16.1.9 DOCUMENTATION OF STATISTICAL METHODS

This appendix includes

Document	**Date, Version**
Statistical Analysis Plan	Version 1.0 Date 16 August 2019

Statistical Analysis Plan

Sponsor: Zealand Pharma A/S

Protocol Number ZP4207-17086 (ZEA-DNK-02170)

Study Title:
A phase 3, randomized, double-blind, placebo- and active-controlled, parallel-arm trial to assess the efficacy, safety, and pharmacokinetics of dasiglucagon relative to placebo and GlucaGen® when administered as a rescue therapy for severe hypoglycemia in children with T1DM treated with insulin

Protocol Version 3.0: 08 January 2019

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Version	Date
Draft 0.1	10APR2019
Draft 0.2	06JUN2019
Draft 0.3	14JUN2019
Draft 0.4	28JUN2019
Draft 0.5	17JUL2019
Draft 0.6 – pre-final version	22JUL2019
1.0	16AUG2019

Approval

Upon review of this document, including the table, listing, and figure shells, the undersigned approves the statistical analysis plan. The analysis methods and data presentation are acceptable.

Signature	Date
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[redacted] *Statistical Project Director* *Zealand Pharma A/S*	[redacted]

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LIST OF ABBREVIATIONS

ADA	anti-drug antibody
AE	adverse event
BMI	body mass index
AESI	adverse event of special interest
CDISC	Clinical Data Interchange Standards Consortium
CFR	Code of Federal Regulations
CSR	clinical study report
CRO	contract research organization
ECG	electrocardiogram
eCRF	electronic case report form
FAS	full analysis set
ICH	International Council for Harmonisation
IMP	investigational medicinal product
IV	intravenous(ly)
LLOQ	lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MRT	mean residence time
NPH	neutral protamine Hagedorn
PD	pharmacodynamic(s)
PK	pharmacokinetic(s)
PPS	per protocol set
PR	PR interval; ie, the measure of the time between the start of the p wave and the end of the r wave in the heart's electrical cycle
QRS	QRS interval; ie, the measure of the time between the start of the q wave and the end of the s wave in the heart's electrical cycle
QT	QT interval; ie, the measure of the time between the start of the q wave and the end of the t wave in the heart's electrical cycle
QTc	corrected QT interval
QTcF	QTc according to Fridericia's formula

SAE	serious adverse event
T1DM	type 1 diabetes mellitus
TLF	tables, listings, and figures

Plasma concentrations of dasiglucagon/GlucaGen

$AUC_{0\text{-}30min}$	Area under the plasma concentration versus time curve from 0 to 30 minutes post-dose
$AUC_{0\text{-}300min}$	Area under the plasma concentration versus time curve from 0 to 300 minutes post-dose
$AUC_{0\text{-}inf}$	Area under the plasma concentration versus time curve from 0 to infinitly post-dose
C_{max}	Maximum of all valid plasma concentration measurements from 0 to 300 minutes post-dose
t_{max}	Time to maximum of plasma concentration measurements
λ_z	Terminal elimination rate constant
$t_{½}$	Terminal plasma elimination half-life
CL/f	Total body clearance
V_z/f	Volume of distribution
MRT	Mean residence time

Plasma glucose concentrations

$AUE_{0\text{-}30min}$	Plasma glucose response as area under the effect curve above baseline from time 0 to 30 minutes

1. INTRODUCTION

This document outlines the statistical methods to be implemented during the analyses of data collected within the scope of Zealand Pharma A/S protocol ZP4207-17086. The purpose of this plan is to provide specific guidelines from which the statistical analyses will proceed. Any deviations from this plan will be documented in the clinical study report (CSR).

2. STUDY DOCUMENTS

The following study documents are used for the preparation of the statistical analysis plan (SAP):

- Protocol version 3.0, dated 08 January 2019
- Annotated electronic case report form (eCRF) version 1.0, 11 September 2018
- Data management plan version 1.0, 23 August 2018

3. STUDY OBJECTIVES

3.1 Primary Objective

To demonstrate that dasiglucagon is superior to placebo following a single injection of 0.6 mg of dasiglucagon in treating hypoglycemia in children with type I diabetes mellitus (T1DM)

3.2 Secondary Objective

- To confirm that a single dose of dasiglucagon [0.6 mg] is comparable to a single dose of GlucaGen® [1 mg/mL] in treating hypoglycemia in children with T1DM (in accordance with the label, children below 25 kg body weight will be administered 0.5 mg GlucaGen®)
- To assess safety profile of dasiglucagon in children with T1DM
- To assess pharmacokinetic (PK) profile of dasiglucagon in children with T1DM

4. STUDY DESIGN AND PLAN

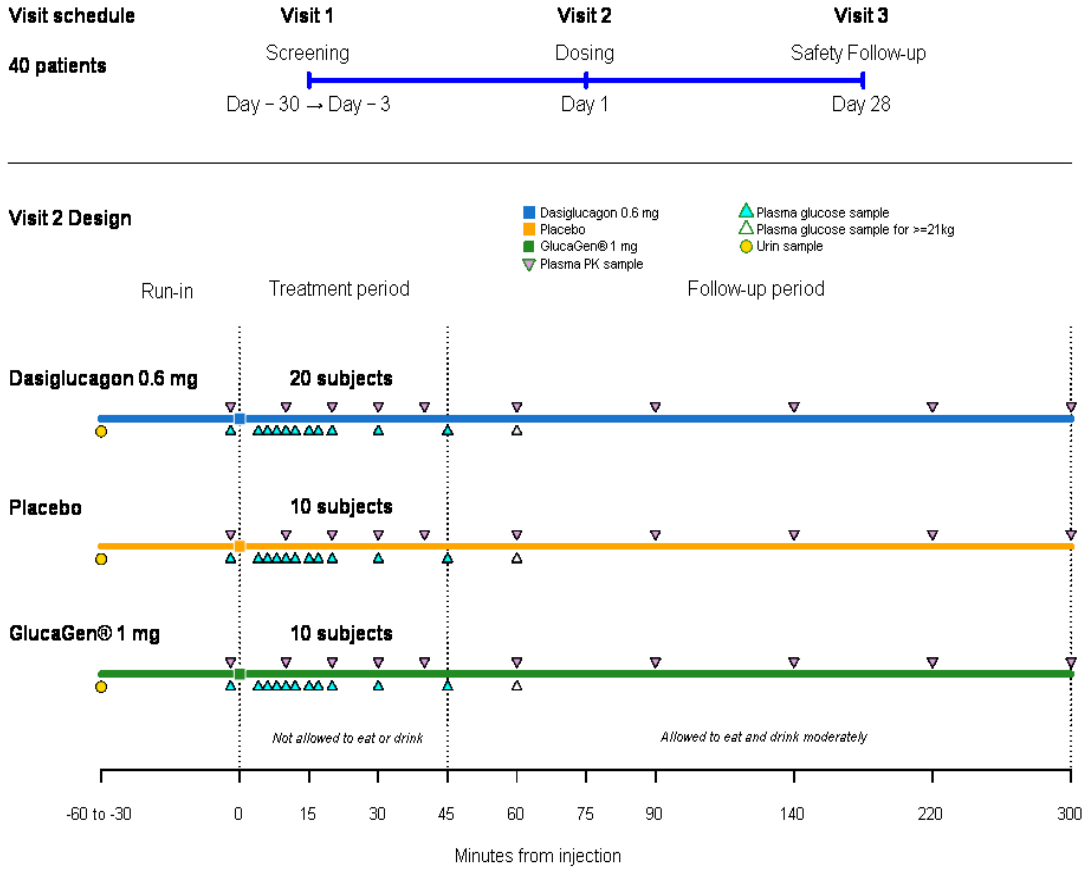
This is a phase 3, randomized, double-blind, placebo- and active-controlled, parallel-arm trial designed to assess efficacy, safety and PK of dasiglucagon versus placebo and versus GlucaGen® in children with T1DM. At the time of protocol finalisation it was anticipated that it will be conducted at 2-3 centers in Europe and 1-2 centers in the USA.

The trial will include the following periods (as illustrated in Figure 4-1).

- A screening period from Day -30 to Day -3

- A treatment period, from Day 0 to Day 1 (day of randomization and single dosing with trial product). Unblinded trial personnel will do the handling, preparation and administration of trial product. All trial assessments will be done by blinded trial personnel
- A follow-up visit at Day 28 (the end-of-trial visit)

Figure 4-1 Overview of the Trial Design



Abbreviation: PK=pharmacokinetic

The schedule of assessments (refer to the study protocol) gives an overview of the trial procedures. Patients should attend all visits on the designated day or as close to it as possible.

5. DETERMINATION OF SAMPLE SIZE

The primary comparison is between the dasiglucagon and placebo treatment arms. From phase 2 results, the median time to an increase of 20 mg/dL of the 0.6 mg dose was approximately 10 minutes. For placebo-treated patients, the median time to recovery is assumed to be more than 50 minutes. Assuming an exponential time-to-recovery distribution with median times of 10 and 50 minutes, a 2-sided log-rank test will be able to detect a difference between dasiglucagon 0.6 mg

and placebo with 90% power with a follow-up time of 45 minutes at a 5% significance level with 20 patients randomized to the dasiglucagon arm and 10 patients to placebo.
GlucaGen® is included as a reference to compare the responses and AE profile to dasiglucagon with those to a marketed product. It is expected that 10 patients in the GlucaGen® group will suffice for the comparison.

6. GENERAL ANALYSIS CONSIDERATIONS

The statistical analyses will be reported using summary tables, listings, and figures (TLFs). The International Council for Harmonisation (ICH) numbering convention will be used for all TLFs. Unless otherwise noted, all statistical testing will be 2-sided and will be performed at the 0.05 significance level. Tests will be declared statistically significant if the calculated *P* value is ≤0.05.

All data obtained in this trial and documented in the eCRFs will be listed and summarized with statistics or frequency tables as appropriate. In case of termination of the trial, all data collected up to that time point will be included into the analysis.

Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums and valid cases. Other summaries (eg, quartiles, 5%, 95% intervals) may be used as appropriate. For PK parameters except Tmax, geometric mean and geometric % CV will be calculated.

Categorical variables will be summarized by counts and by percentage of patients in corresponding categories. Percentages for missing values are omitted and do not account for the percent calculation of other categories. Percentages are routinely based on the total category count excluding the missing category if not otherwise mentioned. Percentages showing a rate relative to the total number of patients in this group are given in special tables (eg, adverse event [AE] tables). Footnotes will specify the percent basis in those cases.

All summary tables will be presented by treatment group if possible and also include a total summary column.

Individual patient data obtained from the eCRFs, external vendors, and any derived data will be presented by patient in data listings.

The analyses described in this plan are considered a priori, in that they have been defined prior to breaking the blind.

Any analyses performed subsequent to breaking the blind will be considered post hoc and exploratory. Post hoc analyses will be labeled as such on the output and identified in the CSR.

All analyses and tabulations will be performed using SAS® software Version 9.4 or higher. Pharmacokinetic and pharmacodynamic (PD) analyses will be performed using Phoenix®

WinNonlin® Version 6.4 or higher. Tables, listings, and figures will be presented in ASCII or RTF format.

The process for SAS program validation and quality control (QC) for programs and outputs is documented in the Synteract working instruction "SAS programming quality control." Study-specific QC requirements can be found in Appendix B: SAS Programming QC Requirements.

7. NOTATION OF TREATMENT GROUPS AND VISITS

Notation of treatment groups

The following notation of **treatment groups** will be used throughout the report:

Full notation (as used in the study protocol)	***Notation as used throughout all tables, listings, and figures***
Dasiglucagon, liquid formulation, 1 mg/mL, 0.6 mL	**dasiglucagon**
1 mg lyophilized powder for reconstitution (GlucaGen®, Novo Nordisk)	**GlucaGen**
Placebo treatment: Placebo, liquid formulation, 0.6 mL	**Placebo**

Visit terminology

Visit	***Notation as used throughout all tables, listings, and figures***
V1 Screening	Screening
V2 Dosing	Dosing
V3 Follow up	Follow up

8. ANALYSIS SETS

For the statistical analysis, the randomized patients will be divided up into the following datasets. The following definitions are applicable:

Safety analysis set — All patients who were randomized and received at least 1 dose of trial product. Treatment assignment will be based on the treatment actually received.

Full analysis set (FAS) — All patients of the safety analysis set. Treatment assignment will be based on the randomized treatment. Assignment to the stratification factor injection site will be based on the planned

	and not the actual used injection site.
Per protocol set (PPS)	All patients of the FAS for whom no relevant protocol deviations were documented. Treatment assignment will be based on the randomized treatment. Assignment to the stratification factor injection site will be based on the planned and not the actual used injection site.

The analysis of the primary endpoint will be based on the FAS. A secondary analysis of the primary endpoint will be based on the PPS. Safety analysis will be based on the safety analysis set.
The decision whether a protocol deviation is relevant or not for the exclusion of patients from the PPS will be made case-by-case in a data review meeting before breaking the blind.

9. STUDY POPULATION

9.1 Patient Disposition

Patient disposition information will be summarized for all patients by treatment group. Summaries will include: the number of patients screened, the number of randomized patients, and the number of patients in each analysis set.

The number of patients who completed or discontinued the study will be tabulated by treatment. In addition, for patients who discontinued, the primary reason will be tabulated by treatment group.

Patient numbers and percentages in each country and patient numbers and percentages in each country and center will be presented by treatment group.
In additon, the number of patient numbers and percentages of US versus non-US countries will be tabulated by treatment group.

9.2 Protocol Deviations

A listing of all protocol deviations including the deviation designation (relevant/non-relevant), category, and indication of whether the deviation led to an exclusion of a patient from the PPS will be presented in a data listing.

9.3 Eligibility

A listing of patients not fulfilling any eligibility criteria will be created. This listing will consider and differentiate eligibility criteria at screening as well as the re- check of dosing day exclusion criteria.

9.4 Demographic and Baseline Characteristics

Demographic variables include: age, age group (6-11 years, 12-17 years), sex, childbearing potential, ethnicity, and race.

Summary statistics will be presented for the above-mentioned variables by treatment group.

Other baseline characteristics include: diabetes history, medical history and body measurements (height, weight, BMI).
BMI will be additionally classified into the following categories:
<25
25-<30
30-<35
>=35
A summary table for BMI by BMI class and country will be created. In addition, this table will show BMI classes of US versus non-US countries.

Diabetes history
Time since diagnosis of diabetes 1 (based on date of informed consent and start date of diabetes 1) (years) will be tabulated with descriptive statistics by treatment group. If the day is not available, the calculation of duration will be based on month and year only, setting the start day to 1. In case only the year is available, the start day will be 1 and the start month will be January.

Body measurements

Separate descriptive statistics will be presented for body measurements (height, weight, BMI) by treatment group.

Medical history
The verbatim term of the medical history condition/event will be coded using Medical Dictionary for Regulatory Activities (MedDRA), version 22.0.

A summary will be prepared by treatment group. The summary will show the system organ class and preferred terms ordered by descending order of incidence of system organ class and preferred term within each system organ class.

Demographic and baseline characteristics will be summarized for the safety analysis set and FAS. If the safety analysis set and FAS are identical, then it will be sufficient to state this in the table output section.

Other information documented at screening
Analyses of other screening or baseline variables as listed below, which are documented at screening/baseline and/or have further evaluations after the screening/baseline visit will be described in subsequent sections.

- Physical examination
- Vital signs
- 12-lead electrocardiogram (12-lead ECG)
- Central safety laboratory (hematology, biochemistry, coagulation, urinalysis)
- Antibody serum sample for immunogenicity measurements

9.5 Concomitant Medications and Current Diabetes Treatment

Concomitant medication and current diabetes treatment verbatim terms in the eCRFs will be mapped to Anatomical/Therapeutic/Chemical (ATC) class and preferred names using the WHODrug Global (version March 2018).

All concomitant medications and current diabetes treatment will be listed as documented in the eCRF. In this listing the WHODrug coding including the drug name as documented in the eCRF, the drug name used for the coding, the preferred term, the ATC code and the ATC term will be included as well.
Coding will be done using ATC level 4, which will be presented in the listings.

Concomitant medications and current diabetes treatment will be summarized for each treatment by WHO ATC class (level 2) and preferred name. These summaries will present the number and percentage of patients using each medication. Patients may have more than 1 medication per ATC class and preferred name. At each level of patient summarization, a patient is counted once if he/she reported 1 or more medications at that level. Each summary will be ordered by descending order of incidence of ATC class and preferred name within each ATC class.

In case the centers also captured true prior medications, this will only be listed and a flag will be included in the raw data listing denoting whether the medication is prior or concomitant.

The distinction between previous and concomitant medication will be done as follows:

- Prior medication is all medication which stopped before the first investigational medicinal product (IMP) administration within the trial context, independent from start date.
- Concomitant medication is all medication that started prior to the first IMP administration and is still ongoing or stopped at date of first study drug intake - or medication that started at/after the date of the first drug intake.
- If the start or stop date is incomplete and the allocation to previous or concomitant is not clear, the medication will be considered to be concomitant.

10. EFFICACY ANALYSES

The primary efficacy analysis will be based on the FAS. Analogous supportive sensitivity analyses will be conducted in the PPS, but without inference intent.

10.1 Efficacy Variables

The **primary** efficacy variable is:

- Time to plasma glucose recovery. Plasma glucose recovery is defined as first increase in plasma glucose of ≥20 mg/dL (1.1 mmol/L) from baseline during the hypoglycemic clamp procedure[1] without administration of rescue intravenous (IV) glucose. Time to recovery is considered only within the first 45 minutes from baseline.
  In this trial, plasma glucose for pharmacodynamics is reported with the unit 'mmol/l'. For consistency, these results are converted into the unit 'mg/dl' by using the conversion factor 0.0555 (i.e. Glucose [mg/dl]=Glucose [mmol/l] /0.0555).

Secondary efficacy variables include the following:

- Plasma glucose recovery within 30 minutes, within 20 minutes, within 15 minutes, and within 10 minutes after study drug injection without administration of rescue IV glucose.
- Plasma glucose changes from baseline at 30 minutes, at 20 minutes, at 15 minutes, and at 10 minutes after study drug injection or at the time of rescue IV glucose.

10.2 Baseline Values

Unless otherwise noted, baseline is defined as the last non-missing value recorded prior to the first dose of study drug. Unscheduled visits will be used in the determination of baseline values, when applicable.

10.3 Adjustments for Covariates

The model for the primary efficacy will include adjustments for the following covariates:

- Age group: 6-11 years, 12-17 years
- Injection site: abdomen/thigh

10.4 Handling of Dropouts or Missing Data

Only non-missing cases will be analyzed, ie, no imputation technique like last observation carried forward will be applied. Summaries will be based on observed data only.

10.5 Interim Analysis and Data Monitoring

There are no planned interim analyses for this study.

[1] For simplification the addition 'during the hypoglycemic clamp procedure' will be omitted further on.

10.6 Examination of Subgroups

No subgroup analysis is planned.

10.7 Multiple Comparison/Multiplicity

For the confirmatory analyses of the primary and secondary endpoints, patients treated with either dasiglucagon 0.6 mg and or placebo will be compared. A hierarchical procedure will be applied for the control of multiplicity. The primary and secondary endpoints will be evaluated on the FAS.

For the confirmatory analyses, the following a priori-defined hierarchical inferential test order will be applied for the control of the type 1 error rate across the planned multiple comparisons. The primary endpoint and secondary endpoints will be inferentially evaluated within the FAS in the following order, where inference will proceed at the 2-sided 0.05 criterion significance level until the first failure to reject the null hypothesis for a dasiglucagon versus placebo comparison:

- Primary: Time to plasma glucose recovery
- Secondary 1-4: Plasma glucose recovery within 30 minutes, within 20 minutes, within 15 minutes, and within 10 minutes after study drug injection without administration of rescue IV glucose.
- Secondary 5-8: Plasma glucose changes from baseline at 30 minutes, at 20 minutes, at 15 minutes, and at 10 minutes after study drug injection or at the time of rescue.

The GlucaGen® versus placebo comparisons will not be included in the inferential testing hierarchy, since the efficacy of GlucaGen® is previously established, and these comparisons are intended to support the validity of the study for the dasiglucagon versus placebo comparisons. Moreover, the comparison of dasiglucagon versus GlucaGen® is not part of this hierarchial testing procedure.

10.8 Multicenter Studies

This is a multicenter study, having approximately 5 centers participating in the study. The factor center will not be accounted for in the primary statistical analysis model.

11. METHODS OF EFFICACY ANALYSIS

11.1 Primary Efficacy Analyses

The primary endpoint, time to plasma glucose recovery, will be summarized using Kaplan-Meier estimates per treatment group.

The actual time points at 0, 4, 6, 8, 10, 12, 15, 17, 20, 30, 45 and 60 minutes will be used in the analyses.

Kaplan-Meier plots will be created showing the the estimated survival function for each treatment in one plot.

In the primary analysis, recovery cannot be achieved in those subjects where rescue IV glucose treatment is administered. Those subjects who receive rescue IV glucose will be censored (and set to 'not recovered') at 45 minutes after dosing.

For patients who did not recover within 45 minutes after dosing, time to recovery is censored at 45 minutes.

The stratified log-rank test will be applied to compare the dasiglucagon 0.6 mg treatment group to the placebo group. The same method will be applied to compare dasiglucagon 0.6 mg with GlucaGen®, but not considered for the confirmatory hierarchial testing procedure.

In order to facilitate this, SAS procedure proc lifetest is used. The following code will be used, but minor variations can be applied during programming:

```
proc lifetest data=xx  plots=survival(atrisk=0 10 15 20 30 45);
   time aval * Status(0);
   strata age site/ group= treat test=logrank diff=all;
   run;
```

where "aval" is the time to plasma recovery, and "status" is a censor variable for patients who receive IV glucose. Age group and injection site are the stratification variables and "treat" the planned treatment assignment.

The unstratified result of the log-rank test can be obtained from the following code:

```
proc lifetest data=xx  plots=survival(atrisk=0 10 15 20 30 45);
   time aval * Status(0);
   strata treat / test=logrank diff=all;
   run;
```

In sensitivity analyses, the time to plasma glucose recovery will be analyzed

1) without censoring for those subjects who require rescue IV glucose before 45 minutes and

2) with censoring at the time of administration of rescue IV glucose before 45 minutes.

As a supportive analysis to the stratified log-rank test for the time to plasma glucose recovery, dasiglucagon will be compared to placebo using a Wilcoxon test stratified by age group and injection site.

To graphically describe recovery in time, a histogram showing the proportion of patients that recovered at each time interval will be created, one for each treatment group.

The primary endpoint will additionally be analyzed using a discrete-time Cox proportional hazards (CPH) time to event statistical model, if the hazards by treatment group can be assumed

proportional using a graphical comparison of log-minus-log survival curves and no more than two-thirds of the recovery times are censored in each treatment group. The CPH model will be used for descriptive purposes, with treatment group, age group and injection site modeled as categorical effects, and baseline plasma glucose modelled as a continuous covariate. The treatment group hazard ratios of active versus placebo, will be estimated together with the 95% confidence intervals, and pairwise treatment group inferences (dasiglucagon vs placebo, GlucaGen vs placebo, dasiglucagon vs GlucaGen) will be evaluated using least-square mean and standard deviation estimates.

Due to the discrete nature of blood sampling in time, and the fact that there must be a true, but unmeasured, ordering of the recovery times, the method using the "exact discrete" partial likelihood for tied failure times will be applied. In SAS, this is implemented in the `phreg` procedure with the option `ties=discrete`. The influence of age and injection site on time to recovery will also be evaluated in the proportional hazards model by a 'type 3' test in the `phreg` procedure.

In addition, separate CPH models will be calculated to evaluate homogenicity for the following factors:

Sex, BMI class, ethnicity, race, US/non-US.

These additonal homogenicity models are only presented for the primary efficacy analysis, but not for subseqent variants of that analysis.

To obtain an estimate of these true, but unassessed, patient recovery times, a linear interpolation (between the two time points before and after recovery is observed) will be carried out to estimate the patients' actual time of recovery. These derived recovery times will be described and analysed in the same manner as for the discrete times above.

Let t_1 and t_2 be the 2 time points before and after recovery is observed and y_1 and y_2 be the corresponding changes from baseline in glucose concentrations, where y_1 is below 20 mg/dL and y_2 is greater than 20 mg/dL.

The interpolated time point t_{ext} is calculated then as:

$$t_{ext} = t_1 + \frac{(20 - y_1) * (t_2 - t_1)}{(y_2 - y_1)}$$

This linear interpolation is only used as a supportive analysis to the primary analysis model using proc lifetest.
In this statistical model, `ties=exact` will be used.

11.2 Secondary Efficacy Analyses

The secondary efficacy endpoints are plasma glucose recovery within 10, 15, 20 and 30 minutes after trial product injection, ie, achieving a ≥20 mg/dL increase in plasma glucose from baseline at 0 to 10, 15, 20, and 30 minutes.
Actual timepoints of sampling will be used for this calculation.
If a patient has received an IV glucose treatment before recovery, the patient is set to "not recovered" in the analysis of the 4 endpoints, corresponding to censoring in the time-to-recovery analysis for the primary endpoint. The 10-, 15-, 20-, and 30-minute recovery rates of dasiglucagon and Placebo will be compared by a Cochran-Mantel-Haenszel test stratified by age group and injection site. The treatment responder rates with the 95% confidence intervals will be presented for the 10-, 15-, 20-, and 30-minute endpoints.

If due to small or zero cell counts the Cochran-Mantel-Haenszel test fails, non-stratified Fisher exact tests will be applied instead.

Plasma glucose changes from baseline at 10, 15, 20, and 30 minutes after trial product injection will be analyzed in an analysis of variance with factors treatment (3 levels), age group (2 levels), and injection site (2 levels) for each endpoint. If the rescue IV glucose was administered before 10, 15, 20, or 30 minutes, respectively, the patient's plasma glucose changes from baseline will be determined from the value at the time of rescue IV glucose administration.
The change from baseline is calculated using the nominal sampling time.

Least-square mean adjusted treatment means will be presented with their 95% confidence intervals including the 95% confidence intervals for the treatment difference. The analysis of variance at each of the 4 time points will also be used to test the difference of dasiglucagon and Placebo adjusted for age group and injection site.

12. PHARMACOKINETIC ANALYSES

Plasma dasiglucagon and glucagon concentrations will be described and the following parameters are calculated and summarized with descriptive statistics:

PK parameter	PK parameter abbreviation	Calculation
Area under the plasma dasiglucagon or GlucaGen® concentration versus time curve from 0 to 30 minutes post-dose	$AUC_{0\text{-}30min}$	Linear trapezoidal rule for the ascending part of the concentration-time curve, logarithmic trapezoidal rule for the descending part.
Area under the plasma dasiglucagon or GlucaGen® concentration versus time curve	$AUC_{0\text{-}300min}$	Linear trapezoidal rule for the ascending part of the concentration-time curve, logarithmic trapezoidal rule for the

PK parameter	PK parameter abbreviation	Calculation
from 0 to 300 minutes post-dose		descending part.
Area under the plasma dasiglucagon or GlucaGen® concentration versus time curve from 0 to infinitely post-dose	$AUC_{0\text{-}inf}$	(AUClast + $Clast_{obs}$)/ λ_z, where $Clast_{obs}$ is the concentration corresponding to Tlast (time of last measurable (positive) concentration).
Maximum of all valid plasma dasiglucagon or GlucaGen® concentration measurements from 0 to 300 minutes post-dose	C_{max}	Taken directly from analytical data, selected from individual concentration data. The time when the first occurrence of Cmax is taken as Tmax.
Time to maximum of plasma dasiglucagon or GlucaGen® concentration measurements	t_{max}	Taken directly from analytical data, selected from individual concentration data
Terminal elimination rate constant of plasma dasiglucagon or GlucaGen®	λ_z	Calculated by linear regression of the terminal linear portion of the log concentration vs. time curve. At least 3 concentrations in the terminal elimination phase will be required to calculate λz.
Terminal plasma elimination half-life of dasiglucagon or GlucaGen®	$t_{½}$	Ln(2)/ λ_z
Total body clearance of plasma dasiglucagon or GlucaGen®	CL/f	Dose/ $AUC_{0\text{-}inf}$
Volume of distribution of plasma dasiglucagon or GlucaGen®	V_z/f	Dose/ (λ_z * $AUC_{0\text{-}inf}$) or CL/f/ λ_z
Mean residence time of plasma dasiglucagon or GlucaGen®	MRT	AUMCinf/ $AUC_{0\text{-}inf}$ where AUMCinf is the area under the first moment curve as estimated by WinNonlin.

The PK metrics as listed above will be obtained by non-compartmental analysis using the computer programs Phoenix® WinNonlin® Version 6.4.

12.1 Data Handling

Plasma dasiglucagon and GlucaGen® are determined at pre-dose, and at 10, 20, 30, 40, 60, 90, 140, 220, and 300 minutes after dosing. The actual time of blood sampling should not deviate from the nominal time by more than ±1 minute between t=5 minutes and t=90 minutes, ±5

minutes between t=140 minutes and t=240 minutes. Pre-dose is defined as within 2 minutes prior to dosing).

Summary tables and figures for plasma concentrations:

i.) For all pre-dose samples, the sampling time will be set to zero.
ii.) For post-dose samples, the planned sampling time will be used in summary tables and the actual sampling times will be used for all figures of individual concentrations.
iii.) All concentration values < lower limit of quantification (LLOQ) will be set to zero.
iv.) Missing post-dose values will not be replaced.

Determination of PK metrics:

i.) For all pre-dose samples, the sampling time will be set to zero.
ii.) For post-dose samples, the actual sampling time will be used.
iii.) All pre-dose concentration values will be set to zero.
iv.) Post-dose concentration values < LLOQ before t_{max} will be set to zero if there are no further concentrations > LLOQ at later time points.
v.) Post-dose concentration values < LLOQ before t_{max} will be set to the lower limit of quantitation if there are further concentrations > LLOQ at later time points.
vi.) Post-dose concentration values < LLOQ after t_{max} will be ignored if there are no further concentrations > LLOQ at later time points.
vii.) Post-dose concentration values < LLOQ after t_{max} will be ignored if there are further concentrations > LLOQ at later time points.
viii.) Missing post-dose values will not be replaced.

PK metrics will be determined by Synteract. Plasma concentration data will be transferred from an external laboratory (York Bioanalytical Solutions (YBS), MLM laboratories) to Synteract as detailed in separate data transfer specifications.

12.2 Presentation of Plasma Concentrations and PK metrics

Individual plasma concentration results:
A raw data listing will be provided displaying the concentration as reported, the result used in summary tables and mean time-concentration curves, and the change from pre-dose result. Results will be displayed using 3 significant digits.

Summary statistics of plasma concentration table:
Summary statistics of the plasma concentration by treatment group and time point will be presented. In addition, the change from pre-dose will be summarized. Results will be displayed using 3 significant digits.

PK metrics:

Summary statistics of PK metrics will be presented by treatment group. Results will be displayed using 3 significant digits.

Figures:

1. Mean concentrations versus nominal time by treatment group using the original (untransformed) scale of concentrations. The curves of each treatment group will be put into 1 graph, having an overlay plot in the end with 2 curves for each treatment group. (Samples from patients receiving placebo will not be analyzed by the laboratories that will be analyzing for dasiglucagon and GlucaGen®.)
2. Mean concentrations versus nominal time by treatment group using the log scale of concentrations. The curves of each treatment group will be put into 1 graph, having an overlay plot in the end with 2 curves for each treatment group. (Samples from patients receiving placebo will not be analyzed by the laboratories that will be analyzing for dasiglucagon and GlucaGen®.)
3. Individual dasiglucagon and glucagon concentrations versus nominal time curves using the original concentration scale overlaying all patients per treatment group will be prepared.

13. PHARMACODYNAMIC ENDPOINTS

Plasma glucose is determined at pre-dose and at 4, 6, 8, 10, 12, 15, 17, 20, 30, and 45 minutes (and as well at 60 minutes if the patient´s body weight is ≥21 kg) after dosing. The actual time of blood sampling should not deviate from the nominal time by more than ±30 seconds until the 20-minute collection time point, and by more than ±1 minute for the subsequent collection time points. Pre-dose is defined as within 2 minutes prior to dosing

The pharmacodynamic endpoint is the plasma glucose response as area under the effect curve above baseline from time 0 to 30 minutes ($AUE_{0\text{-}30min}$). $AUE_{0\text{-}30min\ will}$ be calculated using SAS software.

Individual plasma glucose concentration results:
A raw data listing will be provided displaying the concentration as reported, the result used in summary tables and mean time-concentration curves and the change from pre-dose result.

Summary statistics of plasma glucose concentration table:
Summary statistics of the plasma glucose concentration by treatment group and time point will be presented. In addition, the change from pre-dose will be summarized.

Pharmacodynamic metrics:
Summary statistics of pharmacodynamic metrics will be presented by treatment group.

Figures:

1. Mean glucose concentrations versus nominal time by treatment group using the original (untransformed) scale of concentrations. The curves of each treatment group will be put into 1 graph, having an overlay plot in the end with 2 curves for each treatment group.
2. Individual glucose concentrations versus nominal time curves using the original concentration scale overlaying all patients per treatment group will be prepared.

14. SAFETY ANALYSES

All safety analyses will be based on the safety set.

14.1 Extent of Exposure

14.1.1 Insulin administration prior to the hypoglycemia induction procedure

All details with regard to insulin administration prior to the hypoglycemia induction procedure will be listed. This includes whether the patient used multiple daily injections, long-acting insulin, short-acting insulin (except insulin glulisine [Apidra®]), insulin NPH, or insulin glulisine (Apidra®) or an insulin pump.

A summary table will be prepared showing the number (percentage) of patients who used any of the following:

- Multiple daily injections
- Insulin NPH
- Insulin pump
- Insulin glulisine (Apidra®)

14.1.2 Hypoglycemia induction procedure

All details with regard to the hypoglycemia induction procedure will be listed.
A summary table will be prepared showing the number (percentage) of patients where the hypoglycemia induction procedure was performed, the total amount of insulin administered to induce hypoglycemia and the total amount of glucose administered during the induction procedure.

14.1.3 Trial medication administration

All details with regard to the trial medication administration will be listed.
A summary table will be prepared showing the number (percentage) of patients where the trial medication was administered.

14.1.4 Post-treatment rescue glucose infusion

All details with regard to the post-treatment rescue glucose infusion will be listed.
A summary table will be prepared showing the number (percentage) of patients where glucose was given as rescue medication.

The time to first IV glucose infusion, after IMP administration (IV glucose infusion prior to IMP administration should not be included, as it is part of hypoglycemic clamp procedure) will be described with descriptive statistics. No statistical tests will be performed.

Time to first IV glucose infusion [minutes] is calculated as:

Time of start of first glucose administration – Time of administration of study medication.
No censoring is done in case no IV glucose infusion is given, ie, the descriptive statistics only show data when an infusion was given.

14.2 Local Tolerability

Local tolerability at the injection site is assessed at 30, 120, and 300 minutes after dosing and at Follow-up.
The following symptoms are assessed:

- Spontaneous pain
- Pain on palpation
- Itching
- Redness
- Edema
- Induration/Infiltration
- Other types of reaction

All details of local tolerability assessment are listed. Any local reaction will also be reported as AE.

The analysis of local tolerability will include a summary table displaying counts and percentages of patients experiencing local symptoms by time point, symptom and grade (intensity).

The category “other types of reactions” will not be included in this summary due to lack of a distinct unique reaction term.

14.3 Adverse Events

All AE summaries except for 1 overview table will be restricted to treatment-emergent AEs (TEAEs), which are defined as those AEs that occurred after dosing and those existing AEs that worsened during the study. A manual check is done for AEs that start prior dosing and continue after dosing whether the intensity of the AE worsened.

If it cannot be determined whether the AE is treatment emergent due to a partial onset date, then it will be counted as such unless the end date is before dosing. Verbatim terms in the eCRFs will be mapped to preferred terms and system organ classes using the MedDRA, version 21.0 or higher.

Each AE summary will be displayed by treatment group.

Causal relationship: Causal relationship between the occurrence of an AE and the administration of the study drug is assessed by the investigator according to classification scheme 0=not related, 1=unlikely related, 2=possibly related and 3=probably related. Probable and possible relationship are subsumed under the category related. All AEs must have a causal relationship assigned. In case of a missing relationship, a query will be raised in order to obtain causality assessment. In case no clarification of relationship via query is possible the missing relationship will be set to related for the analysis.

Severity: Severity grading will differ between 1=mild, 2=moderate and 3=severe. For AEs having a missing severity, the severity will not be imputed and kept as missing.

14.3.1 Summary of adverse events

An overview AE summary table will be prepared showing the number and percentage of patients with at least 1 event and the total number of events for the following selections:

1. AEs during screening
2. TEAEs
3. TEAEs, which are adverse events of special interest (AESIs)
4. TEAEs, which are an other important event
5. TEAEs, which are injection site reactions based on investigator assessment in CRF
6. Injection site reactions based on special search category provided by Zealand
7. Study drug-related TEAEs
8. Serious TEAEs (SAEs)
9. Study drug-related serious TEAEs (serious study drug-related TEAEs)
10. Deaths

The summary table is based on the number of AE verbatim terms.

14.3.2 Adverse event tables

In addition, frequency tables will be prepared by MedDRA terms (system organ class, preferred term) showing the following:

1. All TEAEs
2. TEAEs, which are AESIs
3. TEAEs, which are an other important event
4. TEAEs, which are injection site reactions based on investigator assessment in CRF
5. Study-drug related TEAEs
6. TEAEs by causal relationship to study drug
7. TEAEs by severity
8. Serious TEAEs (SAEs)
9. Special search category TEAEs

The analysis of AEs will include summary tables displaying counts and percentages of patients experiencing AEs by system organ class and preferred term. If a patient has more than 1 AE which codes to the same preferred term, the patient will be counted only once for that preferred term. The total number of events documented per system order class and preferred term will also be displayed. Summaries will be ordered by descending order of incidence of system organ class and preferred term within each system organ class based on the frequency (proportion of patients) in the dasiglucagon group.

The special search category should include the following MedDRA tems:

Events of hypoglycemia
- SMQ Hypoglycemia (narrow)

Hemodynamic events
- Zealand custom search
- External file with PT to be provided by pharmacovigilance

Allergic reactions
- SMQ: Hypersensitivity (narrow)

Events related to QT interval prolongation
- SMQ: Torsade de pointes/QT prolongation (broad)

Renal disorders
- SMQ: Acute renal failure (broad)

Hepatic disorders

- SMQ: Drug related hepatic disorders (broad)

Medication errors
- SMQ: Medication errors (broad)

Rare events
- Zealand custom search
- External file with PTs to be provided by pharmacovigilance

Injection site reactions
- Zealand custom search
- External file with PTs to be provided by pharmacovigilance

All details of adverse events will be listed. A separate listing for additional details for AEs of special interest is prepared.

14.4 Clinical Laboratory Evaluation

14.4.1 General

- High (H)/Low (L) flags will be presented in laboratory listings including the specific lab reference range, where appropriate. If normal ranges are not available, the flagging cannot be performed.
- All data will be listed in the CSR as raw data. For the summaries the most recent value will be used in case several measurements have been performed at 1 visit.

Tabulations will be prepared for each laboratory parameter by treatment group:

1. Laboratory results with continuous variables will be presented with descriptive statistics for each scheduled time point. They will be marked whether they are below (L), within or above (H) the respective reference range. The numbers in each category (above/below/within reference range) will be counted and percentages presented for each laboratory test result, visit and time point.
2. If laboratory values are categorical, the results (eg, positive/ negative) will be presented with counts and percentages for each visit and time point available.
3. Presentation of "change from baseline" values: Change from baseline will be evaluated for all laboratory parameters. The change will be calculated by building the difference between the screening visit (V1) and the follow-up visit (V3). Change from baseline values will be presented with descriptive statistics in case of continuous parameters.

14.4.2 Hematology

Tabulation will follow presentation as suggested in section 14.4.1, items #1 to #3. No figures will be prepared.

14.4.3 Biochemistry

Tabulation will follow presentation as suggested in section 14.4.1, items #1 to #3. No figures will be prepared.

14.4.4 Coagulation

Coagulation parameters at screening will be tabulated with descriptive statistics by treatment group.

14.4.5 Urinalysis

Tabulation will follow presentation as suggested in section 14.4.1, items #1 to #3. No figures will be prepared.

14.4.6 Pregnancy test

Data results of pregnancy test will be tabulated with counts/percentages for each visit by treatment group.

14.4.7 Alcohol breath test

Data on alcohol breath test will be listed.

14.5 Vital Signs

Vital signs will be summarized using descriptive statistics at baseline and at each postbaseline time point.
Categorical analysis of pulse rate will be done using the following thresholds:

	Class 1	Class 2
Pulse rate	<=120 bpm	>120 bpm

14.6 Physical Examination

Physical examination results will be included in data listings only.

14.7 Electrocardiogram

The number of patients with normal/abnormal clinically significant/abnormal not clinically significant investigator assessments of 12-lead ECG will be tabulated with counts/percentages by treatment group and visit.

Descriptive measures by visit for each ECG parameter will be presented by treatment group for each visit.

In addition, a categorical summary of corrected QT interval (QTc) values will be presented. At each visit, the number of patients with QTc according to Fridericia's formula (QTcF) values of >450 ms, >480 ms, and >500 ms will be presented. At each postbaseline time point, the number of patients with change from baseline values in QTcF of >30 ms and >60 ms will be presented.

14.8 Immunogenicity

Occurrence of ADA will be analyzed descriptively per treatment group. No statistical tests are planned.

ADA will be derived from the number of patients having an ADA-positive sample during the course of the trial. Determination of the number of patients will include counting:

1. Patients, who were ADA-negative at baseline and ADA-positive after drug administration (=**treatment-induced ADA patients)**
2. Baseline ADA-positive patients with significant increases (≥5-fold) in ADA titer after drug administration (= **treatment-boosted ADA patients)**

Both patient numbers will be summed up for the overall ADA incidence nominator. The nominator will be derived by dividing by the number of evaluable patients (see sec. Definitions: Evaluable patients = *A patient with at least one sample taken after drug administration during the treatment or follow-up that is appropriate for ADA testing (with reportable result).*). Patients, who were baseline-positive patients without any samples available after drug administration, will be excluded from the number of evaluable patients. Note that for ADA-positive patients unscheduled dosing visits are performed and results from those visits have to be respected as well.

15. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

The following changes have been made in the SAP compared to the protocol:

- The statistical analyis for the primary efficacy parameter has been reworded and additional sensitivity and supportive analysis have been added.
- For the secondary efficacy variables, the terminology was changed from '… within 30 (20 or 15 or 10) min' to '…at 30 (20 or 15 or 10) min'.

1. REFERENCES

US Department of Health and Human Services (DHHS), Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Guidance for industry: E9 Statistical principles for clinical trials. September 1998 ICH [cited 2018 Aug 03]. Available from: https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073137.pdf

2. APPENDICES

Appendix A: Presentation of Data and Programming Specifications

General

- Specialized text styles, such as bold, italics, borders, shading, superscripted, and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters are to be used in tables and data listings.
- Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used on a table, figure, or data listing.
- Hexadecimal character representations are allowed (eg, μ, α, ß).
- All footnotes will be left justified and at the bottom of a page. Footnotes must be used sparingly and must add value to the table, figure, or data listing.

Tables

- Formal organization of tabulations may be changed during programming, if appropriate, eg, tables for the different variables may be combined into a single table, or tables with more than 1 variable may be split into several tables.
- Means and medians will be presented to 1 more decimal place than the raw data. Standard deviations will be presented to 2 more decimal places than the raw data. Minimums and maximums will be reported with the same number of decimal places as the raw data.
- Percentages will be presented to the tenths place.
- For frequency counts of categorical variables, categories whose counts are zero will be displayed for the sake of completeness.
- For all inferential analyses, *P* values will be rounded to 3 decimal places (or at the highest level of precision) with a leading zero (0.001). *P* values less than 0.001 will be presented as "<0.001."
- The last footnotes will be
  - "Source: xxx", where xxx indicates the source **table number**(s) if applicable (in case aggregated results like mean or median are plotted) or the source listing(s) (in case individual responses are plotted) and/or source dataset(s) (eg, ADaM).
  - "PROGRAM SOURCE: ...\\xx.sas, DATA CUT OFF DATE: DDMMMYYYY, RUN DATE: DDMMYY hh:mm".
    where extract date is the date stamp of the data snapshot used.

Figures

- Legends will be used for all figures with more than 1 variable or item displayed.
- Figures will be in black and white but can be in color to add value to the clarity and readability of a figure. Lines must be wide enough to see the line after being copied.
- The last footnotes will be
  - "Source: xxx", where xxx indicates the source listing number(s) and/or source dataset(s) (eg, ADaM).
  - "PROGRAM SOURCE: ...\\xx.sas, DATA CUT OFF DATE: DDMMMYYYY, RUN DATE: DDMMYY hh:mm".

where extract date is the date stamp of the data snapshot used.

Listings

- Formal organization of the listing may be changed during programming, if appropriate, eg, additional variables may be included, change in the column order, or the listing may be split into multiple parts due to space constraints.
- If not otherwise specified, all data listings will be sorted by treatment, center, patient number, visit, and date/time, as appropriate.
- All date values will be presented in a SAS date (eg, 29AUG2001) format.
- All observed time values will be presented using a 24-hour clock HH:MM:SS format (eg, 01:35:45 or 11:26). Seconds will only be reported if they were measured as part of the study.
- The last footnote will be
  - "PROGRAM SOURCE: ...\\xx.sas, DATA CUT OFF DATE: DDMMMYYYY, RUN DATE: DDMMYY hh:mm".
    where extract date is the date stamp of the data snapshot used.

Missing or incomplete dates (ie, AEs and concomitant medications)

The most conservative approach will be systematically considered. If the AE onset date is missing/incomplete, it is assumed to have occurred during the study treatment phase (ie, considered a TEAE) except if the partial onset date or other data, such as the stop date, indicates differently. Similarly, a medication with partial start and stop dates could be considered as both a prior and concomitant treatment.

Standard Calculations

Variables requiring calculation will be derived using the following formulas:

Days – A duration expressed in days between 1 date (date1) and another later date (date2) is calculated using the formula a follows:
Duration in days = date2 – date1 + 1

Months – A duration expressed in months is calculated using the INTCK function of SAS as follows: months=intck('month','date1'd,date2'd, 'continuous').

Years – A duration expressed in years between 1 date (date1) and another later date (date2) is calculated as follows:
Duration in years = intck(‘year,'date1'd,date2'd, 'continuous').

Height – Height entries made in inches (in) are converted to centimeters (cm) using the following formula:
Height (cm) = height (in) × 2.54.

Weight – Weight entries made in pounds (lb) are converted to kilograms (kg) using the following formula:
Weight (kg) = weight (lb)* 0.453592.

Temperature – Temperature entries in degrees Fahrenheit are converted to degrees centigrade using the following formula:
Temperature (degrees centigrade) = 5/9 × [temperature (degrees Fahrenheit) – 32].

Body Mass Index (BMI) – BMI is calculated using height (cm) and weight (kg) using the following formula:
BMI (kg/m^2) = weight (kg)/[[height (cm)/100]^2].

Change from baseline – Change from baseline will be calculated as:
Change = postbaseline value – baseline value.

Appendix B: SAS Programming QC Requirements

Programmer/Validator Review

1. **Program Review**
   - **1.1.** **Program name** follows standard naming conventions and is consistent with other study program names.
   - **1.2.** **Program header** uses standard template with all relevant information completed.
   - **1.3.** **Program flow** is logical (ie, header → initialization code → macro variable definitions → format definitions → main body).
   - **1.4.** **Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.
   - **1.5.** **Hard coding**, if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.
   - **1.6.** **SAP derivation rules**, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.
   - **1.7.** **Permanent intermediate datasets** utilized as source data have either been fully validated elsewhere or are fully validated within the scope of this QC.
   - **1.8.** **Program runs** properly and output dataset is generated as intended.

2. **SAS Log Review**
   - **2.1.** **Scan of entire log** confirming that each data step and procedure completed properly.
   - **2.2.** **Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.
   - **2.3.** **Other messages** such as “PUT” or “INFO” messages (eg, overwritten variables following merge) are handled appropriately, if they are found in log.

3. **Output Review**
   - **3.1.** **Output file name** follows standard naming conventions and is consistent with other study output file names.
   - **3.2.** **Titles and footnotes** are verified against mock table/listing/figure (if available). Discrepancies, including footnotes added for clarification, are noted and verified.
   - **3.3.** **Column/row header text** is verified against mock table/listing/figure and/or CRF.
   - **3.4.** **Format and sorting order** are correct relative to mock table/listings/figure and/or CRF.
   - **3.5.** **Pages breaks** are as intended throughout the document.
   - **3.6.** **Significant digits** are appropriate for summary results (eg, mean is 1 more digit than collected on the CRF).
   - **3.7.** **Analysis population totals** are verified as correct based on SAP definitions and are consistent with other tables using the same population(s).
   - **3.8.** **Inappropriate data:** checked for outliers, invalid numbers, missing results, etc.

4. Dataset Structure (for SDTM/TDM/ADaM)

4.1. **Pinnacle 21 validator is run.** Any errors or warnings are updated or explained.

5. Verification of Data

5.1. SDTM/TDM/Analysis datasets (ADaM or ADaM-Like)

5.1.1. Programmer

- Each SDTM/TDM/Analysis dataset is opened and data are reviewed for consistency with the protocol, SAP, and/or CRF (no additional QC programming is necessary).

5.1.2. Validator

- Validation is performed against the protocol, SAP, and/or CRF. A spot-check of source data against the output dataset is performed on at least 2 patients. Each CRF section/form should be populated at least once for the spot-check. If a section/ form is repeated (eg, at several visits) 1 repeat per patient has to be spotchecked.

5.2. Tables

5.2.1. Program Review

- Verify that the appropriate datasets, variables, analysis populations, parameters/tests, and visits/time points are used.
- Verify that all keyword and positional parameters of the standardized macro call are accurate and are implemented as intended.

5.2.2. Output Review

- All expected data (parameters/tests, visits/time points, interventions, totals, etc.) are included on the output.
- Units and the range of values are confirmed to be consistent.
- Percentages are based on the correct denominator and confirmed to not exceed 100%.
- Counts within subgroups or subsets of data are checked for internal consistency (eg, subset counts do not exceed overall counts).

5.3. Listings

- Listing content is as expected (eg, listing includes all enrolled patients, all expected visits)
- Variables directly from source dataset are spot-checked for accuracy and completeness.
- Derived or calculated variables are compared to corresponding source data and manual calculation for at least 2 patients are done.

5.4. Figures

- Manual comparison to the corresponding table, where the table is validated and at least 25% of the data points on the figure are compared to the corresponding value on the table.
- Manual calculations (if feasible based on small Ns or frequency counts).

6. Documentation

6.1. The Programmer and Validator must document completion of QC (eg, date of QC and method used) in **BIO-0205-TMP-002 Program Status Document.**

6.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.

6.3. The following must be retained electronically within the study folder by the Validator as supporting documentation:

- If a spot-check of patient data is performed, output that clearly identifies the patients and CRF forms/sections that are checked
- Pinnacle 21 report generated at time of QC including comments

Appendix C: List of Tables, Figures, and Listings

The following proposal for section 14 and 16.2 is completed according to ICH E3 guidelines. The ICH heading numbers and description are in **bold**. Minor changes from this planned index do not need to be amended in the SAP.

Formal organization of tabulations may be changed during programming, if appropriate, eg, tables for the different variables may be combined into a single table, or tables with more than 1 variable may be split into several tables.

Section 14: Tables, Figures, and Graphs

Table Number	Table Title	Analysis Set	Comment
14	**TABLES, FIGURES, AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT**		
14.1	**DEMOGRAPHIC DATA**		
14.1.1	Patient number by country	All patients	
14.1.2	Patient number by country and center	All patients	
14.1.3	Patient disposition	All patients	
14.1.4	Trial termination form	Safety analysis set	
14.1.5	Demographic characteristics	Safety analysis set	
14.1.6	Demographic characteristics	FAS	
14.1.7.	Baseline characteristics		
14.1.7.1	Diabetes history	Safety analysis set	
14.1.7.2	Body measurements (height, weight, BMI)	Safety	

Table Number	Table Title	Analysis Set	Comment
		analysis set	
14.1.7.3	BMI by country	Safety analysis set	
14.1.7.4	Medical history	Safety analysis set	
14.1.8	Concomitant medication/ current diabetes treatment	Safety analysis set	
14.2	**Efficacy data**		
14.2.1	Primary efficacy endpoint		
14.2.1.1	Time to plasma glucose recovery - summary table	FAS	Patients who receive IV glucose will be censored (ie, set to 'not recovered') at 45 minutes after dosing
14.2.1.2	Time to plasma glucose recovery - Kaplan Meier survival curve	FAS	
14.2.1.3	Time to plasma glucose recovery - summary table	PP	
14.2.1.4	Time to plasma glucose recovery - Kaplan Meier survival curve	PP	
14.2.1.5	Sensitivity analysis - time to plasma glucose recovery without censoring for those subjects who require rescue IV glucose before 45 minutes - summary table	FAS	Without censoring for those subjects who require rescue IV glucose before 45 minutes
14.2.1.6	Sensitivity analysis - Time to plasma glucose recovery without censoring for those subjects who require rescue IV glucose before 45 minutes - Kaplan Meier survival curve	FAS	
14.2.1.7	Sensitivity analysis - time to plasma glucose recovery with censoring data at the actual time when the patients received glucose IV - summary table	FAS	With censoring data at the actual time when the patients received glucose IV.
14.2.1.8	Sensitivity analysis - Time to plasma glucose recovery with	FAS	

Table Number	Table Title	Analysis Set	Comment
	censoring data at the actual time when the patients received glucose IV - Kaplan Meier survival curve		
14.2.1.9	Time to plasma glucose recovery - histogram	FAS	
14.2.1.10	Time to plasma glucose recovery – using linear interpolation of the time to recovery – summary table	FAS	
14.2.1.11	Time to plasma glucose recovery – using linear interpolation of the time to recovery – Kaplan Meier survival curve	FAS	
14.2.2	Secondary efficacy endpoints		
14.2.2.1	Plasma glucose recovery within 10, 15, 20 and 30 minutes after trial product injection	FAS	Including p-values from CMH or Fisher's exact test and 95% CIs for response rates of each treatment group
14.2.2.2	Plasma glucose - untransformed results at 10, 15, 20 and 30 minutes after trial product injection	FAS	
14.2.2.3	Plasma glucose - change from baseline results and inferential test statistics at 10, 15, 20 and 30 minutes after trial product injection	FAS	Results from ANCOVA will be displayed here
14.3	**Safety data**		
14.3.1	**Displays of Adverse Events**		
14.3.1.1	Overall summary of adverse events	Safety analysis set	
14.3.1.2	TEAEs by system organ class and preferred term	Safety analysis set	
14.3.1.3	TEAEs of special interest by system organ class and preferred term	Safety analysis set	
14.3.1.4	Other impotant TEAEs by system organ class and preferred term	Safety analysis set	

Table Number	Table Title	Analysis Set	Comment
14.3.1.5	TEAEs, which are injection site reactions	Safety analysis set	
14.3.1.6	Study drug-related TEAEs by system organ class and preferred term	Safety analysis set	
14.3.1.7	TEAEs by system organ class and preferred term and causal relationship	Safety analysis set	
14.3.1.8	TEAEs by system organ class and preferred term and severity	Safety analysis set	
14.3.1.9	SAEs by system organ class and preferred term	Safety analysis set	
14.3.1.10	Special search category TEAEs	Safety analysis set	
14.3.2	Listings of deaths, other serious and significant adverse events		This is a cross-reference to listing 16.2.7.4
14.3.3	Narratives of deaths, other serious and certain other significant adverse events		This is a cross-reference to section 12.3.2 of the CSR
14.3.4	Extent of exposure		
14.3.4.1	Insulin administration prior to the hypoglycemia induction procedure	Safety analysis set	
14.3.4.2	Hypoglycemia induction procedure	Safety analysis set	
14.3.4.3	Trial medication	Safety analysis set	
14.3.4.4	Post-treatment rescue glucose infusion	Safety analysis set	
14.3.5	**Other safety data**		
14.3.5.1	ECG		

Table Number	Table Title	Analysis Set	Comment
14.3.5.1.1	ECG, overall interpretation	Safety analysis set	
14.3.5.1.2	ECG, descriptive statistics of all ECG parameters	Safety analysis set	
14.3.5.1.3	ECG, categorical analysis of QTc results	Safety analysis set	
14.3.5.1.4	ECG, categorical analysis of QTc results, change from baseline	Safety analysis set	
14.3.5.2	Laboratory data		
14.3.5.2.1	Hematology	Safety analysis set	
14.3.5.2.2	Clinical chemistry	Safety analysis set	
14.3.5.2.3	Coagulation	Safety analysis set	
14.3.5.2.4	Urinalysis - pH	Safety analysis set	
14.3.5.2.5	Urinalysis - quantitative results, count of abnormal results	Safety analysis set	
14.3.5.2.6	Pregnancy test		
14.3.5.3	Local tolerability	Safety analysis set	
14.3.5.4	Vital signs		
14.3.5.5	Pulse rate – categorical analysis	Safety analysis set	
14.3.5.6	Immunogenicity - occurrence of ADA	Safety analysis set	

Table Number	Table Title	Analysis Set	Comment
14.4	**Pharmacokinetic (PK) and pharmacodynamic (PD)**		
14.4.1	Pharmacokinetics		
14.4.1.1	Summary statistics of plasma dasiglucagon and GlucaGen concentration table	FAS	
14.4.1.2	PK metrics	FAS	
14.4.1.3	Figure: Mean analyte concentrations versus time - original scale	FAS	
14.4.1.4	Figure: Mean analyte concentrations versus time - log scale	FAS	
14.4.1.5	Figure: Individual analyte concentrations versus time curves - original scale	FAS	
14.4.2	Pharmacodynamics		
14.4.2.1	PD metrics	FAS	
14.4.2.2	Figure: Mean glucose concentrations versus time - original scale	FAS	
14.4.2.3	Figure: Individual glucose concentrations versus time curves - original scale	FAS	

Section 16.2: List of Data Listings

ICH Listing Number	Listing Title	Comment
16.2	**PATIENT DATA LISTINGS**	
16.2.1	**Discontinued patients**	
16.2.1.1	Patient disposition	
16.2.1.2	Trial termination	
16.2.2	**Protocol deviations**	
16.2.2.1	Patients not fulfilling any inclusion/exclusion criteria	
16.2.3	**Patients excluded from the efficacy analysis**	
16.2.3.1	Patients Excluded from analysis	
16.2.4	**Demographic data**	
16.2.4.1	Informed consent and demographics	
16.2.4.2	Baseline characteristics (body measurements)	
16.2.4.3	Diabetes history	
16.2.4.4	Medical history	
16.2.5	**Compliance and/or drug concentration data**	
16.2.5.1	Visit dates	
16.2.5.2	Randomisation	
16.2.5.3	Insulin administration prior to the hypoglycemia induction procedure	
16.2.5.4	Hypoglycemia induction procedure	
16.2.5.5	Study drug administration	
16.2.5.6	Post-treatment rescue glucose infusion	
16.2.5.7	Plasma dasiglucagon/GlucaGen sampling and concentrations	
16.2.5.8	Plasma dasiglucagon/GlucaGen pharmacokinetic metrics	
16.2.6	**Individual efficacy response data**	
16.2.6.1	Plasma glucose sampling and concentrations	

ICH Listing Number	Listing Title	Comment
16.2.6.2	Plasma glucose pharmacodynamic metrics	
16.2.6.3	Time to plasma glucose recovery	Derived including derived parameters
16.2.7	**Adverse events listings**	
16.2.7.1	Adverse events - CRF entries	
16.2.7.2	Adverse events - MedDRA coding	
16.2.7.3	Adverse Event of Special Interest - additional details	
16.2.7.4	Death and serious adverse events	
16.2.7.5	Adverse events – leading to withdrawal from study	
16.2.7.6	Adverse events – patients with positive ADA result	
16.2.7.7	Adverse events - plasma glucose measurements in case of hypogylcemia	
16.2.8	**Listing of individual laboratory measurements by patient, when required by regulatory authorities**	
16.2.8.1	Hematology	incl. derived data CFB
16.2.8.2	Biochemistry	incl. derived data CFB
16.2.8.3	Coagulation	incl. derived data CFB
16.2.8.4	Urinalysis	
16.2.8.5	Pregnancy test	
16.2.8.6	Alcohol breath test	
16.2.9	**Other data**	
16.2.9.1	Vital signs	
16.2.9.2	Physical examination	
16.2.9.3	Electrocardiogram	incl. derived data CFB
16.2.9.4	Concomitant medication and current diabetes treatment	
16.2.9.5	Local tolerability	

ICH Listing Number	Listing Title	Comment
16.2.9.6	Immunogenicity results	

Appendix D: Table Layouts

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14.1.1: Patient number by country, all patients

Country	Sreening Failure (N=xxx)	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Country 1	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Country 2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
US	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
NON-US	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.1.2: Patient number by country and center, all patients

Country	Center Number	Sreening Failure (N=xxx)	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Country 1	xx	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	xx	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Country 2	xx	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	xx	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...						
Country xx	xx	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	xx	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.1.3: Patient disposition, all patients

Number of	Sreening Failure (N=xxx)	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
patients screened	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
patients randomised		n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
patients in safety analysis set		n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
patients in full analysis set		n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
patients in per protocol set		n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.1.4: Trial termination, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Did the patient complete the study?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Primary reason for non-completion				
Adverse event	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Death	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...				

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Programmer Note: Populate all possible reasons for non-completion from e-CRF

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14.1.5: Demographic characteristics, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Age				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Age groups				
6-11 years	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
12-17 years	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Gender				
Male	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Female	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Child bearing potential				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.1.5 Demographic characteristics, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Race				
American indian or alaska native	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Asian	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Ethnic				
Hispanic or latino	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Nothispanic or latino	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Not allowed to ask per local regulations	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy

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Programmer Note: Populate all possible races from e-CRF

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14.1.6: Demographic characteristics, FAS

- ➔ Repetiton of table 14.1.5 with different selection of population.
- ➔ If identical (like expected) it will be sufficient to state they are identical.

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14.1.7.1: Diabetes history, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Time since diagnosis of diabetes 1 [years]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

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14.1.7.2: Body measurements (height, weight, BMI), Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Height [cm]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Weight [kg]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Body mass index [kg/m2]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Body mass index class				
<25 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
25-<30 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
30-<35 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
>35 kn/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.1.7.3: BMI by country, Safety analysis set

Country		dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Country 1	<25 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	25-<30 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	30-<35 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	>35 kn/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...					
Country xx	<25 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	25-<30 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	30-<35 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	>35 kn/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
US	<25 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	25-<30 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	30-<35 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	>35 kn/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
NON-US	<25 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	25-<30 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	30-<35 kg/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	>35 kn/m2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.1.8: Medical history, Safety analysis set

System organ class Preferred term	Number of Patients (%) Event Count dasiglucagon (N=xxx)	 Placebo (N=xxx)	 GlucaGen (N=xxx)	 Total (N=xxx)
Any medical history	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 1				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 2				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class xx				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
...				

Note: At each level of summation (SOC class, preferred name), patients reporting more than 1 event are counted only once for the patient count.
Table is sorted by descending patientcount on the PT level
Percentages are based on total no. of patients in each treatment group

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14.1.8: Concomitant Medications/ Current Diabetes Treatment, Safety analysis set

	Number of Subjects (%) Medication Count			
ATC class (level 2) **Preferred name**	**dasiglucagon (N=xxx)**	**Placebo (N=xxx)**	**GlucaGen (N=xxx)**	**Total (N=xxx)**
Any medication/ treatment	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
ATC class 1				
PT Name 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
ATC class 2				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
ATC class xx				
PT Name 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Name xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
...				

Note: At each level of summation (overall, ATC class, preferred name) patients reporting more than 1 medication/ treatment are counted only once.
Table is sorted by descending total patient count
Percentages are based on total no. of subjects in each treatment group

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14.2.1.1: Time to plasma glucose recovery - summary table, FAS

Primary model

	Treatment			
	dasiglucagon (N=xxx)	GlucaGen (N=xx)	placebo (N=xx)	p-values
Status (N)	Xx	xx	xx	
Recovered[1]	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	
Censored[2]	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	
Time to recovery (minutes)				
25th percentile	xx.x	xx.x	xx.x	
Median (95% CI)	xx.x (xx.x ; xx.x)	xx.x (xx.x ; xx.x)	xx.x (xx.x ; xx.x)	
75th percentile	xx.x	xx.x	xx.x	
Dasiglucagon versus Placebo P-value (log-rank test – stratified)				x.xxxx
P-value (log-rank test – non-stratified)				x.xxxx
P-value (Wilcoxon test) - stratified				x.xxxx
Dasiglucagon versus GlucaGen				
P-value (log-rank test – stratified)				x.xxxx
P-value (log-rank test – non-stratified)				x.xxxx
Cox proportional hazards[3]				
Hazard ratio	xx.xx	xx.xx	1	
95% profile CL	(xx.xxx ; xx.xxx)	(xx.xxx ; xx.xxx)		
P-values				
Dasiglucagon versus Placebo				x.xxxx
Dasiglucagon versus Glucagen				x.xxxx
Glucagen versus Placebo				x.xxxx
Type 3 test for Age				x.xxxx
Type 3 test for injection site				x.xxxx

1: Increase of plasma glucose of 20 mg/dL within 45 min without iv glucose
2: Did not recover within 45 min or received iv glucose before 45 min
3: Cox proportional hazard model with treatment, age and injection site as fixed effects and baseline plasma glucose as covariate

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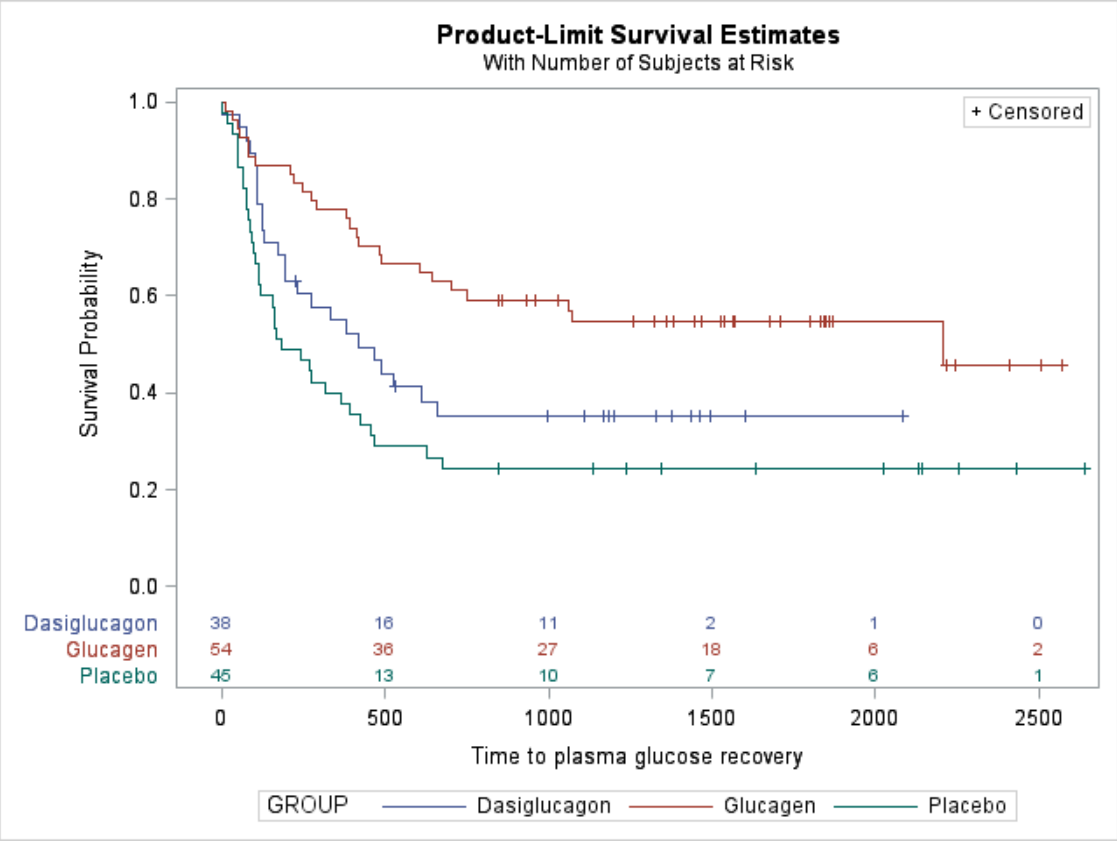
Homogenicity models

	Treatment		
	dasiglucagon (N=xxx)	GlucaGen (N=xx)	placebo (N=xx)
Cox proportional hazards[1]			
<Sub-group level 1>			
Hazard ratio	xx.xx	xx.xx	1
95% profile CL	(xx.xxx ; xx.xxx)	(xx.xxx ; xx.xxx)	
<Sub-group level 2>			
Hazard ratio	xx.xx	xx.xx	1
95% profile CL	(xx.xxx ; xx.xxx)	(xx.xxx ; xx.xxx)	
.. .			
<Sub-group level i>			
Hazard ratio	xx.xx	xx.xx	1
95% profile CL	(xx.xxx ; xx.xxx)	(xx.xxx ; xx.xxx)	

1: Cox proportional hazard model with treatment, age and injection site as fixed effects and baseline plasma glucose as covariate

14.2.1.2: Time to plasma glucose recovery - Kaplan Meier survival curve, FAS



Note: this is a generic example using example data from SAS Institute; number of patients at risk are adapted to 0, 10, 15, 20, 30 and 45min.

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14.2.1.3: Time to plasma glucose recovery - summary table, PP

➔ Repetiton of table 14.2.1.1 with different selection of population. Only page 1 output presented here.

14.2.1.4: Time to plasma glucose recovery - Kaplan Meier survival curve, PP

➔ Repetiton of table 14.2.1.2 with different selection of population.

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14.2.1.5: Sensitivity analysis - time to plasma glucose recovery without censoring for those subjects who require rescue IV glucose before 45 minutes - summary table, FAS

➔ Repetiton of table 14.2.1.1 with different selection of population. Only page 1 output presented here.

14.2.1.6: Sensitivity analysis - time to plasma glucose recovery without censoring for those subjects who require rescue IV glucose before 45 minutes - Kaplan Meier survival curve, FAS

➔ Repetiton of table 14.2.1.2 with different selection of population.

14.2.1.7: Sensitivity analysis - time to plasma glucose recovery with censoring for those subjects who require rescue IV glucose before 45 minutes - summary table, FAS

➔ Repetiton of table 14.2.1.1 with different selection of population. Only page 1 output presented here.

14.2.1.8: Sensitivity analysis - time to plasma glucose recovery with censoring for those subjects who require rescue IV glucose before 45 minutes - Kaplan Meier survival curve, FAS

➔ Repetiton of table 14.2.1.2 with different selection of population.

14.2.1.9: Time to plasma glucose recovery - histogram, FAS

➔ Layout will be established during programming

14.2.1.10: Time to plasma glucose recovery - using linear interpolation of the time to recovery, FAS

➔ Repetiton of table 14.2.1.1 using linear interpolated time to recovery data. Only page 1 output presented here.

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14.2.2.1: Plasma glucose recovery within 10, 15, 20 and 30 minutes after trial product injection, FAS

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	p-value[1] dasiglucgon versus Placebo
Plasma glucose recovery within 10min				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	
95% CIs for response rate (Category 'Yes')	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	x.xxxx
Plasma glucose recovery within 15min				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	
95% CIs for response rate (Category 'Yes')	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	x.xxxx
Plasma glucose recovery within 20min				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	
95% CIs for response rate (Category 'Yes')	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	x.xxxx
Plasma glucose recovery within 30min				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	
95% CIs for response rate (Category 'Yes')	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	x.xxxx

If a patient has received an IV glucose treatment before recovery, the patient is set to 'not recovered'.
[1] p-values calculated using a Cochran-Mantel-Haenszel test stratified by age group and injection site.

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14.2.2.2: Plasma glucose - untransformed results at 10, 15, 20 and 30 minutes after trial product injection

Variable	Time Point		dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Result	Pre-dose	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	10 min after dosing	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	15 min after dosing	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	20 min after dosing	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	30 min after dosing	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

If the rescue IV glucose was administered before 10, 15, 20, or 30 minutes, respectively, the patient's plasma glucose changes from baseline is determined from the value at the time of rescue IV glucose administration.

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14.2.2.2: Plasma glucose - change from baseline results and inferential test statistics at 10, 15, 20 and 30 minutes after trial product injection

Variable	Time Point		dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)	p-value[1] (95% CI) dasiglucgon versus Placebo
Change from Baseline	10 min after dosing	n	xx	xx	xx	xx	
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx.x	xx.x	xx.x	xx.x	
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	x.xxxx
		LS-mean	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
		95%CI (LS-mean)	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]
	15 min after dosing	N	xx	xx	xx	xx	
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx.x	xx.x	xx.x	xx.x	
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	x.xxxx
		LS-mean	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
		95%CI (LS-mean)	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]
	20 min after dosing	n	xx	xx	xx	xx	
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx.x	xx.x	xx.x	xx.x	
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	x.xxxx
		LS-mean	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
		95%CI (LS-mean)	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]
	30 min after dosing	n	xx	xx	xx	xx	
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	
		Median	xx.x	xx.x	xx.x	xx.x	
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	x.xxxx
		LS-mean	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
		95%CI (LS-mean)	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]	[xx.x; xx.x]

If the rescue IV glucose was administered before 10, 15, 20, or 30 minutes, respectively, the patient's plasma glucose changes from baseline is determined from the value at the time of rescue IV glucose administration.
[1] p-values calculated using an analysis of variance (ANOVA) with factors treatment, age group and injection site
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14.3.1.1: Overall summary of adverse events, Safety analysis set

	Number of Subjects (%) Event Count			
	dasiglucagon (N=xxx)	**Placebo (N=xxx)**	**GlucaGen (N=xxx)**	**Total (N=xxx)**
Adverse events during screening	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Treatment-emergent AEs (TEAEs)	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
TEAEs, which are adverse events of special interest (AESIs)	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
TEAEs, which are another important event	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
TEAEs, which are injection site reactions	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Study drug-related TEAEs [1]	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Serious TEAEs (SAEs)	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Study drug-related serious TEAEs	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Deaths	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx

...

[1] Study drug-related TEAEs: TEAEs which were assessed by the investigator as possibly related or probably related, or without assessment of relationship.
Table is based on number of verbatims.
Patients reporting more than 1 event are counted only once for the patient count.
Percentages are based on total no. of subjects in each treatment group

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14.3.1.2: TEAEs by system organ class and preferred term, Safety analysis set

	Number of Subjects (%) Event Count			
System organ class **Preferred term**	**dasiglucagon (N=xxx)**	**Placebo (N=xxx)**	**GlucaGen (N=xxx)**	**Total (N=xxx)**
Any adverse event	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 1				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 2				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class xx				
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
...				

Note: At each level of summation (SOC class, preferred name) patients reporting more than 1 event are counted only once for the patient count.
Table is sorted by descending subject count on the PT level in the dasiglucagon group.
Percentages are based on total no. of subjects in each treatment group

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14.3.1.3: TEAEs of special interest by system organ class and preferred term, Safety analysis set

➔ Repetiton of table 14.3.1.2 with different selection of the AE analysis dataset.

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14.3.1.4: Other important TEAEs by system organ class and preferred term, Safety analysis set

➔ Repetiton of table 14.3.1.2 with different selection of the AE anaylsisy dataset.

14.3.1.5: TEAEs, which are injection site reactions, Safety analysis set

➔ Repetiton of table 14.3.1.2 with different selection of the AE analysis dataset.

14.3.1.6: Study drug-related TEAEs by system organ class and preferred term, Safety analysis set

➔ Repetiton of table 14.3.1.2 with different selection of the AE anaylsisy dataset.

14.3.1.7: TEAEs by system organ class and preferred term and causal relationship, Safety analysis set

	dasiglucagon (N=xxx)		Placebo (N=xxx)		GlucaGen (N=xxx)	
System organ class **Preferred term**	**Related[1]**	**Not Related[2]**	**Related[1]**	**Not Related[2]**	**Related[1]**	**Not Related[2]**
Any adverse event	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 1						
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 2						
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx

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Note: At each level of summation (SOC class, preferred name) patients reporting more than 1 event are counted only once for the patient count.
[1] Includes all events reported as 'Possible', 'Probable' or missing relationship.
[2] Includes all events reported as 'Not related or 'Unlikely'.
Table is sorted by descending subject count on the PT level in the dasiglucagon group.
Percentages are based on total no. of subjects in each treatment group.

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14.3.1.8: TEAEs by system organ class and preferred term and severity, Safety analysis set

	dasiglucagon (N=xxx)			Placebo (N=xxx)			GlucaGen (N=xxx)		
System organ class **Preferred term**	**Mild**	**Moderate**	**Severe**	**Mild**	**Moderate**	**Severe**	**Mild**	**Moderate**	**Severe**
Any adverse event	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 1									
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
SOC class 2									
PT Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term 3	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
PT Term xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx

Note: At each level of summation (SOC class, preferred name) patients reporting more than 1 event are counted only once for the patient count.
Table is sorted by descending subject count on the PT level in the dasiglucagon group.
Percentages are based on total no. of subjects in each treatment group.

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14.3.1.9: SAEs by system organ class and preferred term, Safety analysis set

➔ Repetiton of table 14.3.1.2 with different selection of the AE anaylsisy dataset.

14.3.1.10: Special search category TEAEs, Safety analysis set

➔ Repetiton of table 14.3.1.2 with different selection of the AE anaylsisy dataset.

14.3.2: Listings of deaths, other serious and significant adverse events, Safety analysis set

Please refer to listing 16.2.7.4.

Programmer Note: Create a empty table with that reference as message

14.3.3: Narratives of deaths, other serious and certain other significant adverse events, Safety analysis set

Please refer to listing 16.2.7.4.

Programmer Note: Create a empty table with that reference as message

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14.3.4.1: Insulin administration prior to the hypoglycemia induction procedure, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Is the subject using multiple daily injections?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n
Has the subject taken insulin NPH?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n
Is the subject using an insulin pump?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n
Was insulin glulisine (Apidra) administered in the last 5 hours prior to initiation of the hypoglycemic induction procedure?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n

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14.3.4.2: Hypoglycemia induction procedure, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Was the hypoglycemia induction procedure performed?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n
Total amount of insulin administered to induce hypoglycemia [IU]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Total amount of glucose administered during the induction procedure [mL]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

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14.3.4.3: Trial medication, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Was the trial medication administered?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n

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14.3.4.4: Post-treatment rescue glucose infusion, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Was glucose given for rescue?				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n
Time to first IV glucose infusion [min]				
Mean (SD)	n	xx	xx	xx
Median	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Min, Max	Median	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx

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14.3.5.1.1: ECG, overall interpretation, Safety analysis set

Visit	Time Point	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Screening		NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	Pre-dose	NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	20min post dose	NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	35min post dose	NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	45min post dose	NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	60min post dose	NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	300min post dose	NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.3.5.1.1: ECG, overall interpretation, Safety analysis set

Visit	Time Point	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Follow up		NORMAL	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / NOT CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		ABNORMAL / CLIN. SIG.	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

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14.3.5.1.2: ECG, descriptive statistics of all ECG parameters, Safety analysis set

Parameter	Visit/ TimePoint	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Mean heart rate [bpm]	Screening	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Dosing/ Pre-dose	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Dosing/20 min after dosing	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	...					
	Follow up	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: This table is continued for each of the following ECG parameter: PR Interval Aggregate [msec], QRS Duration Aggregate[msec], QT Interval Aggregate[msec], QTcF Interval Aggregate[msec]

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14.3.5.1.3: ECG, categorical analysis of QTc results, Safety analysis set

Visit	Time Point	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Screening		QTcF values of >450 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >480 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >500 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	Pre-dose	QTcF values of >450 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >480 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >500 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	20min post dose	QTcF values of >450 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >480 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >500 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...						
Follow up		QTcF values of >450 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >480 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF values of >500 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

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14.3.5.1.4: ECG, categorical analysis of QTc results, change from baseline, Safety analysis set

Visit	Time Point	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Dosing	20min post dose	QTcF CFB >30 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF CFB >60 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	35min post dose	QTcF CFB >30 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF CFB >60 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...						
Follow up		QTcF CFB >30 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		QTcF CFB >60 ms	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: Baseline is the pre-dose result at visit 1 Screening

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14.3.5.2.1: Hematology, Safety analysis set

Treatment	Visit	n	Mean	Median	SD	Min	Max	CFB -Mean	CFB- SD	Below reference range n(%)	Within reference range n(%)	Above reference range n(%)
Laboratory parameter test name 1												
dasiglucagon	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Placebo	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Glucagon	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Total	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Laboratory parameter test name 2												
dasiglucagon	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Placebo	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Glucagon	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
Total	Screening	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	-	-	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	xx	xx.xx	xx.xx	xx.xxx	xx.x	xx.x	xx.xx	xx.xxx	n (xx.x%)	n (xx.x%)	n (xx.x%)
...												

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: Each laboratory test parameter is either displayed one per page or as shown here two on 1 page if possible.

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14.3.5.2.2: Clinical chemistry, Safety analysis set

➔ Repetiton of table 14.3.5.2.1 with different selection of the lab analysis dataset.

14.3.5.2.3: Coagulation, Safety analysis set

➔ Repetiton of table 14.3.5.2.1 with different selection of the lab analysis dataset.

14.3.5.2.4: Urinalysis - pH, Safety analysis set

➔ Repetiton of table 14.3.5.2.1 with different selection of the lab analysis dataset.

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14.3.5.2.5: Urinalysis - quantitative results, count of abnormal results, Safety analysis set

Urine parameter	Visit	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Urine parameter 1	Screening	Below reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Within reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Above reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Dosing	Below reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Within reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Above reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	Below reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Within reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Above reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Urine parameter 2	Screening	Below reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Within reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Above reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Dosing	Below reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Within reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Above reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Follow up	Below reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Within reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Above reference range	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

...

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

14.3.5.2.6: Pregnancy test, Safety analysis set

Visit	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Screening	Negative	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Positive	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	Negative	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Positive	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Follow up	Negative	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
	Positive	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

Screening: Serum pregnancy test
Dosing,Follow up: Urine stick pregnancy test. Prior to the start of the insulin-induced hypoglycemic procedure.

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

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14.3.5.3: Local tolerability, Safety analysis set

Local Symptom	Visit/ Time point	Grade (Intensity)	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Spontaneous Pain	30min after dosing	None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	120min after dosing	None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	300min after dosing	None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Follow up	None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Percentages are based on total no. of subjects in each treatment group

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: Table is produced with same SAS macro like Aes (npcttab).

14.3.5.4: Vital signs, Safety analysis set

Parameter	Visit/Time Point	Result	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Systolic blood pressure [mmHg]	Screening	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Dosing/ Prior start of hypoglycemic procedure	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
	Dosing/ 30min post dose	n	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
...						
	Follow up	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
		n	xx	xx	xx	xx

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: This table is continued for each of the following Vital signs parameter: Systolic blood pressure [mmHg], Pulse rate [bpm] and body temparature [°C]

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14.3.5.5: Pulse rate - categorical analysis, Safety analysis set

Visit	Time Point	Class	dasiglucagon (N=xxx)	GlucaGen (N=xxx)	Placebo (N=xxx)	Total (N=xxx)
Screening		Class1	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Class2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	Prior start of hypoglycemic procedure	Class1	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Class2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Dosing	30min post dose	Class1	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Class2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
...						
Follow up		Class1	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
		Class2	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: This table is repeated (as byvars) for each of the following Vital signs parameter: Systolic blood pressure [mmHg], Pulse rate [bpm] and body temparature [°C]

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14.3.5.6: Immunogenicity - occurrence of ADA, Safety analysis set

	dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Occurrence of ADA				
No	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Yes	n (xx.x%)	n (xx.x%)	n (xx.x%)	n (xx.x%)
Missing	n	n	n	n

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

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14.4.1.1: Summary statistics of plasma dasiglucagon and GlucaGen concentration table, FAS

Treatment	Variable		Pre-dose	10min	20min	30min	40min	60min	90min	140min	220min	300min
Glucagon	Result	n		xx	xx	xx	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
	Change from baseline	n		xx	xx	xx	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
dasiglucagon	Result	n		xx	xx	xx	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
	Change from baseline	n		xx	xx	xx	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Pre-dose results LLOQ are set to 0 pmol/mL
Results are rounded to 3 significant digits

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note: The mean (SD) column above is broken into 2 lines above, but if possible put it in one row

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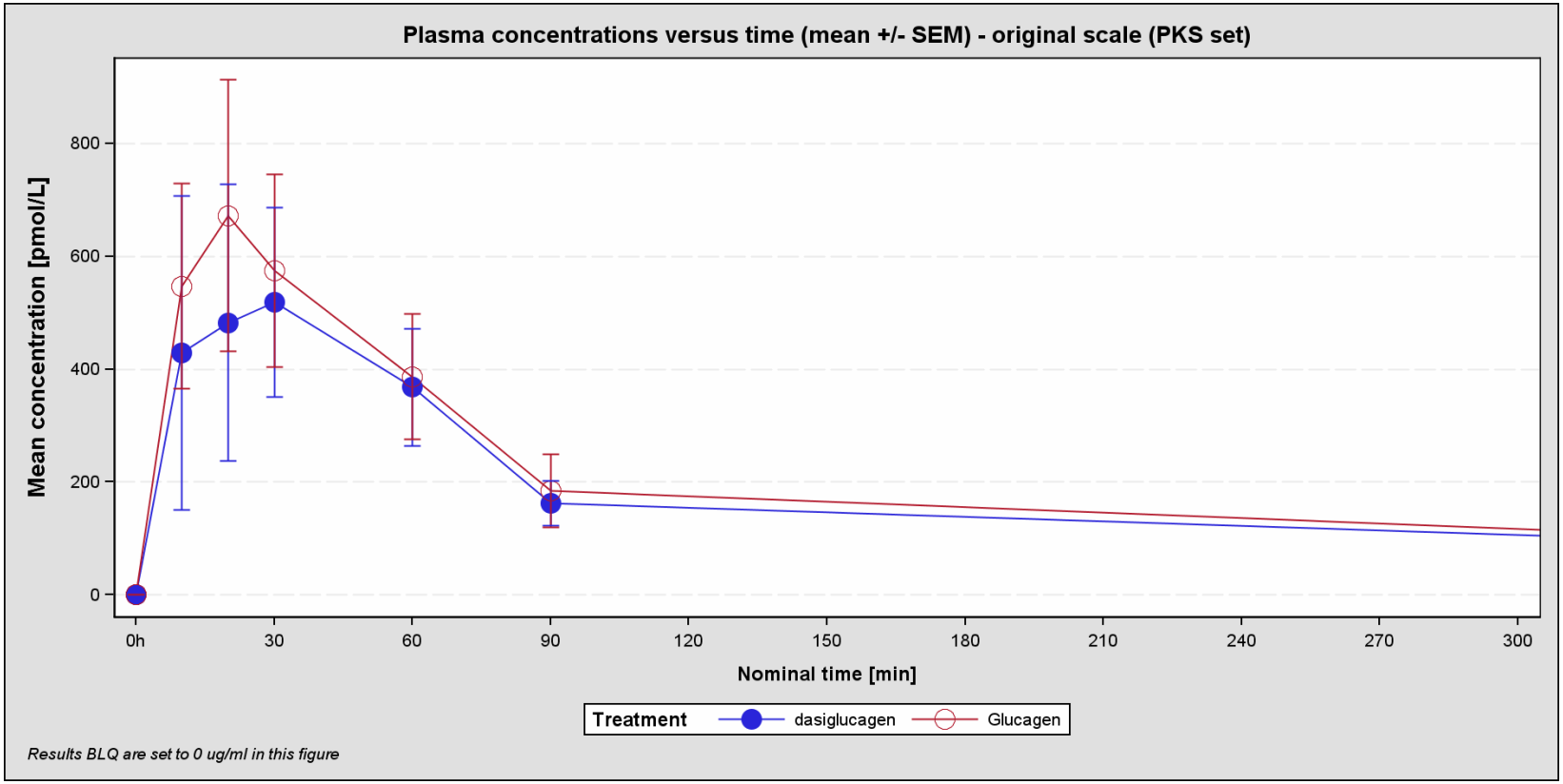
14.4.1.2: PK metrics, FAS

PK Parameter		dasiglucagon (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Cmax [pmol/L]	n	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx
	Geom. Mean	xx, xx	xx, xx	xx, xx
	Gem. Mean CV %	xx, xx	xx, xx	xx, xx
Tmax [h]	n	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx
...				

Results are rounded to 3 significant digits

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

14.4.1.3: Figure: Mean analyte concentrations versus time - original scale, FAS



PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy

RUN DATE: ddmmyyy hh:mm CET

NOTE: This is a generic example using example data not real data

14.4.1.4: Figure: Mean analyte concentrations versus time - log scale, FAS

➔ Repetiton of figure 14.4.1.3 using logarithmic y-scale

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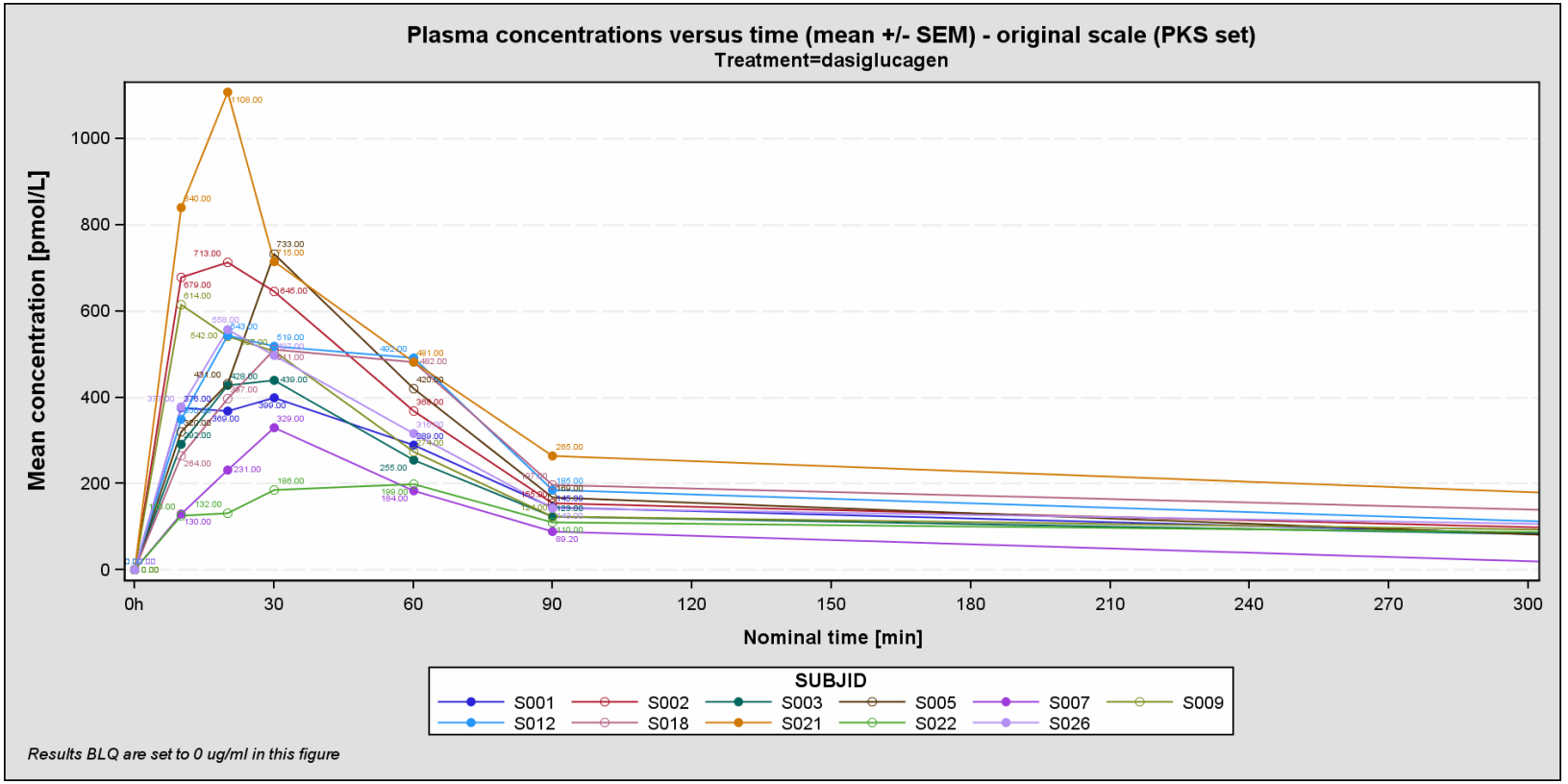
14.4.1.5: Figure: Individual analyte concentrations versus time curves- original scale, FAS



PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

NOTE: This is a generic example using example data not real data and coloring will be the same as in the figure before; x-axis and sampling scheme will be adapted to the study specifics

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14.4.2.1: PD metrics, FAS

PK Parameter		dasiglucagon (N=xxx)	Placebo (N=xxx)	GlucaGen (N=xxx)	Total (N=xxx)
Cmax [pmol/L]	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Tmax [h]	n	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
...					

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

14.4.2.2: Figure: Mean glucose concentrations versus time - original scale, FAS

➔ Repetiton of figure 14.4.1.3 using glucose concentration and adapted sampling scheme

14.4.2.3: Figure: Individual glucose concentrations versus time curves - original scale, FAS

➔ Repetiton of figure 14.4.1.4 using glucose concentration and adapted sampling scheme

Appendix E: Listing Layouts

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Listing 16.2.x
Title, Population (if applicable)

Treatment	Subject ID	Parameter	Visit	Time Point	Variable 1	Variable 2	Variable 3	Variable 4	Variable xxxx
xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

PROGRAM SOURCE:###, DATA CUT OFF DATE: ddmmmyyyy RUN DATE: ddmmyyy hh:mm CET

Programmer Note:

- *Listings are sorted by treatment, Subject ID, Parameter, Visit and timepoint as applicable and available.*
- *Listings usually will display all data avaiölable and not restricted to any analysis set if not defined otherwise in the SAP*