

Statistical Analysis Plan

Study Title: The INSPIRE Study: InVivo Study of Probable Benefit of the Neuro-Spinal Scaffold™ for Safety and Neurologic Recovery in Subjects with Complete Thoracic AIS A Spinal Cord Injury

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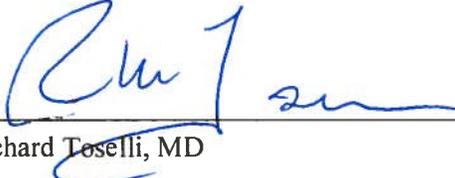
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Signatory Page

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1. LIST OF ABBREVIATIONS AND ACRONYMS

Abbreviations and Acronyms	Description
AE	Adverse Event
ADE	Adverse Device Effect
AIS	American Spinal Cord Injury Association Impairment Scale
ASIA	American Spinal Cord Injury Association
BMI	Body Mass Index
BDI-II	Beck Depression Inventory II
CDE	Common Data Elements
CDISC	Clinical Data Interchange Standards Consortium
CDMS	Clinical Data Management System
CI	Confidence Interval
CFB	Change From Baseline
DPC	DP Clinical Inc.
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HDE	Humanitarian Device Exemption
ICH	International Conference on Harmonisation
IDE	Investigational Device Exemption
ISNCSCI	The International Standards for Neurological Classification of Spinal Cord Injury
ITT	Intent-To-Treat
LEMS	Lower Extremity Motor Score
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic resonance imaging
NINDS	National Institute of Neurological Disorders and Stroke
NLI	Neurological Level of Injury
ODS	Output Delivery System

Abbreviations and Acronyms	Description
QC	Quality Control
QLI-SCI III	Ferrans and Powers Quality of Life Index - Spinal Cord Injury III
PCFB	Percent Change From Baseline
PLGA-PLL	Poly((lactic-co-glycolic acid)-co-poly-(L-lysine))
PT	Preferred Term
RTF	Rich Text Format
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SCI	Spinal Cord Injury
SCIM	Spinal Cord Independence Measure
SD	Standard Deviation
SOC	System Organ Class
SOP	Standard Operating Procedure
SSEP	Somatosensory Evoked Potential
TESE	Treatment Emergent Safety Event
UADE	Unanticipated adverse device effect
TLFs	Tables, Listings and Figures
WHODrug	World Health Organization Drug Dictionary
ZPP	Zone of Partial Preservation

2. INTRODUCTION

This Statistical Analysis Plan (SAP) is prepared to provide a more technical and detailed elaboration of the principal statistical features stated in the protocol. The SAP will ensure that the tables, listings, and figures that will be produced and statistical methods that will be used are complete and accurate and will allow valid conclusions to be drawn. In the development of this SAP, the following documents were used:

- Protocol InVivo-100-101 (version 12.1), June 29 2017
- Electronic Case Report Form (eCRF), October 7 2017

The principles in the following guidance documents are followed in preparation of this SAP:

- International Conference on Harmonisation (ICH) E3 (1995): Structure and Content of Clinical Study Reports [1]
- ICH E6 (1996): Guideline for Good Clinical Practice [2]
- ICH E9 (1998): Statistical Principles for Clinical Trials [3]

In the event that a discrepancy is found between the descriptions in the statistical section of the protocol and this document, the description in this document supersedes the descriptions in the statistical section of the protocol.

3. STUDY OVERVIEW

InVivo Therapeutics Corporation has developed an investigational *Neuro-Spinal Scaffold*TM or “Scaffold” for the treatment of Spinal Cord Injury (SCI) to address this unmet medical need.

A prospective, open label, multicenter, non-randomized, single arm pivotal study of this investigational product is being conducted to assess its overall safety and probable benefit. Participation will be limited to subjects suffering from complete AIS A functional spinal cord injury T2 – T12 presentation. The Scaffold is intended for use only in subjects presenting with recent (≤ 7 days since injury) spinal cord injuries that do not involve penetrating injury to the cord or complete severing of the cord. With the exception of Scaffold implantation, subjects are treated according to standard of care at a qualified trauma center, have comprehensive post-injury rehabilitation, and are followed on-study for a period of 10 years from Scaffold implantation.

3.1 Study Objectives

3.1.1 Primary Objectives

To evaluate whether the Scaffold is safe and demonstrates probable benefit for the treatment of complete T2-T12 spinal cord injury.

3.1.2 Regulatory Objective

This is a Humanitarian Device Exemption (HDE) Probable Benefit study to demonstrate safety and probable benefit in support of future studies and an HDE application with subsequent approval.

3.2 Study Design

This is an HDE probable benefit, open-label, non-randomized, single-arm, multicenter study to evaluate the safety and probable benefit of the poly(lactic-co-glycolic acid)-b-poly(L-lysine) Scaffold (“Scaffold”) in subjects with thoracic AIS A traumatic spinal cord injury at neurological level of injury of T2–T12.

The study will be conducted at up to 40 sites in the U.S, Canada and the European Union by qualified Investigators who have been trained on the surgical Scaffold implant procedure in order to obtain 16 subjects (overriding the 20 subjects planned in the protocol) in the Primary Endpoint Analysis Set, defined as all subjects with a successful Scaffold implant, no major

protocol deviations that affect data quality (Section 6.1.2), and a complete 6-month Primary Endpoint Follow-up Visit. After receiving the Scaffold and following discharge, subjects will participate in a comprehensive rehabilitation program (Section 7.3 of protocol). For the first 24-months after implantation of the Scaffold, Follow-up and Long-term Follow-up assessments will be conducted at either the study site or the rehabilitation center depending on the preference of the Investigator and subject, and provided appropriate Institutional Review Board (IRB)/Research Ethics Committee (REC)/Research Ethics Board (REB) approvals are in place. The Long-term Follow-up annual visits for years 3 through 10 will be conducted over the telephone.

A schedule of assessments can be found in Section 3.2.2.

The European Multicenter Study about Spinal Cord Injury (EMSCI) database was used to set the benchmark for the Objective Performance Criterion (OPC) in this HDE Probable Benefit study. This large database of almost 2,600 subjects is being updated continuously. A recent paper including almost 400 subjects with thoracic (T2–T12) complete (AIS A) SCI (same population evaluated in this study) [4] carefully delineated the ISNCSCI-based neurologic outcomes over 48 weeks for subjects segmented by three thoracic level groupings (T2–T5, T6–T9, T10–T12) as well as outcomes for the entire thoracic group. This paper clearly demonstrates that outcomes are poorer for higher level injuries. The subjects in this HDE Probable Benefit study will have similar demographics and mechanisms of injury as in the EMSCI database.

Although standard of care in rehabilitation has changed significantly over the past several decades with introduction of new experimental devices such as exoskeletons, nothing has been demonstrated to improve neurologic outcome in patients with thoracic complete SCI. As evidence of the lack of effect of rehabilitation modernization with respect to AIS category changes, the results are similar for the U.S. Model Systems, EMSCI, and Sygen databases. Published data from the EMSCI, U.S. Model Systems, and Sygen databases found approximately 13%–16% of subjects (thoracic AIS A) spontaneously improved AIS grade by one or more level at six or more months post-injury [4–6]. The neurologic outcomes published from these databases are very consistent, establishing community norms for spontaneous neurologic recovery after SCI. As level of injury is the one criterion which does appear to influence neurologic outcome, assuming a similar distribution of location of injury as these larger databases, establishing a study success goal or OPC of at least 25% of subjects demonstrating an improved AIS grade by one or more level at the 6-month Primary Endpoint Follow-up Visit post-Scaffold implantation is a rigorous efficacy requirement in this population. Thus, the current study will be deemed a success if at least 25% of subjects demonstrate an improved AIS grade by one or more levels at 6-month Primary Endpoint Follow-up Visit post-Scaffold implantation (the final visit for the Primary Endpoint).

3.2.1 Sample Size Considerations

The study planned to enroll up to 36 subjects to ensure 20 subjects in the Primary Endpoint Analysis Set (Section 5.1). The sample size was determined for the purpose of the study without a formal statistical null hypothesis.

At the time of Primary Endpoint Analysis, it was determined to close enrollment with 16 subjects meeting the Primary Endpoint Analysis Set criteria.

3.2.2 Study Assessments Schedules

Study assessments are described in detail in the protocol, and summarized below in Table 1.

Table 1: Summary of Study Procedures

Visit Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14-21	Unscheduled Visit
Visit Name	Screening	Surgery	24-hours Post-implant	48-hours Post-implant	72-hours Post-implant	1-week Post-implant	Hospital Discharge	1-month Follow-up	2-months Follow-up	3-months Follow-up	Primary Endpoint 6-months	12-months Long-term Follow-up	24-months Long-term Follow-up	Annual Telephone Visits ⁶	
Visit Windows		±96 hrs	±6 hrs	±6 hrs	±8 hrs	±1 day	-	±3 days	±4 days	±7 days	±30 days	±30 days	±30 days	±60 days	
Informed Consent	X														
Demographics and Medical/Surgical History	X														
Skeletal Maturity/Bone Age (ages 16–17)							X ⁷								
Complete Physical Examination	X						X				X	X	X		X
Screening Labs ¹	X														
Comprehensive Metabolic Panel ² , Hematology ³	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Erythrocyte Sedimentation Rate, C-Reactive Protein	X						X	X	X	X					X
Vital Signs (for intraop vitals, see Section 7.7.3)	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Vital Capacity for subjects not ventilator dependent	X	X	X	X	X	X	X								
Neuro Exam (include hip abd/add, great toe flex/ext)	X	X ⁴	X ⁴	X ⁴	X ⁴	X	X	X	X	X	X	X	X		X
Pain Assessment							X	X	X	X	X	X			X
ISNCSCI exam	X	X ⁵					X	X	X	X	X	X	X		X
MRI (without contrast)	X				X					X	X	X	X		
SSEP (Section 7.7.10)		X													
Pulmonary function monitoring (Section 7.7.11)		X	X	X	X										
Intraoperative Ultrasounds with photograph		X													
Scaffold Implantation with videography		X													
Bowel, Bladder and Sexual Function Assessments								X	X	X	X	X			X
SCIM III, QLI-SCI III, BDI-II							X	X	X	X	X	X			
Prior & Concomitant Meds/Interventions/Procedures	X	X	X	X	X	X	X	X	X	X	X	X			X
Rehabilitation Therapy Log							X	X	X	X	X	X			
Annual General Health Assessment														X	
End of Study (Year 10 or last study visit only)														X	
Safety Event Monitoring		X	X	X	X	X	X	X	X	X	X	X	X	X	X

1 Screening Labs include a serum Pregnancy Test, Blood Alcohol/Urine Drug Toxicology, Blood Type, and Coagulation Test (PT, PTT, INR).
 2 CMP: BUN, glucose, creatinine, sodium, potassium, chloride, calcium, total protein, albumin, total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, carbon dioxide.

3 Hematology: CBC w/Diff, WBC, RBC, platelet count, hemoglobin differential counts.
 4 Following surgery, site will perform neurological exam per standard of care.
 5 Confirmatory ISNCSCI must be within 8 hrs before surgery.
 6 Annual visits for years 3 - 10 are telephone contacts and not clinic visits.
 7 May be performed anytime between screening and Hospital Discharge.

4. STUDY ENDPOINTS AND DEFINITIONS

4.1 Primary Efficacy Endpoint

The primary endpoint is the AIS grade at the 6 month follow-up visit. Improvement in AIS grade of one or more levels (i.e. a grade of B, C, D, or E) at the 6 month follow-up visit will be considered a success.

4.2 Secondary Efficacy Endpoints

Secondary efficacy endpoints include:

1. Changes in neurological level of injury (NLI), sensory scores, motor scores
2. Changes in spinal cord anatomy
3. Changes in bowel function, bladder function and sexual function

4.3 Exploratory Efficacy Endpoints

Exploratory efficacy endpoints include:

1. Changes in bowel function, bladder function, and sexual function
2. Changes in pain
3. Changes in SCIM III overall and Area scores
4. Changes in QLI-SCI III

4.4 Safety Endpoints

Safety endpoints will include the following:

1. General safety assessments
 - Incidence of all safety events (AEs/ADEs) of any kind/seriousness
 - Incidence of all serious safety events (SAEs/SADEs)
 - Incidence of unanticipated ADEs (UADEs)
2. Incidence of the following safety events for assessment of the potential risk associated with the use of Scaffold
 - Scaffold migration or malposition
 - Untoward physiologic reaction to PLGA-PLL materials
 - Scaffold-related loss of motor or sensory neurologic function
 - Increased inflammatory response

- Persistent cerebrospinal fluid leak
 - Damage to adjacent structures post Scaffold implant
 - Re-operation or removal of the Scaffold
 - Hemorrhage into or around the spinal cord causing neurologic deficit or possible need for further surgery
 - Surgical infection
 - Increased anesthesia time

 - Adhesion between the spinal cord and dura
 - Postoperative symptomatic or asymptomatic intraspinal cyst or syrinx
 - Post-Scaffold implant on-ventilator time for subjects with sensory deterioration of 2 or more dermatomes determined by either ISNCSCI pinprick or light touch exam as compared to subjects without sensory deterioration of 2 or more dermatomes.
3. Incidence of the following safety events for assessment of the potential risk associated with neurosurgical procedures
- Soft tissue wound infection or dehiscence
 - Surgical injury to the cord

 - Cerebrospinal fluid (CSF) leakage
 - Progressive neurological deterioration beyond that normally expected
 - Bacterial meningitis
 - Cord abscess
 - Failure to alter the natural course of healing from a spinal cord injury
4. Incidence of the following safety events for assessment of the most common general risks of surgery and spinal surgery:
- Adverse reactions to the anesthetic
 - Post-operative pneumonia
 - Blood clots in the legs or elsewhere (deep vein thrombosis) that may travel to the lungs (pulmonary embolus)
 - Infection at the site of surgery
 - Blood loss during surgery requiring a transfusion

- Injury to the nerves or spinal cord resulting in pain or further paralysis
 - Instrumentation breaking, dislodging, or irritating the surrounding tissues
 - Pain from the surgery itself
5. Findings of clinical laboratory tests, including routine blood chemistry and hematology tests
 6. Findings from vital signs measurements
 7. New onset or worsening of depression by Beck Depression Inventory II (BDI-II)

4.5 Definitions

4.5.1 Study Day and Subject-Years

This is the first in human feasibility study of the Scaffold. Various reference time points will be selected for assessment of changes in safety and exploratory efficacy endpoints in the study. Time will be measured as Study Day defined according to Clinical Data Interchange Standards Consortium (CDISC) standard. That is, the date of the start of open spine surgery is Study Day 1. The date before the surgery is Study Day -1. All measurements taken will be displayed in chronological order of the study day to visualize the profile of changes over time.

Last study day for a subject is the subject's last clinical visit date or the date of last telephone contact, whichever is on a later day. If this date is missing for a subject, the last date found in the clinical database (e.g., clinical lab test date or date of vital sign collection) will be used as the last study date for the subject.

Total days on study are the total number of days a subject has been followed up after had the surgery. Mathematically it can be calculated as follows:

$$\text{Total days on study} = \text{last study date} - \text{date of surgery} + 1$$

4.5.2 Study Day and Study Reference Period

For events that occurred after the implantation of the Scaffold:

Study Day = visit date – date of surgery + 1

For events occurred before implantation of the Scaffold:

Study Day = visit date – date of surgery

4.5.3 **Baseline and Change from Baseline**

Time points that can be used as a “baseline” for assessments are primarily the assessment, immediately prior to the open spine surgery, but also may include at screening or at hospital discharge as denoted in their respective analysis.

Unless indicated otherwise change from baseline (CFB) will be calculated as follows:

- CFB = Value at Visit - Baseline

5. STATISTICAL ANALYSIS GENERAL CONSIDERATIONS

The results will be presented primarily via data tabulation by subject ID and time course because this is an early feasibility study with a small sample size. Group descriptive statistics and cumulative statistics will be presented, as appropriate.

5.1 Analysis Populations

The following analysis populations will be prepared for this study:

Screened Set:

The screened population will include all subjects who signed the informed consent form and were screened for participation in this study. This population will be used when describing disposition throughout the study.

Safety Set:

The Safety Set includes all enrolled subjects (i.e. subjects who have signed an Informed Consent Form) that passed the screening assessments. The Safety Set will serve as the analysis set for listings, where data will be presented stratified by screen failures and non-screen failures (as designated by the subject status eCRF page, determined by eligibility procedures at the Screening visit and surgery).

Safety Set Excluding Screen Failure Subjects:

A subgroup of the Safety Set, "Safety Set Excluding Screen Failures" will be considered the subjects in the safety set, but excluding subjects identified as screen failures on the subject status eCRF page. This set will be used for safety table summaries.

All Treated Analysis Set:

The All Treated Analysis Set includes all subjects who have a successful Scaffold implant. The All Treated Analysis Set will serve as the analysis set for all efficacy endpoints.

Primary Endpoint Analysis Set:

The Primary Endpoint Analysis Set includes all subjects who have a successful Scaffold implant, no major protocol deviations that affect data quality, and who have completed the 6-month Primary Endpoint Follow-up Visit. The Primary Endpoint Analysis Set will serve as the analysis set for the primary efficacy endpoint.

5.2 Test Hypothesis and *P*-Value Justification

No formal statistical hypothesis was used to determine the sample size. No formal statistical tests are planned for the study.

5.3 Procedures for Handling Missing Data and Outliers

Unless indicated otherwise, no imputation will be done for missing data. However, missing adverse event start dates or partial start dates that result in the assessment of the event beginning before or after the implantation will result in the event being considered as having started after the initiation of device implantation.

Safety events with missing intensity assessments will be tabulated as “Severe” and safety events with missing relationship causality will be tabulated as “Definitely Related” for the purpose of analysis (with a footnote stating it was derived as such); and the missing data will be presented in the data listing as is.

The clinical database will be locked after all subjects complete their 6-month Primary Endpoint Follow-up Visits for the Primary Endpoint Analysis and writing of the Clinical Study Report is completed.

5.4 Interim Evaluations and Primary Analysis

One interim evaluation was performed at the time the first 5 subjects received the Scaffold implant and completed the 6-month post-Scaffold implantation Follow-up Visit. The purpose of the interim evaluation was to support conversion of the pilot study into an HDE probable benefit study enrolling up to 36 subjects to achieve 20 subjects in the Primary Endpoint Analysis Set.

Subjects who received the Scaffold are to be followed for 24-months in clinic, and then the subjects will be followed annually by telephone contact for an additional 8 years. At the time of the last subject in the Primary Endpoint Analysis set completes the 6 Month Post-Implantation Visit, the Primary Analysis of all available data will be presented in tables, listings, and figures and a Clinical Study Report will be prepared. Data collected during the Long-term Follow-up will be reported via the format of Investigation Device Exemption (IDE) annual update.

A Data Safety Monitoring Board (DSMB) will be formed to evaluate safety and efficacy on an on-going basis. The DSMB will be notified of all serious safety events, safety events of interest, and study stopping rules. The DSMB may recommend that the study enrollment be put on hold or the study be terminated should safety events occur that are Scaffold-related and distinct from a safety event that may be associated with standard of care open spine surgery or sequelae considered part of the normal course of a non-penetrating SCI (contusion injury) following such surgery.

Additional safety reviews or ad-hoc analyses may be scheduled as recommended by the DSMB or the sponsor.

6. STATISTICAL ANALYSIS METHODOLOGY

All data collected for this study will be presented in summary tables, listings, and figures (TLFs) as indicated in Appendix 1 of this SAP. Shells for TLFs with enough detail for programming will be provided as a guide to develop the programming SAS codes. These shells will be in sufficient detail to simulate the actual TLFs when they are created from the locked database.

The results will be presented primarily via data tabulation and listed by subject ID and time course because this is an HDE Probable Benefit study with a small sample size. Group descriptive statistics and cumulative statistics will be utilized if appropriate.

Tabulations for continuous data will use a standard set of summary statistics: number of observations available (n), mean, standard deviation (SD), median, and range (minimum, maximum).

Categorical or dichotomous data will be tabulated using counts and percentages. The numerator and denominator for each percentage calculation will be specified in the footnotes of table shells.

Data listings will present all information recorded in eCRFs and any derived variable(s) included in the analysis datasets for all subjects and visits.

6.1 Study Subjects

6.1.1 Subject Disposition

The summary tables will provide frequency counts for subject disposition (all enrolled [Safety Set], screen failures, Unsuccessful Scaffold Implantation [with and without durotomy performed], subjects with successful implantation of the Scaffold [All Treated Set], subjects who completed the 12-month post-implantation visit, subjects who completed the 24-month post-implantation visit, subject in the Primary Endpoint Analysis Set, and subjects who withdrew early from the study and reason for discontinuation).

6.1.2 Protocol Deviations

A protocol deviation is any change, divergence, or departure from the study design or procedure defined in the protocol.

The following categories will be used to group protocol deviations:

1. Eligibility Not Met
2. Study Assessment Noncompliance
3. Other

The following are categorical reasons used to document why a protocol deviation occurred:

1. Subject Illness
2. Clinical Error
3. Investigator/Staff Decision
4. Other

A subset of the protocol deviations can be identified as a major protocol deviation as described below:

Major Protocol Deviation: A major protocol deviation that may significantly affect the completeness, accuracy, and/or reliability of the study data or that might significantly affect a subject's rights, safety, or well-being.

To determine inclusion in the Primary Endpoint Analysis set, major protocol deviations will be categorized into the following subgroups:

- Major Data Protocol Deviations - protocol deviations related to the completeness, accuracy, and/or reliability of the study data.
- Major Good Clinical Practice (GCP) Protocol Deviation - protocol deviations related to subject's rights, safety, or well-being but do not affect the completeness, accuracy, and/or reliability of the study data.

Subjects with Major Data Protocol Deviations that occurred in the time period through the 6 Month Primary Endpoint Visit will be excluded from the Primary Endpoint Analysis Set.

Subjects with only no protocol deviations or subjects with minor and/or Major GCP Protocol Deviations will not be excluded from the Primary Endpoint Analysis Set.

All documented protocol deviations in the study will be reviewed on an ongoing basis to identify all Major Protocol Deviations by a data review team including representatives from clinical operations, medical, data management, and statistics, and sent to the sponsor for approval. Final decisions will be documented and archived.

Number and proportion of subjects with protocol deviations (major/all other deviations) may also be tabulated by protocol deviation category if data warrants. Subjects excluded from each analysis set will be tabulated.

6.1.3 Demographics

A demographic and baseline characteristics table will be presented for the Safety Set. The summary will include descriptive statistics for age, sex, race, ethnicity, weight, height, BMI at baseline, as well as the cause of spinal cord injury. Skeletal maturity will be summarized through Risser Staging for subjects aged 16 and 17 if applicable.

6.1.4 Medical and Surgical History

At the Screening visit, the general medical and surgical procedures history will be recorded on the eCRF, Medical/Surgical History data will be listed.

6.1.5 Concomitant Medications, Interventions, and Procedures

Prior and concomitant medications will be coded to the therapeutic drug classes and generic drug names using the World Health Organization Drug (WHODrug) classifications version March 2014 [8]. All prior and concomitant medications, interventions and procedures will be tabulated by Anatomical-Therapeutic-Chemical (ATC) Level 3 Code and Preferred Term.

Concomitant interventions and procedures will be listed by subject.

6.2 Efficacy Analysis

The primary analysis of the study will be presented upon completion of the 6 Month Primary Endpoint Follow-up Visit (6 Months post-Scaffold) for the subjects in the Primary Endpoint Analysis Set. For the purposes of the Primary Endpoint Analysis, the Primary Efficacy Endpoint Analysis will be performed on the Primary Endpoint Analysis set. All secondary, exploratory, and other efficacy analyses will be performed on the All Treated Set.

Additional efficacy and subgroup analyses may be performed for information obtained after the 6 Month Primary Endpoint Follow-up Visit (12 month and 24 month post-Scaffold follow-up visits), as needed.

6.2.1 Primary Endpoint Analysis

The Primary Endpoint Analysis will be performed when the 16th subject in the Primary Endpoint Analysis completes the 6-month post-implantation visit.

The primary endpoint analysis is the proportion of subjects from the Primary Endpoint Analysis Set who have an improvement of at least 1 grade on AIS assessment at the 6-month Primary Endpoint Follow-up Visit. The number and percent of subjects with an improvement of at least 1 grade on AIS assessment will be presented. If the proportion of subjects who demonstrate an improvement of at least 1 grade on AIS is at or above 25% the study will be deemed a success using this preset Objective Performance Criterion (OPC) of $\geq 25\%$ as a measure of success.

The primary endpoint analysis will also be conducted utilizing the All Treated Analysis Set. This analysis will be performed in the same manner as described above as a confirmatory analysis. In addition, a sensitivity analysis will be performed that will impute a value for any missing AIS grade at the 6-month Primary Endpoint Follow-up Visit. Any subject who does not have a 6-month Primary Endpoint Follow-up Visit for any reason including premature study withdrawal, will have the primary endpoint imputed to not having an improvement of at least 1 grade on AIS assessment at the 6-month Primary Endpoint Follow-up Visit unless they were assessed as AIS C or better at the last two study visits.

Additionally, the AIS grade will be tabulated by subject at each visit in the All-Treated Set. The number and percentage of subjects with each AIS grade will be tabulated at each visit.

6.2.2 Secondary Efficacy Analysis

6.2.2.1 *Change Neurological Level of Injury*

The Neurological Level of Injury (NLI) at the screening visit, pre-surgery visit, 1-month, 2-months, 3-months, 6-months, 12-months and 24-months will be summarized for the All Treated Set. Observed values and change from the baseline will be presented. The confirmatory ISNCSCI exam performed within 8 hours prior to surgery (pre-surgery ISNCSCI) will be used as baseline visit. The zone of partial preservation will also be presented

6.2.2.2 *Change in ISNCSCI Motor Scores*

The ISNCSCI motor scores, including the Right Side Muscle Motor Score, Left Side Muscle Motor Score, LEMS and Motor Total Score, at the screening visit, pre-surgery visit, 1-month, 2-months, 3-months, 6-months, 12-months and 24-months will be summarized for the All Treated Set. Observed values and change from the baseline will be presented. The confirmatory ISNCSCI exam performed within 8 hours prior to surgery (pre-surgery ISNCSCI) will be used as baseline visit.

Individual Motor Total Score and Change from Baseline will be graphically displayed by visit. The mean Motor Total Score (SD) will also be plotted over time.

6.2.2.3 *Change in ISNCSCI Sensory Scores*

The ISNCSCI sensory scores, including the Light Touch Score, Pin Prick Score, and Sensory Total Score, at the screening visit, pre-surgery visit, 1-month, 2-months, 3-months, 6-months, 12-months and 24-months will be summarized for the All Treated Set. Observed values and change from the baseline will be presented. The confirmatory ISNCSCI exam performed within 8 hours prior to surgery (pre-surgery ISNCSCI) will be used as baseline visit.

Individual Sensory Total Score, Light Touch Score, and Pin Prick Score and their Changes from Baseline will be graphically displayed by visit. The mean Sensory Total Score (SD) will also be plotted over time.

6.2.2.4 *Change in Spinal Cord Anatomy*

MR Images (axial and sagittal T1 and T2-weighted images at minimum) are obtained at Screening and 72-hours, 3-months, 6-months, 12-months, and 24-months post-implant. Characteristics of spinal cord anatomy will be assessed by a Board-certified neuroradiologist central reader and will include the following analyses: spinal cord dimensions (above, at, and below level of injury), lesion size and location, cyst presence or absence including size and location, if present. Observed values at 72 hours post-implant and change (in Edema size, Hemorrhage, scaffold detection, cyst and spinal cord adhesion) from baseline will be presented. The Screening MRI will be used as the baseline. These analyses will be performed on the All Treated Analysis Set.

The following will be tabulated by subject at the baseline and 72 hour time points:

- Edema location
- Edema - Sagittal Plane Superior-Inferior (millimeters [mm]), with change from baseline
- Hemorrhage location
- Hemorrhage - Sagittal Plane Superior-Inferior (mm), with change from baseline
- Scaffold Detection at 72 hours (Yes/No)

The following will be tabulated by subject for the 3 Month Visit, 6 Month Visit, 12 Month Visit, and 24 Month Visit:

- Presence of cyst (Yes/No)
- Cyst location
- Cyst size - Sagittal Plane x Axial Plane (mm)
- Spinal Cord Adhesion (Yes/No)
- Spinal Cord Adhesion Location

6.2.3 **Exploratory Analysis**

6.2.3.1 *Change in Bowel Function*

Bowel function will be assessed using the questionnaire from the International Spinal Cord Injury Data Sets – Bowel Function Basic Data Set – Data Form. The following bowel function assessments will be summarized in descriptive tables by subject and for the overall

population at each time point (1-month, 2-months, 3-months, 6-months, and 12-months post-Scaffold implantation):

- 1) Subjects with awareness of the need to defecate
- 2) Main method for bowel defecation and bowel care procedure
- 3) Supplementary method for bowel defecation and bowel care procedure
- 4) Average time required for defecation and frequency of defecation
- 5) Frequency of fecal incontinence
- 6) Need to wear pad or plug
- 7) Use of laxatives and use of medication affecting bowel function/constipating agents
- 8) Perianal problems since last visit

Observed values and any changes of baseline (1-month post-implantation) will be assessed qualitatively. If data warrants additional exploratory work may be carried out to gain a better understanding of subject characteristics and the degree of improvement.

6.2.3.2 *Change in Bladder Function*

Bladder function will be assessed using the questionnaire from the International Spinal Cord Injury Data Sets – Lower Urinary Tract Function Basic Data Set – Data Form. The following bladder function assessments will be summarized in descriptive tables by subject and for the overall population at each time point (1-month, 2-months, 3-months, 6-months, and 12-months post-Scaffold implantation):

- 1) Number of subjects reported yes to question of ‘Awareness of the need to empty bladder (yes/no)’ at each time point.
- 2) Frequency of major bladder emptying methods at each time point
- 3) Frequency of supplementary bladder emptying methods at each time point
- 4) Distribution of average number of voluntary bladder-emptying per day at each time point
- 5) Distribution of subjects with any involuntary urine leakage at each assessment time points
- 6) Distribution of subjects taking medications for urinary tract

7) Distribution of subjects with surgical procedures on urinary tract and list of type of surgery at each time point

Observed values and any changes of baseline (1-month post-implantation) will be assessed qualitatively. If data warrants additional exploratory work may be carried out to gain a better understanding of subject characteristics and the degree of improvement.

6.2.3.3 *Change in Sexual Function*

Sexual function will be assessed using the International Spinal Cord Injury Male and Female Sexual Function Basic Data Sets (version 2.0). The sexual function assessments are designed to record data on sexual function for individuals with spinal cord lesions, and to standardize the collection and reporting of information on sexual function in daily practice.

The site will interview the subject on various aspects of their sexual function, including their interest in discussing sexual issues and any sexual dysfunction related to the spinal cord injury, and will complete the required assessments.

Sexual function will be assessed prior to hospital discharge and at post-Scaffold implant study visits at 1, 2, 3, 6 and 12-months.

Due to no sexual data collected at the time of the Primary Endpoint Analysis, Sexual Function will be presented only after the Long-term Follow-up Period of all subjects has been completed.

6.2.3.4 *Change in Pain*

Pain will be assessed at all study visits beginning at Hospital Discharge through the 12 Month Long-Term Follow-up Visit using the International Spinal Cord Injury Pain Basic Data Set Data Collection Form Version 2.0 (Appendix G of the protocol). Pain assessment findings by time profile will be prepared for each subject. Pain assessments at the hospital discharge will be used as the reference time point for the assessment of change in pain intensity.

There are 3 pain assessments at each time point: worst, second worst, and third worst pain assessments. However, pain assessments will focus on the worst pain problems that a subject had during the last 7 days. The following pain assessments will be tabulated by subject and summarized:

- Reported pain score for the worst pain at each time point. A subject's pain score at a given time point is the average pain intensity reported by the subject during the worst

pain assessment at that time point, where a lower score corresponds to less pain (i.e. lower score corresponds to improvement).

- Number of pains reported by subject (0 to ≥ 5) at each time point, where fewer reported pains are better
- Reported quality of life scores at each time point for pain “interferes with activities,” “interferes with mood,” and “interferes with sleep” (0 to 10), where a lower score corresponds with a higher quality of life (i.e. lower score corresponds to improvement).

The number of subjects with improvement, worsening, and no change in pain assessments will be tabulated.

Worst pain scores and quality of life scores will be plotted by individual and by mean over time.

6.2.3.5 *Change in SCIM III*

The Spinal Cord Independence Measure (SCIM) III will be assessed (Appendix I of the protocol) at discharge and at months 1, 2, 3, 6, and 12. SCIM III results at discharge will be used as the reference time point (baseline) to assess changes in subjects’ quality of life at months 1, 2, 3, 6, and 12. The Spinal Cord Independence Measure (SCIM) III covers 19 tasks, all activities of daily living, grouped into four areas of function: Self-Care (Questions 1-4, scored 0-20), Respiration and Sphincter Management (Questions 5-8, scored 0-40), Mobility in Room and Toilet (Questions 9-11) and Mobility Indoors and Outdoors on Even Surface (Questions 12-17) (Mobility Questions 9-17, Scored 0-40). The final total SCIM III is the sum of all scores and ranges from 0 to 100, with 0 being requiring total assistance and 100 being completely independent.

SCIM III total score and each domain score will be calculated for each subject at hospital discharge and at months 1, 2, 3, 6, and 12. Change from baseline (Hospital Discharge) in SCIM III will also be derived at each post baseline time point. SCIM III total score, scores for each area of function, change from baseline for total score and functional score will be tabulated by subject and summarized overall at each time point. Additionally, the scores for sphincter management – bladder and bowel (out of 15 and out of 10, respectively) and the change from baseline will be tabulated by subject over time and summarized at each time point.

Subjects with improvement, worsening, and no change from baseline in their quality of life as determined by their SCIM III assessments will be tabulated. Improvement will be defined as an increase in SCIM III score/subscore from baseline, while worsening will be defined as a decrease in score/subscore.

SCIM III total individual and mean scores (with SD) will be plotted over time.

6.2.3.6 Change in QLI-SCI III

The Ferrens and Powers Quality of Life Index – Spinal Cord Injury (QLI-SCI) III will be assessed (Appendix J of the protocol) at discharge and at months 1, 2, 3, 6, and 12. QLI-SCI III results at discharge will be used as the reference time point (baseline) to assess changes in subjects' quality of life at months 1, 2, 3, 6, and 12. QLI-SCI contains two parts that measure the satisfaction (1=Very Dissatisfied to 6=Very Satisfied) and importance (1=Very Unimportant to 6=Very Important) with 37 aspects of quality of life. Importance ratings are used to weight satisfaction responses, so that scores reflect satisfaction with the aspects of life that are valued by the individual. The QLI produces five scores: quality of life overall and in four domains (health and functioning, social and economic domain, psychological/spiritual domain, and family). The scores are calculated as follows:

Subscale Scores:

The subscale questions are distributed as follows:

Health and Functioning Subscale:

- 1. Health
- 2. Health care
- 3. Pain
- 4. Energy (fatigue)
- 5. Ability to take care of yourself
- 6. Ability to go places
- 7. Ability to clear lungs
- 8. Control over life
- 9. Chances for living as long as you would like
- 14. Sex life
- 20. Ability to take care of family responsibilities
- 21. Usefulness to others
- 22. Worries
- 29. Things for fun

- 30. Chances for a happy future

Social and Economic Scale:

- 17. Friends
- 19. Emotional support from people other than your family
- 23. Neighborhood
- 24. Home
- 25/26. Job/Not having a job
- 27. Education
- 28. Financial needs

Psychological/Spiritual Subscale:

- 31. Peace of mind
- 32. Faith in God

- 33. Achievement of personal goals
- 34. Happiness in general
- 35. Life satisfaction in general
- 36. Personal appearance
- 37. Self

Family Subscale:

- 10. Family health
- 11. Children
- 12. Ability to have children
- 13. Family happiness
- 15/16. Spouse, lover, or partner/Not having a spouse, lover, or partner
- 18. Emotional support from family

For each of these four subscales, the score is calculated as follows:

- 1) Recode satisfaction scores: To center the scale at zero, subtract 3.5 from satisfaction response for each item (this will produce responses of -2.5, -1.5, -0.5, +0.5, +1.5, +2.5).
- 2) Weight the satisfaction responses with the paired importance responses: multiply the recoded satisfaction response by the raw importance response for each pair of items.
- 3) Obtain preliminary sum for the subscale score: Add the weighted responses from step 2 together for each corresponding subscale item.

- 4) Obtain final subscale score: Divide the preliminary sum from step 3 by the number of complete item pairs answered in each corresponding subscale (this prevents bias from missing data). To eliminate negative numbers in the final score, add 15 to each score. Each final subscale score will have a range of 0-30, where 30 is the highest quality of life and 0 is the lowest quality of life.

Overall QLI-SCI III Score:

The calculation for the overall (total) QLI-SCI III Score is similar to the subscales:

- 1) Recode satisfaction scores: To center the scale at zero, subtract 3.5 from satisfaction response for each item (this will produce responses of -2.5, -1.5, -0.5, +0.5, +1.5, +2.5)
- 2) Weight the satisfaction responses with the paired importance responses: multiply the recoded satisfaction response by the raw importance response for each pair of items
- 3) Obtain preliminary sum for the overall total score: Add the weighted responses from step 2 together.
- 4) Obtain final overall total QLI-III score: Divide the preliminary sum from step 3 by the total number of complete item pairs answered. To eliminate negative numbers in the final score, add 15 to each score. This final overall total QLI-III score will have a range of 0-30, where 30 is the highest quality of life and 0 is the lowest quality of life.

QLI-SCI III total score and subscale scores will be calculated for each subject at hospital discharge and at months 1, 2, 3, 6, and 12. Change from baseline (Hospital Discharge) in SCIM III will also be derived at each post baseline time point. QLI-SCI III total score, subscores, change from baseline for total score and subscores will be tabulated by subject and summarized overall at each time point.

Subjects with improvement, worsening, and no change from baseline in their quality of life as determined by their QLI-SCI III assessments will be tabulated. Improvement will be defined as an increase in QLI-SCI III score/subscore from baseline, while worsening will be defined as a decrease in score/subscore.

6.3 Safety Analysis

Safety analysis will be performed using all subjects in the Safety Population Excluding Screen Failure Subjects. The safety data will be presented descriptively and no formal statistical analyses are planned. The following sections provide the safety presentations for the Safety Set Excluding Screen Failure Subjects.

The primary safety analysis of the study will be presented upon completion of the 6 Month Primary Endpoint Follow-up Visit (6 Months post-Scaffold) for the subjects in the Safety Set Excluding Screen Failures.

Additional safety Analysis may be performed for information obtained after the 6 Month Primary Endpoint Follow-up Visit (12 month and 24 month post-Scaffold follow-up visits) upon the completion of collection of clinical data, as needed.

6.3.1 Extent of Exposure

The Scaffold is a bioresorbable material, and based upon pre-clinical testing, is expected to be completely cleared from the site of implant within four to eight weeks. A summary of study participation will be provided but no analysis of extent of exposure is applicable for this study.

6.3.2 Safety Events

The Medical Dictionary for Regulatory Activities (MedDRA) (Version 17) [5] will be used to classify all safety events (AEs, ADEs, Safety Events of Interest [associated with the potential risk with the use of Scaffold, risk associated with neurological procedures, and general risks of surgery and spinal surgery] SAEs, SADEs and UADEs) with respect to system organ class (SOC) and preferred term (PT). ADEs will be considered any safety event that is at least possibly related to the Scaffold or the procedure to implant the Scaffold. The safety event dataset will be reviewed by the study team to identify all events and to group the identified events into different categories for the analysis, particularly the Safety Events of Interest.

Summary tables will provide the total number of safety events of each type (AEs, ADEs, Safety Events of Interest, SAEs, SADEs and UADEs, Safety Events Leading to Discontinuation) and the number and proportion of subjects with each type of safety event.

Events will be tabulated for the overall study period and separately for the 6- Month Primary Endpoint Follow-up period. Within each tabulation, subjects within the Safety Set that had a successful Scaffold implant will be tabulated separately.

The following tables will be produced:

- Topline Summary of All Safety Events
- AEs, SAEs by SOC, PT and Intensity
- ADEs, SADEs, and UADEs by PT and Intensity
- Safety Events of Interest by PT and Intensity

In addition, tables providing all AEs and SAEs by SOC, PT, and Intensity will be presented for the All Treated Set.

The calculation of safety event percent will be based on the number of subjects per safety event system organ class and preferred term, where:

Percent of Subjects Experiencing Each Safety Event =

$$\text{Number Subjects with Safety Event} * 100 / \text{Total Number of Subjects}$$

When tabulating a proportion, if a subject has multiple safety events classified to the same category, that subject will be tabulated once under the worst severity for that safety event category. Summary tables will be presented by seriousness and severity. All safety event information will be provided in data listings.

6.3.3 Clinical Laboratory Tests

Laboratory values will be collected at all study visits up to and including Month 24 (with the exception of Erythrocyte Sedimentation Rate and C-Reactive Protein labs). For each clinical laboratory parameter, values at each time point will be categorized as “Low,” “Normal,” or “High” and then categorized as “Clinically Significant” or “Not Clinically Significant,” as determined by the investigator. Changes from screening, pre-implantation, 24 hours post implantation, and hospital discharge in these categories will be tabulated.

The number and percentage of subjects with Low, High, Clinically Significant Low, and Clinically Significant High results will be presented by visit for each parameter.

6.3.4 Vital Signs

For each vital sign, values at each time point will be categorized as “Low,” “Normal,” or “High” and then categorized as “Clinically Significant” or “Not Clinically Significant,” as determined by the investigator. Changes from screening, change from the day of spine surgery (as measured before the surgery) and change from hospital discharge at each visit will be summarized without formal statistical testing.

Summary statistics (N, mean, and SD) of each parameter will be presented by visit.

The number and percentage of subjects with Low, High, Clinically Significant Low, and Clinically Significant High results will be presented by visit for each parameter.

6.3.5 Physical Examination and Neurological Examination Results

Physical examination results will be classified into ‘Normal’, ‘Abnormal, Not Significant’, and ‘Abnormal, Clinically Significant’ categories, and summarized by body system. Results will be listed.

Neurological examination results will be classified into ‘Normal’ and ‘Abnormal’ categories, and summarized for 11 body systems. Five tendon reflexes will be scored on a five-point (0-4) scale for both the right and left side. Additionally, voluntary abdominal muscle contraction, hip adduction/adduction, and toe flexion/extension on the right and left sides will be scored into 0=‘absent’ and 1=‘present’. Scores will be tabulated by subject across time, and a change from absent to present will be considered an improvement in condition.

6.3.6 Beck Depression Inventory II

The Beck Depression Inventory II (BDI-II), created by Aaron T. Beck, is a 21-question multiple-choice self-report inventory, one of the most widely used psychometric tests for measuring the severity of depression. In its current version, the BDI-II is designed for individuals aged 13 and over, and comprises items relating to symptoms of depression such

as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, and lack of interest in sex.

The BDI-II is scored by adding up the score (0—3) of each of the 21 questions, and the assessment of the scores are as described below.

- 0—13 Minimal depression
- 14—19 Mild depression
- 20—28 Moderate depression
- 29—63 Severe depression

A score of 17 or higher may indicate the presence of depression and further evaluation by a mental health professional should be considered. A subject who gives a rating of 2 or 3 on item 2 (hopelessness) or item 9 (suicide ideation) should be closely scrutinized for suicide potential.

The BDI-II will be used to assess the subject's mood at hospital discharge and at months 1, 2, 3, 6, and 12. Observed values for total score and changes from baseline will be presented. BDI-II results will be listed.

6.3.7 Subgroup Analysis

No subgroup analyses are planned for the Primary Endpoint Analysis.

Separate efficacy tabulations may be performed for the subjects enrolled prior to conversion of the study from a pilot study to a pivotal probable benefit study, if necessary. Additionally, if sufficient data are available, separate efficacy analyses may also be performed on the subset of pediatric subjects (under age 22 at time of enrollment).

Separate Safety Event tabulations may be performed for the subjects enrolled prior to conversion of the study from a pilot study to a pivotal probable benefit study, as necessary.

7. TESTING/QUALITY CONTROL PLAN AND SOFTWARE/SYSTEM

All statistical programs will be written in SAS[®] version 9.3 [9]. Statistical programs will be tested and reviewed for Quality Control (QC) by a second programmer/biostatistician not involved in the programming as per DP Clinical (DPC)'s standard operating procedure (SOP). In addition, DPC's SOP will be followed to ensure that the information is complete, consistent, and accurately reflects the data stored in Clinical Data Management System (CDMS) database. Further all tables, listings, and figures (TLFs) will undergo a QC process by an independent biostatistician/programmer to ensure that the information is complete, consistent, and accurately reflects the data stored in CDMS.

7.1 Programming Specifications for TLFs

Appendix 1 provides a list of all the TLFs that are planned to be produced.

7.2 Formatting Conventions

The following formatting conventions will be used to output TLFs:

- TLFs are outputted by SAS Output Delivery System (ODS) into Rich Text Files (RTF) format.
- Tables and Listings will include borders around all headings and data cells.
- Output will be in landscape orientation with margins of 1.5 inches on top, and 1 inch for right, left, and bottom.
- The default font to be in tables/listings/figures will be Courier New.
- Preferred and minimum font size:

Portion of Output	Preferred	Minimum
Page Header	10 pt	8 pt
Title	10 pt	8 pt
Column header	10 pt	8 pt
Cells	10 pt	8 pt
Footnote	10 pt	8 pt
Page Footer	10 pt	8 pt

- Data will be centered within columns when the maximum length of the data being displayed is less than or equal to the maximum width of the column

heading. When the maximum length of the data being displayed exceeds the maximum width of the column heading, the data will be left-justified.

- Column headings should be in initial capital characters. For numeric variables, include “unit” in the column heading when appropriate.
- In figures, axes will be labeled appropriately.

7.3 Standard Text Conventions

7.3.1 Header

All output (table, listing, or figure) will have the following header:

InVivo Therapeutics
Protocol: InVivo-100-101

Page xx of XX

All output will have the date and time (date and time output was generated) and internal page number in the footer. Tables/Listings/Figures should be internally paginated (i.e., page numbers should appear sequentially within each output).

7.3.2 Title

At least three (3) lines, in general, will be reserved for the entire title.

- The first line is for the table/listing/figure number;
- The second line is for the actual title; and
- The third line is reserved for the analysis population descriptor.

All titles will be centered, as shown in the following example:

Table 14.3.2.1
Overall Incidence of Safety Events
Safety Population

7.3.3 Footnotes

Unless otherwise specified, footnotes will appear on all pages within the tables and listings as follows:

- Footnotes will be in the format of “Note: followed by 2 spaces, then the footnotes”, as shown in the following example:

Note: SD = Standard Deviation; SEM = Standard Error of the Mean.

- Each line of a complete footnote should end with a period.
- When an abbreviation (e.g. TESE, SAE, ITT, etc.) appears first time in the whole set of TLFs for a study, a footnote should be provided at least once; and it is up to the study statistician, to decide whether there is a need to repeat the same footnote for the rest of TLFs.
- A footnote serves as a brief explanation/clarification /definition /concept of a flag symbol or a character, an abbreviation, a terminology, etc., that appears in or relates directly to the displayed content of a table/listing/figure.
- Footnotes will not contain detailed/technical elaboration of, for example, a mathematical/statistical formula, a statistical term/test, or an algorithm for deriving a parameter value, which should be addressed in the text of the SAP.
- All footnotes will be at the lowest line of the page immediately above the footer. There will be one space between the last footnote and the footer.
- For Tables, first footnote will provide source listings and/or analysis datasets names for cross-referencing.

7.3.4 Footer

The following footer should appear at the very bottom of each page of a table, a listing, or a figure generated in SAS in the lower left corner:

Program: PGMNAME.sas; Creation Date and Time: MMDDDDYYYY HH:MM
Data Cutoff: DDMMYY:HH:MM:SS – Output Generated MMM DD, YYYY

where PGMNAME = SAS program name.

7.4 Statistical Conventions

7.4.1 Statistics Reported

- Unless otherwise specified, the mean and standard deviation (SD) will be displayed to one more decimal place than the original value, while minimum and maximum will be reported in the format of the original data, e.g.:

Original: xx

Mean and SD: xx.x

Minimum and maximum: xx

- Descriptive statistics in this template include: **Mean, Median, Standard Deviation (SD), Minimum, Maximum, and N**. In addition, 95% CI will be presented when appropriate.
- Unless specified in the actual TLF shells for a study, all percentages will be rounded to 1 decimal place in all tables/listings/figures. Rounding will take place after all calculations have been performed.
- Use of N versus n:
 - N = total number of subjects or subjects in the population.
 - n = total number of subjects or subjects in the specific category.

7.4.2 SAS Procedure Output

If appropriate, SAS procedure output may be formatted and saved as source for references and will be included in Appendix.

7.4.3 Tables Summarizing Categorical Data

The following specifications apply to tables that summarize categorical data:

- Percent of events should be left blank (including the parentheses) if the number of events is zero.
- If the categories of a parameter are ordered, then all categories between the maximum possible category and the minimum category will be included, even if $n=0$ for a given category between the minimum and maximum level for that parameter.
- If the categories are not ordered, then only those categories for which there is at least one subject represented will be included.
- A missing category will be added to any parameter for which information is not available for any subjects.

7.4.4 Subject Data Listings

In general, individual subject data listings should include all subjects with data. However, if a subject data listing includes only subjects who met a certain condition, and there were no subjects who met that condition, then a “message” will appear indicating that no subjects met the condition for inclusion in that listing.

8. REFERENCES

[1] ICH E3 (1995): Structure and Content of Clinical Study Reports. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

[2] ICH E6 (1996): Guideline for Good Clinical Practice. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

[3] ICH E9 (1998): Statistical Principles for Clinical Trials. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

[4] Zariffa, J., et al., Characterization of neurological recovery following traumatic sensorimotor complete thoracic spinal cord injury. *Spinal Cord*, 2011. 49(3): p. 463-71.

[5] Fawcett, J.W., et al., Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal Cord*, 2007. 45(3): p. 190-205.

[6] Lee, B.B., et al., The global map for traumatic spinal cord injury epidemiology: update 2011, global incidence rate. *Spinal Cord*, 2014. 52(2): p. 110-6.

[7] MedDRA Version 17.0 (March 2014). International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

[8] The WHO Drug Dictionary (WHO-DD) (March 2014). World Health Organization (WHO) Uppsala Monitoring Center (UMC).

[9] SAS[®] for Windows[®] Version 9.3. SAS Inc. Cary, North Carolina USA.

9. APPENDICES

9.1 Planned Tables, Listings, and Figures

Table Number	Table Name
Table 14.1.1.1	Summary of Subject Enrollment by Site and Analysis Set – Safety Set Excluding Screen Failure Subjects
Table 14.1.1.2	Reasons for Screen Failures – Safety Set Excluding Screen Failure Subjects
Table 14.1.1.3	Subject Disposition – Safety Set Excluding Screen Failure Subjects
Table 14.1.2	Summary of Protocol Deviations – Safety Set Excluding Screen Failure Subjects
Table 14.1.3	Summary of Demographic and Baseline Characteristics – Safety Set Excluding Screen Failure Subjects
Table 14.1.4	Prior and Concomitant Medications - Safety Set Excluding Screen Failure Subjects
Table 14.2.1.1.1	Primary Efficacy Analysis - Primary Endpoint Analysis Set
Table 14.2.1.1.2	Primary Efficacy Analysis - All Treated Set
Table 14.2.1.1.3	Primary Efficacy Analysis - Sensitivity Analysis
Table 14.2.1.2	AIS Scores - Efficacy Analysis - All Treated Set
Table 14.2.1.3	Number of Subjects Each AIS Grade at Each Post-Implantation Time Point - All Treated Set
Table 14.2.2.1	Neurological Level of Injury - Efficacy Analysis - All Treated Set
Table 14.2.2.2	Subject Neurological Level of Injury (NLI) and Zone of Partial Preservation at Assessment Time Points - All Treated Set
Table 14.2.2.3	Number of Subjects With Changes in Neurological Level Direction from Reference Time Points – All Treated Set
Table 14.2.3.1.1	Subject ISNCSCI Sensory Total Score and Changes from Reference Time Points - All Treated Set
Table 14.2.3.1.2	Mean ISNCSCI Sensory Total Score and Changes from Reference Time Points - All Treated Set
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