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Statistical Analysis Plan

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1. Version History

Version	Summary of Changes	Author(s)/Title
1.0	Please reference CBP10060 Version A: BP for CEP302 HCL in Pediatric Subject approved via Agile. • Change in Version from alphabetical to numeric (Statistical Analysis Plan Template Version 3.0 was used). • Statistical Analysis Plan was based on CEP302 Version F. • Added in term of Age2-6 years old subject in Section 5 Investigation Plan per CEP302 Version F. • Changes in Section 6 Determination of Sample Size per CEP302 Version F. • Changes in Section 7.1.3 Analysis Sets: from "Continued Access Phase: The subject disposition, adverse event and device performance data will be presented." to "Continued Access Phase: Safety data will be summarized and presented." per CEP302 Version F. • Changes in Section 7.2 General Methodology – "SG ≤ 54 mg/dL was added" per CEP302 Version F. • Added Exploratory Analyses in Section 7.12 per CEP302 Version F. • Added Exploratory Analyses in Section 10 Statistical Appendices. • Added SG ≤ 54 mg/dL in Section 10 Statistical Appendices. • Updated Distribution of Subject BMI in Section 10 Statistical Appendices using CDC criteria.	[redacted]

2. List of Abbreviations and Definitions of Terms

Abbreviation	Definition
A1C	Glycosylated hemoglobin
AE	Adverse Event
ADE	Adverse Device Effect
ASIC	Application Specific Integrated Circuit
BMI	Body Mass Index
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CGM	Continuous Glucose Monitoring
CGMS	Continuous Glucose Monitoring System
CL	Closed Loop
CSII	Continuous Subcutaneous Insulin Infusion
DCCT	Diabetes Control and Complications Trial

DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Form
EC	Ethics Committee
EIS	Electrochemical Impedance Spectroscopy
ER	Emergency Room
FDA	United States Food and Drug Administration
FST	Frequent Sample Testing
GCRC	General Clinical Research Center
hCG	Human chorionic gonadotropin
HCL	Hybrid Closed Loop
HFE	Human Factors Engineer
HL	HelpLine
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	Informed Consent Form
IDE	Investigational Device Exemption
IFU	Instructions for Use
IRB	Institutional Review Board
IV	Intravenous
LSL	Low Suspend Limit
MedDRA	Medical Dictionary for Regulatory Activities
NDC	National Drug Code
NGSP	National Glycohemoglobin Standardization Program
OC-RDC	Oracle Clinical Remote Data Capture
OLS	Clinical Online Store
PC	Personal Computer
QC	Quality Control
RF	Radio Frequency
SAE	Serious Adverse Event
SADE	Serious Adverse Device Events
SG	Sensor Glucose
SGV	Sensor Glucose Value
SMBG	Self-Monitoring of Blood Glucose
SSL	Secure Socket Layer
TDD	Total Daily Dose

TSH	Thyroid-stimulating hormone
UADE	Unanticipated Adverse Device Effect

3. Introduction

Closed loop technology has been shown to reduce both hypoglycemia and hyperglycemia, as well as reduce glycemic variability.

Previous studies have evaluated prototype versions of the Medtronic closed-loop insulin delivery systems in pediatric patients, as well as adolescents and young adults. Researchers at the Yale University School of Medicine studied the performance of both a hybrid closed-loop algorithm and a fully closed loop algorithm using the Medtronic MMT-715 insulin pump, the Medtronic Sof-sensor and MiniLink transmitter and a control algorithm running on a laptop computer [Weinzimer et al, 2008]. Seventeen subjects between the ages of 13 and 20 years old participated in the study with eight subjects undergoing testing with a fully closed-loop algorithm, and the remaining nine subjects being evaluated using the hybrid closed-loop algorithm. This study demonstrated that a fully closed loop artificial pancreas using an external glucose sensor is feasible and effective in adolescents with type 1 diabetes.

The Type 1 Diabetes TrialNet Study Groups used this same system to evaluate inpatient hybrid closed-loop control (HCLC) initiated shortly after the diagnosis of type 1 diabetes [Diabetes Research in Children Network Study Group, 2013]. Forty eight subjects between the ages of 7.8 and 37.7 years old participated in the intensive treatment group and received inpatient HCLC followed by outpatient sensor augmented pump therapy. Forty six of the 48 subjects were less than 18 years old. The study found that inpatient HCLC safely initiated soon after the diagnosis of type 1 diabetes resulted in the rapid decrease in blood glucose levels within 24 hours of initiation and that while using HCLC, about 80% of the glucose levels were in the target range of 71-180 mg/dL, with minimal hypoglycemia.

Researchers at Princess Margaret Hospital for Children and the University of Western Australia in Perth, Australia studied a closed-loop system consisting of the Medtronic Paradigm Veo insulin pump, the Medtronic Enlite sensor, MiniLink transmitter and a fully closed-loop algorithm running on BlackBerry Storm smartphone in eight subjects between the ages of three and 21 years old [O'Grady et al, 2012]. These subjects underwent a total of 145 hours of closed-loop control over 16 nights. During these experiments, the closed-loop algorithm maintained venous plasma glucose in target (between 70 and 144 mg/dL) 78% of the time. This study also demonstrated the feasibility of a portable, automated, closed-loop system for overnight glucose control in adolescents and young adults with type 1 diabetes.

4. Study Objectives

The purpose of this study is to demonstrate that the hybrid closed loop system and the Low Management Suspend before Low feature are safe.

5. Investigation Plan

This study is a single-arm, multi-center, Home and Hotel Clinical Investigation in pediatric subjects with type 1 diabetes on insulin pump therapy.

Once 10 adult subjects in the pivotal closed loop study have completed participation (i.e. performed last study visit), the DSMB will determine whether it is safe for the pediatric subjects in this study to begin enrollment. As part of this review, the DSMB will look at data from all enrolled subjects in the adult study at this time.

Staged enrollment for 2-6 years age group:
The younger ages (2-4 years) will not be enrolled until it has been shown that all Safety criteria for the 5-6 year olds have been met as follows: Once the DMC (Data Monitoring Committee) have reviewed data for 10 subjects (5-6 years of age) during the first month of the study period and have determined that study participation is safe, subjects 2-4 years of age will be permitted to enroll.

Run-in Period
A total of up to 200 subjects (age 2-13) will be enrolled at up to 15 investigational centers (14 in the US, 1 in the Europe, Middle East and Africa (EMEA) region) in order to reach 120 subjects who will complete the HCL study. The run-in period will primarily be used to allow subjects to become familiar with the new study devices. During the run-in period, subjects will be using the Study Pump (670G) with the Sensor Augmented Pump function only activated (i.e. SmartGuard Low Management features OFF and Auto Mode OFF). At the end of the CGM run-in period at Run-in Visit 4, subjects 7-13 years of age will be asked to undergo 12 hours (maximum) of Low Management Suspend before Low frequent sample testing on the first day of sensor wear. Testing will begin during the day and extend for an overnight stay at the clinic. Subjects 2-6 years of age will not undergo frequent sample testing procedures at this visit.

Manual Mode: Run-in Pump Settings **before** frequent Sample testing, i.e.: Low Management Suspend before Low

- High and Low Setup limits and alert(s) will be set at investigator discretion
  - Low Setup Limit may not be set lower than 65mg/dL
  - For subjects 2-6 years of age, Low Setup Limit should be set at 80mg/dL and no lower than 70mg/dL
- SmartGuard –Low Management must be OFF during this period
- SmartGuard – Auto Mode must be OFF during this period

Manual Mode: Run-in Settings Pump **during** frequent Sample testing, i.e. Low Management Suspend before Low:

- Low Setup limit for subjects 7-13 years must be set at 65 mg/dL
- Subjects 2-6 years of age will not participate in frequent sample testing, but will still complete Visit 4.
- Alert before low should be ON
- Resume basal alert should be ON

Prior to wearing study devices, all subjects and their parent(s)/guardian(s)/companion(s) will be trained on the devices as well as diabetes management principles, such as the treatment of hyperglycemia and hypoglycemia. In addition, there will be training regarding the need to have access to oral glucose in case of hypoglycemia and glucagon. Subjects and their parent(s)/guardian(s)/companion(s) will be instructed to monitor blood glucose using self-monitoring of blood glucose (SMBG) 4-6 times a day. As a precaution, subjects and their parent(s)/guardian(s)/companion(s) will be told that they should keep their own insulin pump supplies in a safe place in case they should be asked during the study to revert back to their own pump. Subjects and their parent(s)/guardian(s) will also be instructed that they should always have back up to their study pump on hand such as insulin and syringe in case of study pump issues (i.e. infusion set occlusion with high glucose).

Study Period – At Home

Following the two week run-in period using the Study Pump (670G), all subjects will participate in a 3-month study period. Prior to entry into Auto Mode, subjects will use the pump in Manual Mode during the first 6 days of the study period in order to collect data on insulin utilization and sensor glucose levels which will be used by the closed loop algorithm. After this 6 day period, the subjects will be allowed to enter Auto Mode. When subjects are in Manual Mode, the SmartGuard Low Management feature is recommended (optional) to be set to Suspend Before Low with a limit setting of 70 mg/dL.

Subjects will be required to have a companion 18 years or older with them during the night for the duration of the study period. The companion will need to be under the same roof, but not necessarily in the same bedroom. During the Hotel stay where subjects are monitored closely, the presence of a companion is not necessary.

Subjects less than 11 years of age should call a parent if they are transitioned out of Auto Mode or for any questions about use of Auto Mode. For subjects 11-13 years of age it is at the investigator's or parents' discretion to determine if a parent should be called in the event of an exit from Auto Mode.

A lockable pouch for the pump may be distributed to subjects at the investigator's discretion. Since the pump version used in this study does not include Block Mode, the purpose of the pouch is to prevent subjects from changing pump settings.

Settings:

- Manual Mode:
  - High Setup limit recommended to be set at 300 mg/dL
    - Alert setting options may be set per investigator discretion
    - Low Setup limit recommended to be set at 70 mg/dL
    - Low Setup Limit may not be set lower than 65mg/dL
    - For subjects 2-6 years of age, Low Setup Limit should be set at 80mg/dL and no lower than 70mg/dL
  - It is recommend (optional) to have the SmartGuard Low Management turned ON
  - Alarms that are fixed in Manual Mode:
    - When Sensor glucose at or below 50 mg/dL

- Auto Mode:
  - High Setup limit recommended to be set at 300 mg/dL
    - Alert setting options may be set per investigator discretion
  - Low Setup limit recommended to be set at 70 mg/dL
    - Low Setup Limit may not be set lower than 65mg/dL
    - For subjects 2-6 years of age, Low Setup Limit should be set at 80mg/dL and no lower than 70mg/dL
  - The Temp Target is recommended to be used when subject exercises
  - Alarms that are fixed in Auto Mode:
    - When Sensor glucose at or below 50 mg/dL
    - When sensor glucose at or above 300 mg/dL for one hour
    - When sensor glucose at or above 250 mg/dL for 3 hours

Study Period - Hotel Study

Subjects 7-13 years of age will participate in a Hotel study (6 days, 5 nights), with the remainder of the study period to be spent at home. The Hotel study may be conducted at either a clinic (GCRC is acceptable), a Hotel or a house as long as staffing, meal and activity requirements are met. Subjects may leave to go to school but must return after school or school activities have finished for the day.

During the hotel stay, subjects will also participate in a daily exercise/activity regimen for a minimum of 4 hours spread throughout the day; exercise/activity may also take place in the evening. With respect to meals, subjects will be allowed to eat as they normally do.

Subjects 2-6 years of age are not required to participate in a hotel study. Instead, they will participate in an out-of-home study for 5 consecutive days, 4-6 hours per day. During that 5 day period, subjects should engage in significant activity/exercise. Such activities could include utilizing gym play areas appropriate for toddlers and young children, swimming, and playground games. Evidence of geographic location and exercise/activity will be documented by daily photograph. In addition, investigational center staff will be present daily for the 4-6 hours of exercise during the 5 day period.

Auto Mode Frequent Sample testing

While in Auto Mode, subjects 7-13 years of age will undergo daytime and/or nighttime Frequent Sample Testing (FST) during the Hotel study with i-STAT® used as a reference value.

Subjects 7-13 years:

Overnight frequent sample testing (10PM to 7AM) in Auto Mode will be every 30 minutes; daytime frequent sample testing (7AM to 10PM) in Auto Mode will be every 60 minutes. The exact times of FST may differ, but the interval for testing should remain as described.

Subjects 2-6 years:

During one of the days of the out-of-home study subjects should undergo frequent sample testing for 4-6 hours using SMBG as a reference method. The frequent sample testing period will be supervised by investigational center staff. Frequency of testing is every 30 minutes.

Note 1: The Auto Mode Frequent Sample Testing may be performed at any time during the hotel study (7-13 years) or the out-of-home study (2-6 years).

Note 2: It is important that calculation of total blood draw be maintained throughout the study so that the total amount of blood volume does not exceed the maximum each subject is allowed. If the maximum is reached, FST will be stopped.

All participating investigational centers will target 3-6 subjects (7-13 years) to undergo a hotel study on Day 7 to Day 14 in Month 1 of the study period. On Days 1-6 of the Study period, during which data necessary for Auto Mode initiation is collected, subjects will not be permitted to turn Auto Mode ON. Entry into Auto Mode will occur on day 7 whether at home or in hotel. A minimum of 4 subjects are recommended to participate in each of the hotel studies. However, the sponsor has discretion to allow more or less subjects to attend a hotel stay should the site request this.

The remaining subjects at each site will be assigned to participate in hotel studies during the last 2 months of the study period:

Month 2 (Day 36-Day 66): 1-2 Hotel Studies N = minimum 20 subjects from all participating research centers will participate in hotel study during month 2. On Days 1-6 of the Study period, during which data necessary for Auto Mode initiation is collected, subjects will not be permitted to turn Auto Mode ON.
Month 3 (Day 67-Day 96): 1-2 Hotel Studies N = minimum 20 subjects from all participating research centers will participate in hotel study during month 2. On Days 1-6 of the Study period, during which data necessary for Auto Mode initiation is collected, subjects will not be permitted to turn Auto Mode ON.

Since all subjects 7-13 years of age are expected to participate in a Hotel Study, each site may conduct 3 - 4 Hotel Studies to ensure that all subjects have the opportunity to take part. After the initial hotel study, sites may schedule additional hotel studies per sponsor discretion.

Continued Access Program: Devices and Supplies:

Subjects will be given the opportunity to extend the use of their study devices for a period of up to 2 years after the end of the study period or until product is available commercially for children 2-13 years of age. If subjects choose to participate in this optional continued access program, they will retain the study devices at the end of study period. During the continued access period, subjects will come in for office visits every 3 months. At each of the quarterly visits, subjects will be asked about the occurrence of adverse events and device complaints. They will also be tested for A1C at each of those visits.

Continued Access Program - Participation in ancillary studies not outlined in this protocol:

Subjects will be permitted to participate in other studies during the continued access period of the study with Sponsor permission, provided that the studies do not include the use of drugs or devices, i.e. devices not used in this study.

6. Determination of Sample Size

A total of up to 200 subjects (age 2-13) will be enrolled at up to 15 investigational centers (14 in the US, 1 EMEA) in order to reach 120 subjects who will complete the HCL study. A minimum of 20 subjects 2-6 years of age will be enrolled (N=10 5-6 years of age, N=10 2-4 years of age). There will be 4-20 subjects per site.

7. Statistical Methods

7.1. Study Subjects

7.1.1. Disposition of Subjects

The number of subjects enrolled in the study will be presented by periods (Run-in, Study, and Continued Access Period). The number of subjects discontinuing prior to study completion will be also summarized.

7.1.2. Clinical Investigation Plan (CIP) Deviations

All protocol deviations will be presented.

7.1.3. Analysis Sets

Run-In Phase and Study Phase:

- Intention to Treat (ITT) Population

  The Intention to Treat (ITT) population will include all subjects who start the study phase.

- Per Protocol (PP) Population

  The Per Protocol (PP) population will include all subjects who start the study phase and are in Auto Mode ≥ 80% of the time.

- Efficacy Population

  The primary analysis will be performed on the ITT population. Sensitivity analysis will be performed on PP population.

- Safety Population

  The Safety Population will include all enrolled subjects.

Continued Access Phase:

Safety data will be summarized and presented.

7.2. General Methodology

DURING HOME PERIOD:

Descriptive Endpoints

- The mean change in A1C will be presented from baseline to end of study
- Change of Total Daily Dose (TDD) of insulin from baseline to end of study
- Change of weight from baseline to end of study
- Time spent in Auto Mode versus time spent in Manual Mode

- Time in different range (% of SG): SG < 50, 54, 60, 70 mg/dL, 70 mg/dL ≤ SG ≤ 180 mg/dL, SG > 180, 250 mg/dL, 350 mg/dL
- Number of Events, AUC and Time in the hyperglycemic range: sensor glucose (SG) > 180, 250, 350 mg/dL
- Number of Events, AUC and Time in the hypoglycemic range: SG < 50, 54, 60, and 70 mg/dL

Safety Data Summarized

- Serious Adverse Events (SAE), Serious Adverse Device Effects (SADE)
- Unanticipated Adverse Device Effects (UADE)
- Incidence of Severe Hypoglycemia
- Incidence of DKA

STUDY PERIOD DURING HOTEL

Descriptive Endpoints

- **During the Run-In Period**
  Low Management Suspend before Low Evaluation:
  - Success rate of prevention of hypoglycemia (i.e. 1 - percent of Low Management Suspend before Low experiments that have 2 or more consecutive reference glucose values of <= 65 mg/dL)
  - Low Management Suspend before Low Performance
  - Sensor performance
- **During the Hotel Period in the Study Period**
  Auto Mode Evaluation:
  - Time in different range (% of i-STAT): BG < 50, 54, 60, 70 mg/dL, 70 mg/dL ≤ BG ≤ 180 mg/dL, BG > 180, 250 mg/dL
  - Number of Events, AUC and Time in the hyperglycemic range: i-STAT® glucose > 180, 250, 350 mg/dL
  - Number of Events, AUC and Time in the hypoglycemic range: i-STAT® glucose < 50, 54, 60, and 70 mg/dL

7.3. Center Pooling

Data will be pooled for analysis.

7.4. Handling of Missing Data

For ITT population, the missing data in A1C measurements will be handled by the multiple imputation approach using imputation regression method, where the independent variables in the regression model are age, gender, baseline HbA1C and BMI. The imputation will be performed five times using the MI procedure and the analysis results will be combined to form one inference using the MIANALYZE procedure in SAS 9.4. The primary analysis population for the change in A1C endpoint will be the ITT population with multiple imputations.

All available device data will be used for the analysis. No imputation will be applied for the device data.

7.5. Adjustments for Multiple Comparisons

No adjustments will be made.

7.6. Demographic and Other Baseline Characteristics

Subject characteristics, including age, gender, ethnicity, diabetes History, height, weight, BMI and baseline HbA1C will be summarized by descriptive statistics (mean, standard deviation, minimum, median, and maximum) for continuous variables and by counts and percentages for categorical variables.

7.7. Treatment Characteristics

No Applicable.

7.8. Interim Analyses

After 1200 patient days an interim report will be generated.

7.9. Health Outcomes Analyses

Descriptive summary will be used to characterize data from questionnaires that are given to subjects to record feedback.

7.10. Exploratory Analyses

7.10.1. Analysis of Primary Endpoint

The primary effectiveness endpoint is change in A1C from baseline to end of 3-month treatment period, defined as A1C measured at the 3-month treatment visit minus A1C measured at the screening visit. The goal is to show simple superiority in reducing A1C from baseline to end of 3-month study period.

7.10.2. Analysis of Secondary Endpoint

The secondary endpoints are hierarchically ordered and will be evaluated in the fixed sequence from endpoint 1 to 3 during the study phase.

- **Secondary Endpoint: % of Time in Euglycemic (70-180 mg/dL)**
  The overall mean change in % of time in euglycemia (70-180 mg/dL) from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).
- **Secondary Endpoint: % of Time in Hyperglycemic (>180 mg/dL)**
  The overall mean change in % of time in hyperglycemia (> 180 mg/dL) from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).
- **Secondary Endpoint: % of Time in Hypoglycemic (<70 mg/dL)**
  The overall mean change in % time in hypoglycemia (< 70 mg/dL) from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).

7.10.3. Sample Size Justification

7.12.3.1 Sample Size for Primary Endpoint

The overall mean change in A1C from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).

The hypothesis is mathematically expressed as:

$Ho: \mu \geq 0\%$

$Ha: \mu < 0\%$

Where μ is the mean of % of change in A1C (3-month -baseline). The null hypothesis will be rejected if

the one-sided 97.5% upper confidence limit of the mean change in A1C is less than 0%.

Assuming the mean of change in A1C from baseline to the 3-month follow-up visit is zero, the standard deviation of change in A1C is 1.1%, SAS power and sample size calculator show size calculator shows that a total of 80 subjects (7-13 years old) will provide 90% power to detect the difference of 0.4% and with one-sided type I error of 0.025.

A minimum of 95 subjects will be enrolled to account for subject attrition.

7.12.3.2 Sample Size for Secondary Endpoint: % of Time in Euglycemic (70-180 mg/dL)

The overall mean change in % of time in euglycemia (70-180 mg/dL) from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).

$Ho: \mu \leq 0\%$

$Ha: \mu > 0\%$

Where μ is the mean of change in % of time in euglycemia (3-month - baseline). The null hypothesis will be rejected if the one-sided 97.5% lower confidence limit of the mean change in % of time in euglycemia is greater than 0%.

Assuming the mean of change in time in euglycemia (%) from baseline to the 3-month follow-up visit is zero, the standard deviation of change in percentage time in euglycemia is 11.0%, SAS power and sample size calculator shows that a total of 80 subjects (7-13 years old) will provide 90% power to detect the difference of 4.0% and with one-sided type I error of 0.025.

A minimum of 95 subjects will be enrolled to account for subject attrition

7.12.3.3 Sample Size for Secondary Endpoint: % of Time in Hyperglycemic (>180 mg/dL)

The overall mean change in % of time in hyperglycemia (> 180 mg/dL) from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).

The hypothesis is mathematically expressed as:

$Ho: \mu \geq 0\%$

$Ha: \mu < 0\%$

Where μ is the mean of change in % of time in hyperglycemia (3-month - baseline). The null hypothesis will be rejected if the one-sided 97.5% upper confidence limit of the mean change in % of time in hyperglycemia is less than 0%.

Assuming the mean of change in time in hyperglycemia (%) from baseline to the 3-month follow-up visit is zero, the standard deviation of change in percentage time in hyperglycemia is

11.0%, SAS power and sample size calculator shows that a total of 80 subjects (7-13 years old) will provide 90% power to detect the difference of 4% and with one-sided type I error of 0.025.

A minimum of 95 subjects will be enrolled to account for subject attrition

7.12.3.4 Sample Size for Secondary Endpoint: % of Time in Hypoglycemic (<70 mg/dL)

The overall mean change in % time in hypoglycemia (< 70 mg/dL) from baseline to the end of study will be estimated and compared by a simple superiority paired test and a significance level of 0.025 (one-sided).

The hypothesis is mathematically expressed as:

$Ho: \mu \geq 0\%$

$Ha: \mu < 0\%$

Where μ is the mean of change in % of time in hypoglycemia (3-month - baseline). The null hypothesis will be rejected if the one-sided 97.5% upper confidence limit of the mean change in % of time in hypoglycemia is less than 0%.

Assuming the mean of change in time in hypoglycemia from baseline to the 3-month follow-up visit is zero, the standard deviation of change in percentage time in hypoglycemia is 4.0%, SAS power and sample size calculator shows that a total of 80 subjects (7-13 years old) will provide 90% power to detect the difference of 1.5% and with one-sided type I error of 0.025.

A minimum of 95 subjects will be enrolled to account for subject attrition

8. Validation Requirements

Level I or Level II validation are required for analysis output. Level I requires that the peer reviewer independently programs output and then compares the output with that generated by the original Statistical Programmer. Level II requires that the peer reviewer reviews the code; where appropriate, performs manual calculations or simple programming checks to verify the output.

9. References

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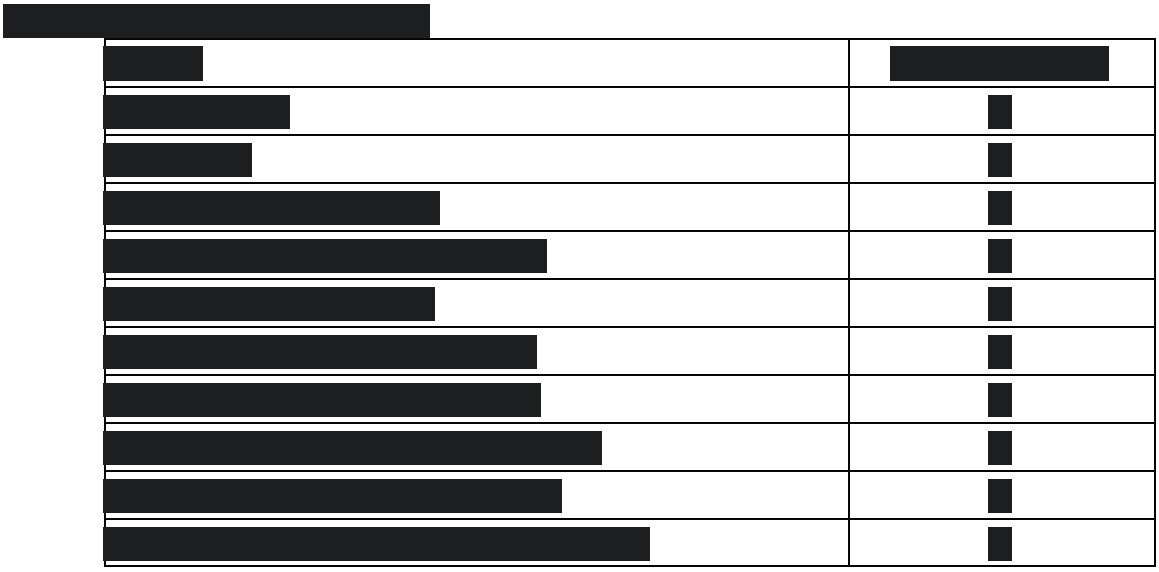
10. Statistical Appendices

[redacted]



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