Statistical Analysis Plan for the ^{13}C-Methacetin Breath Test using the BreathID® MCS System for Conatus phase 2 study of Emricasan, an Oral Caspase Inhibitor, under Protocol IDN-6556-17 (IND111463)

SAP for Protocol No. CON-EX-0217 NCT03462576

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1.0	August 08, 2019	Gil Guggenheim	Initial Release

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1 ABBREVIATIONS

AE - Adverse Event
CDOB - Cumulative Delta over Baseline
CI - Confidence Interval
CL - Confidence Limits
CO_2 - Carbon dioxide
cPDRxx - Cumulative Percentage Dose Recovery at xx minutes from ingestion
CRF - Case Report Form
CSR - Clinical Study Report
CTP - Child-Turcotte-Pugh (score)
DOB - Delta over Baseline
eCRF - Electronic Case Report Form
EGD - Esophagogastroduodenoscopy
GCP - Good Clinical Practice
HCC - Hepatocellular Carcinoma
HE - Hepatic Encephalopathy
HR - Hazard Ratio
IDE - Investigational Device Exemption
ITT - Intent to treat (population)
MBT - ^{13}C-Methacetin Breath Test
MCS - Molecular Correlation Spectrometry
MELD - Model for Endstage Liver Disease
NAFLD - Nonalcoholic Fatty Liver Disease
NASH - Nonalcoholic Steatohepatitis
OPTN - Organ Procurement and Transplantation Network
PDR - Percent Dose Recovered (expressed as % per hour)
PP - Per Protocol (population)
SAE - Serious Adverse Event
SAP - Statistical Analysis Plan
SBP - Spontaneous Bacterial Peritonitis
SD - Standard Deviation
SF - Screen Failures
SUSAR - Suspected unexpected serious adverse reaction
TIPS - Transjugular Intrahepatic Shunt
UADE - Unanticipated Adverse Device Effect
US - United States (of America)
USA - United States of America

2 INTRODUCTION

This Statistical Analysis Plan (SAP) (for Exalenz' companion study protocol: CON-EX-0217) was developed based on the original study protocol version 2.0, dated 24 May 2017 and is a more detailed companion to the "Statistical Methods" section of the study protocol.

The companion protocol and this SAP describe how Exalenz intends to use the clinical data being obtained during the study conducted by Conatus Pharmaceuticals Inc. (Conatus) for study IDN-6556-17 (Emricasan) being conducted under IND 111463.

When differences exist in methods, descriptions or explanations provided in the protocol and this SAP, the SAP prevails.

Since this study is a companion to a pharmaceutical company's study, the data management for the main study can independently determine as to when a data freeze or a data lock shall be performed. Therefore, for the Exalenz companion protocol purposes, any amendments to the SAP will be made prior to Exalenz independently accessing the data from the database freeze or lock. In case additional analyses not described in the final SAP or deviations from the final SAP are required, they will be documented in the clinical study report (CSR).

3 STUDY OBJECTIVES AND ENDPOINTS

3.1 Study Objectives

The data generated in this companion study will be used to validate an algorithm developed under parallel Exalenz studies. Additionally, the companion study aims to evaluate the capabilities of the MBT to assess the severity of Nonalcoholic Steatohepatitis (NASH), predict clinical outcome (hepatic decompensation) events and monitor changes of MBT results in subjects with and without NASH treatment.

3.1.1 Primary Objective

- To validate the ability of the MBT to predict any hepatic decompensation event (considering all hepatic decompensation events as defined in section 8.4.1) using a predefined cut-off of $PDR_{peak} \leq 5.5\%/h$ (see **Appendix A** for detailed description of parameter calculation).

3.1.2 Secondary Objective

- To validate the ability of the MBT to predict any hepatic decompensation event (considering all hepatic decompensation events as defined in section 8.4.1) using a second predefined cut-off of $PDR_{peak} \leq 7.5\%/h$.
- To validate the ability of the MBT to predict hepatic decompensation events within one year (for each of the two predefined cut-offs independently).
- To validate the ability of the MBT to predict hepatic decompensation events when using all the repetitions of the MBT measurements (time dependent parameter) (for each of the two predefined cut-offs independently).
- To validate the ability of the MBT to predict hepatic decompensation events within six months (for each of the two predefined cut-offs independently).
- To validate the ability of the MBT to predict new hepatic decompensation events (considering only reported hepatic decompensation events, as defined in section 8.4.2.5 as per Conatus protocol IDN-6556-17) as observed throughout the study (for each of the two predefined cut-offs independently).

3.1.3 Exploratory Objective

- To validate the ability of the MBT to predict specific types of hepatic decompensation events (for each of the two predefined cut-offs independently).
- To describe the change in MBT between the emricasan treatment arms and the placebo arm, thus assessing the response to treatment.

3.1.4 Safety Objective

All adverse events, serious adverse events (SAE), suspected unexpected serious adverse reactions (SUSAR) and unanticipated adverse device effects (UADE) will be reported according to local regulations. No breath-test related adverse events are expected. For more information please refer to the Investigator's Brochure.

3.2 Study Endpoints

3.2.1 Primary Endpoint

The primary efficacy endpoint is the event-free survival (considering all hepatic decompensation events including events based on the reported AEs or SAEs, as defined in section 8.4.1).

3.2.2 Secondary Endpoints

The secondary efficacy endpoints for this study include:

- The event-free survival (considering all hepatic decompensation events including events based on the reported AEs or SAEs, as defined in section 8.4.1)
- The one-year event-free survival
- The event free survival when using all the repetitions of the MBT measurements (time dependent parameter).
- The six-month event-free survival
- The event-free survival (considering only reported hepatic decompensation events, as defined in section 8.4.2.5 as per Conatus protocol IDN-6556-17)

3.2.3 Exploratory Endpoints

- The specific type of hepatic decompensation event-free survival
- Absolute mean and percent mean change in MBT parameters between MBT visits (for each treatment arm)

3.2.4 Safety Endpoint Measure

Safety endpoints includes all AE's in general and by seriousness, severity related to the MBT. No breath-test related adverse events are expected.

4 STUDY DESIGN

Please refer to Conatus' protocol IDN-6556-17.

This study is a companion protocol that will use the data generated by Conatus' study of emricasan under protocol IDN-6556-17. The IDN-6556-17 study is a Phase 2, multicenter, double-blind, randomized, placebo-controlled, dose-response study to evaluate the safety and efficacy of emricasan in improving event-free survival based on a composite clinical endpoint (where all-cause mortality, new decompensation events, and Model for Endstage Liver Disease (MELD) score progression are counted as events as defined in section 8.4.2.5) in subjects with decompensated NASH cirrhosis.

The study treatment duration will be at least 48 weeks with study visits every 4 weeks up to week 48 and every 8 weeks after week 48. All subjects will continue treatment until the last subject in the study reaches 48 weeks in the study. This subject will undergo the assessments of the final treatment visit at week 48. For all other subjects, the final treatment visit should take place on their last study visit prior to or on the day of the final treatment visit of the last subject who has been in the study for 48 weeks.

As part of the IDN-6556-17 study, the MBT will be performed during a screening visit, every 24 weeks and at the final treatment visit, to assess whether emricasan compared to placebo improves liver metabolic function as determined by the Methacetin Breath Test.

The data obtained in this study will be sequestered from Exalenz in order to allow potential pooling of the data received from Conatus' study as well as other parallel recruiting studies, if applicable, where both the MBT and clinical outcome (e.g. hepatic decompensation events) will be available. Once sufficient data will be accrued, it will be used to validate the algorithm

developed using data from IDE# G080227 and other clinical data accumulated by Exalenz to date. Additional analyses may be performed by Exalenz on the data to be received from this Conatus study after validation of the aforementioned algorithm.

4.1 Sample Size Considerations

The plan is to enroll a subset of subjects that will be screened under Conatus' IDN-6556-17 study. This Conatus study plans to enroll 210 subjects (70 subjects per treatment arm) to be randomly assigned to 1 of 3 treatment groups, 2 doses of emricasan (25 mg or 5 mg) or placebo in a 1:1:1 ratio. A 45% screen failure (SF) rate is estimated. It is expected that approximately 90% of the patients enrolled will perform the MBT. The total number of MBT results expected ranges between 120 and 310 at screening and up to 200 at respective study visits with 24-week intervals and at the final treatment visit.

5 GENERAL CONSIDERATIONS FOR HANDLING OF MISSING DATA

5.1 Premature Withdrawal and Missing Data

For patients who are withdrawn from the study prior to study completion, all data compiled up to the point of discontinuation will be used for analysis. All withdrawals will be included in all analyses up to the time of withdrawal.
There will be no imputation for missing data.

6 SIGNIFICANCE LEVELS AND HANDLING OF TYPE I ERROR

6.1 Type I Error

The overall significance level for this study is 5% using two-tailed tests, except for treatment by site interaction that will be tested at a significance level of 10%.

6.2 Hierarchy Approach for Secondary Endpoint Analysis

The hierarchy approach will be adopted for the primary and secondary endpoints to control type I error due to multiple endpoint testing. Thus the primary endpoint will first be analyzed and only if $p<0.05$, will the secondary endpoint be analyzed. This approach will maintain the overall study type I error by continuing to analyze the next end-point in the hierarchy only if the previous endpoint analysis was found significant. The hierarchy approach is extended for the secondary endpoints as well, according to the order that they appear in section 3.2.2 above.

7 ANALYSIS SETS

7.1 Safety Analysis Set

The Safety analysis set will include all subjects (randomized and non-randomized into the Conatus emricasan study under protocol IDN-6556-17) that initiated at least one MBT (had taken Methacetin), even if the MBT was not completed or the result was not valid.

7.2 Intent To Diagnose (ITD) Analysis Set

The intent to diagnose (ITD) analysis set will include all subjects that were randomized into the Conatus emricasan study under protocol IDN-6556-17 and that had at least one valid MBT result.

7.3 Per Protocol (PP) Analysis Set

The per protocol (PP) analysis set will include all subjects from the ITD analysis set who did not have any major protocol deviations and exclude any subject that had a previous transjugular intrahepatic shunt (TIPS) or bariatric surgery that may affect the efficacy of the breath test.

7.4 Statistical Analysis of Analysis Sets

The safety analysis set will serve as the principal data analysis set for the safety.

The PP analysis set will serve as the principal analysis set for the efficacy analyses.

The primary and secondary efficacy assessments will also be performed on the ITD analysis set.

8 STATISTICAL ANALYSES

8.1 General Considerations for Data Analyses

All analyses will be performed using either SAS® v9.4 or higher (SAS Institute, Cary NC, US) or the R software version 3.6 or higher (R Development Core Team. Vienna, Austria).

The standard summary statistics for continuous variables are: N, mean, standard deviation, median, minimum and maximum. The standard summary statistics for categorical variables are: count and proportion.

Any statistical tests performed, will be two-sided. The required significance level of findings will be equal to or lower than 5%. Where confidence limits are appropriate, the confidence level will be 95%. Nominal p-values and unadjusted confidence intervals will be presented.

8.2 Baseline Definitions

The study baseline will be defined as the last available, non-missing observation prior to first study drug (emricasan or placebo) administration, unless specifically mentioned otherwise.

For survival models: The first valid MBT test will be defined as the baseline and day 0 of follow up. For MELD scores, the first value measured on or after the day of the first valid MBT will serve as baseline value, even if there are later MELD results available prior to first study drug (emricasan or placebo) administration. The MELD progression outcome, 4 point increase in MELD, will thus be calculated by comparing each MELD score to the first available MELD score on or after the first valid MBT date.

8.3 Disposition of Patients

Subject dispositions will be summarized based on all subjects screened into the study, and for each treatment group.

The following subject disposition information will be presented:

- The number and percentage of subjects who had valid MBT for each visit.
- The number and percentage of reasons for not having a valid MBT for each visit.
- The number and percentages of subjects that were excluded from the PP analysis set, by reason for exclusion.

8.4 Efficacy Analyses

All hepatic decompensation events will be summarized descriptively in summary tables for each event type described in the following sections.

8.4.1 Primary Endpoint

The MBT parameter used to predict hepatic decompensation event is PDR_{peak}. Any PDR_{peak} value of less or equal to 5.5 %/h (see **Appendix A** for detailed description of parameter calculation) will be considered as 'high risk' and any value above that threshold will be considered as 'lesser risk'. The dichotomic MBT result will be tested for significance using the Cox proportional hazards regression model with site and Conatus protocol IDN-6556-17 randomized arm as covariates. If the Conatus protocol IDN-6556-17 randomized arm factor is found non-significant (i.e. p-value > 0.05), then this factor will not be a covariate for the main analysis to be performed. If the Conatus protocol IDN-6556-17 randomized arm factor is found statistically significant (i.e. p-value ≤ 0.05), then the main analysis will be performed keeping this factor as a covariate (to 'adjust' the analysis for treatment).

The following list defines the hepatic decompensation events for the primary endpoint:

- Liver-specific mortality
- Liver transplant
- New and/or recurrent hepatic decompensation events

  - Variceal hemorrhage that required 'non-drug therapy' (e.g. variceal ligation, sclerotherapy) based on the AE log or requiring hospitalization
  - Portal hypertensive gastropathy hemorrhage requiring hospitalization
  - Occurrence of large gastroesophageal varices or any varices with red wale sign (classified as severe in the AE log) and that required 'non-drug therapy' (e.g. variceal ligation or sclerotherapy) based on the AE log to avoid hemorrhage
  - Ascites requiring diuretics (in a subject without prior history of ascites requiring diuretics) or refractory ascites requiring 'non-drug therapy' (e.g. paracentesis) based on the AE log (in a subject with history of ascites requiring diuretics).
  - Any onset of hepatic encephalopathy (HE) requiring hospitalization (classified as SAE) in the absence of known co-morbidities or alternative causes.
  - Hepatorenal syndrome requiring hospitalization
  - Spontaneous bacterial peritonitis (SBP) requiring hospitalization
- MELD score progression defined as any increase ≥4 points from baseline

These hepatic decompensation events are identified using the study's 'new decompensation event' dataset as well as events listed in the AE and SAE logs, the reason for (early) termination, the comment and the lab results (incl. MELD scores) datasets. All potential hepatic decompensation events will be adjudicated through a medical review prior to the primary efficacy analysis and blinded to the breath test results. Once defined and adjudicated, the first of the hepatic decompensation events after the first valid MBT will be used for the respective event-free survival analysis.

All MELD scores will be calculated using the formula from the US Organ Procurement and Transplantation Network (OPTN) Policy from 2016 (**Appendix B**). MELD score progression will not include subjects who are started on anticoagulants after the first valid

MBT (and prior to the identified MELD progression event) that can affect the PT or INR at the time of MELD assessment.

The time-to-first event will be derived as the number of days between the day of the screening MBT test and the date when the first hepatic decompensation event occurs or when a subject is censored (i.e., event/censored date minus screening MBT date plus 1). Subjects will be censored at their last study visit for the following reasons:

- If a subject discontinues the study prior to the end of the study without experiencing a hepatic decompensation event
- If a subject reaches the Final Treatment visit without experiencing a hepatic decompensation event
- If a subject developes hepatocellular carcinoma (HCC)

Survival analysis will be conducted using the Cox proportional hazard model. The model summary will include the number of subjects in the model, and a table with each covariate in a separate line specifying the coefficient's value, Hazard Ratio, Hazard Ratio 95% Confidence Interval and p-value. In addition, a Kaplan-Meier plot for event-free survival will be presented, stratified by MBT parameter along with the MBT parameter log-rank p-value. Additionally a crosstab table of MBT parameter and events will be presented.

8.4.2 Secondary Endpoints

8.4.2.1 The overall event-free survival with a second predefined cut-off

The event free survival will be analyzed in the same manner as the primary endpoint analysis with the exception that the dichotomic MBT result will be based on a second predefined cut-off: Any PDR_{peak} value of less or equal to 7.5 %/h (see **Appendix A** for detailed description of parameter calculation) will be considered as ‘high risk’ and any value above that threshold will be considered as ‘lesser risk’.

8.4.2.2 The one-year event-free survival

The one-year event free survival will be analyzed in the same manner as the primary endpoint analysis with the exception of censoring all subjects after 1 year (365 days) from baseline MBT date.

This analysis will be repeated while using the second pre-defined cut-off described in the first secondary endpoint (section 8.4.2.1).

8.4.2.3 The event free survival when using all the repetitions of the MBT measurements (time dependent parameter)

The event free survival will be analyzed in the same manner as the primary endpoint analysis with the exception of using all repetitions of the MBT measurements while dividing the prediction times to the intervals between tests by applying the Time dependent covariate method.

This analysis will be repeated while using the second pre-defined cut-off described in the first secondary endpoint (section 8.4.2.1).

8.4.2.4 The six-month event-free survival

The six-month event free survival will be analyzed in the same manner as the primary endpoint analysis with the exception of censoring all subjects after six months (180 days) from baseline MBT date.

This analysis will be repeated while using the second pre-defined cut-off described in the first secondary endpoint (section 8.4.2.1).

8.4.2.5 The event-free survival considering only new hepatic decompensation events as defined in Conatus study protocol IDN-6556-17

The event free survival will be analyzed in the same manner as the primary and secondary endpoint analyses (sections 8.4.1, 8.4.2.1, 8.4.2.3 and 8.4.2.4) taking only hepatic decompensation events into consideration as defined and adjudicated in the Conatus study protocol IDN-6556-17:

1. All-cause mortality
2. New decompensation events

a. Variceal hemorrhage (including recurrent variceal hemorrhage) documented by endoscopy and requiring hospitalization
b. New onset ascites requiring diuretics (in a subject without prior history of ascites requiring diuretics)
c. New onset HE ≥ grade II requiring hospitalization in the absence of other co-morbidities or alternative causes (in a subject without prior history of HE ≥ grade II)
d. Hepatorenal syndrome requiring hospitalization (either type 1 or 2)
e. SBP requiring hospitalization

3. MELD score progression defined as any increase ≥4 points from baseline

This analysis will be repeated while using the second pre-defined cut-off described in the first secondary endpoint (section 8.4.2.1).

8.4.3 Exploratory Endpoints

8.4.3.1 The specific hepatic decompensation type event free survival

The specific types of hepatic decompensation events or combinations of them for event free survival will be analyzed in a similar manner as the primary endpoint analysis. The following list contains all the separate analyses that will be performed:

1. All-cause mortality
2. Liver-specific mortality
3. Liver-specific mortality **or** liver transplant
4. Liver transplant
5. Variceal hemorrhage that required 'non-drug therapy' (e.g. variceal ligation, sclerotherapy) based on the AE log or requiring hospitalization **or** portal hypertensive gastropathy hemorrhage requiring hospitalization
6. Variceal hemorrhage that required 'non-drug therapy' (e.g. variceal ligation, sclerotherapy) based on the AE log or requiring hospitalization **or** portal hypertensive gastropathy hemorrhage requiring hospitalization **or** occurrence of

large varices or varices with red wale signs (classified as severe in the AE log) and that required 'non-drug therapy' (e.g. variceal band ligation or sclerotherapy) based on the AE log to avoid hemorrhage

7. New onset ascites requiring diuretics (in a subject without prior history of ascites requiring diuretics)
8. SBP requiring hospitalization
9. New onset ascites requiring diuretics (in a subject without prior history of ascites requiring diuretics) **or** any occurrence of refractory ascites requiring 'non-drug therapy' (e.g. paracentesis) based on the AE log (in a subject with history of ascites requiring diuretics) **or** SBP requiring hospitalization
10. New onset HE ≥ grade II requiring hospitalization (classified as SAE) in the absence of other co-morbidities or alternative causes (in a subject without prior history of HE ≥ grade II)
11. Any onset of HE requiring hospitalization (classified as SAE) in the absence of known co-morbidities or alternative causes
12. Hepatorenal syndrome requiring hospitalization
13. MELD score progression defined as any increase ≥4 points from baseline
14. All hepatic decompensation events defined in section 8.4.1, except for MELD score progression.

This analysis will be repeated while using the second pre-defined cut-off described in the first secondary endpoint (section 8.4.2.1).

8.4.3.2 Absolute mean and percent mean change in MBT parameters

The absolute and percent change in MBT parameters will be summarized descriptively by summarizing the PDR_{Peak} and $cPDR_{30min}$ (see **Appendix A**) changes and percent changes for each treatment group. Due to the small sample expected in this analysis (missing values were not related to outcome), no statistical tests will be applied on that endpoint.

8.5 Treatment by Site Interaction

Site by MBT dichotomy interaction will be added to the primary efficacy model as a covariate to test for site effect on the endpoints.

For sites with less than 10 subjects, the following pooling of sites method will be applied: Sites will be sorted from smallest to largest based on the number of randomized subjects with valid baseline MBT results. The smallest site will be pooled with the second smallest, and if necessary with the next sites in line until the site group reaches 10 subjects or more. The site value for those sites will be assigned "Site Group 1". Then the next site in line, if lower than 10 subjects, will be pooled with the sites after it until the site group reaches 10, and so forth until all sites or site groups have at least 10 subjects.

8.6 Safety Analyses

All safety analyses will be conducted on the safety analysis set.

All safety data will be presented by patient in listings (including assessments of abnormality and clinical significance, where applicable) and summarized appropriately,

No inferential statistical testing will be performed for safety variables.

APPENDIX A - MBT PARAMETER & ALGORITHM CALCULATION

1. MBT PARAMETER OF INTEREST

- The MBT parameter of interest for the primary and all the secondary endpoints to be calculated is the PDR_{peak} measured in %/h, which is the maximum rate of metabolized ^{13}C-Methacetin observed within a breath test. When applying a predefined test cut-off on the PDR_{peak}, the dichotomic test result is obtained.
- An additional parameter to be used for the assessment of treatment response as part of an exploratory endpoint is the $cPDR_{30min}$, which is the cumulative percentage dose recovery of the metabolized ^{13}C-Methacetin 30 minutes after ingestion of the test substrate.

2. MBT PREDICTIVE TEST ALGORITHM CALCULATION

The following steps shall be followed to calculate the parameter of interest and the resulting dichotomized test result.

1. Subjects visit height and weight as well as all delta over baseline (DOB) measures with corresponding time point (T) shall be retrieved from the database.
2. DOB values must be sorted by time from lowest to highest time before any calculation, while a first pair of data points should always be added with time T_0=0 min and DOB_0 =0.
3. In order for a test to be valid, the following conditions should be met:
    a. Height should be within acceptable range: 120 cm – 240 cm.
    b. Weight should be within acceptable range: 35 kg – 200 kg.
    c. The last time point (T) should be after 30 minutes.
4. **PDR:** The DOBs shall be transformed into percentage dose recovery rates (PDRs) by normalizing the DOB using patient body weight and height at each observed time point (i) by using the following formula:

$$PDR_i = 0.01817853 \cdot DOB_i \cdot Weight^{0.5378} \cdot Height^{0.3963}$$

While Weight is in kg, and Height is in cm

5. **PDR_{peak}**: PDR_{peak} is defined as the maximum PDR.

$$PDR_{peak} = \max(PDR_0, PDR_1, PDR_2, \dots, PDR_{24})$$

6. **Cut-off**: The cut-off to be applied for the predictive MBT test for assessment of event-free survival is 5.5 %/h.
    - Any PDR_{peak} value **below, or equal to** 5.5%/h is considered as **high risk for development of hepatic decompensation events**.
    - Any PDR_{peak} value **greater than** 5.5%/h is considered as **lesser risk for development of hepatic decompensation events**.

7. **Second Cut-off**: A second cut-off to be applied for the predictive MBT test for assessment of event-free survival is 7.5 %/h.
    - Any PDR_{peak} value **below, or equal to** 7.5%/h is considered as **high risk for development of hepatic decompensation events**.
    - Any PDR_{peak} value **greater than** 7.5%/h is considered as **lesser risk for development of hepatic decompensation events**.

An additional parameter will be used for the exploratory endpoint analysis of treatment response: **$cPDR_{30min}$**

8. **$cPDR_{30min}$**: The following formula will be used to obtain $cPDR_{30min}$:

    - Find 'a', the index for which:

$$T_{a-1} < 30 \leq T_a$$

    - Calculate **PDR_{30min}**:

$$PDR_{30min} = PDR_{a-1} + \frac{PDR_a - PDR_{a-1}}{T_a - T_{a-1}} \cdot (30 - T_{a-1})$$

    - Finally, calculate **$cPDR_{30min}$**:

$$cPDR_{30min} = \sum_{i=1}^{a-1} \left(\frac{\frac{T_i - T_{i-1}}{60} \cdot (PDR_i + PDR_{i-1})}{2} \right) + \frac{\frac{30 - T_{a-1}}{60} \cdot (PDR_{30min} + PDR_{a-1})}{2}$$

No cut-offs are being applied on this parameter for the planned analyses.

APPENDIX B – MELD SCORE FORMULA FROM US OPTN POLICY (2016)

Subjects receive an initial MELD(i) score equal to:

initial MELD(i) = 0.957 x Loge(creatinine mg/dL) + 0. 378 x Loge(bilirubin mg/dL) + 1.120 x Loge (INR) + 0.643

Laboratory values less than 1.0 will be set to 1.0 when calculating a subject's MELD score.

The following subjects will receive a creatinine value of 4.0 mg/dL:

- Subjects with a creatinine value greater than 4.0 mg/dL
- Subjects who received two or more dialysis treatments within the prior 7 days
- Subjects who received 24 hours of continuous veno-venous hemodialysis (CVVHD) within the prior 7 days

The MELD score derived from this calculation will be rounded to the tenth decimal place and then multiplied by 10. The maximum MELD score is 40.

For candidates with an initial MELD score greater than 11, the MELD score is then re-calculated as follows:

MELD = MELD(i) + 1.32*(137-Na) – [0.033*MELD(i)*(137-Na)]

Sodium values less than 125 mmol/L will be set to 125, and values greater than 137 mmol/L will be set to 137.

Resources:

https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf Section 9.1.D on Page 169