

STATISTICAL ANALYSIS PLAN

A Prospective Image Reevaluation Study to Assess the Efficacy of ^{18}F-*m*FBG PET Imaging in Subjects with Neuroblastoma

Protocol No.: IRP101-305

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LIST OF ABBREVIATIONS

CIs	Confidence intervals
CSR	Clinical Study Report
CT	Computed tomography
DEP	Diagnostic efficacy population
eCRFs	Electronic Case Report Forms
EP	Enrolled population
GCP	Good Clinical Practice
ICL	Imaging Core Laboratory
IRC	Independent Review Charter
IP	Investigational product
IRTM	Image Review Training Manual
MR	Magnetic resonance
NPA	Negative percent agreement
NPV	Negative predictive value
OSoR	Objective Standard of Reference
PET	Positron Emission Tomography
PPA	Positive percent agreement
PPV	Positive predictive value
SAP	Statistical Analysis Plan
SD	Standard deviation
SOP	Standard Operating Procedure
TLF	Tables, Listings , and Figures
UN/UNK	Unknown

1. INTRODUCTION

This Statistical Analysis Plan (SAP) provides the outline for the statistical analysis of the data collected for Innervate Radiopharmaceuticals LLC protocol IRP101-305, titled “A Prospective Image Reevaluation Study to Assess the Efficacy of ^{18}F-*m*FBG PET Imaging in Subjects with Neuroblastoma” Version 2.0 06 April 2026 and the related Objective Standard of Reference Charter Version 3.1 31 Jul 2026.

Any deviations from the SAP after database lock, reasons for such deviations, and all alternatives or additional statistical analyses that may be performed will be described in the Clinical Study Report (CSR).

If this SAP differs from the statistical considerations in the protocol, details will be given in Section 16.

2. PROJECT OVERVIEW

2.1. Description of Study Design

This is a prospective image re-evaluation study designed to assess the performance of ^{18}F-*m*FBG PET imaging in detecting the presence of neuroblastoma. Eligible participants will have undergone ^{18}F-*m*FBG PET imaging in a research trial or locally-authorized clinical use and have: a) an established diagnosis of active neuroblastoma; or b) an established diagnosis of neuroblastoma in remission; or c) no history or current evidence of neuroblastoma based on signs, symptoms, imaging findings, and laboratory results.

This is a study involving blinded interpretation of existing ^{18}F-*m*FBG PET images. No cases will be administered ^{18}F-*m*FBG. Previously collected ^{18}F-*m*FBG PET images will be evaluated by 5 independent radiologists and/or nuclear medicine physicians. They will have access to limited clinical information on the reason case was undergoing evaluations at the time of ^{18}F-*m*FBG imaging but be blinded to all other case information. Blinded readers will record the findings on ^{18}F-*m*FBG scans judged consistent with presence of neuroblastoma and the disease status (+ or -) of the cases.

Case-level performance of ^{18}F-*m*FBG PET will be assessed on the basis of positive and negative percent agreement with presence of at least 1 lesion identified by a blinded reader confirmed as neuroblastoma on clinical standard-of-care imaging and histopathology evaluations. Region/organ system level diagnostic performance will be assessed on the basis of positive and negative percent agreement between the blinded ^{18}F-*m*FBG scan interpretations and disease status in the corresponding region on clinical standard-of-care imaging and histopathology evaluations. Both assessments will utilize the clinical information gathered as part of the trials or locally-authorized clinical use in which the ^{18}F-*m*FBG scans were acquired and relevant clinical follow-up available at the imaging sites.

As no cases will be administered investigational product (IP) (^{18}F-*m*FBG) in this study, no safety data will be collected.

Objective Standard of Reference (OSoR) Algorithm

In neuroblastoma patients, definitive histological evidence of disease is almost always obtained from the primary tumor, either at initial detection or after a first course of therapy to reduce symptoms or mass effect on surrounding structures. Thereafter, standard clinical monitoring includes routine periodic bilateral iliac crest bone marrow sampling but only infrequent sampling of other tissues that may be suspicious for tumor on diagnostic imaging. As such, although histopathologic evidence of tumor represents the highest quality evidence for the OSoR, that evidence is usually only available within a few months of the initial disease diagnosis. Thereafter, anatomic and functional imaging are the dominant components of disease monitoring for response to therapy and subsequent surveillance. Acknowledging this reality, the OSoR algorithm is hierarchical in design, with consideration of data from tissue assessment in close proximity to ^{18}F-*m*FBG (if available) first, followed by sequential review of imaging findings over a longer time domain. Anatomic imaging (CT and MRI) is generally considered the first-line technique for characterizing soft-tissue disease, while functional imaging, specifically scans using *m*IBG, FDG, and dotatate, are central to assessment of bone and bone marrow, sometimes referred to as osteomedullary disease, as well as for characterizing indeterminate soft tissue findings on anatomic imaging.

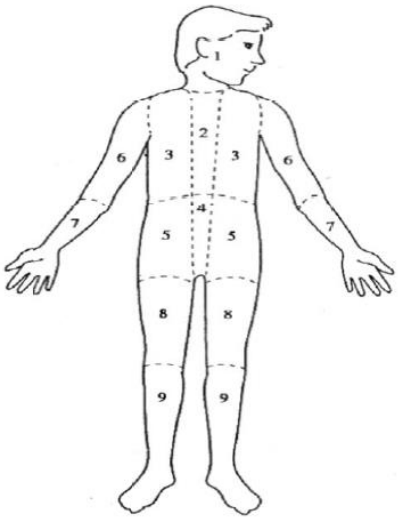
The OSoR algorithm was designed to use the collected imaging procedure reports without further review of the images themselves. Considering the variability in language used by

different interpreters, the most efficient and realistic approach was to divide the scan findings into 3 categories. Details of the 3 categories are described in the OSoR Charter Section 6.2.

For the purposes of the OSoR algorithm, the 3 categories (findings indicative of tumor, equivocal findings and negative studies) are used to produce a binary categorization: Disease+ or Disease-. The algorithm includes all available data within ±90 days of ^{18}F-*m*FBG imaging, as well as findings from 91-180 days post-^{18}F-*m*FBG that allow characterization of findings identified on the reference scan.

Confirmation of ^{18}F-*m*FBG positive findings will be based on Curie score regions (Figure 1) for the primary efficacy analysis and based upon anatomic regions for secondary efficacy analyses.

Figure 1: Curie Score Methodology



Regions 1-9 represent disease detected in the osteomedullary system. All soft tissue findings are recorded as present in region 10 (not shown).

Disease status categorization as positive or negative will rely on the composite of information from relevant procedures available for review by 2 independent trained Interpreters. To maintain the objectivity of the assessment, each Interpreter must follow a pre-specified group of decision rules, namely the OSoR decision algorithm. This algorithm provides 2 mechanisms for defining positive disease: 1) Definitive histopathology for neuroblastoma or imaging findings consistent with the disease from the reference date ±30 days; or 2) the aggregate of abnormal histopathology, imaging and biomarker results from within ±90 days of the reference date, with the additional requirement of correspondence of these findings to at least one abnormal finding on ^{18}F-*m*FBG imaging. In addition to these primary sources of case-level disease confirmation, findings from 90-180 days after the reference date may provide comparable evidence of disease if there is an anatomic region match on the later procedure for an abnormality originally identified only on ^{18}F-*m*FBG imaging.

Experienced pediatric imaging specialists (“Interpreters”) will perform the OSoR review. The primary objective of this review is to determine if, at the case-level, a case is positive for neuroblastoma (NB+). The secondary objective for NB+ cases is to determine if at least one OSoR data element is positive in the same Curie score or anatomic region as reported on the ^{18}F-*m*FBG PET scan. Conversely, for cases judged as negative for neuroblastoma (NB-), the expectation is that there will be no positive findings on the ^{18}F-*m*FBG PET scan. Details

of the process of deciding the OSoR by Interpreters are described in the OSoR Charter Section 6.3.

2.2. Objectives and Endpoints

2.2.1. Primary Objectives and Endpoints

The primary objective of this study is to demonstrate that ^{18}F-*m*FBG PET scintigraphy (PET/CT or PET/MR) is sensitive and specific on a case-level in confirming or excluding the presence of neuroblastoma.

The primary endpoint is focal increased uptake (presence or absence) on ^{18}F-*m*FBG PET/CT or PET/MR imaging, reported as Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) for detecting neuroblastoma as determined by comparing clinical standard of care imaging and/or histopathology with comparable anatomic regions judged positive/negative by ^{18}F-*m*FBG.

2.2.2. Secondary Objectives and Endpoints

A secondary objective is to demonstrate that ^{18}F-*m*FBG PET scintigraphy (PET/CT or PET/MR) is sensitive and specific on a region/organ system-level in confirming or excluding the presence of neuroblastoma.

The secondary efficacy endpoint will be focal increased uptake (presence or absence) on ^{18}F-*m*FBG PET/CT or PET/MR imaging in prespecified anatomic regions, reported as PPA and NPA for detecting neuroblastoma as determined by comparison with clinical standard of care imaging and/or histopathology in those regions.

Another secondary objective is to assess inter-reader variability.

3. SAMPLE SIZE

The sample size determination is based on the expected values of PPA and NPA for ^{18}F-*m*FBG PET. Calculation of N is shown in Table 1. These sample size estimates provide 80% power to demonstrate that the lower limit of the two-sided 95% exact binomial confidence interval is greater than 50%. The last column displays the smallest observed rate for which the lower bound of the two-sided 95% confidence interval will be >50%.

Table 1: Sample Size Calculation

Power 80%	Alternative Hypothesis Rate	Required Sample Size	Smallest Observed Rate
	70.0%	49	63.3%
	72.5%	37	64.9%
	75.0%	30	66.7%
	77.5%	25	72.0%
	80.0%	20	75.0%
	82.5%	17	76.5%
	85.0%	15	80.0%
	87.5%	12	83.3%
	90.0%	12	83.3%
	92.5%	9	88.9%
	95.0%	9	88.9%

Based on experience with trials involving blinded image evaluation (PPA tending to be lower than for informed image reads), expected PPA is 80%. Expected NPA is 85%. As such, the minimum required numbers of positive and negative cases is 20 and 15 respectively. Therefore, the minimum total sample size is 35 cases.

As a prospective image reevaluation study, adequate correlative information from the original trials and associated clinical follow-up will be available to allow definitive determination of the disease status of all cases. Sufficient images will be collected to assure that the numbers of positive and negative disease status cases meet the minimum criteria specified above. It is estimated that the number of evaluable cases included in this study will be between 40 and 50.

4. RANDOMIZATION AND BLINDING

As a trial utilizing existing images, selection of studies for inclusion could be a source of bias. Whereas participants were entered in the previous trials or locally-authorized clinical use in accordance with specific enrolment criteria, the primary basis for inclusion of images in the present study was the ability of site investigators to release those images in compliance with institutional policies and maintenance of case anonymity. As partial mitigation, the choice of submitted images was made by the site investigator, not the study sponsor. The study design also provides partial mitigation, in that the presence or absence of tumor was established in the original trials (or locally-authorized use) by accepted medical methods, prior to development of the present trial protocol. A final mitigation is that only images from cases whose neuroblastoma disease status was unequivocally established at the trial sites will be utilized in this study.

4.1. Method of Assigning Cases Numbers

A unique allocation number will be assigned to each case whose images are included in the study. No case may be entered into the study more than once.

The allocation number will be unique for each case in the study and will consist of an identification of 5 digits: 2 for the site and 3 for the case (e.g., 02001: first case at site No. 2).

Once an allocation number is assigned, it cannot be reassigned even if the case image files are deemed unusable. Allocation numbers will be assigned by the Sponsor.

4.2. Independent Image Review

All image data files and processed/reconstructed PET images will be transferred to the Imaging Core Laboratory (ICL) for blinding, randomization, image processing, evaluation, and data analysis as described in protocol Section 6.1.1.2 and protocol Section 6.1.1.3. ^{18}F-*m*FBG images will be qualitatively examined by 5 independent readers. Readers will be aware that the trial involves neuroblastoma cases. The readers will be informed of the reason the case was undergoing evaluations at the time of ^{18}F-*m*FBG imaging, in accordance with instructions in the Independent Review Charter (IRC) supporting this protocol. The readers will be blinded to all other clinical information. Readers will have access to anatomic cross-sectional images (CT or MRI) acquired as part of the PET exam.

All activities of each reader will be overseen by ICL personnel in accordance with the IRC.

5. STATISTICAL CONSIDERATIONS

5.1. Standard Operating Procedures and Software

Data will be handled and processed per the sponsor representative's (Avance) Standard Operating Procedures (SOPs), which are written based on the principles of Good Clinical Practice (GCP).

5.2. General Considerations

All data collected during the study (data originating from the electronic Case Report Forms (eCRFs) or electronic transfers will be presented in the data listings. Assessment-based listings will be sorted by parameter name (alphabetically unless specifically stated otherwise), Case ID, visit and timepoint (if applicable).

Unless otherwise stated, the following methods will be applied:

- Continuous variables: Descriptive statistics will include the number of non-missing values (n), arithmetic mean, standard deviation (SD), median, minimum, and maximum values.

  The minimum and maximum values will be displayed to the same decimal precision as the source data, the arithmetic mean and median values will be displayed to one more decimal than the source data, and the SD values will be displayed to two more decimals than the source data for the specific variable.

  The appropriate precision for derived variables will be determined based on the precision of the data on which the derivations are based, and statistics will be presented in accordance with the abovementioned rules.

- Categorical variables: Descriptive statistics will include frequencies and percentages per category. The denominator in all percentage calculations will be the number of Cases in the relevant analysis population with non-missing data, unless specifically stated otherwise. Percentages will be rounded to one decimal place and will not be displayed for zero frequencies.

- Presentation of p-values and confidence intervals: 95% confidence intervals will be computed, and reported to three decimal places, p-values will be displayed up to three decimal places and as "<0.001" if the value is below 0.001.

- Result display convention: Results will be center aligned in all summary tables and data listings. Case ID, visit, and parameter labels and comments may be left aligned if required.

- Date and time display conventions: The following display conventions will be applied in all outputs where dates and/or times are displayed:
  - Date only: DD-MMM-YYYY
  - Date and time: DD-MMM-YYYY /HH:MM

- If only partial information is available, unknown components of the date or time will be presented as UN/UNK (Unknown), for example "UN-UNK-2022".

- Total Curie Score: Total Curie Score will be computed as the sum of Curie Score from the ten Regions.

5.3. Adjustments for Covariates

No adjustments for covariates will be carried out for this study.

5.4. Handling of Dropouts or Missing Data

In general, all data will be analyzed as collected and missing values will not be imputed or replaced unless stated otherwise.

Imaging Missing Data Rules: For imaging data, if the Curie score regions are missing, these will be imputed as follows:

- For Interpreter review, if final review conclusion is negative, all Curie score regions and anatomic locations will be imputed as negative for the corresponding interpreter review.
- For the blind reader review, if the image quality is not “Not Evaluable” and “Confirm if Neuroblastoma(s) is present” is recorded as No, the number of lesions in all Curie score regions will be imputed as 0. If the image quality is “Not Evaluable”, the number of lesions in all regions will not be imputed.

5.5. Multicenter Studies

The cases from previous clinical trials or locally-authorized clinical use will be entered into this study and the analysis will be applied for the pooled data.

5.6. Multiple Comparisons/Multiplicity

No multiplicity adjustment will be carried out for this study.

5.7. Active-Control Studies Intended to Show Equivalence

Not applicable for this study.

5.8. Examination of Subgroups

Subgroup analyses for efficacy endpoints are defined in Section 14.2.4.

5.9. Treatment Group and Visit Display Conventions

As this is a retrospective study with only cases who have undergone ^{18}F-*m*FBG PET imaging in a previous trial or locally-authorized clinical use, no treatment group or visit display is relevant.

6. ANALYSIS POPULATIONS

6.1. Diagnostic Efficacy Population (DEP)

The diagnostic efficacy population (DEP) will include all cases who completed a ^{18}F-*m*FBG scan in the previous trials or locally-authorized clinical use, and whose images were available for blinded interpretation.

7. CASE ENROLMENT

The information regarding cases' inclusion and exclusion will be reported in the listing for the DEP and sorted by Case ID.

8. ANALYSIS POPULATION

As there is only one analysis set, the DEP, no summary tables or data listings describing the analysis populations will be presented.

9. PROTOCOL DEVIATIONS

No Protocol Deviation information will be reported for this study.

10. DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

The demographics variables to be reported are listed below:

- Age (years)
- Sex

Demographic variables will be summarized for the DEP overall with descriptive statistics.

A listing of demographics will be provided for the DEP and sorted by Case ID.

11. MEDICAL HISTORY

Medical history information will be reported in the listing to include if neuroblastoma or non-neuroblastoma was recorded for each case in this study.

12. PRIOR AND CONCOMITANT MEDICATION

No prior and concomitant medication information will be reported for this study.

13. TREATMENT COMPLIANCE AND EXPOSURE

^{18}F-*m*FBG exposure will be summarized for the DEP overall with descriptive statistics.

Listings of ^{18}F-*m*FBG administration information will be provided for the DEP sorted by Case ID.

14. EFFICACY

The primary and secondary efficacy endpoints will be assessed using the DEP. Measurements used in the calculation of efficacy endpoints are positive percent agreement (PPA), negative percent agreement (NPA), positive predictive value (PPV) and negative predictive value (NPV) from the results of the independent readings of ^{18}F-*m*FBG imaging.

PPA = No. of True Positives / No. of cases with positive Disease Status

NPA = No. of True Negatives / No. of cases with negative Disease Status

PPV = No. of True Positives / No. of cases with a positive blinded image read

NPV = No. of True Negatives / No. of cases with a negative blinded image read

Where:

- True Positive (TP) is defined as a case with Disease Status of active neuroblastoma and abnormal uptake on ^{18}F-*m*FBG PET imaging identified as neuroblastoma.
- True Negative (TN) is defined as a case in which active neuroblastoma has been ruled out according to the Disease Status, and there is no abnormal uptake consistent with active tumor on ^{18}F-*m*FBG PET imaging.

Table 14.1: Calculation of Primary Endpoints:

	OSoR Positive	**OSoR Negative**	
Blinded Image Read Positive	a(TP)	b(FP)	PPV a / (a + b)
Blinded Image Read Negative	c(FN)	d(TN)	NPV d / (c + d)
	PPA a / (a + c)	NPA d / (b + d)	Accuracy (a + d) / (a + b + c + d)

14.1. Primary Efficacy Endpoints

The primary efficacy endpoint is focal increased uptake (presence or absence) on ^{18}F-*m*FBG PET/CT or PET/MR imaging, reported as case-level PPA and NPA for detecting neuroblastoma as determined by comparing clinical standard of care imaging and/or histopathology with comparable anatomic regions judged positive/negative by ^{18}F-*m*FBG. A correct interpretation by a reader requires either: a) identification of abnormal ^{18}F-*m*FBG uptake in an anatomical (Curie score) region in which neuroblastoma was identified in the Objective Standard of Reference (OSoR) assessment (OSoR+); or b) no identification of abnormal ^{18}F-*m*FBG uptake in any anatomical (Curie score) region in a case with OSoR-.

The results of the independent readings of ^{18}F-*m*FBG imaging will be presented as independent measures. For each reader, PPA and NPA of ^{18}F-*m*FBG for identification of neuroblastoma at a case-level will be calculated along with corresponding exact binomial 2-sided confidence limits.

For each reader, the primary analyses will test the following, using a two-sided exact binomial test at the α=0.05 significance level:

- H0: $p_a = 0.50$ vs. H_1: $p_a \neq 0.50$, where "p_a" corresponds to PPA or NPA

^{18}F-*m*FBG imaging will be deemed diagnostically efficacious for each reader if lower bounds for 95% confidence intervals (CIs) for all calculations of PPA and NPA are greater than 50%.

For descriptive information only, estimates with 95% confidence interval of PPV, NPV and accuracy will be provided.

If there are DEP cases with missing scan data (scan considered incomplete or uninterpretable by a reader), two analyses will be performed, one assuming scans with missing data would have been interpreted positive for neuroblastoma and one assuming the scans would have been interpreted negative for neuroblastoma. If there are cases with missing scan data, the reader success criteria described above must be met for both sets of sensitivity analyses.

14.2. Secondary Efficacy Endpoints

Descriptive summaries of each endpoint will be presented along with the associated statistical assessments indicated below.

For cases with conclusion of NBeq (±30 days or ±90 to 180 days data review) from Interpreters, two analyses will be performed, one excluding NBeq and one assuming NBeq would have been interpreted negative for neuroblastoma.

14.2.1. Anatomic Region-Level Efficacy

The secondary efficacy endpoint will be focal increased uptake (presence or absence) on ^{18}F-*m*FBG positron emission tomography (PET) / computed tomography (CT) or PET/ magnetic resonance (MR) imaging in prespecified Curie score regions and anatomic regions, reported as PPA and NPA for detecting neuroblastoma as determined by comparison with clinical standard of care imaging and/or histopathology in those regions. For each prespecified anatomic region in a case, a correct interpretation by a reader requires either: a) identification of abnormal ^{18}F-*m*FBG uptake in the region with neuroblastoma identified on the OSoR assessment (OSoR+); or b) no identification of abnormal ^{18}F-*m*FBG uptake in the region with no evidence of neuroblastoma on the OSoR assessment. Secondary efficacy analyses will be performed when feasible, i.e., when there is correlative imaging or histopathology results for comparison with ^{18}F-*m*FBG scan findings.

14.2.2. Inter-reader and OSoR Inter-Interpreter variability

Variation of primary efficacy imaging assessments will be considered for each pair of independent blinded reviewers. A kappa statistic with a value > 0.40 for inter-reader or inter-interpreter agreement will be considered acceptable, as per the suggested guidelines by Landis and Koch, where a value of 0.41 – 0.60 is considered as moderate level of agreement. The inter-reader agreement for blinded readers will be compared between different pairs of readers using the kappa (κ) value:

$$\kappa = (p_o - p_e) / (1-p_e)$$

where p_o is the relative observed agreement among readers and p_e is the hypothetical probability of chance agreement.

The relative observed agreement will be defined as $p_o = (a+d) / (a + b + c + d)$.

The hypothetical probability of chance agreement will be defined as $p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2$

A value of κ lower than 0.41 will be explored further to determine if there is an underlying cause for this low value.

Since κ is highly dependent on marginal distributions, the proportion of agreement will also be used to assess Inter-reader and Inter-Interpreter variation with respect to case-level assessment (Table 14.2).

Table 14.2: Agreement between Two Blinded Readers with Respect to Imaging Uptake

		Reader 1	
		Abnormal	Normal
Reader 2	Abnormal	a	b
	Normal	c	d

To further characterize the proportion of agreement between each pair of reviewers, two-sided 95% confidence intervals for kappa value will be provided.

14.2.3. Additional efficacy analyses and summaries

Summaries of agreement between OSoR results and blinded reader results on Curie score regions and anatomic locations will be provided with descriptive statistics defined in Section 5.2.

Summaries of OSoR inter-Interpreter variability on Curie score regions and anatomic locations will be provided with descriptive statistics defined in Section 14.2.2.

In order to determine the effects of time from dose administration to ^{18}F-*m*FBG on the image quality, summaries of time from dose administration to ^{18}F-*m*FBG regarding to the image quality score will be provided with descriptive statistics defined in Section 5.2, excluding non-neuroblastoma cases recorded in the medical history.

14.2.4. Subgroup analyses and summaries

In order to determine reader performance on cases with neuroblastoma recorded in the medical history and correlative data review days on reader image, subgroup analyses for PPA, NPA and image quality will be performed for cases with neuroblastoma recorded in medical history and by correlative data review days (±30 Days, ±90 Days to 180 Days).

Summaries of PPA and NPA by OSoR interpreter (the decision from Interpreter 1 or Interpreter 2) will be provided with descriptive statistics defined in Section 14.2.1.

14.3. Neuroblastoma On-Site Assessment

All available information on case's neuroblastoma assessment will be reported in the listing sorted by Case ID for the DEP, including histopathology, imaging, body region and biomarker, and details regarding results in relation to neuroblastoma.

The neuroblastoma assessment will be summarized for the DEP overall with descriptive statistics defined in Section 5.2.

15. SAFETY

As no cases will be administered investigational product (IP) (^{18}F-*m*FBG) in this study, no safety data will be collected.

16. CHANGES TO THE PROTOCOL

Protocol	Change(s) in SAP	Reason	SAP Sections
In section 9.4.3.2, the calculation of kappa value used $z = (\kappa 1 - \kappa 2) / [\sigma 2 (\kappa 1) - \sigma 2(\kappa 2)]^{1/2}$	The kappa calculation used $\kappa = (p_o - p_e) / (1-p_e)$	To be consistent with previous Innervate studies	14.2.2
NA	Adding anatomic locations by blinded readers	Request from the sponsor	14.2.3
NA	Adding OSoR inter-Interpreter variability on Curie score regions	Request from the sponsor	14.2.3
NA	Adding time from dose administration to ^{18}F-*m*FBG regarding to the image quality score	Request from the sponsor	14.2.3
NA	Subgroup analysis on neuroblastoma recorded in medical history and correlative data review days	Request from the sponsor	14.2.4

17. FINAL ANALYSIS

The final analysis will be conducted after all images have been assessed by blinded readers, the clinical database has been locked, and the analysis population has been approved.

The final analysis will be based on the final version of the SAP. Any deviations from the planned analysis will be documented in the CSR.

The data listings and summary tables, and associated figures, planned to be generated from the study data are listed in the Tables, Listings, and Figures (TLF) Mock Shell table of contents, which is attached to this SAP. The numbering and titles may vary in the final presentation, depending on the amount of data to be presented.

Final Tables, Figures, and Listings will be provided to the Sponsor in RTF and PDF format, and in a form suitable for inclusion as appendices to the Clinical Study Report.

APPENDIX 1: TIME AND EVENTS SCHEDULE

Table 1: Study Schedule of Activities

Procedure	Enrollment (Site)	Blinded Reads (ICL)	Statistical Analysis (CRO)
Inclusion/Exclusion	X		
Medical History	X		
Disease Status Determination	X		
Availability of mFBG Imaging digital files	X		
Image Interpretation		X	
Data Analysis			X

ICL: Imaging Core Laboratory; CRO: Clinical Research Organization



TFL MOCK SHELLS

A Prospective Image Reevaluation Study to Assess the Efficacy of 18F-mFBG PET Imaging in Subjects with Neuroblastoma

Protocol No.: IRP101-305

Sponsor Name and Address:	Innervate Radiopharmaceuticals LLC 175 Elm Road, Englewood NJ 07631 808-856-1406
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GENERAL COMMENTS

- Where a count is not applicable, the layout will be displayed as "-".
- Where a count is 0, the percentage will not be shown (e.g., 0 (0.0%) will be displayed as 0).
- The denominator in all percentage calculations will be the number of Cases in the relevant analysis population and treatment group, unless specifically stated otherwise.
- Unless otherwise stated, parameters will be listed in alphabetical order.
- The minimum and maximum values will be presented to the same number of decimal places as recorded in the raw data.
- Arithmetic mean and the median will be presented to one more decimal place than the raw data, while standard deviation (SD) will be presented to two more decimal places than the raw data.
- Percentages will be rounded to one decimal place, with the denominator being the number of Cases in the relevant analysis sets with non-missing data, unless otherwise specified. 100% will be displayed without decimal places.
- Results will be center aligned in all summary tables and listings. Case ID, Visit, and comments/descriptions may be left aligned if required.
- Column widths and text-wrapping may be altered in final output to best present the data.
- Footnotes may be added/amended if required.
- All outputs will be presented in Courier New font, Size 8. Outputs will be created in rich text file (.rtf) and portable document (.pdf) formats with one file created for each output.
- Due to programming constraints, tables with many columns may require some columns be displayed on a separate page. In such cases, all identifier columns must be repeated across pages.

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Table 14.1.1.1
Summary of ^{18}F-*m*FBG Administration
(Diagnostic Efficacy Population)

	Overall (N=XX)
^{18}F-*m*FBG Administered Activity (mCi)	
N	XX
Mean (SD)	XX.XXX (XX.XXXX)
Median	XX.XXX
Min, Max	XX.XX, XX.XX

Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Reference Listing: 16.2.5.1

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Table 14.1.1.2
Summary of On-site Disease Determination
(Diagnostic Efficacy Population)

	Overall (N=XX)
Time from Dosing Administration to mFBG (min)	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX, XX
Treating Site Disease Interpretation	
Positive	XX (XX.X%)
Negative	XX (XX.X%)
Reason for Assessment	
Staging – Diagnosis	XX (XX.X%)
Mid-Therapy Evaluation	XX (XX.X%)
End-of-Therapy Evaluation	XX (XX.X%)
Relapse/Recurrence Evaluation	XX (XX.X%)
Surveillance	XX (XX.X%)
Unknown	XX (XX.X%)

Note: Percentages are based on diagnostic efficacy population.
Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Reference Listing: 16.2.5.2

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Table 14.1.2.1
Summary of Case Demographics and Baseline Characteristics
(Diagnostic Efficacy Population)

Parameter **Statistic**	**Overall (N=XX)**
Age (years)	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX, XX
Gender	
Male	XX (XX.X%)
Female	XX (XX.X%)

Note: Percentages are based on diagnostic efficacy population. Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviations: SD = Standard Deviation; Min = Minimum; Max = Maximum; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.4.1

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Table 14.2.1.1.1
Agreement between ^{18}F-*m*FBG Imaging Read and Objective Standard of Reference
(Diagnostic Efficacy Population)

Blinded Image Reader	Blinded Reader Result	Cases with missing ^{18}F-*m*FBG scan data as Positive						Cases with missing ^{18}F-*m*FBG scan data as Negative					
		OSoR Positive	OSoR Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value	OSoR Positive	OSoR Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value
1	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
2	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
3	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
4	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
5	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPA and NPA. P-values are from a two-sided exact binomial test, testing whether the proportion (PPA or NPA) equals 0.5.
PPA = a / (a+c)
NPA = d / (b+d)

Abbreviation: PPA = Positive Percent Agreement; NPA = Negative Percent Agreement; CI = Confidence Interval; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference.
Reference Listing: 16.2.6.1 and 16.2.6.2

Programming Note:

- If it is confirmed that there are no missing scan data after DBL, only columns under "Cases with missing ^{18}F-*m*FBG scan data as Positive" table header should be retained with this table header removed.

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Table 14.2.1.1.2
Agreement between ^{18}F-*m*FBG Imaging Read and Objective Standard of Reference for Neuroblastoma Recorded in Medical History
(Diagnostic Efficacy Population)

Blinded Image Reader	Blinded Reader Result	Cases with missing ^{18}F-*m*FBG scan data as Positive						Cases with missing ^{18}F-*m*FBG scan data as Negative					
		OSoR Positive	OSoR Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value	OSoR Positive	OSoR Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value
1	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
2	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
3	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
4	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
5	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPA and NPA. P-values are from a two-sided exact binomial test, testing whether the proportion (PPA or NPA) equals 0.5.
PPA = a / (a+c)
NPA = d / (b+d)

Abbreviation: PPA = Positive Percent Agreement; NPA = Negative Percent Agreement; CI = Confidence Interval; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference.
Reference Listing: 16.2.6.1 and 16.2.6.2, 16.2.4.2

Programming Note:

- If it is confirmed that there are no missing scan data after DBL, only columns under "Cases with missing ^{18}F-*m*FBG scan data as Positive" table header should be retained with this table header removed.
- Only include cases with Neuroblastoma as Yes in medical history

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Table 14.2.1.1.3
Agreement between ^{18}F-*m*FBG Imaging Read and ±30 Days Review Conclusion by Interpreter
(Diagnostic Efficacy Population)

Interpreter: 1/2

Blinded Image Reader	Blinded Reader Result	Cases with NBeq Excluded						Cases with NBeq data as Negative					
		±30 Days Conclusion Positive	±30 Days Conclusion Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value	±30 Days Conclusion Positive	±30 Days Conclusion Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value
1	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
2	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
3	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
4	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
5	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPA and NPA. P-values are from a two-sided exact binomial test, testing whether the proportion (PPA or NPA) equals 0.5.
PPA = a / (a+c)
NPA = d / (b+d)

Abbreviation: PPA = Positive Predictive Agreement; NPA = Negative Predictive Agreement; CI = Confidence Interval; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference.
Reference Listing: 16.2.6.1 and 16.2.6.2

Programming Note:

- If it is confirmed that there are no missing scan data after DBL, only columns under "Cases with missing ^{18}F-*m*FBG scan data as Positive" table header should be retained with this table header removed.

Table 14.2.1.2.1
Positive and Negative Predictive Values and Accuracy between ^{18}F-*m*FBG Imaging Read and Objective Standard of Reference
(Diagnostic Efficacy Population)

Blinded Image Reader	Blinded Reader Result	Cases with missing ^{18}F-mFBG scan data as Positive					Cases with missing ^{18}F-mFBG scan data as Negative				
		OSoR Positive	OSoR Negative	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)	OSoR Positive	OSoR Negative	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
1	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
2	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
3	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
4	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
5	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPV, NPV and accuracy.
PPV = a / (a+b)
NPV = d / (c+d)
Accuracy = (a+d) / (a+b+c+d)
Abbreviation: ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference; PPV = Positive Predictive Value; NPV = Positive Predictive Value.
Reference Listing: 16.2.6.1

Programming Note:

- If it is confirmed that there are no missing scan data after DBL, only columns under "**Cases with missing ^{18}F-mFBG scan data as Positive**" table header should be retained with this table header removed.
- Include all the blinded reader results

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Table 14.2.1.2.2
Positive and Negative Predictive Values and Accuracy between ^{18}F-*m*FBG Imaging Read and ±30 Days Review Conclusion by Interpreter
(Diagnostic Efficacy Population)

Interpreter: 1/2

Blinded Image Reader	Blinded Reader Result	Cases with NBeq Excluded					Cases with NBeq as Negative				
		±30 Days Conclusion Positive	±30 Days Conclusion Negative	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)	±30 Days Conclusion Positive	±30 Days Conclusion Negative	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
1	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
2	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
3	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
4	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			
5	Positive	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX[a]	XX[b]	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)	XX.X (XX.X, XX.X)
	Negative	XX[c]	XX[d]				XX[c]	XX[d]			

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPV, NPV and accuracy.
PPV = a / (a+b)
NPV = d / (c+d)
Accuracy = (a+d) / (a+b+c+d)
Abbreviation: ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference; PPV = Positive Predictive Value; NPV = Positive Predictive Value.
Reference Listing: 16.2.6.1

Table 14.2.1.3.1
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 1 vs. Reader 2)
(Diagnostic Efficacy Population)

Reader	Image Reader Result	Image Reader 2			
		^{18}F-*m*FBG Result			
		Abnormal	Normal	k	P_o
Image Reader 1	Abnormal	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Normal	XX[c]	XX[d]		

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Kappa Statistic (κ) = (p_0 - p_e) / (1-p_e), where p_0 = observed agreement among raters and p_e = probability of chance agreement. Proportion of Agreement (p_o) = (a+d)/(a + b + c + d) As per Landis and Koch guidelines, p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2. k value between 0.41 and 0.60 is considered as moderate level of agreement.

Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.6.2

Table 14.2.1.3.2
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 1 vs. Reader 3)
(Diagnostic Efficacy Population)

Programming Note:
- Repeat Table 14.2.1.3.1 for readers 1 vs. reader 3.

Table 14.2.1.3.3
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 1 vs. Reader 4)
(Diagnostic Efficacy Population)

Programming Note:
- Repeat Table 14.2.1.3.1 for readers 1 vs. reader 4.

Table 14.2.1.3.4
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 1 vs. Reader 5)
(Diagnostic Efficacy Population)

Programming Note:
- Repeat Table 14.2.1.3.1 for readers 1 vs. reader 5.

Table 14.2.1.3.5
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 2 vs. Reader 3)
(Diagnostic Efficacy Population)

Programming Note:
- Repeat Table 14.2.1.3.1 for readers 2 vs. reader 3.

Table 14.2.1.3.6
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 2 vs. Reader 4)
(Diagnostic Efficacy Population)

Programming Note:
- Repeat Table 14.2.1.3.1 for readers 2 vs. reader 4.

Table 14.2.1.3.7
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 2 vs. Reader 5)
(Diagnostic Efficacy Population)

Programming Note:
- Repeat Table 14.2.1.3.1 for readers 2 vs. reader 5.

Table 14.2.1.3.8
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 3 vs. Reader 4)
(Diagnostic Efficacy Population)

Programming Note:

- Repeat Table 14.2.1.3.1 for readers 3 vs. reader 4.

Table 14.2.1.3.9
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 3 vs. Reader 5)
(Diagnostic Efficacy Population)

Programming Note:

- Repeat Table 14.2.1.3.1 for readers 3 vs. reader 5.

Table 14.2.1.3.10
Agreement between Blinded Readers with Respect to Imaging Uptake (Reader 4 vs. Reader 5)
(Diagnostic Efficacy Population)

Programming Note:

- Repeat Table 14.2.1.3.1 for readers 4 vs. reader 5.

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Table 14.2.1.4.1
Summary of Scan Image Quality Scores by OSoR Assessment
(Diagnostic Efficacy Population)

Reader Identifier	OSoR Assessment	Scan Quality	Overall (N=XX)
Reader 1	Positive	Excellent	XX (XX.X%)
		Good	XX (XX.X%)
		Fair	XX (XX.X%)
		Poor	XX (XX.X%)
		Uninterpretable	XX (XX.X%)
	Negative	Excellent	XX (XX.X%)
		Good	XX (XX.X%)
		Fair	XX (XX.X%)
		Poor	XX (XX.X%)
		Uninterpretable	XX (XX.X%)
Reader 2			
Etc.			

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.6.1, 16.2.6.2

Programming Note:
- Include all the blinded reader results

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Table 14.2.1.4.2
Summary of Scan Image Quality Scores by Neuroblastoma Recorded in Medical History
(Diagnostic Efficacy Population)

Reader Identifier	Neuroblastoma Recorded in Medical History	Scan Quality	Overall (N=XX)
Reader 1	Positive	Excellent	XX (XX.X%)
		Good	XX (XX.X%)
		Fair	XX (XX.X%)
		Poor	XX (XX.X%)
		Uninterpretable	XX (XX.X%)
	Negative	Excellent	XX (XX.X%)
		Good	XX (XX.X%)
		Fair	XX (XX.X%)
		Poor	XX (XX.X%)
		Uninterpretable	XX (XX.X%)
Reader 2			
Etc.			

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.4.2, 16.2.6.2

Programming Note:
- Include all the blinded reader results

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Table 14.2.1.4.3
Summary of Time from Dose Administration to ^{18}F-*m*FBG Imaging on Scan Image Quality Scores with Neuroblastoma Positive from Medical History (Diagnostic Efficacy Population)

Blinded Image Reader	Time from Dose Administration to ^{18}F-*m*FBG	Scan Quality				
		Excellent	Good	Fair	Poor	Uninterpretable
1	n	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)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
2	n	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)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Etc.						

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.5.2, 16.2.6.2

Programming Note:
- Include all the blinded reader results

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Table 14.2.1.5
Summary of ^{18}F-*m*FBG Total Curie Score by Blinded Reader
(Diagnostic Efficacy Population)

	Overall (N=XX)
Reader 1	
N	XX
0	XX.X (XX.X%)
>0	XX.X (XX.X%)
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX, XX
Reader 2	
N	XX
0	XX.X (XX.X%)
>0	XX.X (XX.X%)
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX, XX
Etc.	

Note: Percentages are based on diagnostic efficacy population. Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviations: SD = Standard Deviation; Min = Minimum; Max = Maximum; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.6.2

Programming Note:
- Curie Score is the sum of scores across ten regions.
- >0 include Curie Score 1, 2 and 3

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Table 14.2.1.6.1
Agreement between ^{18}F-*m*FBG Imaging Read and Intra-Objective Standard of Reference on Curie Score Regions by Interpreter (Diagnostic Efficacy Population)

Curie Score Region: 1/2/3/4/5/6/7/8/9/10

Blinded Image Reader	Blinded Reader Result	Cases with missing ^{18}F-*m*FBG scan data as Positive						Cases with missing ^{18}F-*m*FBG scan data as Negative					
		Interpreter 1 Result Positive	Interpreter 1 Result Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value	Interpreter 1 Result Positive	Interpreter 1 Result Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value
1	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
2	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
3	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
4	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
5	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPA and NPA. P-values are from a two-sided exact binomial test, testing whether the proportion (PPA or NPA) equals 0.5.
PPA = a / (a+c)
NPA = d / (b+d)

Abbreviation: PPA = Positive Percent Agreement; NPA = Negative Percent Agreement; CI = Confidence Interval; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1, 16.2.6.2

Programming Note:

- Curie score region for blinded reader read Zone 1 corresponds to Curie score region 1.
- Repeat the table for Interpreter 1 and Interpreter 2

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Table 14.2.1.6.2
Agreement between ^{18}F-*m*FBG Imaging Read and Intra-Objective Standard of Reference on Anatomic Regions by Interpreter
(Diagnostic Efficacy Population)

Anatomic Region: Head/Neck/Chest/Abdomen/Pelvis/Extremities

Blinded Image Reader	Blinded Reader Result	Cases with missing ^{18}F-*m*FBG scan data as Positive						Cases with missing ^{18}F-*m*FBG scan data as Negative					
		Interpreter 1 Result Positive	Interpreter 1 Result Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value	Interpreter 1 Result Positive	Interpreter 1 Result Negative	PPA (95% CI)	PPA p-value	NPA (95% CI)	NPA p-value
1	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
2	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
3	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
4	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				
5	Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX	XX[a]	XX[b]	XX (XX.X, XX.X)	X.XXX	XX (XX.X, XX.X)	X.XXX
	Negative	XX[c]	XX[d]					XX[c]	XX[d]				

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Exact binomial two-sided 95% CIs are presented for PPA and NPA. P-values are from a two-sided exact binomial test, testing whether the proportion (PPA or NPA) equals 0.5.
PPA = a / (a+c)
NPA = d / (b+d)

Abbreviation: PPA = Positive Percent Agreement; NPA = Negative Percent Agreement; CI = Confidence Interval; ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1, 16.2.6.2

Programming Note:

- Repeat the table for Interpreter 1 and Interpreter 2

Table 14.2.1.7
Agreement between On Site Neuroblastoma Assessment and Objective Standard of Reference
(Diagnostic Efficacy Population)

On Site Assessment	OSoR Positive	OSoR Negative	**k**	**P_o**
Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
Negative	XX[c]	XX[d]		

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Kappa Statistic (κ) = (p_0 - p_e) / (1-p_e), where p_0 = observed agreement between on site assessment and the OSoR, and p_e = probability of chance agreement.
Proportion of Agreement (p_o) = (a+d)/(a + b + c + d) As per Landis and Koch guidelines, p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2. k value between 0.41 and 0.60 is considered as moderate level of agreement.

Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1, 16.2.5.2

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Table 14.2.1.8.1
Agreement between Interpreter 1 and Interpreter 2 on Objective Standard of Reference
(Diagnostic Efficacy Population)

Interpreter 1 Result	Interpreter 2 Positive	Interpreter 2 Negative	**k**	**P_o**
Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
Negative	XX[c]	XX[d]		

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Kappa Statistic (κ) = (p_0 - p_e) / (1-p_e), where p_0 = observed agreement between OSoR interpreters, and p_e = probability of chance agreement.
Proportion of Agreement (p_o) = (a+d)/(a + b + c + d) As per Landis and Koch guidelines, p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2. k value between 0.41 and 0.60 is considered as moderate level of agreement.

Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1

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Table 14.2.1.8.2
Agreement between Interpreter 1 and Interpreter 2 on ±30 Days Data Review Conclusion
(Diagnostic Efficacy Population)

Interpreter 1 Result	Cases with NBeq data Excluded				Cases with NBeq data as Negative			
	Interpreter 2 Positive	Interpreter 2 Negative	k	P_o	Interpreter 2 Positive	Interpreter 2 Negative	k	P_o
Positive	XX[a]	XX[b]	XX (XX.X, XX.X)	XX (XX.X, XX.X)	XX[a]	XX[b]	XX (XX.X, XX.X)	XX (XX.X, XX.X)
Negative	XX[c]	XX[d]			XX[c]	XX[d]		

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Kappa Statistic (κ) = (p_0 - p_e) / (1-p_e), where p_0 = observed agreement between OSoR interpreters, and p_e = probability of chance agreement.
Proportion of Agreement (p_o) = (a+d)/(a + b + c + d) As per Landis and Koch guidelines, p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2. k value between 0.41 and 0.60 is considered as moderate level of agreement.

Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1

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Table 14.2.1.8.3
Agreement between Interpreter 1 and Interpreter 2 on Curie Score Regions
(Diagnostic Efficacy Population)

Curie Score Region	Interpreter 1 Result	Interpreter 2 Positive	Interpreter 2 Negative	**k**	**P_o**
1	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
2	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
3	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
4	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
5	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		

Etc.

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Kappa Statistic (κ) = (p_0 - p_e) / (1-p_e), where p_0 = observed agreement between OsoR interpreters, and p_e = probability of chance agreement.
Proportion of Agreement (p_o) = (a+d)/(a + b + c + d) As per Landis and Koch guidelines, p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2. k value between 0.41 and 0.60 is considered as moderate level of agreement.

Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1

Programming Note:
- Curie score region for blinded reader read Zone 1 corresponds to Curie score region 1.

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Table 14.2.1.8.4
Agreement between Interpreter 1 and Interpreter 2 on Anatomic Regions
(Diagnostic Efficacy Population)

Anatomic Region	Interpreter 1 Result	Interpreter 2 Positive	Interpreter 2 Negative	**k**	**P_o**
Head	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
Neck	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
Chest	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
Abdomen	Positive	XX[a]	XX[b]	X.XX (X.XXX, X.XXX)	X.XX (X.XXX, X.XXX)
	Negative	XX[c]	XX[d]		
Etc.					

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Kappa Statistic (κ) = (p_0 - p_e) / (1-p_e), where p_0 = observed agreement between OSoR interpreters, and p_e = probability of chance agreement.
Proportion of Agreement (p_o) = (a+d)/(a + b + c + d) As per Landis and Koch guidelines, p_e = (a+b)(a+c) +(c+d)(b+d)/ (a + b + c + d)^2. k value between 0.41 and 0.60 is considered as moderate level of agreement.

Abbreviation: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR= Objective Standard of Reference.
Reference Listing: 16.2.6.1

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Table 14.2.1.9
Summary of Objective Standard of Reference Requiring Participation from the Third Interpreter
(Diagnostic Efficacy Population)

Statistic	Overall (N=XX)
Participation from the Third Interpreter	
Yes	XX (XX.X%)
No	XX (XX.X%)

Note: Percentages are based on diagnostic efficacy population. Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviations: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.6.1

Table 14.2.1.10
Summary of Objective Standard of Reference Change from Interim Assessment with ^{18}F-*m*FBG Blinded Read Data Review
(Diagnostic Efficacy Population)

	Overall (N=XX)	
Statistic	OSoR Positive	OSoR Negative
±30 days Review Conclusion		
Interpreter 1		
Positive	XX (XX.X%)	XX (XX.X%)
Negative	XX (XX.X%)	XX (XX.X%)
NBeq	XX (XX.X%)	XX (XX.X%)
Interpreter 2		
Positive	XX (XX.X%)	XX (XX.X%)
Negative	XX (XX.X%)	XX (XX.X%)
NBeq	XX (XX.X%)	XX (XX.X%)

Note: Percentages are based on diagnostic efficacy population. Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviations: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference.
Reference Listing: 16.2.6.1

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Table 14.2.1.11
Summary of Neuroblastoma Correlative Procedures
(Diagnostic Efficacy Population)

Statistic	Overall (N=XX)
Histopathology Procedure Type	
Bone Marrow	XX (XX.X%)
Biopsy	XX (XX.X%)
Surgery	XX (XX.X%)
Histopathology Result in Relation to Neuroblastoma	
Positive	XX (XX.X%)
Negative	XX (XX.X%)
Image Procedure Type	
CT	XX (XX.X%)
FDG PET	XX (XX.X%)
mIBG	XX (XX.X%)
MRI	XX (XX.X%)
Ultrasound	XX (XX.X%)
Image Body Region Examined	
Abdomen / Spine	XX (XX.X%)
Abdomen; Spine; Left leg	XX (XX.X%)
Brain	XX (XX.X%)
Brain, Neck/Thorax, Abdomen, Spine	XX (XX.X%)
Etc.	
Image Result in Relation to Neuroblastoma	
Positive	XX (XX.X%)
Negative	XX (XX.X%)
Equivocal	XX (XX.X%)
Not Applicable	XX (XX.X%)
Biomarker Type of Analysis	
Urine	XX (XX.X%)

Statistic	Overall (N=XX)
Biomarker Result in Relation to Neuroblastoma	
Positive	XX (XX.X%)
Negative	XX (XX.X%)
Equivocal	XX (XX.X%)

Note: Percentages are based on diagnostic efficacy population. Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Cases can be counted multiple times if more than one procedure was collected. The sum of percent for each procedure type can exceed 100%.
Abbreviations: ^{18}F-*m*FBG = meta-fluorobenzylguanidine (^{18}F).
Reference Listing: 16.2.6.3

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Listing 16.2.1.1
Inclusion and Exclusion
(Diagnostic Efficacy Population)

Case ID	Inclusion Met / Exclusion Did not Meet
XXXXX	(Yes/No)
XXXXX	(Yes/No)
XXXXX	(Yes/No)
XXXXX	(Yes/No)

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.

Programming Notes:

- *Sort order: Case ID*

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Listing 16.2.4.1
Demographic Characteristics
(Diagnostic Efficacy Population)

Case ID	Age (Years)	Sex
XXXXX	XX	Male
XXXXX	XX	Female
XXXXX	XX	Male
XXXXX	XX	Female

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.

Programming Notes:

- *Sort order: Case ID*

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Listing 16.2.4.2
Neuroblastoma Recorded in Medical History
(Diagnostic Efficacy Population)

Case ID	Confirmed Neuroblastoma
XXXXX	(Yes/No)
XXXXX	(Yes/No)
XXXXX	(Yes/No)
XXXXX	(Yes/No)

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.

Programming Notes:

- *Sort order: Case ID*

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Listing 16.2.5.1
^{18}F-*m*FBG Administration
(Diagnostic Efficacy Population)

Case ID	Image Date	Administered Activity (mCi)
XXXXX	DD-MMM-YYYY	XX.XX
XXXXX	DD-MMM-YYYY	XX.XX
XXXXX	DD-MMM-YYYY	XX.XX
XXXXX	DD-MMM-YYYY	XX.XX
XXXXX	DD-MMM-YYYY	XX.XX
XXXXX	DD-MMM-YYYY	XX.XX

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.

Abbreviation: ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F).

Programming Notes:

- *Sort order: Case ID;*

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Listing 16.2.5.2
On Site Disease Determination
(Diagnostic Efficacy Population)

Case ID	Treating Site Disease Interpretation	Time from Dosing Administration to ^{18}F-*m*FBG (min)	Reason for Assessment
XXXXX	(Negative/Positive)	XXX	(Staging-Diagnosis/ Mid-Therapy Evaluation/ End-of-Therapy Evaluation/ Relapse/Recurrence Evaluation/ Surveillance/ Unknown)
XXXXX	(Negative/Positive)	XXX	(Staging-Diagnosis/ Mid-Therapy Evaluation/ End-of-Therapy Evaluation/ Relapse/Recurrence Evaluation/ Surveillance/ Unknown)
XXXXX	(Negative/Positive)	XXX	(Staging-Diagnosis/ Mid-Therapy Evaluation/ End-of-Therapy Evaluation/ Relapse/Recurrence Evaluation/ Surveillance/ Unknown)
XXXXX	(Negative/Positive)	XXX	(Staging-Diagnosis/ Mid-Therapy Evaluation/ End-of-Therapy Evaluation/ Relapse/Recurrence Evaluation/ Surveillance/ Unknown)
XXXXX	(Negative/Positive)	XXX	(Staging-Diagnosis/ Mid-Therapy Evaluation/ End-of-Therapy Evaluation/ Relapse/Recurrence Evaluation/ Surveillance/ Unknown)
XXXXX	(Negative/Positive)	XXX	(Staging-Diagnosis/ Mid-Therapy Evaluation/ End-of-Therapy Evaluation/ Relapse/Recurrence Evaluation/ Surveillance/ Unknown)

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.

Abbreviation: ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F).

Programming Notes:

- *Sort order: Case ID;*

Listing 16.2.6.1
Objective Standard of Reference
(Diagnostic Efficacy Population)

Case ID	Interpreter ID	Neuroblastoma (±30 Days Review)	Neuroblastoma (±90 to 180 Days Review)	Neuroblastoma (Final Conclusion)	Was Disease Status Changed with Blinded Reader Data Review	NB Positive Curie Score Region	Anatomical Zones
XXXX	1	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Yes/No)	X (XXXXX); X; X; X	(Head (XXXXX) /Neck/Chest/Abdomen/Pelvis/ Extremities)
	2	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Yes/No)	X (XXXXX); X; X; X	(Head (XXXXX) /Neck/Chest/Abdomen/Pelvis/ Extremities)
XXXX	1	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Yes/No)	X (XXXXX); X; X; X	(Head (XXXXX) /Neck/Chest/Abdomen/Pelvis/ Extremities)
	2	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Yes/No)	X (XXXXX); X; X; X	(Head (XXXXX) /Neck/Chest/Abdomen/Pelvis/ Extremities)
	3	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Yes/No)	X (XXXXX); X; X; X	(Head (XXXXX) /Neck/Chest/Abdomen/Pelvis/ Extremities)
XXXX		(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Positive/Negative/Abnormal but equivocal to NB/ NE)	(Yes/No)	X (XXXXX); X; X; X	(Head (XXXXX) /Neck/Chest/Abdomen/Pelvis/ Extremities)

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Final Conclusion of neuroblastoma is the OSoR.
Abbreviation: ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F); OSoR = Objective Standard of Reference; NB = Neuroblastoma; NE = Not Evaluable.

Programming Notes:

- *Sort order: Case ID and Interpreter ID*
- *For multiple Curie Score Region, combine all NB+ into "NB Positive Curie Score Region" separate by ";" If any comments for the Curie Score Region, add it to the corresponding Curie Score Region number*
- *For multiple Anatomical Zones, combine all into "Anatomical Zones" separate by ";" If any comments for the Anatomical Zones, add it to the corresponding Anatomical Zones*

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Listing 16.2.6.2
^{18}F-*m*FBG Blinded Reviewer Assessment Data
(Diagnostic Efficacy Population)

Case ID	Reader Identifier	Visit Date	Image Quality	Scan Consistent with Neuroblastoma	Curie Score Region	Total Curie Score	Grid Zone	Organ System
XXX	1	DD-MMM-YYYY	Good	Yes	X; X; X	XX	XXXXXX	XXXXXX
							XXXXXX	XXXXXX
							Etc.	
	2	DD-MMM-YYYY	Fair	No		XX		
	3	DD-MMM-YYYY	Fair	Yes	X; X; X	XX	XXXXXX	XXXXXX
							Etc.	
	4	DD-MMM-YYYY	Fair	Yes	X; X; X	XX	XXXXXX	XXXXXX
							Etc.	
	5	DD-MMM-YYYY	Fair	Yes	X; X; X	XX	XXXXXX	XXXXXX

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation. Total Curie Score is the sum of Curie Score in the ten regions.
Abbreviations: NA = Not Assessed; ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F).

Programming Notes:

- *Sort order: Case ID, visit Date*
- *Curie Score Regions are Zone 1 to Zone 10. All Curie Score will be combined into "Curie Score Regions"*

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Listing 16.2.6.3
Neuroblastoma Correlative Procedures
(Diagnostic Efficacy Population)

Case ID	Histopathology Available/ Date/ Days from ^{18}F-*m*FBG Scan	Histopathology Procedure Type (Specify Site If Biopsy)	Histopathology Result in Relation to Neuroblastoma/ Relevant Details	Image Available/ Date/ Days from ^{18}F-*m*FBG Scan	Image Procedure Type/ Result in Relation to Neuroblastoma/ Relevant Details	Biomarker Available / Date/ Days from ^{18}F-*m*FBG Scan	Biomarker Type of Analysis/ Result in Relation to Neuroblastoma	Follow-Up Information (If Yes, Specify Details)
XXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Bone/Marrow/Biopsy, XXXX/ Surgery)	(Positive/Negative)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(CT/FDG/PET/mIBG/MRI/Ultrasound)/ (Positive/Negative/Equivocal/Not Applicable)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	XXXX/ (Positive/Negative/Equivocal)	(Yes, XXXX/No)
XXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Bone/Marrow/Biopsy, XXXX/ Surgery)	(Positive/Negative)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(CT/FDG/PET/mIBG/MRI/Ultrasound)/ (Positive/Negative/Equivocal/Not Applicable)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	XXXX/ (Positive/Negative/Equivocal)	(Yes, XXXX/No)
XXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Bone/Marrow/Biopsy, XXXX/ Surgery)	(Positive/Negative)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(CT/FDG/PET/mIBG/MRI/Ultrasound)/ (Positive/Negative/Equivocal/Not Applicable)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Positive/Negative/Equivocal)	(Yes, XXXX/No)
XXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Bone/Marrow/Biopsy, XXXX/ Surgery)	(Positive/Negative)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(CT/FDG/PET/mIBG/MRI/Ultrasound)/ (Positive/Negative/Equivocal/Not Applicable)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	XXXX/ (Positive/Negative/Equivocal)	(Yes, XXXX/No)
XXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Bone/Marrow/Biopsy, XXXX/ Surgery)	(Positive/Negative)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(CT/FDG/PET/mIBG/MRI/Ultrasound)/ (Positive/Negative/Equivocal/Not Applicable)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Positive/Negative/Equivocal)	(Yes, XXXX/No)
XXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(Bone/Marrow/Biopsy, XXXX/ Surgery)	(Positive/Negative)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	(CT/FDG/PET/mIBG/MRI/Ultrasound)/ (Positive/Negative/Equivocal/Not Applicable)/ XXXXXXXXXX	(Yes/No)/ DD-MMM-YYYY/ XX	XXXX/ (Positive/Negative/Equivocal)	(Yes, XXXX/No)
Etc.								

Note: Diagnostic efficacy population includes all enrolled cases who completed a ^{18}F-*m*FBG scan in the previous trials and whose images were available for blinded interpretation.
Abbreviation: ^{18}F-mFBG = meta-fluorobenzylguanidine (^{18}F).

Programming Notes:

- *Sort order: Case ID*
- *If histopathology procedure type is Biopsy, specify site*

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