, or any other medication, in it.

c. Correct.

d. Incorrect. A device is not being used in this study.

Slide 48

Tests and Procedures
Slide 49

The following things will happen at each visit….

• Your height, weight, waist, hips and blood pressure will be measured
• Your blood will be drawn (2 tubes, which is about 3 tablespoons)
• How far you walk in 6 minutes will be measured
• A rectal exam to check the size of your prostate and for the presence of nodules will be done (at Months 3 and 12)

Slide 50

You will be asked about ….

• the medicines that you take (prescription and over-the-counter drugs and herbal or supplements)
• health events, by asking you to describe new health problems that you have or changes to conditions that you already have. You will be asked if you had a heart attack or stroke, but should report all of your health problems.

Slide 51

You will be asked about ….

• trouble urinating
• difficulty doing ordinary things like washing up in the morning or grocery shopping

Slide 52

You will be asked about ….

• any falls you may have had and what happened
• your memory, and you will do tests to see what you remember
You will be asked about ....

- depression and moods
- your interest in sex
- your feelings of energy and tiredness

You will be asked to....

- respond to a few questionnaires at home using a phone system that lets you answer questions in the privacy of your home (or anywhere).
- The sexual diary, tiredness, depression and mood questionnaires will be done at home using this system.
- You will be taught how to use this phone system, called IVR, by the research staff.

What is Interactive Voice Response (IVR)?

IVR is a computer based phone response system. You may have used a similar system when calling the gas or electric company.

Recorded messages will guide you through the steps of answering the questions. You will use the phone number pad to answer them.

Your answers will be stored in an electronic computer file by your study code number. Your voice will not be recorded.
Check Your Understanding Statement:
A rectal exam is being done to check for colon cancer.
True. Incorrect. A rectal exam is being done to check for prostate enlargement and the presence of nodules in the prostate.
False. Correct. A rectal exam is being done to check for prostate enlargement and the presence of nodules in the prostate.

Check Your Understanding Statement:
It is not important to report changes in health conditions like diabetes, since it is not related to taking testosterone.
True. Incorrect. All of the changes in your health status are important to report. This may be informative about what is happening to all of the men in the study.
False. Correct. All of the changes in your health status are important to report. This may be informative about what is happening to all of the men in the study.

Check Your Understanding Statement:
You will be asked to report all of the medicine that you take, even over-the-counter medicines.
True. Correct. It is important to report as accurately as possible all of the medicine that you take, even over the counter medicines.
False. Incorrect. It is important to report as accurately as possible all of the medicine that you take, even over the counter medicines.

Check Your Understanding Statement:
You should not report trouble urinating because that happens to most men, as they get older.
True. Incorrect. You should report any problems or changes that happen to the way you urinate.
False. Correct. You should report any problems or changes that happen to the way you urinate.
Slide 58

Check Your Understanding

You will respond to questions using the IVR system by:

- a. Speaking slowly so your voice can be recorded
- b. Using the number pad on the phone
- c. Using a computer to go to a website

Check Your Understanding Statement:
You will respond to questions using the IVR system by:

- a. Incorrect. Your voice will not be recorded in the IVR system.
- b. Correct. You will use the number pad on the phone to answer questions.
- c. Incorrect. It is not necessary to use a computer to answer these questions. You will use the number pad on the phone to answer questions.

Slide 59

Risks and Benefits

Slide 60

What are the risks of this study?

There is a chance that using testosterone may make some conditions worse. You will be checked for these before and during the study.

The risks that you should understand are described in the following slides:

Slide 61

Prostate cancer
There could be small areas of cancer in the prostate that are not harmful and are not causing a health problem to you now. Using testosterone could change these small prostate cancers that are not harmful, into harmful ones. Presently, there is not enough information to know about the effects of taking testosterone on prostate cancer.
Slide 62

You will have rectal exams to check your prostate, and blood tests to learn your PSA result, which is the prostate cancer blood test. You will be asked questions about your prostate health and medical history.

Your prostate and the risk of developing prostate cancer will be monitored closely over the course of the study. Regular screening such as the kind you will receive in this study, helps detect prostate cancer in its early stages.

Slide 63

Benign Prostatic Hyperplasia (BPH)
BPH is the condition of having an enlarged prostate gland. Using testosterone may increase the size of the prostate, which could cause a decrease in urine flow.

You may see this as difficulty in starting and finishing when you urinate.

Presently there is not enough information to know about the effects of taking testosterone on BPH. You will be checked for this condition throughout the 1st year. The research team will act on changes that you report by referring you to the study urologist.

Slide 64

High red blood cell count
Testosterone normally increases the number of red blood cells, which is why men have higher red blood cell counts than women.

It is possible that using testosterone could increase the number of red blood cells that you have to higher than normal. This might increase the chance of stroke.

During the 1st year, your blood count will be checked frequently. Increases above normal will be investigated. You may be told to use less gel or you may be told to stop using the testosterone gel altogether.

Slide 65

Sleep apnea
Testosterone may increase the risk of sleep apnea, a condition in which not enough oxygen gets into the blood during sleep. This may result in excessive daytime sleepiness.

The connection between testosterone and sleep apnea is not known, so you will be asked about it regularly.

If you have been told that you have sleep apnea you can be in the study only if you are being treated for it.
There is some risk in doing the study tests. It may be hard for you to do the walking test or climb the stairs. The study staff will be there to assist you at all times, but you can rest or stop at any time.

Having blood taken from you has a small risk of temporary mild pain, bruising or infection. It is possible that you could faint. There will be trained technicians to draw your blood.

You may feel it is hard to answer some questions because they are so personal.

All of your answers are considered private and will not be shared with anyone.

The information that you give will be given a code number. Your name or other personal information will not be connected to your answers.

You may find that the memory tests are tiring.

You should just try to do the best you can. There are no passing or failing grades on these tests, and you should not practice taking these tests at home to do better.
Slide 70

Using Testosterone Safely

There are safety precautions that you must follow when using testosterone gel. You must be careful not to allow others to touch the gel on your skin. It is important to wash your hands, allow the gel to dry completely after you put it on, and to keep the skin covered.

Slide 71

If a prostate biopsy is needed, there are risks of bleeding and infection. You will be given detailed instructions before the procedure to reduce these possibilities.

Slide 72

Lastly, there is a chance that there are side effects that are not yet known.

Slide 73

Benefits

You may not get any benefit from being in this study. You may feel better or stronger, or you may not.

By being in this study, you may help medical science gain a better understanding of testosterone treatment.
Check Your Understanding

Changes in the prostate will be checked by measuring the PSA level in your blood, doing a rectal exam and asking questions about urinating.

Testosterone may cause an increase in the number of red blood cells.

Check Your Understanding Statement:

Changes in the prostate will be checked by measuring the PSA level in your blood, doing a rectal exam and asking questions about urinating.

True. Correct. Measuring the PSA level in your blood, doing a rectal exam and asking questions about urinating are procedures that monitor you for changes in your prostate cancer risk and enlargement of your prostate.

False. Incorrect. Measuring the PSA level in your blood, doing a rectal exam and asking questions about urinating are procedures that monitor you for changes in your prostate cancer risk and enlargement of your prostate.

Check Your Understanding Statement:

Testosterone may cause an increase in the number of red blood cells.

True. Correct. Testosterone may cause an increase in the number of red blood cells. This may not occur, may be small or could be significant. This will be monitored over the course of the study and may require a change in the dose or discontinuation of testosterone gel.

False. Incorrect. Testosterone may cause an increase in the number of red blood cells. This may not occur, may be small or could be significant. This will be monitored over the course of the study and may require a change in the dose or discontinuation of testosterone gel.

Check Your Understanding Statement:

Using testosterone will make you physically stronger.

True. Incorrect. It is not known for certain that testosterone will improve your physical strength.

False. Correct. It is not known for certain that testosterone will improve your physical strength.

Check Your Understanding Statement:

Using testosterone may enlarge your prostate gland.

True. Correct. It is possible that testosterone could make your prostate become enlarged. This may or may not happen to you.

False. Incorrect. It is possible that testosterone could make your prostate become enlarged. This may or may not happen to you.
Check Your Understanding Statement:
Using testosterone will cause you to have sleep apnea.
True. Incorrect. The connection between testosterone and sleep apnea is not clear.
False. Correct. The connection between testosterone and sleep apnea is not clear.

Check Your Understanding Statement:
You will have a prostate biopsy at the end of the study.
True. Incorrect. You will not automatically have a prostate biopsy at the end of the study. A prostate biopsy may be done if the prostate cancer risk signs (your PSA level and rectal exam) change. A urologist will determine if you should have a prostate biopsy.
False. Correct. You will not automatically have a prostate biopsy at the end of the study. A prostate biopsy may be done if the prostate cancer risk signs (your PSA level and rectal exam) change. A urologist will determine if you should have a prostate biopsy.

More Important Information

Will you be paid for being in this research study?
You will be paid a small amount of money, which will be given to you as you complete study visits.
You will be reimbursed for travel expenses and parking.
You will be given coupons for meals while you are at the research clinic visits.
Slide 79

What if you want to leave the research study after you begin?

You can leave the study at any time.

Dropping out of the study will not interfere with your future care.

---

Slide 80

Will confidential health information be collected as part of this study?

Some private information about your health will be collected like your medical history, and your answers to questions about your physical function, sexual function, and other questionnaires.

All information (including blood samples) collected in this study is kept strictly private by using study code numbers to collect information instead of names. This code number will be on the blood samples and questionnaires and in the computer that saves your responses.

Your contact information will be locked securely in files at the research clinic and used only by the staff to contact you.

---

Slide 81

The information collected in the study is saved in a highly secure computer system. Only those people who are working to analyze the information will be able to look at it.

Authorized study representatives may review and copy data collected from this study and your medical records. Your name will never appear in any articles that are published of the results from this research.

---

Slide 82

What will you do with the blood you collect?

Any blood that is left over after measuring testosterone, PSA and other tests will be saved at the Mayo Clinical Trial Services Central Laboratory for 5 years or more.

These saved samples might be helpful in the future, if new tests are discovered that would enhance knowledge about testosterone. You will not be able to find out anything about these tests.
Slide 83
What happens if you are injured during the study?
If you are injured because of taking part in this research study, you should contact the study doctor or staff right away at the phone numbers provided on the front page of this form. They will advise you about what to do next.

Slide 84
What if you have questions about the study?
Your rights and protection as a research participant are very important. If you have any questions, concerns or complaints about this research study, or if you have questions about your rights as a research subject, feel free to contact the Principal Investigator listed on the front page of this form. You may also call your Institutional Office of Regulatory Affairs with any question, concerns or complaints.

Check Your Understanding
Blood samples that are taken for the study will be saved for several years.

True
False

To protect your personal information, the study will use study code numbers, secure computer technology and restrict access to study information to authorized personnel.

True
False

Check Your Understanding Statement:
Blood samples that are taken for the study will be saved for several years. True. Correct. Such samples may be useful for future research studies.

False. Incorrect. Such samples may be useful for future research studies.

Check Your Understanding Statement:
To protect your personal information, the study will use study code numbers, secure computer technology and restrict access to study information to authorized personnel. True. Correct. Your personal information will be kept confidential.

False. Incorrect. Your personal information will be kept confidential.
Check Your Understanding Statement:
You will be paid a lump sum of money at the end of the study.
True. Incorrect. You will be paid as you complete certain research visits. Your travel expenses and meals will be provided.
False. Correct. You will be paid as you complete certain research visits. Your travel expenses and meals will be provided.

Check Your Understanding Statement:
If you have a complaint about this research study, you may not contact anyone but the research study staff.
True. Incorrect. Your rights as a research participant are very important. You may contact the investigator, staff, the office of regulatory affairs and/or research administration at this institution to discuss your concerns.
False. Correct. Your rights as a research participant are very important. You may contact the investigator, staff, the office of regulatory affairs and/or research administration at this institution to discuss your concerns.

Check Your Understanding Statement:
If you start the study, it does not matter if you leave before you finish all of the research study visits.
True. Incorrect. You are free to leave the study at any time without effect to your healthcare. However, it is best to collect a complete set of information about your participation for the entire length of the study whenever possible.
False. Correct. You are free to leave the study at any time without effect to your healthcare. However, it is best to collect a complete set of information about your participation for the entire length of the study whenever possible.
Slide 88

Summary

Slide 89

• The Testosterone Trial is being done to find out if older men who take testosterone will have improvement in walking, more interest in sex, improved memory and improved energy level.
• There are 4 trials in this research study focused on:
  • Physical Function
  • Sexual Function
  • Memory
  • Energy

Slide 90

If you decide to be in the study, you will …
• be in the study for 2 years.
• use testosterone or placebo gel every day for 1 year.
• go to 7 research clinic visits in the first year.
• report regularly about your health status and medicines.
• use an automated phone system to answer questions from home.
• be asked personal questions.

Slide 91

During research clinic visits, you will …
• take a walking test.
• have your height, weight, waist, hips and blood pressure measured.
• have blood drawn.
• have a rectal exam (at Month 3 and 12).
• be asked questions about physical ability, sexual interest, your memory and energy level.
Slide 92

You will be monitored for changes in …

• your prostate size and PSA.
• your red blood count.
• how you urinate.
• how you sleep.
• other medical conditions that are new to you, and changes in those that you have known about.

Slide 93

• There may be risks involved in taking testosterone that are not known.
• If you start the study and then decide to leave, it will not have an affect on your health care.
• If you have concerns about your rights as a research participant, you may contact the investigator, research staff, and the office of regulatory affairs or research administration.

Slide 94

If you have questions or concerns…

Please discuss them with someone from the research team.

You may want to discuss this research study with your spouse or significant other as well as with your doctor.

Slide 95

Comments?

We appreciate your feedback!
If you would like to make comments about the tutorial, please do so by clicking the box on the right.
Slide 96

Conclusion

Thank you for using this program and for considering participating in this research study.

Slide 97

Administrative Section

Tutorial management toolkit -
- View Check Your Understanding output.
- View Comments.
- View audit trail.
- Check version control.

Slide 98

Sample Output –
Check Your Understanding

<table>
<thead>
<tr>
<th>Module</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Participating in the Trial</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>4 Testosterone Trials in 1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tests and Procedures</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Risks and Benefits</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>More Important Information</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Comments</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

N.A. = Not applicable
INFORMED CONSENT DOCUMENT
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: The Testosterone Trial

Main Study Consent Form

P.I. Name and Department
Co-P.I. Name(s)
Telephone Numbers(s), 24-Hour Emergency Number
IRB # of Protocol
Sponsor: National Institute on Aging

Invitation to Participate

You are being invited to take part in a research study. The Testosterone Trial is a research study in men over the age of 65 who have a low blood level of the main male hormone, testosterone. This research study is being done to see if taking testosterone for one year will improve walking, sexual function, memory, and energy.

This is a consent form. The information in this consent form will tell you about what will happen during the study and the possible risks and benefits, so that you can decide whether or not to participate. The form also includes other important information about the research study, including the health information we will collect. Please read this form carefully before deciding whether you want to take part. If there is anything you do not understand, please ask questions.

Participation in this research study is voluntary. You do not have to take part in this study if you do not want to. If you do take part, you can leave at any time.

The National Institute on Aging (NIA) of the National Institutes of Health (NIH) and Solvay Pharmaceuticals are providing most of the funding for this study. This study will be conducted at 18 sites in the United States. The University of Pennsylvania, Philadelphia, PA, will manage the study.

It is expected that 1200 men will take part in this study. Each man’s participation will last two years.

Why am I being asked to take part in this study?

You are being invited to take part in this study because you are 65 years of age or older and have complaints or symptoms that might be related to a low testosterone level. Testosterone is a hormone produced by the testes and is responsible for the development of normal male muscles, bone strength, energy level, and sexual function. In many men the amount testosterone in their blood gradually decreases with age.
Some research suggests that this fall in testosterone might cause some of the unwanted effects of aging.

**What is the purpose of this research study?**

The main purpose of this research study is to determine if taking testosterone improves walking, sexual function, memory, and energy levels of men with low testosterone. Other purposes are to find out if testosterone treatment improves the ability to perform daily activities, improves mood and lowers the tendency to fall.

**How long will I be in this research study?**

If you qualify, you will take part in the study for 2 years. During the first year you will receive treatment with testosterone or with a placebo, which looks like medication but does not have the active ingredient in it. Also during the first year you will come to the research clinic for seven visits for different types of testing, and you will also answer questions from home by telephone. During the second year you will come to the research clinic once and answer questions by telephone once.

**What is involved in this research study?**

The first step is to find out if you qualify to take part in the study. You will be eligible if your blood testosterone is low, if you have a problem that could be caused by low testosterone, and if you do not have a problem that testosterone treatment could make worse. If you qualify for one or more of the four separate studies (called trials) that are part of this study, you will take part in the trials that you choose. The four trials are called:

- Physical Function Trial
- Sexual Function Trial
- Cognitive Function Trial
- Vitality Trial

You will be treated for one year. During this year you will be tested for the possible desirable and undesirable effects of testosterone. During the year after treatment, you will be followed to make sure that your general health remains good. The following sections describe the clinic visits, tests and procedures in this study.

**Eligibility**

The test results from Screening Visits 1 and 2 show that you qualify for one or more of the four separate trials. If you agree to participate, you will move to the next step and take a few more tests at the Baseline Visit at the research clinic.

**Study Treatment Assignment**

If you agree to participate, you will be assigned to one of two treatment groups. One group will receive testosterone in a gel which is applied to the skin every day. The other group will receive a matching placebo gel, which does not contain testosterone. (The 2 gels will appear the same, but one will have testosterone in it and the other will not.)
You will be assigned to a treatment group by a computer program. Neither you, the study doctors, nor the study staff will know if you are assigned to the group that is treated with testosterone or the group that is treated with the placebo.

**How Will I Take the Treatment**
Testosterone gel and placebo gel both come in an upright tube with a pump on top. The gel is applied once a day. You will push down on the pump with one hand and will catch the gel (which is a combination of alcohol and water) in the palm of the other hand. Both gels look, feel and smell the same. You will then spread the gel on the skin of your abdomen, chest or upper arm. After letting the gel dry, which usually takes about 2-3 minutes, you should wash your hands. You must cover the area where the gel is applied, because it is very important to keep the testosterone from touching anyone else. This is especially important for women or children, who might develop male features, such as facial hair, if they were exposed to testosterone.

**The Four Trials**
If you are eligible for more than one trial, you may choose to participate in only one trial or as many trials for which you qualify and are interested in. Some tests will be given to all participants in the study. Other tests will be given only to those who take part in a particular trial. The following is an explanation of the tests used in each of the four trials.

1. **Physical Function Trial:** We will measure how far you can walk in a certain period of time. Another test is a measure of stair climbing. There are also questions about daily physical function.

2. **Sexual Function Trial:** The tests in this trial will be questionnaires about your ability to have sex and erections. One of them you will answer from home by telephone, and the others you will complete at the research clinic.

3. **Cognitive Function Trial:** The tests in this trial will be about your memory, such as how well you can remember a paragraph that is read aloud to you by someone and how well you can remember designs and drawings.

4. **Vitality Trial:** The test in this trial will be a questionnaire about your energy level that you will answer from home by telephone. Other tests will be questionnaires about mood and emotional state that will be done at the research clinic.

**Description of Tests and Procedures**
The list below describes each test and procedure that will be done during the course of the study. The tests are grouped by those everyone will have, followed by tests that are only for those taking part in a specific trial.

**Interactive Voice Response (IVR)**
Some of the tests involve questionnaires. Some of the questionnaires you will answer with paper and pencil at the research clinic, and others you will answer from home using a computer-based telephone system called IVR. For IVR, recorded messages will guide you through the questions. You will answer the questions using the phone.
number pad. Your answers will be kept in a secure computer file by a code number that cannot be traced back to your name or other private information.

**Tests for Everyone in All Trials**

Most of the tests and procedures will happen every 3 months when you come to the research clinic. The table on the last page shows what will happen each time you come to the research clinic and when we call you on the phone between visits.

**Blood Draw**

Blood will be taken once a month for the first 3 months and then every 3 months. Testosterone will be measured each time. Prostate-specific antigen (PSA), a blood test for prostate cancer, will be measured at baseline, 3 and 12 months. Hemoglobin (a test for red blood cells) will be measured every three months.

**Physical Measurements**

We will measure your height, weight, waist, hips and blood pressure.

**Rectal Exam**

This exam involves putting a gloved finger in the rectum, to feel for hardness or lumps in the prostate. It will be done at the 3 and 12 month visits.

**Walking Test**

You will be asked to walk for 6 minutes down a corridor at a normal pace. The distance you walk and how fast you walk will be measured.

**Your Medicine**

You will be asked to bring all of the medicines (prescription, over-the-counter and herbal or supplements) you are taking to the research clinic at each visit. We will also ask about medicines during monthly phone calls.

**Health Problems and Changes**

You will be asked to describe new health problems that may have happened or changes to conditions that you already have at each visit and phone call.

**Urination Questions**

You will be asked a few questions about problems with passing urine.

**Activities of Daily Living**

You will be asked about difficulties in general activities of daily living, such as bathing or making lunch, as well during the previous month.

**Falls**

You will be asked if you have experienced a fall during the previous 3 months.
**General Memory Test**
You will be asked questions that test your memory and thinking at baseline and at 12 months.

**Memory Questions**
You will be asked 6 questions about your memory compared to when you were younger. This test will be done at this screening visit in everyone and after 12 months in those participating in the Cognitive Function Trial. This test will take less than 5 minutes.

**Memory for Words**
Two paragraphs will be read aloud to you by someone and you will be asked what you remember. This test will be done every 6 months.

**Sex Diary**
You will be asked 6 questions about your sexual activity and feelings using the IVR phone system. This test will be done once a day for 7 days and repeated every 3 months.

**Depression Questions**
You will be asked several questions about whether you feel depressed. You will use the IVR phone system to answer these questions.

**Good and Bad Mood Questions**
You will be asked questions that are about your mood. You will use the IVR phone system to answer these questions.

**Tiredness Questions**
You will be asked questions about your energy level and tiredness. You will use the IVR phone system to answer these questions.

**Change in the Way You Feel**
You will be asked to compare how you feel now to how you felt at the start of the study.

**Tests for Participants in the Physical Function Trial Only- given every 3 months**

**Stair Climbing Test**
You will be asked to climb a standard (12-step) staircase at your normal pace.

**Physical Function Questions**
You will be asked questions about how you can move and your physical abilities.
Tests for Participants in Sexual Function Trial Only- given every 3 months

Erection Questions
You will be asked questions about your ability to have erections and sex.

Function Questions
You will be asked questions about your sexual thoughts and activities.

Tests for Participants in the Cognitive Function Trial Only- given every 6 months

Memory for Designs Test
You will be asked to remember designs that you have been shown from memory.

Memory for Drawings Test
You will be asked to pick out a drawing that you are shown from a set of many other drawings.

Connect the Dots Test
You will be asked to connect lines between numbered and lettered points on a page.

Tests for Participants in the Vitality Trial Only- given every 3 months

Quality of Life Questions
You will be asked how you feel about your quality of life in several areas. This test has 11 questions. This test will be done using the IVR phone system.

Different Moods Questions
You will be asked about your mood and feelings of anger from a list of words that describe different ways that you might feel. This test will be done using the IVR phone system.

Study Schedule
The chart below shows the schedule of tests during the time that you are in the study. In the 1st year there are 7 research site visits and 6 phone contacts. In the 2nd year there is 1 research site visit and 1 phone contact.

<table>
<thead>
<tr>
<th>Study Phase</th>
<th>Treatment Phase (1 Year)</th>
<th>Post-treatment Phase (1 Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monthly Clinic Visits or Phone Contacts</td>
<td></td>
</tr>
<tr>
<td>Visits</td>
<td>M 1 M 2 M 3 M 4 M 5 M 6 M 7 M 8 M 9 M 10 M 11 M 12 M 18 M 24</td>
<td></td>
</tr>
<tr>
<td>Contact Type</td>
<td>C C C P P C P P C P P C C P</td>
<td></td>
</tr>
<tr>
<td>Base line</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

C = Clinic visit in person; P = phone contact

V1.20080627
The research clinic visits and phone calls, and the tests and questionnaires that will be done are listed below.

**Baseline Visit**

For everyone:

- Blood draw (2 tablespoons)
- Measurements of height, weight, waist, hip, blood pressure
- Rectal exam
- Walking test
- Medicines you are taking
- Health problems and changes
- Questionnaires at the research clinic about urinating, daily activities, falls, memory and mental sharpness
- Questionnaires at home using IVR phone system about interest in sex, depression, moods, tiredness and mental sharpness

For men in specific trials:

- Physical Function Trial: stair climbing test and physical abilities questionnaire
- Sexual Function Trial: questionnaires at the research clinic about erections and sexual function and questionnaires at home using IVR phone system about sexual thoughts and interest
- Cognitive Function Trial: questionnaires at the research clinic about memory for designs and drawings
- Vitality Trial: questionnaires at home using IVR phone system about moods and feelings about your quality of life

At the baseline visit you will be given the study gel and you will be shown how to use it. This visit will take 3 – 4 hours.

**Months 1 and 2 Visits**

At these visits you will be asked about the following:

- Blood draw (1 tablespoon) for testosterone level only
- Medicines you are taking
- Health problems and changes

You will be asked to bring your used study gel container with you to these visits and we will review the instructions for gel use. These visits will take about 30 minutes.

**Month 3 Visit**

You will be asked to bring your used study gel container with you to this visit and we will review the instructions for gel use. We will do the following tests and questionnaires with you:
All Participants

- Blood draw (2 tablespoons) for testosterone level, PSA, hemoglobin and hematocrit
- Measurements of height, weight, waist, hip, blood pressure
- Rectal exam
- Walking test
- Medicines you are taking
- Health problems and changes
- Questionnaires at the research clinic about urinating, daily activities, falls, memory and mental sharpness
- Questionnaires at home using IVR phone system about interest in sex, depression, moods, tiredness and mental sharpness

For men in specific trials:

- Physical Function Trial: stair climbing test and physical abilities questionnaire
- Sexual Function Trial: questionnaires at the research clinic about your erections and sexual function and questionnaires at home using IVR phone system about your sexual thoughts and interest
- Vitality Trial: questionnaires at home using IVR phone system about your moods and feelings about your quality of life

This visit will take 2 1/2 – 3 1/2 hours.

Months 4 & 5 Phone Contact
You will be contacted by telephone for these visits. The following assessments will occur for all subjects:

- Medicines you are taking
- Health problems and changes
- Review of instructions for using the study gel

These calls will take approximately 15 minutes.

Month 6 Visit
You will be asked to bring your used study gel container with you and review the instructions for gel use. We will do the following tests and questionnaires with you:

All participants:

- Blood draw (2 tablespoons) for testosterone level, hemoglobin and hematocrit
- Measurements of height, weight, waist, hip, blood pressure
- Walking test
- Medicines you are taking
- Health problems and changes
- Questionnaires at the research clinic about urinating, daily activities, falls, memory and mental sharpness
- Questionnaires at home using IVR phone system about interest in sex, depression, moods, tiredness and mental sharpness

**For men in specific trials:**
- Physical Function Trial: stair climbing test and physical abilities questionnaire
- Sexual Function Trial: questionnaires at the research clinic about erections and sexual function and questionnaires at home using IVR phone system about your sexual thoughts and interest
- Cognitive Function Trial: questionnaires at the research clinic about your memory for designs and drawings
- Vitality Trial: questionnaires at home using IVR phone system about your moods and feelings about your quality of life

This visit will take 3 – 4 hours.

**Months 7 & 8 Phone Contact**
You will be contacted by telephone for these visits. The following assessments will occur in all participants:

- Medicines you are taking
- Health problems and changes
- Review of instructions for using the study gel

These phone calls will take approximately 15 minutes.

**Month 9 Visit**
You will be asked to bring your used study gel container with you to this visit and we will review the instructions for gel use. We will do the following tests and questionnaires with you:

**All participants:**
- Blood draw (2 tablespoons) for T level, hemoglobin and hematocrit
- Measurements of height, weight, waist, hip, blood pressure
- Walking test
- Medicines you are taking
- Health problems and changes
- Questionnaires at the research clinic about urinating, daily activities, falls, memory and mental sharpness
- Questionnaires at home using IVR phone system about interest in sex, depression, moods, tiredness and mental sharpness

**For men in specific trials:**
- Physical Function Trial: stair climbing test and physical abilities questionnaire
- Sexual Function Trial: questionnaires at the research clinic about your erections and sexual function and questionnaires at home using IVR phone system about your sexual thoughts and interest
- Vitality Trial: questionnaires at home using IVR phone system about your moods and feelings about your quality of life

This visit will take 2 1/2 – 3 1/2 hours.

**Months 10 & 11 Phone Contact**
You will be contacted by telephone for these visits. The following assessments will occur for all participants:

- Current medicines
- Health problems and changes
- Review the instructions for using the study gel

These phone calls will take approximately 15 minutes.

**Month 12 – End of Treatment Visit**
This is the last visit of the treatment phase. You will be asked to bring your used study gel container with you to this visit. We will do the following tests and questionnaires with you:

**All participants:**

- Blood draw (2 tablespoons) for testosterone level, PSA, hemoglobin and hematocrit
- Measurements of height, weight, waist, hip, blood pressure
- Rectal exam
- Walking test
- Medicines you are taking
- Health problems and changes
- Questionnaires at the research clinic about urinating, daily activities, falls, memory and mental sharpness
- Questionnaires at home using IVR phone system about interest in sex, depression, moods, tiredness and mental sharpness

**For men in specific trials:**

- Physical Function Trial: stair climbing test and physical abilities questionnaire
- Sexual Function Trial: questionnaires at the research clinic about erections and sexual function and questionnaires at home using IVR phone system about sexual thoughts and interest
- Cognitive Function Trial: questionnaires at the research clinic about your memory for designs and drawings
- Vitality Trial: questionnaires at home using IVR phone system about your moods and feelings about your quality of life

This visit will take 3 – 4 hours.

**Months 18 Assessment**
The follow-up visit at Month 18 may be held at the research clinic or at home.
- Blood draw (1 tablespoon) for PSA
- Health problems and changes

**Months 24 Assessment**
The follow-up visit at Month 24 will be by phone to ask about health problems and changes.

**What are the risks of taking part in this research study?**

**Risks of testosterone treatment**

Because testosterone might make certain conditions worse, if you take part in this study you will be tested before and during treatment to check for these conditions and to try to reduce the risk to your health. These are the conditions that testosterone might make worse.

Prostate cancer. About half of men over age 65 have tiny areas of cancer in their prostate glands that appears not to hurt them. The worry is that testosterone treatment in this study could change these harmless tiny prostate cancers into harmful ones. When testosterone was given in previous studies to older men, there was not an increase in prostate cancer, but there is not enough research about older men using testosterone to know for certain how it will affect the chance of prostate cancer. Also, some men who have prostate cancer have an improvement in the cancer if their blood testosterone is lowered.

Men who have had prostate cancer or a pre-cancerous condition called PIN (prostate intra-epithelial neoplasia) will not be in the study. To reduce the chance that men who are in this study could have a worsening of an unknown cancer, only men who have a less than a 30% chance of any prostate cancer and less than a 7% chance of an aggressive prostate cancer will be allowed to be in the study. These possibilities will be figured out by using a combination of blood PSA results, age, race, family history of prostate cancer, absence of a prostate lump, and any results of a prior prostate biopsy, (sticking a needle into the prostate to get a sample to look at under the microscope) if one was done. Also, only men who do not have a prostate lump or hardness on the rectal examination will be in the study, unless a previous biopsy shows that the lump is not cancer.

If your rectal exam does not show a lump, your estimated risk of any prostate cancer is about _____% and of aggressive (called high grade) prostate cancer is about _____%. To check men in this study, we will repeat the blood PSA test at 3 and 12 months of treatment and again 6 months after stopping treatment. If the blood PSA level increases by a certain amount, and the same result is found when we measure it again, we will recommend that you see a urologist to discuss whether you should have a prostate biopsy. At that time, the urologist will go over with you the risk of having a prostate cancer compared to the problems of treatment for prostate cancer if one is found.
Enlarged prostate (Benign prostatic hyperplasia/BPH). Testosterone treatment of older men might also increase the size of the prostate and cause a decrease in urine flow. Other studies of testosterone treatment have not shown worsening of urination problems, but the number of men studied so far is too small to know for sure. To reduce the chance of urination problems in this study, only men who do not have a lot of difficulty urinating will be eligible. This will be known by the score on the urination questionnaire. These questions will be asked again at 3 and 12 months. If the score goes up by 5 or more points, that will lead to us check for the cause of this problem.

High red blood cell count (Erythrocytosis). Testosterone normally increases the number of red blood cells, which is why men have higher red blood cell counts than women. However, if a man had a high red blood cell count when his testosterone was low, increasing the blood testosterone could increase his red blood cell count to higher than normal. This might increase the chance of a stroke. For this reason, only men with blood hemoglobin levels (a measure of red blood cells) below a certain value will be allowed to be in the study. In addition, the hemoglobin levels will be checked again at 3, 6, and 12 months. An increase above normal will lead us to send you to another doctor to find out the cause of the increase. If no cause is found, the amount of gel that you use will be reduced. If the hemoglobin value does not go back to normal within one month, treatment will be stopped.

Sleep apnea. Testosterone may increase the risk of sleep apnea, a condition in which not enough oxygen gets into the blood during sleep, resulting in excessive sleepiness during the day. Although it is not certain that testosterone has this effect, men who have been diagnosed with sleep apnea will be eligible only if they are being treated for it.

Procedure Risks

Physical Function Tests. There is a risk that you may find the Walking Test or the Stair Climbing Test tiring or too hard to finish. Trained personnel will be there to check how you are during these tests. You may stop the test if you need to rest. You may also stop to rest if you become tired because of the number of tests.

Blood Draw. Getting your blood drawn at the research clinic has a very small risk of temporary mild pain, bruising or infection at the place where the needle was stuck in the blood vessel. There is also the possibility of fainting because of anxiety or fear of needles. These risks are decreased by the use of trained people to draw your blood.

Questionnaires. Because some of the questionnaires are personal, some men may feel uncomfortable answering these questions. The most personal questions will be asked over the phone IVR system while you are at home so that you will have privacy. Your answers will not be shared with anyone. All information that is collected will be considered private and only identified by a study code number.

Memory Tests. Testing of your memory may be stressful and tiring because they require you to think hard sometimes. We just want you to try your best. There are no
passing or failing grades on these tests, and you should not practice taking these tests at home to do better.

**Testosterone Gel.** If testosterone gets transferred from your skin to a woman’s or a child’s skin, she or he could develop male features. Transfer can be avoided by washing your hands. It is also important to allow the gel to dry thoroughly after applying it, and to keep the area where the gel was applied covered. The gel contains alcohol and in some men may cause dry skin or skin irritation.

**Prostate Biopsy.** If a prostate biopsy is needed, it has two main risks, which are bleeding and infection. The standard safety measure to lower the chance of bleeding is to avoid medicines that thin your blood and prevent it from clotting normally, like aspirin, anti-inflammatory medicines (such as ibuprofen), and herbal supplements, before and after the procedure. The standard safety measure to lower the chance of infection is to give antibiotics. If you have a prostate biopsy, your doctor will give you complete instructions about taking antibiotics. By using these safety measures, the chance of bleeding or serious infection requiring hospitalization is less than 1%.

**Unknown risks.** There is also a chance of a side effect that is not known at this time.

**Are there any benefits to taking part in this research study?**
You may not get any benefit from participating in this study. You may feel better or stronger, or you may not. Your health status will be checked frequently during the time that you are in the study. By taking part in this study you may improve our understanding of testosterone treatment.

**What happens if I decide not to take part in this research study?**
You are free to decide whether or not to be in this study. Your care at this institution will not change if you choose not to be in this study or if you choose to withdraw from the study anytime after you start.

**How long will I be in the study? What if I want to leave the research study after I begin?**
You will be in the study for 2 years. You are free to leave the study at any time. Dropping out of the study will not interfere with your future care.

**Will confidential health information be collected as part of this study?**
Some private information about your health will be collected. There are forms that ask questions about your medical history, physical function as well as sexual function, memory and how you think, and your energy level and quality of life. Every attempt will be made to keep all information collected in this study strictly private. Authorized representatives of [Insert Institution], the University of Pennsylvania, and the National Institutes of Health may review and copy information collected from this study and your medical records. If any articles are published from the results of this research, you will not be identified by name.
**What happens to the health information if you want to leave the study?**

If you leave from study, no additional information will be collected. Information that has already been collected and are part of the study will remain. You may ask that your stored blood samples be destroyed by writing a request to the Principal Investigator of the study.

**What will you do with the blood you collect?**

Blood that is left over after measuring the testosterone, PSA and other tests will be stored at the Mayo Clinical Trial Services Central Laboratory. It may be used for future studies of the effects of testosterone. Information that identifies the blood as yours will be removed, so that the only connection of the blood to your study results will be a study code number, which you will be given at the time of you consent to be in the study. The blood will be stored through the end of the study, up to 5 years or more. It may be used at any time during that period for other studies of testosterone effects. It is possible that new tests might be available in the future, which could be useful in understanding testosterone. You will not be able to find out the results of these tests.

Researchers who plan to use your blood sample for future research studies will ask permission from the National Institutes of Health and the investigators of this study before using your sample. Samples will be released only to scientists who are qualified and prepared to conduct a research study.

**What will it cost me to take part in this study?**

It will not cost you anything to be in the study. You will be contributing your time and energy.

**Will I be paid for taking part in this research study?**

You will be paid a small amount, which will be given to you as you complete study visits. If you complete the entire study, the total amount will be $750. In addition, you will be reimbursed for travel expenses and parking and you will be provided meal tickets during the study visits.

{This section can be customized per site.}

**What happens if I am injured during the study?**

In the event of a research-related injury, please contact your study doctor right away at the phone numbers provided on the front page of this form.

In the event of any physical injury resulting from the research procedures, medical treatment will be provided without cost to you, but financial compensation is not otherwise available from {Customize this section in accordance with institutional policy.}

You or your insurance company, if any, may be billed for medical expenses associated with this study only if they are believed to be medically necessary and not related to the study. {Customize this section in accordance with institutional policy.}
What if I have questions about the study?
If you have questions, concerns or complaints about being in this research study, or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the {Institutional Office of Regulatory Affairs} with any question, concerns or complaints at Your Institution by calling {XXX)YYY-ZZZZ}. 
SIGNATURE PAGE

I have had this research study explained to me. I have read the informed consent form. I have had the chance to ask questions. My questions have been answered to my satisfaction.

I understand that my signature below means that I voluntarily agree to take part in the research study. I will be given a copy of this form for my records.

Printed Name ______________________________ Signature of Subject ______________________________ Date ______________
(Or Legally Authorized Representative – note relationship to subject)

Printed Name ______________________________ Signature of Witness ______________________________ Date ______________
(Only required if the subject cannot read this consent form)

I have discussed this clinical study with the subject and/or his authorized representative, using language that is understandable and appropriate. I believe that I have fully informed the subject of the nature of this study and its possible benefits and risks.

Printed Name ______________________________ Signature of Person Obtaining Consent ______________________________ Date ______________

SEPARATE SIGNATURE REQUIREMENTS FOR OPTIONAL GENETIC SAMPLE

We are also interested in collecting blood samples to store for future genetic studies. Details of the genetic sub-study are described in the attached genetic consent form. You are not required to take part in this portion of the study in order to be in the main part of the research study.

Please indicate your interest in participating below:

______________ Yes, I would like to know more about the genetic sub-study. If I decide to take part in the sub-study, I will sign a separate consent form.

Please Initial

______________ No, I do not want to participate in the genetic sub-study.

Please Initial
# Study Schedule

## Test or Procedure in All Participants

<table>
<thead>
<tr>
<th></th>
<th>Screen 2</th>
<th>Base-line</th>
<th>M 1 &amp; M 2</th>
<th>M 3</th>
<th>M 4 &amp; M 5</th>
<th>M 6</th>
<th>M 7 &amp; M 8</th>
<th>M 9</th>
<th>M 10 &amp; M 11</th>
<th>M 12</th>
<th>M18</th>
<th>M24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed consent</td>
<td></td>
<td></td>
<td></td>
<td>C</td>
<td>C</td>
<td>P</td>
<td>C</td>
<td>P</td>
<td>C</td>
<td>C</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Blood draw</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your medicine</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health problems &amp; changes</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gel instruction and review</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height, weight, waist, hip, blood pressure</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal exam</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urination questions</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking Test</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short memory test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex Diary – Question 4*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory for words</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tiredness questions</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in the way you feel</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activities of daily living</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Falls</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression questions</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood questions*</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint pain and stiffness questions</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual function questions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervousness and worry questions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory questions</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Word knowledge test ‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

## Tests in Participants in Specific Trials:

### Physical
- Physical Function Questionnaire-10, Stair climb
  - x

### Sexual
- Sex Diary* (complete), Erection questions, Sexual function questions
  - x

### Cognitive
- Memory of designs, drawings, connect the dots, general memory†
  - x

### Vitality
- Quality of life questions*, Different mood questions*
  - x

(Key: * administered by IVR, † 0 and 12 mos, ‡ 0 mo only)
# Title

**Development of an Informed Consent Multimedia Tool for Research**

## Introduction - Proposed Use

This multimedia tool is being developed to accompany the informed consent document of a clinical trial in a geriatric population. Its purpose is to enhance the informed consent process by presenting the information in the informed consent document in a series of brief, focused teaching modules. These modules will include video and audio technology to guide the user through the module. Each module will conclude with a review section called “Check Your Understanding” that asks the user to answer questions about the information that have just seen and heard. A summary of these responses will be made available to the research team presenting the informed consent document to provide a basis for review and clarification of the information presented in the module.

## Audience

The users of this multimedia tool will be the potential participants of the Testosterone Trial, a clinical trial of testosterone efficacy in men aged 65 and older.

## Resources

Funding for development of this tool will be sought from the research study sponsor. Research technology expertise will be contracted through the web services development department in the University of Pennsylvania School of Medicine.

## Personnel

Content will be developed by a collaborative team of the following:

- **Denise Cifelli**, Project Director. Ms. Cifelli, Director of Project Operations and Compliance in the Clinical Research Computing Unit, has led the project development effort from the proposal phase and will continue to direct the project into the implementation phase. She has developed the study protocol, informed consent documents, regulatory documentation and associated monitoring and quality assurance plans.

- **Peter J. Snyder**, MD. Principal Investigator of the Testosterone Trial. Dr. Snyder is an endocrinologist at the University of Pennsylvania, School of Medicine and has conducted testosterone clinical research for over 30 years. He will serve as the subject matter expert for the content presented in the tutorial.

- **Gregg Fromell**, MD, Director, Office of Human Research, University of Pennsylvania, School of Medicine. Dr. Fromell provides expertise on research education and training, research compliance and quality improvement. He will serve as the subject matter expert on the essential elements of informed consent, readability and format of the material.

- **Barry Dornfeld**, PhD. Educational Media Consultant. Dr. Dornfeld of the Center for Applied Research (CFAR) provides expertise in development of content and organization of biomedical knowledge and serves as a reviewer of the multimedia tool.
### Content Development

The content of the tutorial will parallel the information written in the informed consent document. Subject matter experts will review the tutorial for accuracy regarding the testosterone trial (Snyder), the essential elements of informed consent (Fromell) and overall tone, sequencing, cohesion and clarity (Dornfeld).

The tutorial has been developed as a Powerpoint presentation. See Appendix A. This presentation will serve as the template for the development of the tool as a teaching module available from a secure server as well as a portable program.

### Availability of Technology

The tutorial will be developed for use by participants who may access it from a web site on a secure server (hosted at the University of Pennsylvania Biomedical Research Computing environment) on the internet. This will be made available via a computer in a private location at the research clinic to serve those participants who are willing to read the informed consent and participate in the informed consent process during the baseline clinical research visit.

The program must also be available on transportable media (DVD) so that a participant may take the DVD home to read the informed consent document and complete the accompanying tutorial in the privacy of their home, using a standard desk top computer. The requirements for the desk top computer must be of the type that are available on most recent model computer systems and not require “plug-ins” or files that must be downloaded in order to run the tutorial.

### Technology Features

The tutorial must include the following features:

1. **Advance organizer.** The first slide of the tutorial will instruct the user about the features of the tutorial described below. Audio will accompany this first slide as the mouse moves automatically over the features and tags appear to indicate the alternative keystroke that will perform the same function as the mouse. The second slide of the tutorial will describe the Check Your Understanding slides and features using the same audio and video technology.

2. **Table of Contents.** Each segment of the module must be listed separately in a vertical table of contents so that it can be selected by one click of the mouse or keyboard stroke and begin at the first slide of that segment.

3. **Video streams must be sharp and clear.** An indicator will appear over the video file and a tag will instruct the user to click the arrow to play the video.

4. **Volume adjustment keys with mouse-over tag to describe the function.**

5. **Slide navigation keys to return to the previous slide or advance to the next slide.**

6. **Repeat slide key.**

7. **Slide counter to indicate slide number of total slides.** (Example: Slide 3 of 10).

---

Dated April 4, 2008
8. Quit program key. This will allow the user to stop the tutorial and save their responses so that they can resume later and continue from that point.

9. Check Your Understanding features will include the ability to click in a response check box and receive immediate reply indicating if response is correct or incorrect and accompanying information. (See Comment boxes on these slides as an example.)

10. Responses to Check Your Understanding questions will be saved in a data table that can be generated as a report at the end of the program by the participant (if using the program at home) or by the person administering the tutorial (if the process is occurring at the research clinic.) This table should include complete information (the entire question, answers and explanations) be viewable and printable so that it may be used to discuss the informed consent issues that require clarity.

11. The program must allow the user to pause or quit the program and resume where he left off, saving the responses completed to that point.

### Additional Requirements

The tutorial will be provided to the software developer and programmer as a power point presentation. Video images and video streams will be provided and incorporated into the tutorial as indicated in the .ppt file. The project director will have final approval over the selection of the audio portion of the program. (The audio portion must be a male voice.) The functionality (described above) will be pilot tested by the project director before final implementation.

### Terms

To be determined.

### Timeline

To be developed.

### Contact Information

Denise Cifelli
cifelli@mail.med.upenn.edu
Phone 215-573-4534

Dated April 4, 2008
INTERVIEW QUESTIONS FOR POTENTIAL TESTOSTERONE TRIAL PARTICIPANTS (MEN 65 OR OLDER)

EVALUATION OF INFORMED CONSENT DOCUMENT INTERVIEW SCRIPT

Dated: February 9, 2008

Interviewer: I would like to ask your opinion about several things that have to do with a research study that is being planned at several medical centers in the US. It is about the use of testosterone in men aged 65 or older.

Testosterone is not a new drug. It has been available for a few years and doctors can prescribe it. Doctors are conducting this study to try to find out if using testosterone (it is often called “T”) leads to improved physical performance (for example: ability to walk, climb stairs, carry groceries), increased interest in sex, improved memory and improved overall sense of energy and zest for life.

Before starting in the study there would be a few tests that must be done to check your testosterone level and other blood tests, as well as questionnaires that you will be asked to complete. For now, I would like to ask you 15 questions about the research consent form that I will give you to read.

Interviewee initials: ___ ___ ___

1. Are you willing to participate in this interview? ....................................... Yes   No

2. Age __________ years

3. Level of education:
   □ 1 6th grade or less
   □ 2 7th to 12th grade, no high school diploma
   □ 3 High school graduate or equivalent (e.g. GED)
   □ 4 Technical or vocational school degree
   □ 5 Some college education, but not completed degree
   □ 6 College graduate
   □ 7 Professional or graduate degree (e.g. Master’s, PhD, JD, MD)

Directions: I am going to give you several pages to read. It is an informed consent document that describes the research study. Please take your time and read it and let me know when you are finished.

4. On the line below, please rate how easy or difficult it was for you to read the informed consent document.

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very easy</td>
<td>Easy</td>
<td>Somewhat easy</td>
<td>Moderate</td>
<td>Somewhat difficult</td>
<td>Difficult</td>
<td>Very difficult</td>
</tr>
</tbody>
</table>

Comments: ____________________________________________
5. After reading this document, do you understand that you could be in 1, 2, 3 or 4 separate trials depending on the information you give when asked about your physical abilities, sexual interest, memory or energy? ......................... Yes  No

Comments: _________________________________________________________

6. A. Do you understand the explanation about the testosterone gel and placebo (gel without medication) used in this study? .................................................. Yes  No
B. Do you understand that you will not know which gel you are using and that the study doctors, nurses or other study staff members will not know either? .... ................................................................. Yes  No

Comments: _________________________________________________________

7. Do you understand the explanation about using the gel every day for a year and the steps that you should take to be sure that you use it safely? ........ Yes  No

Comments: _________________________________________________________

8. Do you understand the commitment that is being asked of you to in coming to the research site for tests and questionnaires 6 times over the first year and once during the second year?................................................................. Yes  No

Comments: _________________________________________________________

9. A. Do you understand what the IVR phone system is used for? .......... Yes  No
B. What do you think of using your home phone (or cell phone) to answer private questions?

Comments: _________________________________________________________

10. Do you think you will be able to answer personal questions about your physical abilities, sexual life, memory and energy with the people at the research site?... ................................................................. Yes  No

Comments: _________________________________________________________

11. A. Do you understand the risks of being in this study? ......................... Yes  No
B. Do you have concerns about the risks of taking testosterone? ....... Yes  No

Comments: _________________________________________________________

12. A. Do you think being in this study is the kind of thing that you would be interested in doing? ................................................................. Yes  No
B. Would you be willing to talk about it with your spouse, partner, family or friends?................................................................. Yes  No

Comments: _________________________________________________________

13. Do you think it would be helpful to discuss this study with your own doctor? ...... ................................................................. Yes  No

Comments: _________________________________________________________

20080410
14. A. If the information in the consent form were given to you on a CD, would you be able to use a home computer or DVD player to view it?
   i. Computer? ................................................................. Yes  No
   ii DVD player? ................................................................. Yes  No

   B. If you were given a link to a website, would you feel comfortable reading this on the Internet? ................................................................. Yes  No

   Comments: _______________________________________________________

15. Do you have any questions or comments about this informed consent document, the research study or any other topics related to this discussion? ....... Yes  No

   Comments: _______________________________________________________

Thank you very much for your time and for discussing this topic with me!!

Notes:
EVALUATION OF INFORMED CONSENT DOCUMENT
SUMMARY DATA AND COMMENTS

Interview with Potential Subjects about the Testosterone Trial

Dated: April 16, 2008

1. Respondents (n = 8)

<table>
<thead>
<tr>
<th>Initials</th>
<th>Age</th>
<th>Eligible?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ALC</td>
<td>77</td>
<td>No</td>
</tr>
<tr>
<td>2 BLM</td>
<td>67</td>
<td>Yes</td>
</tr>
<tr>
<td>3 PLH</td>
<td>71</td>
<td>No</td>
</tr>
<tr>
<td>4 ABP</td>
<td>65</td>
<td>Yes</td>
</tr>
<tr>
<td>5 LAD</td>
<td>75</td>
<td>Yes</td>
</tr>
<tr>
<td>6 RMC</td>
<td>70</td>
<td>Yes</td>
</tr>
<tr>
<td>7 RSR</td>
<td>80</td>
<td>No</td>
</tr>
<tr>
<td>8 MIK</td>
<td>85</td>
<td>Yes</td>
</tr>
</tbody>
</table>

2. Education

<table>
<thead>
<tr>
<th>Number (Percent)</th>
<th>Level of Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (12.5%)</td>
<td>7th to 12th grade, no high school diploma</td>
</tr>
<tr>
<td>4 (50%)</td>
<td>High school graduate or equivalent (e.g. GED)</td>
</tr>
<tr>
<td>1 (12.5%)</td>
<td>Some college education, but not completed degree</td>
</tr>
<tr>
<td>2 (25%)</td>
<td>College graduate</td>
</tr>
</tbody>
</table>

3. Age Group

<table>
<thead>
<tr>
<th>Range: 65 – 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>65 - 74</td>
</tr>
<tr>
<td>75 - 85</td>
</tr>
</tbody>
</table>
4. Document Readability

<table>
<thead>
<tr>
<th>Number (Percent)</th>
<th>Document Readability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (12.5%)</td>
<td>Very easy</td>
</tr>
<tr>
<td>2 (25%)</td>
<td>Easy</td>
</tr>
<tr>
<td>2 (25%)</td>
<td>Somewhat easy</td>
</tr>
<tr>
<td>2 (25%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>1 (12.5%)</td>
<td>Somewhat difficult</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question Number</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.</td>
<td>Knowledge of 4 separate trials about your physical abilities, sexual</td>
<td>6 (75%)</td>
<td>2 (75%)</td>
</tr>
<tr>
<td></td>
<td>interest, memory or energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 A.</td>
<td>Explanation about the testosterone gel and placebo</td>
<td>8 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>6 B.</td>
<td>Knowledge of treatment or placebo group</td>
<td>7 (87%)</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>7.</td>
<td>Medication use and safety precautions</td>
<td>8 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>8.</td>
<td>Time commitment and trial participation schedule</td>
<td>6 (75%)</td>
<td>2 (75%)</td>
</tr>
<tr>
<td>9.</td>
<td>IVR phone system</td>
<td>6 (75%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>10.</td>
<td>Comfort regarding personal questions about physical abilities, sexual</td>
<td>7 (87%)</td>
<td>1 (13%)</td>
</tr>
<tr>
<td></td>
<td>life, memory and energy with research staff</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 A.</td>
<td>Risks</td>
<td>8 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>11 B.</td>
<td>Specific concerns about testosterone risks</td>
<td>6 (75%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>12 A.</td>
<td>Potential interest</td>
<td>4 (50%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>12 B.</td>
<td>Willingness to discuss with your spouse, partner, family or friends</td>
<td>6 (75%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>13.</td>
<td>Discuss this study with personal physician</td>
<td>8 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>14 A.</td>
<td>Ability to use technology at home – computer</td>
<td>3 (38%)</td>
<td>5 (62%)</td>
</tr>
<tr>
<td>14 B.</td>
<td>Ability to use technology at home – DVD player</td>
<td>4 (50%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>14 C.</td>
<td>Ability to use technology at home – Internet website</td>
<td>2 (25%)</td>
<td>6 (75%)</td>
</tr>
</tbody>
</table>