Subcutaneous vs. Intramuscular Testosterone

Men's Health Boston
200 Boylston Street, A309
Chestnut Hill, MA 02467

SQ vs. IM Protocol

Subcutaneous testosterone therapy in men compared to intramuscular testosterone therapy in men

Author
Abraham Morgentaler, MD
Men's Health Boston

Author
Emily Davidson, BS
Men's Health Boston

Version Date: February 23, 2017

IND No.:	N/A
Protocol No.:	MHB023
Investigators:	Abraham Morgentaler, MD
Sponsor:	Men's Health Boston (Beckman)

Primary Contact Information

For the Sponsor:	Geoff Gleason	Phone:	952-368-2191
	Staff Clinical Studies Scientist	Fax:	952-368-7710
	Beckman Coulter	Email:	ggleason@beckman.com

Sponsor Signature/Document Approval Page

MHB023 – Subcutaneous vs. Intramuscular Testosterone – February 23, 2017

This protocol has been approved by Beckman Coulter, Inc. The following signature documents this approval.

Michael Samoszuk, MD
Vice President and Chief Medical Officer
Beckman Coulter

3/13/2017
Date

Investigator's Agreement

1. I have read this protocol and agree to conduct this trial in accordance with Good Clinical Practice (GCP), all stipulations of the protocol, the Declaration of Helsinki, and applicable regulatory requirements as stated by my human subjects testing oversight body [e.g., independent ethics committee (IEC) or institutional review board (IRB)].

2. I will personally conduct or supervise the described investigation(s). This includes informing all associates, colleagues, and employees assisting in the conduct of the study about their obligations in meeting the above commitments.

3. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

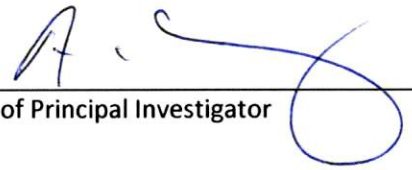
4. I agree that all electronic signatures will be considered the equivalent of a handwritten signature and will be legally binding.

Protocol Title: Subcutaneous vs. Intramuscular Testosterone

Protocol Number: MHB023

Version Number: 1.5

Version Date: February 23, 2017



Signature of Principal Investigator

3/10/17

Date

Abraham Morgentaler, MD

Name of Principal Investigator (printed or typed)

Summary

In this randomized, cross-over study 20 subjects who are undergoing testosterone (T) therapy for the treatment of T deficiency will receive both subcutaneous testosterone therapy and intramuscular testosterone therapy. One group will receive a SQ injection followed by an IM injection and one group will receive an IM injection followed by a SQ injection. The primary objective of this study is to measure testosterone concentration in men after these two treatment routes and determine if there are any significant differences due to modes of administration. Endpoints will include total serum testosterone and calculated free testosterone. A questionnaire will also be administered to assess overall patient experience with each route of administration.

Schedule of activities

	Pre-Enrollment (prior to Day 0)	**Visit 1 Day 0**	**Visit 2 Day 3**	**Visit 3 Day 7**	**Visit 4 Day 14**	**Visit 5 Day 17**	**Visit 6 Day 21**	**End of Study Day 28**
Window	-14 to 0 days	± 0 days	± 2 days	± 2 days	± 2 days	± 2 days	± 2 days	± 2 days
Informed consent	X							
Eligibility assessment[1] • Laboratory testing[2]	SC							
Questionnaires[3]	SC	X			X			X
Testosterone Treatment • Pain rating[4]		SC			SC			
Blood sampling • Beckman Coulter[5]		X	X	X	X	X	X	X
End of study[6]								

[1] Eligibility labs: use the most recent values performed as part of routine clinical care: [1] total testosterone, [2] free testosterone, [3] PSA
[2] Other lab data collected: use the most recent values performed as part of routine clinical care: [1] estradiol, [2] LH, [3] FSH, [4] SHBG, [5] hematocrit
[3] Responses collected for: [1] Low Testosterone Questionnaire | © 2014 Men's Health Boston, [2] International Prostate Symptom Score (IPSS) | American Urological Association
[4] Rating pain after injection on Likert scale
[5] Samples collected for: visits 1, 4, 7: [1] total testosterone, [2] free testosterone, [3] PSA; visits 2, 3, 5, 6: [1] total testosterone, [2] free testosterone, [3] estradiol, [4] LH, [5] FSH, [6] SHBG, [7] hematocrit, [8] PSA
[6] End of study survey – preferred mode of administration

X = Research only
SC = Standard care

Table of contents

List of abbreviations and definitions

AE	Adverse event
IM	Intramuscular mode of administration
SQ	Subcutaneous mode of administration
T	Testosterone
TD	Testosterone deficiency
eCRF	eCase report form
IRB	The institutional review board of record for the study at the participating site

1. Introduction

1.1. Background

Testosterone deficiency (TD) is defined as a clinical syndrome that results from failure of the testis to produce adequate physiological levels of testosterone (T) due to disruption of one or more levels of the hypothalamic-pituitary-testicular axis. TD is characterized by lower than normal concentration of serum testosterone[1]. Reduced T levels in men can cause a variety of symptoms, including decreased libido, erectile dysfunction, decreased volume of ejaculate, loss of body and facial hair, weakness, decreased bone density, decreased lean body mass, increased body fat, and anemia[2].

T deficiency is often treated with testosterone therapy of which various delivery methods are available[3]. Treatment is aimed at inducing and maintaining secondary sex characteristics and improving sexual function, sense of well-being, and bone mineral density[4]. Although testosterone was first synthesized in 1935, treatment options are continually evolving[5].

One standard treatment for TD is intramuscular (IM) injections of exogenous T[6]. However, subcutaneous (SQ) injections may have some advantages compared to IM injections. SQ injections is more convenient and less challenging than IM for men who are candidates for self-injection. SQ also involves a smaller needle and may be less intimidating to patients. This trial will investigate how serum testosterone levels are affected by the route of T administration.

1.2. Rationale and hypothesis

The purpose of this study is to preliminarily determine if the route of delivery of testosterone therapy affects testosterone concentrations in men. Our hypothesis that SQ will provide comparable or acceptable T concentrations as IM, with regard to duration of action and peak or average concentrations.

2. Objectives

2.1. Primary outcome and endpoint (endpoint bulleted below)

The primary objective of this study is to determine how testosterone concentration in men differs based on administration route for T injections in men.

The Primary endpoints are total testosterone concentration and calculated free T concentration following injection, measured by Beckman assays and equipment.

2.2. Secondary outcomes and endpoints (endpoints bulleted below)

The Secondary endpoints are responses to Low Testosterone Questionnaire, International Prostate Symptom Scores, and levels of estradiol, LH, FSH, SHBG, and PSA following injection, measured by Beckman assays and equipment and hematocrit following injection measured by Quest Diagnostics.

3. Study design

In this single-center clinical trial, 20 subjects being treated with testosterone therapy for T deficiency will be randomized to subcutaneous testosterone injection followed by intramuscular testosterone injection or intramuscular testosterone injection followed by subcutaneous testosterone injection. Subjects will be screened for eligibility and subsequently randomized at the baseline visit, then followed for four weeks.

4. Study population

4.1. Inclusion criteria

Each patient must meet all of the following inclusion criteria to be enrolled in the study. For laboratory assessment, use the most recent values performed as part of routine clinical care.

1) Ability to read, write, and understand English
2) Age greater than or equal to 18
3) Diagnosed with testosterone deficiency
4) Pre-enrollment testosterone concentration of less than 350 ng/dL
5) Planning to initiate testosterone treatment at MHB
6) Willing to be followed at MHB for at least one month
7) Willing to provide informed consent for this study

4.2. Exclusion criteria

Patients meeting any of the following exclusion criteria are not to be enrolled in the study. For laboratory assessment, use the most recent values performed as part of routine clinical care.

1) Previous exposure to exogenous T, clomiphene citrate, or other Selective Estrogen Receptor Modulators, unless off therapy for at least 12 weeks
2) American Urological Association Prostate Symptom score of 15 or greater or significant prostatic symptoms
3) History of carcinoma, tumors or induration of the prostate or the male mammary gland, including suspicion thereof
4) Pre-enrollment serum PSA more than 4 ng/ml
5) Serious psychiatric disease or uncontrolled medical illness, as suspected from the history or clinical examination
6) Used any sex hormones or steroidal anabolic drug supplements within 28 days before pre-enrollment testosterone collection or at any time throughout the study
7) Incapable of giving informed consent or complying with the protocol

4.3. Protected populations

Vulnerable populations will not be enrolled in this study.

5. Modes of Administration

During the study, subjects will be assigned to intramuscular injections, followed by subcutaneous injections or subcutaneous injections, followed by intramuscular injections. Subjects will already have been prescribed testosterone treatment at MHB, participation in the study will only alter the route of administration of T. Subjects will be given standard dosage for bi-weekly T injections (200mg).

5.1. Allocation to intervention

Before the study commences, the site will create consecutively numbered envelopes containing randomization schema. Upon a subject enrollment, the next consecutive envelope will be opened to reveal the subject's randomization schema.

6. Subject recruitment and consent

6.1. Subject identification

Potential subjects will be identified by physicians at MHB. Identification will be based on results of standard care labs and review of symptoms in the medical record.

6.2. Screening

A member of the study staff will assess patient eligibility using the Eligibility Checklist. All protected health information used during the screening process of a potential subject will be the minimum necessary for the conduct of this study. Any protected information recorded will be destroyed at the end of the screening process.

For ineligible patients, only the eligibility criteria that were not met (i.e. which criteria excluded the patient from study participation) will be recorded.

6.3. Recruitment and consent

A member of the study staff will explain study procedures in detail to the potential subject. The study staff member will clearly outline that the purpose of the study is to compare the testosterone concentrations following two different routes of testosterone therapy. While any study staff member may conduct the informed consent discussion and obtain informed consent, a study physician will be available at all times for any consent-related questions. Undue coercion will be prevented by stressing that participation in this study is voluntary and the future care of the potential subject will not be affected by his decision regarding participation in this study.

7. Activities and measurements

Subjects planning to initiate testosterone treatment via injection at MHB will be consented into the study. Upon enrollment in the study, the randomization will be completed for each subject.

Blood collection will occur before each injection. Subjects will rate pain on the Likert scale following each injection. After treatment with the first mode of T administration (SQ or IM depending on randomization), subjects will come in for blood draws 3 days and 7 days following the injection. Two weeks after the initial injection, subjects will come in for treatment with the second mode of T administration (SQ or IM depending on randomization). Subjects will come in for blood draws 3 days and 7 days following the second injection. Two weeks after the second injection, subjects will complete an end of study assessment with an Investigator and will complete a survey assessing their satisfaction with treatment. Subjects will likely continue testosterone therapy at Men's Health Boston after completion of the study.

7.1. Data to be recorded

Pre-enrollment

- Low Testosterone Questionnaire
- International Prostate Symptom Score
- Total Testosterone
- Calculated free Testosterone
- Estradiol
- LH
- FSH
- SHBG
- Hematocrit
- PSA

Visits 1 and 4

- Concomitant medication review and adverse event assessment
- Low Testosterone Questionnaire
- International Prostate Symptom Score
- Total Testosterone
- Calculated Free Testosterone
- PSA
- Pain rating following injection

Visits 2, 3, 5, and 6

- Concomitant medication review and adverse event assessment
- Total Testosterone
- Calculated Free Testosterone
- Estradiol
- LH
- FSH
- SHBG
- Hematocrit
- PSA

End of Study

- Concomitant medication review and adverse event assessment
- Low Testosterone Questionnaire
- International Prostate Symptom Score
- Total Testosterone
- Calculated free Testosterone
- PSA
- Survey

7.2. Blood sample collection

At each visit, up to 14mL (approximately 3 teaspoons) of blood will be collected for study purposes. The serum samples (approximately 6mL) will be frozen and shipped to Beckman Coulter for analysis. Whole blood samples (approximately 3mL) will be sent to Quest Diagnostics for analysis.

	At each visit	Total for study
Total amount collected for study	13mL (4 teaspoons)	91mL
Amount of serum shipped to Beckman	6mL	42mL
Amount of whole blood for Quest	4mL	28mL

The Investigator will review all laboratory test results. Laboratory test results that are considered clinically significant by the Investigator will be followed to satisfactory resolution. Laboratory abnormalities are considered to be adverse events only if they result in discontinuation from the study, necessitate therapeutic medical intervention, and/or if the Investigator considers them to be an adverse event.

Beckman Coulter will arrange for samples to be tested for this study. Contact information is listed below:

Name:	**Geoff Gleason** Staff Clinical Studies Scientist Beckman Coulter, Inc.
Address:	Immunoassay Business Center 1000 Lake Hazeltine Drive Chaska, MN 55318
Telephone:	952-368-2191
Email:	ggleason@beckman.com

Quest will analyze whole blood samples for this study. Contact information is listed below:

Name:	**Quest Diagnostics**
Address:	200 Forest Street Marlborough, MA 01752
Telephone:	508-864-6577

Sample collection
Seven blood samples will be obtained throughout the study. Samples will be collected at the following visits:

- Visit 1
- Visit 2
- Visit 3
- Visit 4
- Visit 5
- Visit 6
- End of Study

Sample processing and storage
Whole blood samples from the SST tubes (10mL) will be spun down and resulting serum (6mL) will be transferred to an aliquot tube. Aliquot tubes will be frozen at the site for batch shipping. Whole blood samples from the EDTA tubes (4mL) will remain ambient and will be collected at the site for analysis by Quest Diagnostics. Remaining specimen will be disposed of in biohazard waste receptacle. Beckman Coulter samples will be labeled with a study-specific ID number, date of birth, Visit number, and collection date and time. No other identifiers will be transferred with the samples to the lab. Quest samples will be labeled with a study-specific ID number, date of birth, visit number, and collection date and time. No other identifiers will be transferred with the samples to the lab. The laboratories will not have access to the Master List that links the study-specific ID number with subject identifiers.

Frozen study samples are to be kept at -20°C with an acceptable range of -10° to -30°C. Freezers must maintain constant temperature (i.e. freezers must not be frost-free or defrost automatically). A temperature log will be maintained at the site.

Sample shipping
Frozen samples will be batch shipped at designated times to Beckman Coulter, Inc. Ambient samples will be collected by Quest after each visit.

De-identification of samples
After the master list is destroyed, samples will not be traceable back to individual subjects.

Specimen analysis
Blood sampling will be performed at MHB and analyzed by Beckman Coulter, Inc. and Quest Diagnostics, Inc. Results of the analysis will be provided to MHB and results of the tests may be discussed with subjects, as it pertains to their medical care.

7.3. Data entry

Data collected during this study will be maintained in the subject's source document folder. For the purposes of data analyses, data from the source will be entered into a database or spreadsheet on a designated, password-protected study computer. The subject ID will be entered, not the subject name. Data on the computer will be password-protected and only accessible to the Investigator and delegated study staff members.

7.4. Subject withdrawals

The Investigator or subjects themselves may stop study treatment at any time for safety or personal reasons.

No replacement of subjects who drop out or are withdrawn following administration of testosterone therapy will take place. Subjects who, having been randomized, do not initiate testosterone therapy may be replaced. The replacement subject will start the study from the beginning.

7.5. Stopping rules

The stopping criteria for an individual patient will be:

- Serum total testosterone concentration >1750 ng/dL on two consecutive blood draws
- Hematocrit >54%
- Elevation of one or more liver enzymes >2X upper reference threshold
- Development of subjective and objectively confirmed gynecomastia
- New onset pedal/ankle edema >1+ on a 1-4 scale
- Report of any serious adverse outcomes, including heart attack, heart failure, stroke, depression, hostility, aggression, liver toxicity, male infertility (in accordance with U.S. Food and Drug Administration (FDA) recommendations)
- Report of any withdrawal symptoms associated with abuse of high doses of testosterone, including depression, fatigue, irritability, loss of appetite, decreased libido, insomnia (in accordance with U.S. Food and Drug Administration (FDA) recommendations)
- New onset of prostate cancer (in accordance with U.S. Food and Drug Administration (FDA) recommendations)

8. Data analysis and statistical considerations

8.1. Sample size determination

A total of 20 subjects will enter this study with testosterone deficiency in an age range of 18-70 years. The probability is 80 percent that the study will detect a relationship between the independent and the dependent variables at a two-sided 0.05 significance level, if the true change in the dependent variables is 0.663 standard deviations per one standard deviation change in the independent variable.

8.2. Analysis of endpoints

Subjects will be summarized by age and other demographic variables. All lab results and responses from low T questionnaires will all be quantitatively analyzed.

9. Risks and benefits of trial participation

9.1. Potential risks

Risks associated with blood collection
Risks associated with the blood draw include mild discomfort during needle insertion, the possibility of pain or bruising at the site of the blood draw, the potential for sensations of lightheadedness and very rarely, infection at the site of blood draw.

Risks associated with loss of confidentiality
There is a risk that information recorded about subjects will be shared with people who would not normally have access to this information.

Unknown risks
This study may involve risks to the subject which are currently unforeseeable. We will inform subjects as soon as possible if we discover any information that may affect the subject's health, welfare, or decision to be in this study.

9.2. Mitigation of potential risks

Mitigation of risks associated with blood collection
Blood sample collection will be performed by healthcare workers for whom the procedure is in the legal scope of practice for their positions and who have demonstrated proficiency after training. The amount of extra blood drawn is quite small and the risk of having to under additional needle sticks is low.

Mitigation of risks associated with loss of confidentiality
Subject confidentiality will be protected with the use of password-protected, de-identified data sets. Subject names will not be associated with their subject IDs at any time during the study. Research procedures have been designed to protect subjects' privacy and confidentiality.

9.3. Potential benefits and risk-to-benefit ratio

Potential benefit to the individual subject
There is no direct benefit to individual subjects from being in this study.

Potential benefit to society
The potential benefit to society is the knowledge gained from this research. By further investigating and comparing routes of administration of testosterone therapy, treatments will continue to develop and improve in the future.

Risk-to-benefit ratio
Overall the risks posed to participants in this study are minimal. Research procedures have been designed to protect subjects' privacy and confidentiality. Risk of side effects from blood draws is very low and patients have previously decided to undergo testosterone therapy and are well aware of the risks. The potential benefits in knowledge from this study outweigh the minimal risk to participants.

10. Adverse events and unanticipated problems

10.1. Adverse event definitions

Adverse event (AE)
An adverse event is defined as any untoward or unfavorable medical occurrence in a human subject including any abnormal sign, symptom, or disease temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Include the type and duration of the follow-up of subjects after adverse events.

Serious adverse event (SAE)
A serious adverse event is defined as any adverse event that meets one of the following criteria:

- Results in death; OR
- Is life-threatening; OR
- Requires hospitalization or prolongs existing hospitalization; OR
- Results in significant or persistent disability or incapacity; OR
- Results in a congenital anomaly/birth defect; OR

Additionally, important medical events that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Any SAE occurring in a subject after providing informed consent and until 30 days after completing the study must be documented. Reports of over dosage must be monitored and reported as SAEs.

Unanticipated problem (UP)
An unanticipated problem is defined as an event that meets all of the following criteria:

1) Unexpected in severity, nature, or frequency given the research procedures and the characteristics of the subject population (i.e., problems that are not described in this protocol or other study documents); AND
2) Related or possible related to participation in the research; AND
3) Suggests that research places subjects or others at a greater risk of harm related to the research than was previously known or recognized.

10.2. Severity assessment

The severity of all adverse events will be assessed according to the following scale:

- Mild = does not interfere with the subject's usual function
- Moderate = interferes to some extent with the subject's usual function
- Severe = interferes significantly with the subject's usual function

10.3. Causality assessment

The Site PI will determine the relationship of adverse events to the research intervention using the following scale:

- Definite = AE is clearly related to the study procedures
- Probable = AE is likely related to the study procedures
- Possible = AE is possibly related to the study procedures

- Unlikely = AE is doubtfully related to the study procedures
- Unrelated = AE is clearly not related to the study procedures

10.4. Procedures for recording and reporting adverse events

All adverse events, whether volunteered by the subject, discovered during general questioning by study staff, or detected through a physical examination or other means, will be recorded in the clinic chart (source document) and on the Adverse Events Case Report Form CRF. Each description of an adverse event will include:

- Duration: start and stop dates
- Expectedness
- Severity
- Causality
- Action taken
- Outcome: resolved, continuing requiring no treatment, continuing requiring treatment, hospitalization, or death

Whenever possible, adverse events causing premature study discontinuation should be followed to resolution.

All SAEs occurring after providing informed consent and through 30 days after the subject completes the study must be reported to the FDA per ICH guidelines.

10.5. Other reportable events

Reporting timeframes begin when the site learns of the occurrence of the event.

Event	Definition	Reporting
Breach of confidentiality	The exposure of any study information or communications directly related to a study subject to anyone not named as study staff or the release of a study subject's identifiable information to study staff who were not specified to receive such information in the protocol or IRB application.	Treat as major deviation (below)
Protocol deviation	A deviation is an incident involving a departure from the IRB-approved protocol in the actual conduct of the study. Deviations may result from the action of the participant, investigator, or staff.	See below
Major deviations	Deviations are considered major when the unapproved change(s) in previously approved research activities, implemented without IRB approval, may potentially adversely affect subjects' rights, safety, welfare, or willingness to continue participation, or affect the scientific design of the study and/or the integrity of the resultant data.	Treat as an Unanticipated Problem (above)
Minor deviations	Deviations are considered minor when the unapproved change(s) in previously approved research activities, implemented without IRB approval, do not adversely affect subjects or the integrity of the study data.	Sites are to report cumulative events to AE Coordinator at time of continuing review.
Protocol violation	An incident involving an intentional deviation from the IRB-approved protocol that was not implemented in response to an emergency situation and that may impact a subject's rights, safety, and/or welfare, makes a substantial alteration to risks to subjects, or affects the scientific design of the study and/or the integrity of the resultant data. Violations may also be repeated deviations (major or minor) of the same nature. Violations can represent serious or continuing non-compliance with the federal regulations and guidelines for ethical conduct of human subject research.	Treat as an Unanticipated Problem (above)
Protocol Exceptions	A protocol exception is an IRB-approved deviation for a single subject or a small group of subjects, but is not a permanent revision to the research protocol.	Protocol exceptions must be approved by local IRB prior to implementation.

10.6. Reporting by study sites to local IRB

The Investigator must notify his or her IRB in writing of all SAEs according to the time requirements and policies of the IRB. Additionally, the Investigator must notify the IRB of any other AEs as required by the IRB.

11. Administrative requirements

11.1. Good clinical practice

The study will be conducted in accordance with FDA and ICH guidelines for Good Clinical Practice. All study staff will be thoroughly familiar with the contents of this protocol and associated trial materials.

11.2. Data quality assurance

The investigator is required to prepare and maintain adequate and accurate case histories designed to record all observations and other data pertinent to the study for each study subject. The investigator will indicate in each subject's medical records that the subject has been enrolled in this clinical trial. The following study information should be recorded:

- Sponsor (Beckman Coulter)
- Protocol Number (MHB023)
- Study Enrollment Date (blood draw date)

Source documents (original medical records, lab reports and data, progress notes, signed informed consent forms, Case Report Forms, etc.) must be available for monitoring and inspection by the Sponsor and appropriate Regulatory agencies (e.g. US FDA).

11.3. Electronic case report form completion

CRFs will be completed for each study subject. It is the investigator's responsibility to ensure the accuracy, completeness, clarity and timeliness of the data reported in the subject's CRF. The investigator or designated representative shall complete the CRF as soon as possible after the information is available.

11.4. Study monitoring

Due to financial and staff limitations there are no formal plans to monitor data for this study; however there remains a possibility for this if deemed necessary. All information recorded in the database or spreadsheet for this study must be consistent with the subject's source documentation. Should monitoring occur, the study monitor may review protocol compliance, verify database or spreadsheet against source documentation and ensure the protocol is being conducted according to pertinent regulatory requirements. Any review of medical records will be performed in a manner to ensure patient confidentiality is maintained.

11.5. Ethical consideration

The study will be conducted in accordance with ethical principles founded in the Declaration of Helsinki. The IRB will review all appropriate study documentation in order to safeguard the rights, safety and well-being of the subjects. The study will only be conducted at sites where IRB approval has been obtained. The protocol, informed consent form, written information given to the patients, safety updates, annual progress reports and any revisions to these documents will be provided to the IRB by the investigator.

11.6. Patient confidentiality

All subjects will be assigned a study-specific ID number. The site will maintain a master list linking each subject's medical record number (MRN) with a study-specific ID number. This list is to be maintained electronically in a location separate from any study data and it shall be password-protected.

All data entered into the database or spreadsheet will be associated with the study-specific ID number. HIPAA identifiers to be recorded are month and year of birth, and age of subject.

All study data will be kept for five years after completion of the study. All data will be destroyed by deletion from computer files and/or shredding.

11.7. Investigator compliance

The investigator will conduct the trial in compliance with the protocol approved by the IRB. Changes to the protocol will require written IRB approval prior to implementation, except when the modification is needed to eliminate an immediate hazard(s) to subjects.

11.8. Subject cost and payment

Cost
Subjects will not incur additional costs due to their participation in this study. All laboratory testing done as part of the study will be paid for by the Sponsor.

Payment
For subjects' time and inconvenience related to their participation in this study, they will be paid $25 for each in-clinic study visit that they complete.

12. Funding Sources

This study is financed by the Sponsor, Beckman Coulter, Inc., Chaska, MN.

13. Publication Policy

The Clinical Trial Agreement for this study will stipulate the publication policy.

References

1. Pastuszak AW, Gomez LP, Scovell JM, Khera M, Lamb DJ, & Lipshultz LI. (2015). Comparison of the Effects of Testosterone Gels, Injections, and Pellets on Serum Hormones, Erythrocytosis, Lipids, and Prostate-Specific Antigen. Sex med 2015; 3; 165–173.
2. Smith RP, Khanna A, Coward RM, Rajanahally S, Kovac JR, Gonzales MA, Lipshultz LI. Factors influencing patient decisions to initiate and discontinue subcutaneous testosterone pellets (Testopel) for treatment of hypogonadism. J Sex Med 2013; 10: 2326–33.
3. Morgentaler A, Dobs AS, Kaufman JM, Miner MM, Ridwan Shabsigh R, Swerdloff RS, Wang C. "Long acting testosterone undecanoate therapy in men with hypogonadism: results of a pharmacokinetic clinical study." J Urol 2008; 180.6: 2307–13.
4. Wang C, Cunningham G, Dobs A, Iranmanesh A, Matsumoto AM, Snyder PJ, Weber T, Berman N, Hull L, Swerdloff RS. Long-term testosterone gel (AndroGel) treatment maintains beneficial effects on sexual function and mood, lean and fat mass, and bone mineral density in hypogonadal men. J Clin Endocrinol Metab 2004; 89: 2085–98.
5. Nieschlag E. Testosterone treatment comes of age: new options for hypogonadal men. Clin Endocrinol 2006; 65:275–81.
6. Borst SE, and Yarrow JF. Injection of testosterone may be safer and more effective than transdermal administration for combating loss of muscle and bone in older men. Amer J Phys-Endocrinol Metab 2015; 308: E1035–42.