Subject Screening N° ☐☐ ☐☐☐

VISIT 1 (DAY -3 TO DAY 1)

INFORMED CONSENT

Did the **subject** sign the Informed Consent Form? **Yes** ☐ **No** ☐

Informed Consent signed on |__|__| |__|__| |__|__|__|__|
day month year

Did the **parents/legal guardian** of the subject sign the Informed Consent Form?

Yes ☐ **No** ☐ **NA** ☐ (subject is ≥ 18 years old)

Informed Consent signed on |__|__| |__|__| |__|__|__|__| Parent 1/legal guardian
day month year

Informed Consent signed on |__|__| |__|__| |__|__|__|__| Parent 2/legal guardian
day month year

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

DEMOGRAPHY

Age: |__|__| years

Gender: **M** ☐ **F** ☐

Ethnic Origin:
- Caucasian ☐
- Black ☐
- Asian ☐
- Other, specify: _____ ☐

VISIT 1 (DAY -3 TO DAY 1)

MEDICAL HISTORY

Is the subject currently affected, or was affected in the past, by any significant medical condition, other than the one being studied?

Yes ☐ **No** ☐

*If **YES**, please list in the table below: Please check the Exclusion Criteria for disorders potentially leading to* subjects *exclusion.*

System/Organ	**Disease/Syndrome**	**Start date*** (dd/mm/yyyy)	**Ongoing**	**End date*** (dd/mm/yyyy)
Cardiovascular			☐	
Hematopoietic			☐	
Hemostasis			☐	
Skin and annexes			☐	
Endocrine/Metabolic			☐	
Gastrointestinal/ Hepatic			☐	
Genitourinary/ Renal			☐	
Immunological			☐	
Musculoskeletal			☐	
Neurologic			☐	
Respiratory			☐	
Pulmonary			☐	
Allergies			☐	
Alcoholism and drug addiction			☐	
Psychiatric			☐	
Neoplastic			☐	
Infections and infestations			☐	
Other (specify) _____			☐	
Other (specify) _____			☐	
Other (specify) _____			☐	
Other (specify) _____			☐	

** If complete date is not known, please report "na" (Not Available) for missing data (example: na/02/2015).*

VISIT 1 (DAY -3 TO DAY 1)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	Not Done
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 1 (DAY -3 TO DAY 1)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|
day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐

VISIT 1 (DAY -3 TO DAY 1)

Test	Outcome	Value	Unit	LNL	UNL	Not Done
ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant					☐
Beta-hCG**	☐Positive ☐Negative					☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5*UNL
- Beta-hCG positive

** For female only

VISIT 1 (DAY -3 TO DAY 1)

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____

_____

VISIT 1 (DAY -3 TO DAY 1)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 1 (DAY -3 TO DAY 1)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for LEFT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

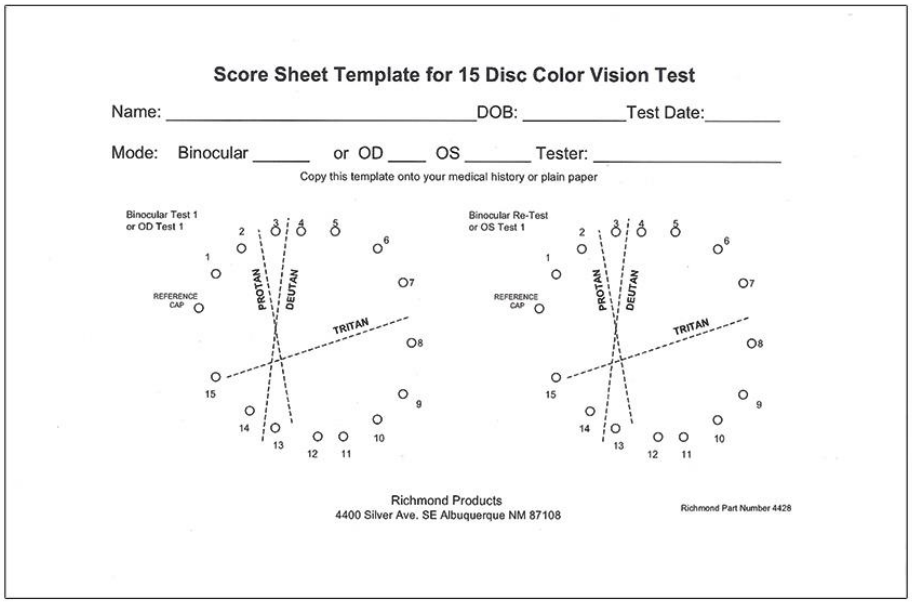
Cylinder: _____

TABO Axis: _____

VISIT 1 (DAY -3 TO DAY 1)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISIT 1 (DAY -3 TO DAY 1)

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 1 (DAY -3 TO DAY 1)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 1 (DAY -3 TO DAY 1)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 1 (DAY -3 TO DAY 1)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC1]: Absolute Change in Thickness
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 1 (DAY -3 TO DAY 1)

COMPUTERIZED VISUAL FIELD EXAMINATION – RIGHT EYE
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – LEFT EYE
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 1 (DAY -3 TO DAY 1)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 1 (DAY -3 TO DAY 1)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 1 (DAY -3 TO DAY 1)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 1 (DAY -3 TO DAY 1)

CONCOMITANT MEDICATIONS AND THERAPIES

Is the patient currently taking any other medication/therapy? **Yes** ☐ **No** ☐

Please record any medication taken by the patient in the Concomitant Medications and Therapies form.

VISIT 1 (DAY -3 TO DAY 1)

INCLUSION CRITERIA

For inclusion in the trial, all of the following inclusion criteria must be fulfilled:

1.	Male and female of any race and > 6 years old	**Yes** ☐ **No** ☐
2.	Positive genetic test for SCA7.	**Yes** ☐ **No** ☐
3.	Signed Informed Consent. (in case of minors, written informed consent must be obtained by parents or legal representative)	**Yes** ☐ **No** ☐

If 'NO' is recorded for any criterion, the patient does NOT fulfil all eligibility criteria and is not eligible. Please complete the *"END OF STUDY FORM".*

EXCLUSION CRITERIA

Subject will not be considered eligible for this trial if he/she fulfills any of the following exclusion criteria:

1.	Female subjects: pregnant or lactating women cannot participate in the study. Women of childbearing potential cannot participate unless willing to use highly effective contraception methods as combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal or transdermal); progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable or implantable; intrauterine device (IUD); intrauterine hormone-releasing system (IUS); bilateral tubal occlusion; vasectomised partner; sexual abstinence. In case of use of oral contraception, women should have been stable on the same pill for a minimum of 3 months before taking study drug. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.	**Yes** ☐ **No** ☐ **NA** ☐
2.	Subjects with a clinically significant or unstable medical or surgical condition that would preclude safe and complete study participation. Such conditions may include cardiovascular, pulmonary, hepatic, renal, severe systemic mycotic infections, metabolic diseases or malignancies.	**Yes** ☐ **No** ☐
3.	Hepatic diseases with serum values of alanine aminotransferase, aspartate aminotransferase or bilirubin > 1·5 times above normal limit	**Yes** ☐ **No** ☐
4.	Any medical or psychiatric condition that may affect the subject ability to give informed consent, or to complete the study, or if the subject is considered by the treating neurologist to be, for any other reason, an unsuitable candidate for this study.	**Yes** ☐ **No** ☐
5.	Known hypersensitivity to any component of riluzole (Glentek).	**Yes** ☐ **No** ☐

If 'YES' is recorded for any criterion, the patient does NOT fulfil all eligibility criteria and is not eligible. Please complete the *"END OF STUDY FORM".*

VISIT 1 (DAY -3 TO DAY 1)

RANDOMIZATION

Is the subject eligible? Yes ☐ No ☐

If NO, please complete "END OF STUDY FORM"

Is the subject entering the treatment phase of the Clinical Study? Yes ☐ No ☐

If NO, check the one most significant reason below:

☐ Consent withdrawal

☐ Did not meet inclusion/exclusion criteria, specify: Inclusion criterion N. |__|__|
Exclusion criterion N. |__|__|

☐ Adverse Event

☐ Other, specify _____

If **YES**, please randomize the patient.

Date of Randomization |__|__| |__|__| |__|__|__|__|
day month year

Random number |__|__|__|__|

VISIT 2 – 3 months (±7 days)

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____

_____

VISIT 2 – 3 months (±7 days)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	**Not Done**
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 2 – 3 months (±7 days)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|
day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Unit	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐

VISIT 2 – 3 months (±7 days)

ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Beta-hCG**	☐Positive ☐Negative						☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5'UNL
- Beta-hCG positive

** For female only

VISIT 2 – 3 months (±7 days)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 2 – 3 months (±7 days)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for LEFT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

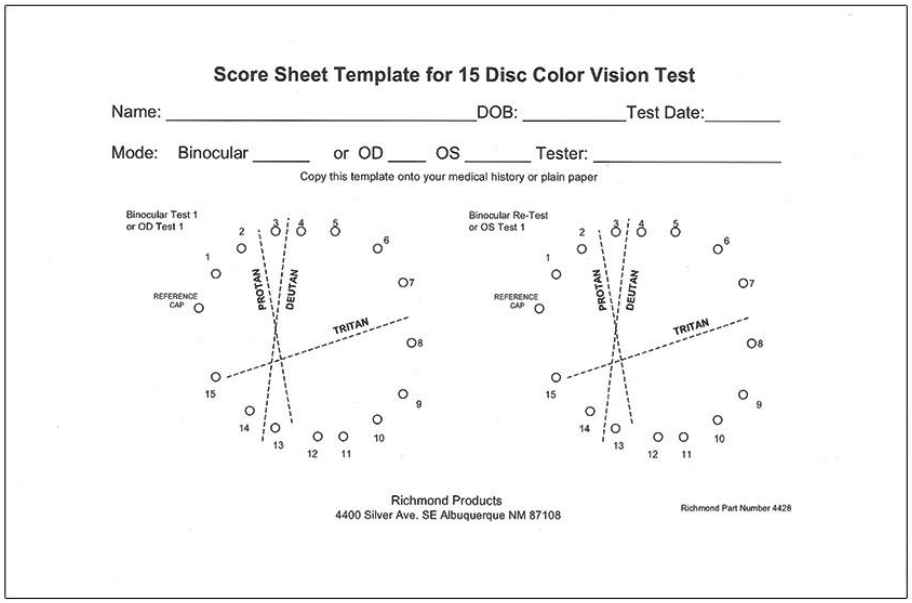
Cylinder: _____

TABO Axis: _____

VISIT 2 – 3 months (±7 days)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 2 – 3 months (±7 days)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 2 – 3 months (±7 days)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 2 – 3 months (±7 days)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC2]: **Absolute Change in Thickness**
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 2 – 3 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION – RIGHT EYE
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – LEFT EYE
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 2 – 3 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 2 – 3 months (±7 days)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 2 – 3 months (±7 days)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 2 – 3 months (±7 days)

CONCOMITANT MEDICATIONS

Has any change in concomitant medications or treatments occurred since the last visit?

Yes ☐ **No** ☐

If Yes, please record on *Previous and Concomitant Medication form* any change in medication/treatment taken by the patient since previous visit and **please fill in the Adverse Event form, as appropriate.**

ADVERSE EVENTS

Has any adverse event occurred since last visit? **Yes** ☐ **No** ☐

If Yes, please **fill in the Adverse Event form.**

VISIT 3 – 6 months (±7 days)

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____

_____

VISIT 3 – 6 months (±7 days)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	Not Done
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 3 – 6 months (±7 days)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|

day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Unit	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐

VISIT 3 – 6 months (±7 days)

ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Beta-hCG**	☐Positive ☐Negative						☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5'UNL
- Beta-hCG positive

** For female only

VISIT 3 – 6 months (±7 days)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 3 – 6 months (±7 days)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

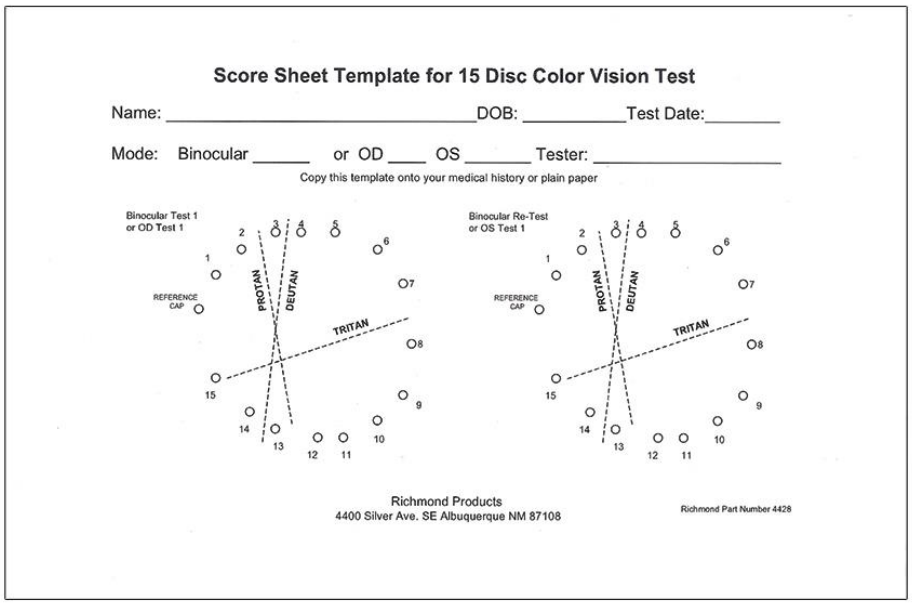
Cylinder: _____

TABO Axis: _____

VISIT 3 – 6 months (±7 days)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISIT 3 – 6 months (±7 days)

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 3 – 6 months (±7 days)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 3 – 6 months (±7 days)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 3 – 6 months (±7 days)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC3]: **Absolute Change in Thickness**
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 3 – 6 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>RIGHT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>LEFT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 3 – 6 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 3 – 6 months (±7 days)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 3 – 6 months (±7 days)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 3 – 6 months (±7 days)

CONCOMITANT MEDICATIONS

Has any change in concomitant medications or treatments occurred since the last visit?

Yes ☐ **No** ☐

If Yes, please record on *Previous and Concomitant Medication form* any change in medication/treatment taken by the patient since previous visit and **please fill in the Adverse Event form, as appropriate.**

ADVERSE EVENTS

Has any adverse event occurred since last visit? **Yes** ☐ **No** ☐

If Yes, please **fill in the Adverse Event form.**

PATIENT'S DIARY DISPENSATION

Was the patient provided with the diary and instructed on how to fill it in?

Yes ☐ **No** ☐

STUDY PRODUCT DISPENSATION

Was the patient provided with the study product? **Yes** ☐ **No** ☐

Number of capsules provided ☐☐☐

Was the patient instructed on how to take the product? **Yes** ☐ **No** ☐

VISIT 4 – 9 months (±7 days)

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____
_____

VISIT 4 – 9 months (±7 days)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	**Not Done**
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 4 – 9 months (±7 days)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|
day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Unit	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐

VISIT 4 – 9 months (±7 days)

ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Beta-hCG**	☐Positive ☐Negative						☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5'UNL
- Beta-hCG positive

** For female only

VISIT 4 – 9 months (±7 days)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 4 – 9 months (±7 days)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

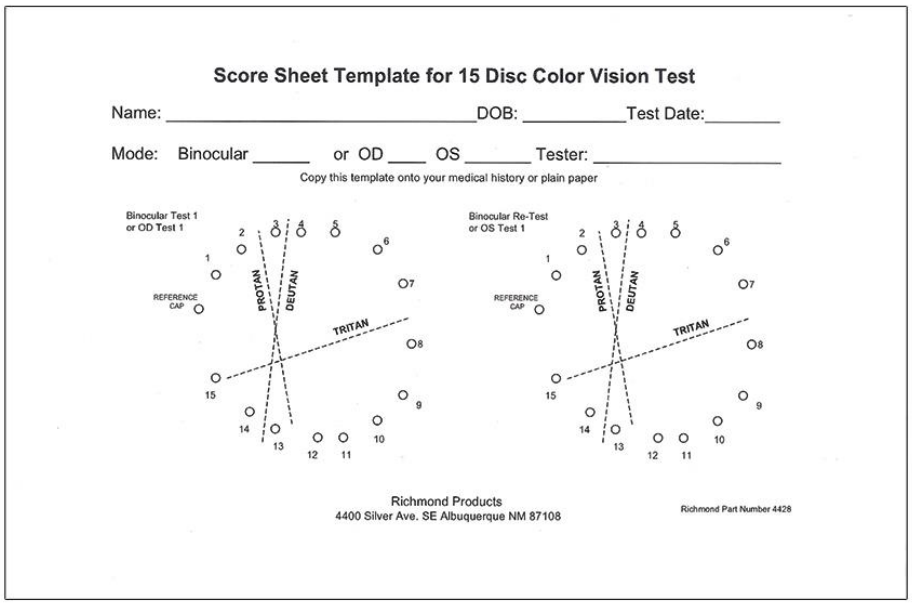
Cylinder: _____

TABO Axis: _____

VISIT 4 – 9 months (±7 days)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 4 – 9 months (±7 days)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 4 – 9 months (±7 days)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 4 – 9 months (±7 days)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC4]: **Absolute Change in Thickness**
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 4 – 9 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>RIGHT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>LEFT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 4 – 9 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 4 – 9 months (±7 days)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 4 – 9 months (±7 days)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 4 – 9 months (±7 days)

CONCOMITANT MEDICATIONS

Has any change in concomitant medications or treatments occurred since the last visit?

Yes ☐ **No** ☐

If Yes, please record on *Previous and Concomitant Medication form* any change in medication/treatment taken by the patient since previous visit and **please fill in the Adverse Event form, as appropriate.**

ADVERSE EVENTS

Has any adverse event occurred since last visit? **Yes** ☐ **No** ☐

If Yes, please **fill in the Adverse Event form.**

VISIT 4 – 9 months (±7 days)

PATIENT'S DIARY VERIFICATION

Has the diary been returned by the patient and reviewed by the Investigator?

☐ **NO**, please explain and re-train patient

_____

☐ **YES**, please specify:

Number of capsules used **recorded** in the diary |__|__|__|

STUDY PRODUCT ACCOUNTABILITY

Did the patient returned the unused study product? **Yes** ☐ **No**

Date of study product return |__|__| |__|__|__| |__|__|__|__|
day month year

Date of first study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Date of last study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Number of capsules returned: _____

Compliance: _____ %

Comments _____

_____

_____

Subject Screening N° ☐☐ ☐☐☐

VISIT 4 – 9 months (±7 days)

PATIENT'S DIARY DISPENSATION

Was the patient provided with the diary and instructed on how to fill it in?

Yes ☐ **No** ☐

STUDY PRODUCT DISPENSATION

Was the patient provided with the study product? **Yes** ☐ **No** ☐

Number of capsules provided ☐☐☐

Was the patient instructed on how to take the product? **Yes** ☐ **No** ☐

VISIT 5 – 12 months (±7 days)

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____
_____

VISIT 5 – 12 months (±7 days)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	**Not Done**
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 5 – 12 months (±7 days)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|
day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Unit	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐

VISIT 5 – 12 months (±7 days)

ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Beta-hCG**	☐Positive ☐Negative						☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5'UNL
- Beta-hCG positive

** For female only

VISIT 5 – 12 months (±7 days)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 5 – 12 months (±7 days)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

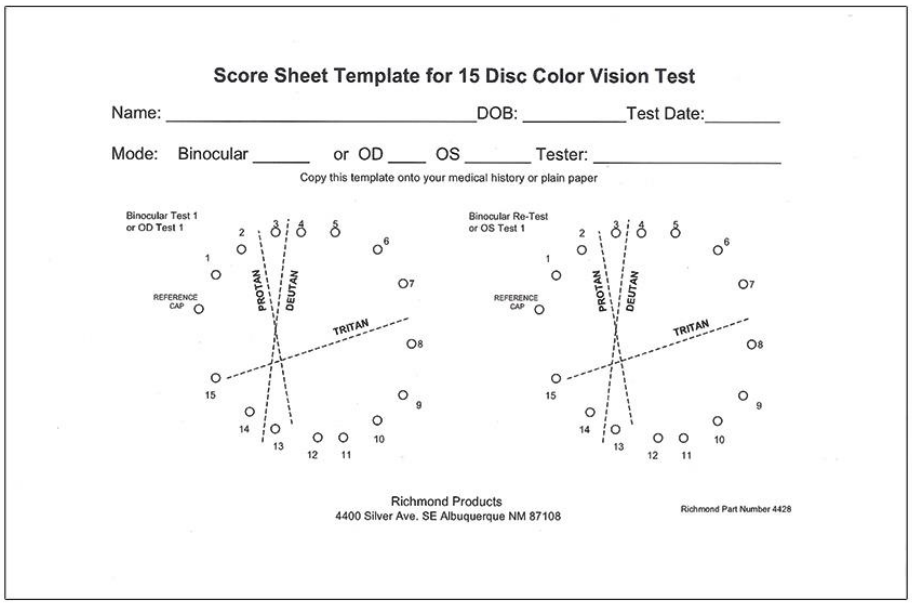
Cylinder: _____

TABO Axis: _____

VISIT 5 – 12 months (±7 days)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISIT 5 – 12 months (±7 days)

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 5 – 12 months (±7 days)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 5 – 12 months (±7 days)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 5 – 12 months (±7 days)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC5]: **Absolute Change in Thickness**
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 5 – 12 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>RIGHT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>LEFT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 5 – 12 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 5 – 12 months (±7 days)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 5 – 12 months (±7 days)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 5 – 12 months (±7 days)

CONCOMITANT MEDICATIONS

Has any change in concomitant medications or treatments occurred since the last visit?

Yes ☐ **No** ☐

If Yes, please record on *Previous and Concomitant Medication form* any change in medication/treatment taken by the patient since previous visit and **please fill in the Adverse Event form, as appropriate.**

ADVERSE EVENTS

Has any adverse event occurred since last visit? **Yes** ☐ **No** ☐

If Yes, please **fill in the Adverse Event form.**

VISIT 5 – 12 months (±7 days)

PATIENT'S DIARY VERIFICATION

Has the diary been returned by the patient and reviewed by the Investigator?

☐ **NO**, please explain and re-train patient

_____

☐ **YES**, please specify:

Number of capsules used **recorded** in the diary |__|__|__|

STUDY PRODUCT ACCOUNTABILITY

Did the patient returned the unused study product? **Yes** ☐ **No**

Date of study product return |__|__| |__|__|__| |__|__|__|__|
day month year

Date of first study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Date of last study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Number of capsules returned: _____

Compliance: _____ %

Comments _____

_____

_____

VISIT 5 – 12 months (±7 days)

PATIENT'S DIARY DISPENSATION

Was the patient provided with the diary and instructed on how to fill it in?

Yes ☐ **No** ☐

STUDY PRODUCT DISPENSATION

Was the patient provided with the study product? **Yes** ☐ **No** ☐

Number of capsules provided ☐☐☐

Was the patient instructed on how to take the product? **Yes** ☐ **No** ☐

VISIT 6 – 15 months (±7 days)

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____

_____

VISIT 6 – 15 months (±7 days)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	Not Done
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 6 – 15 months (±7 days)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|
day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Unit	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐

VISIT 6 – 15 months (±7 days)

ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Beta-hCG**	☐Positive ☐Negative						☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5'UNL
- Beta-hCG positive

** For female only

VISIT 6 – 15 months (±7 days)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 6 – 15 months (±7 days)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

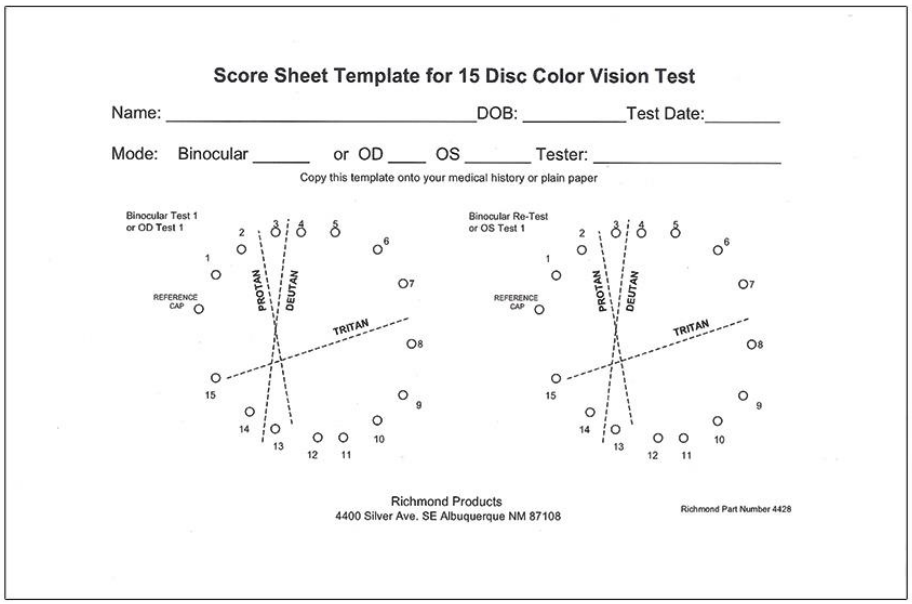
Cylinder: _____

TABO Axis: _____

VISIT 6 – 15 months (±7 days)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISIT 6 – 15 months (±7 days)

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 6 – 15 months (±7 days)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 6 – 15 months (±7 days)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 6 – 15 months (±7 days)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC6]: **Absolute Change in Thickness**
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 6 – 15 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>RIGHT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – <u>LEFT EYE</u>
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 6 – 15 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 6 – 15 months (±7 days)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 6 – 15 months (±7 days)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 6 – 15 months (±7 days)

CONCOMITANT MEDICATIONS

Has any change in concomitant medications or treatments occurred since the last visit?

Yes ☐ **No** ☐

If Yes, please record on *Previous and Concomitant Medication form* any change in medication/treatment taken by the patient since previous visit and **please fill in the Adverse Event form, as appropriate.**

ADVERSE EVENTS

Has any adverse event occurred since last visit? **Yes** ☐ **No** ☐

If Yes, please **fill in the Adverse Event form.**

VISIT 6 – 15 months (±7 days)

PATIENT'S DIARY VERIFICATION

Has the diary been returned by the patient and reviewed by the Investigator?

☐ **NO**, please explain and re-train patient

_____

☐ **YES**, please specify:

Number of capsules used **recorded** in the diary |__|__|__|

STUDY PRODUCT ACCOUNTABILITY

Did the patient returned the unused study product? **Yes** ☐ **No**

Date of study product return |__|__| |__|__|__| |__|__|__|__|
day month year

Date of first study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Date of last study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Number of capsules returned: _____

Compliance: _____ %

Comments _____

_____

_____

Subject Screening N° ☐☐ ☐☐☐

VISIT 6 – 15 months (±7 days)

PATIENT'S DIARY DISPENSATION

Was the patient provided with the diary and instructed on how to fill it in?

Yes ☐ **No** ☐

STUDY PRODUCT DISPENSATION

Was the patient provided with the study product? **Yes** ☐ **No** ☐

Number of capsules provided ☐☐☐

Was the patient instructed on how to take the product? **Yes** ☐ **No** ☐

VISIT 7 – 18 months (±7 days)

Date of visit |__|__| |__|__| |__|__|__|__|
day month year

VITAL SIGNS

Date |__|__| |__|__| |__|__|__|__|
day month year

Height: |__|__|__| (cm)

Weight: |__|__|__|.|__| (kg)

Blood pressure: |__|__|__| / |__|__|__| (mmHg)
Systolic Diastolic

ECG

Date |__|__| |__|__| |__|__|__|__|
day month year

Heart Rate: |__|__|__| bpm

PR interval: |__|__|__| ms

QRS interval: |__|__|__| ms

QT interval: |__|__|__| ms

QTcB: |__|__|__| ms

QTcF: |__|__|__| ms

Please specify if the ECG is:

- ☐ Normal
- ☐ Abnormal, not clinically significant
- ☐ Abnormal, clinically significant

If Abnormal, please specify the abnormality:

_____

_____

VISIT 7 – 18 months (±7 days)

PHYSICAL EXAMINATION

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Please report any positive findings in the table below and cross check with the Medical History Form and/or Surgical History Form.

	Please specify the abnormality	Not Done
Skin		☐
Head		☐
Eyes		☐
Ears, nose, throat		☐
Mouth		☐
Neck		☐
Thyroid		☐
Lymph nodes		☐
Heart		☐
Lungs		☐
Breast		☐
Abdomen		☐
Musculoskeletal		☐
Genitourinary		☐
Extremities		☐
Neurological		☐
Other (specify)		
Other (specify) _____		

VISIT 7 – 18 months (±7 days)

HEMATOLOGY AND BLOOD BIOCHEMISTRY

Date of blood sample collection |__|__| |__|__|__| |__|__|__|__|
day month year

☐ Not Done

Test	Outcome	Value	Unit	LNL	UNL	Unit	Not Done
RBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
WBC	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hemoglobin	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Hematocrit	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Lymphocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Monocytes	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Neutrophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Eosinophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Basophils	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Platelets	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Glucose	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Calcium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
AST*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐

VISIT 7 – 18 months (±7 days)

ALT*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Bilirubin*	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
gGT	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
ALP	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Urea	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Creatinine	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Potassium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Sodium	☐Normal ☐Abnormal NOT Clinically significant ☐Abnormal AND Clinically significant						☐
Beta-hCG**	☐Positive ☐Negative						☐

* According to the exclusion Criteria, the patient cannot be enrolled in the study if:

- AST or ALT or Bilirubin values > 5'UNL
- Beta-hCG positive

** For female only

VISIT 7 – 18 months (±7 days)

OPHTHALMOLOGIC EXAMINATION

BEST CORRECTED VISUAL ACUITY (BCVA) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
RIGHT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

Cylinder: _____

TABO Axis: _____

VISIT 7 – 18 months (±7 days)

BEST CORRECTED VISUAL ACUITY (BCVA) – LEFT EYE

A. Total number of correct letters at 4 meters:	
B. If A ≥ 20, enter 20, otherwise enter a zero (0):	
C. Total number of correct letters at 1 meter (if not tested, enter a zero)	
LEFT EYE: Sum of A, B and C above: Approximate SNELLEN acuity equivalent (smallest line with 1 of fewer error)	

If zero letters are read correctly at 1 meter, indicate best visual acuity for RIGHT EYE:

☐ Count fingers at: ☐ 120 cm ☐ 60 cm ☐ 30 cm

☐ Hand motion

☐ Light perception

☐ No light perception

Refraction

Sphere: _____

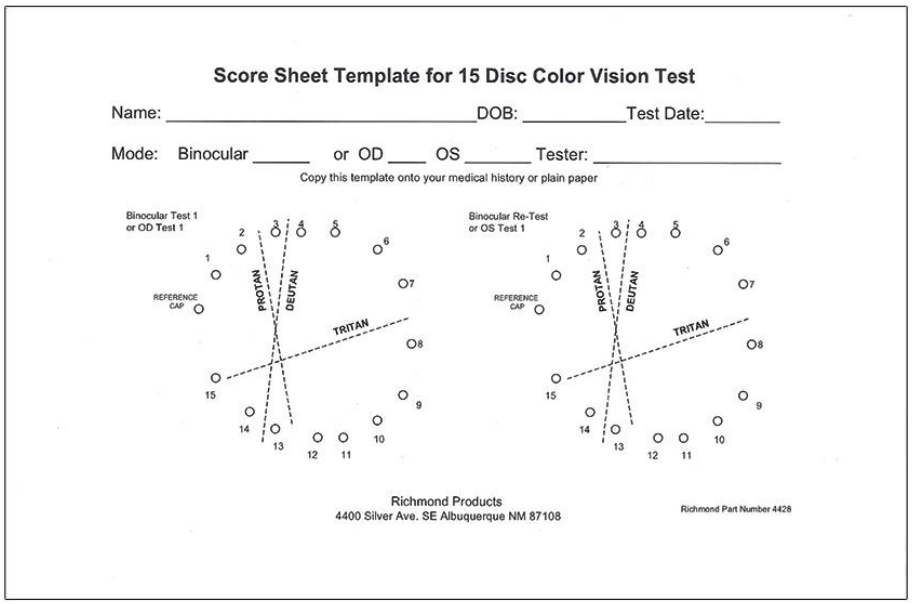
Cylinder: _____

TABO Axis: _____

VISIT 7 – 18 months (±7 days)

COLOR VISION TEST
Farnsworth Munsell Dichotomous D-15 Color Vision Test

Date of examination |__|__| |__|__| |__|__|__|__|
day month year



Color vision:

OD	OS
☐ Normal	☐ Normal
☐ Protan	☐ Protan
☐ Deutan	☐ Deutan
☐ Tritan	☐ Tritan

VISIT 7 – 18 months (±7 days)

VISUAL EVOKED POTENTIALS (VEPs)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Visual evoked potentials are elicited using transient Pattern Reversal stimuli and monocular stimulation. The checkerboard is displayed on a television screen subtending a visual angle of 15°. Contrast is 99%, spatial frequencies equivalent to 60 and 15 arcmin visual angles, separately presented. Recordings at Oz-Fz locations of the 10-20 International System. Measurement of N75 and P100 latencies (ms) and N75 to P100 peak-to-peak amplitude (μV).

RIGHT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 60' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

RIGHT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

LEFT EYE - 15' stimulation

N75 latency: _____ ms

P100 latency: _____ ms

N75-P100 amplitude: _____ μV

☐ Normal (*)

☐ Abnormal (*)

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 7 – 18 months (±7 days)

BASELINE ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

BASELINE ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

Photopic responses (*):

☐ Normal ☐ Abnormal ☐ Absent

30-Hz Flicker responses (*):

☐ Normal ☐ Abnormal ☐ Absent

(*) Responses have to be considered abnormal when values exceed 2,5 standard deviations

VISIT 7 – 18 months (±7 days)

FOLLOW-UP ELECTRORETINOGRAM (ERG) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

FOLLOW-UP ELECTRORETINOGRAM (ERG) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Scotopic, Photopic, Flicker ERG recorded according to the ISCEV International Guidelines (REF).

Scotopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

Photopic responses:

☐ Improved ☐ Stable ☐ Deteriorated

30-Hz Flicker responses:

☐ Improved ☐ Stable ☐ Deteriorated

VISIT 7 – 18 months (±7 days)

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – RIGHT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

MACULAR OPTICAL COHERENCE TOMOGRAPHY (OCT) – LEFT EYE

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Center Point Thickness (CPT)		μm
Central Subfield Mean Thickness (CSMT)		μm

***Center Point Thickness (CPT)**
the average of the thickness values for the 6 radial scans at their point of intersection.
***Central Subfield Mean Thickness (CSMT)**
the mean value of the 128 thickness values obtained in the central subfield.
***Central Subfield (CS)**
the circular area of diameter 1 mm centered around the center point; 128 thickness measurements are made in this circular area in the fast mac protocol.

Commentato [CC7]: **Absolute Change in Thickness**
the difference in the thickness between two measurements made at different times. For example, if measurements M_1 and M_2 are made at two different times, then the absolute change in thickness equals M_2-M_1. The absolute change in thickness is equal to the absolute change in thickening, which is the first of three methods of analyzing OCT changes listed above.
Relative Change in Thickness
the absolute change in thickness divided by the baseline thickness. Using the symbols introduced previously, relative thickness equals $[(M_2-M_1)/M_1]\cdot100\%$, which is the second of three methods of analyzing OCT changes.
Relative Change in Thickening
the absolute change in thickness (or thickening) divided by the baseline thickening. Using the symbols introduced previously, relative change in thickening equals $[(M_2-M_1)/(M_1$-normative mean$)]\cdot100\%$, which is the third of three methods of analyzing OCT changes.

VISIT 7 – 18 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION – RIGHT EYE
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

COMPUTERIZED VISUAL FIELD EXAMINATION – LEFT EYE
Standard automated perimetry (30.2 threshold exam)

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Fixation losees: _____

False POS Errors: _____

False NEG Errors: _____

Test duration: _____

Fovea		dB
GHT		-
MD		dB
PSD		dB

☐ < 5% ☐ < 2% ☐ < 1% ☐ < 0,5%

VISIT 7 – 18 months (±7 days)

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>RIGHT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

COMPUTERIZED VISUAL FIELD EXAMINATION - <u>LEFT EYE</u>
Kinetic perimetry

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____

Test duration: _____

MIR (mean isopter radius): _____

VISIT 7 – 18 months (±7 days)

MICROPERIMETRY- RIGHT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

MICROPERIMETRY- LEFT EYE

*It is recommended the use of standard stimulus (III, White Goldman stimulus).

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

Stimulus size: _____ Test duration: _____

MS (mean sensitivity): _____

Fixation:

☐ Stable (if more than 75% of fixation points fall within a 2° circle)

☐ Relatively unstable (if fewer than 75% fall within a 2° circle but more than 75% fall within a 4° circle)

☐ Unstable (if fewer than 75% fall within a 4° circle)

BCEA (Bivariate Contour Ellipse Area): _____

VISIT 7 – 18 months (±7 days)

SCALE FOR THE ASSESSMENT AND RATING OF ATAXIA (SARA)

Date of examination |__|__| |__|__| |__|__|__|__|
day month year

	Score
Gait	
Stance	
Sitting	
Speech disturbance	

	Score	**Right**	**Left**
Finger Chase			
Nose-Finger Test			
Fast Alternating Hand Movements			
Heel-Shin Slide			

VISIT 7 – 18 months (±7 days)

CONCOMITANT MEDICATIONS

Has any change in concomitant medications or treatments occurred since the last visit?

Yes ☐ **No** ☐

If Yes, please record on *Previous and Concomitant Medication form* any change in medication/treatment taken by the patient since previous visit and **please fill in the Adverse Event form, as appropriate.**

ADVERSE EVENTS

Has any adverse event occurred since last visit? **Yes** ☐ **No** ☐

If Yes, please **fill in the Adverse Event form.**

VISIT 7 – 18 months (±7 days)

PATIENT'S DIARY VERIFICATION

Has the diary been returned by the patient and reviewed by the Investigator?

☐ **NO**, please explain and re-train patient

_____

☐ **YES**, please specify:

Number of capsules used **recorded** in the diary |__|__|__|

STUDY PRODUCT ACCOUNTABILITY

Did the patient returned the unused study product? **Yes** ☐ **No**

Date of study product return |__|__| |__|__|__| |__|__|__|__|
day month year

Date of first study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Date of last study product intake |__|__| |__|__|__| |__|__|__|__|
day month year

Number of capsules returned: _____

Compliance: _____ %

Comments _____

_____

_____

Subject Screening N° ☐☐ ☐☐☐

CONCOMITANT MEDICATIONS AND THERAPIES

Has the subject taken any medication or treatment in the 3 months before Screening visit or during the Study? **Yes** ☐ **No** ☐

Please, use these forms to record any change in medications/treatments taken by subject occurring during the study.

Trade Name	Active Ingredients	Indication*	Single Dose	Units	Frequency	Formulation	Administration Route**	Start Date (dd/mm/yyyy)***	Ongoing	Stop Date (dd/mm/yyyy)***
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____

**if given for AE, enter the exact term from the AE form*

Report the following commonly accepted abbreviations/acronyms: IM (intramuscular), IV (intravenous), NEB (nebulised), NG (naso-gastric), PO (oral), PEG (percutaneous enteral gastrostomy), PV (per vagina), PR (per rectum), PICC (peripherally inserted central catheter), subcut (subcutaneous), subling (sublingual).* ***Abbreviations may not be used for other routes (write the term in full).

**** If complete date is not known, please report "na" (Not Available) for missing data (example: na/02/2015).*

CONCOMITANT MEDICATIONS AND THERAPIES

Please, use these forms to record any change in medications/treatments taken by subject occurring during the study.

Trade Name	Active Ingredients	Indication*	Single Dose	Units	Frequency	Formulation	Administration Route**	Start Date (dd/mm/yyyy)***	Ongoing	Stop Date (dd/mm/yyyy)***
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____

**if given for AE, enter the exact term from the AE form*

Report the following commonly accepted abbreviations/acronyms: IM (intramuscular), IV (intravenous), NEB (nebulised), NG (naso-gastric), PO (oral), PEG (percutaneous enteral gastrostomy), PV (per vagina), PR (per rectum), PICC (peripherally inserted central catheter), subcut (subcutaneous), subling (sublingual).* ***Abbreviations may not be used for other routes (write the term in full)

**** If complete date is not known, please report "na" (Not Available) for missing data (example: na/02/2015).*

CONCOMITANT MEDICATIONS AND THERAPIES

Please, use these forms to record any change in medications/treatments taken by subject occurring during the study.

Trade Name	Active Ingredients	Indication*	Single Dose	Units	Frequency	Formulation	Administration Route**	Start Date (dd/mm/yyyy)***	Ongoing	Stop Date (dd/mm/yyyy)***
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____

**if given for AE, enter the exact term from the AE form*

Report the following commonly accepted abbreviations/acronyms: IM (intramuscular), IV (intravenous), NEB (nebulised), NG (naso-gastric), PO (oral), PEG (percutaneous enteral gastrostomy), PV (per vagina), PR (per rectum), PICC (peripherally inserted central catheter), subcut (subcutaneous), subling (sublingual).* ***Abbreviations may not be used for other routes (write the term in full).

**** If complete date is not known, please report "na" (Not Available) for missing data (example: na/02/2015).*

Subject Screening N° | | | | | |

CONCOMITANT MEDICATIONS AND THERAPIES

Please, use these forms to record any change in medications/treatments taken by subject occurring during the study.

Trade Name	Active Ingredients	Indication*	Single Dose	Units	Frequency	Formulation	Administration Route**	Start Date (dd/mm/yyyy)***	Ongoing	Stop Date (dd/mm/yyyy)***
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____
								__/__/____	☐	__/__/____

**if given for AE, enter the exact term from the AE form*

Report the following commonly accepted abbreviations/acronyms: IM (intramuscular), IV (intravenous), NEB (nebulised), NG (naso-gastric), PO (oral), PEG (percutaneous enteral gastrostomy), PV (per vagina), PR (per rectum), PICC (peripherally inserted central catheter), subcut (subcutaneous), subling (sublingual).* ***Abbreviations may not be used for other routes (write the term in full).
**** If complete date is not known, please report "na" (Not Available) for missing data (example: na/02/2015).*

ADVERSE EVENT

Did the subject experience any Adverse Event after signing the Informed Consent Form?

Yes ☐ **No** ☐

Adverse Event description			
Start Date (dd/mm/yyyy)	|__|__| |__|__| |__|__|__|__|	Start Time (hh:mm)	|__|__| : |__|__|
Outcome	☐ Resolved ☐ Resolved with sequelae ☐ Ongoing	☐ Fatal ☐ Unknown	
End Date (dd/mm/yyyy)	|__|__| |__|__| |__|__|__|__|	End Time (hh:mm)	|__|__| : |__|__|
Severity	☐ Mild ☐ Moderate ☐ Severe	☐ Life-threatening consequences ☐ Death	
Relatedness with study treatment	☐ Certain ☐ Probable ☐ Possible	☐ Doubtful ☐ None ☐ Unknown	
Causality different from study treatment	☐ Pathology being studied ☐ Other pathology, specify_____	☐ Concomitant treatment, specify _____ ☐ Other, specify _____	
Action taken with study treatment	☐ None	☐ Study Treatment permanently discontinued	
Other action taken	☐ None ☐ Medication, specify _____	☐ Other, please specify _____	
Serious Adverse Event?	☐ No	☐ Yes	
TYPE OF SAE	☐ Death ☐ Life-threatening illness or injury ☐ Permanent impairment of a body structure or a body function ☐ In-patient or prolonged hospitalization ☐ Medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function ☐ Foetal distress, foetal death or a congenital abnormality or birth defect		

ADVERSE EVENT

Adverse Event description			
Start Date (dd/mm/yyyy)	|__|__| |__|__| |__|__|__|__|	Start Time (hh:mm)	|__|__| : |__|__|
Outcome	☐ Resolved ☐ Resolved with sequelae ☐ Ongoing	☐ Fatal ☐ Unknown	
End Date (dd/mm/yyyy)	|__|__| |__|__| |__|__|__|__|	End Time (hh:mm)	|__|__| : |__|__|
Severity	☐ Grade 1 (Mild) ☐ Grade 2 (Moderate) ☐ Grade 3 (Severe)	☐ Grade 4 (Life-threatening consequences) ☐ Grade 5	
Relatedness with study treatment	☐ Certain ☐ Probable ☐ Possible	☐ Doubtful ☐ None ☐ Unknown	
Causality different from study treatment	☐ Pathology being studied ☐ Other pathology, specify_____	☐ Concomitant treatment, specify _____ ☐ Other, specify _____	
Action taken with study treatment	☐ None	☐ Study Treatment permanently discontinued	
Other action taken	☐ None ☐ Medication, specify _____	☐ Other, please specify _____	
Serious Adverse Event?	☐ No	☐ Yes	
TYPE OF SAE	☐ Death ☐ Life-threatening illness or injury ☐ Permanent impairment of a body structure or a body function ☐ In-patient or prolonged hospitalization ☐ Medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function ☐ Foetal distress, foetal death or a congenital abnormality or birth defect		

ADVERSE EVENT

Adverse Event description			
Start Date (dd/mm/yyyy)	|__|__| |__|__| |__|__|__|__|	Start Time (hh:mm)	|__|__| : |__|__|
Outcome	☐ Resolved ☐ Resolved with sequelae ☐ Ongoing	☐ Fatal ☐ Unknown	
End Date (dd/mm/yyyy)	|__|__| |__|__| |__|__|__|__|	End Time (hh:mm)	|__|__| : |__|__|
Severity	☐ Grade 1 (Mild) ☐ Grade 2 (Moderate) ☐ Grade 3 (Severe)	☐ Grade 4 (Life-threatening consequences) ☐ Grade 5	
Relatedness with study treatment	☐ Certain ☐ Probable ☐ Possible	☐ Doubtful ☐ None ☐ Unknown	
Causality different from study treatment	☐ Pathology being studied ☐ Other pathology, specify_____	☐ Concomitant treatment, specify _____ ☐ Other, specify _____	
Action taken with study treatment	☐ None	☐ Study Treatment permanently discontinued	
Other action taken	☐ None ☐ Medication, specify _____	☐ Other, please specify _____	
Serious Adverse Event?	☐ No	☐ Yes	
TYPE OF SAE	☐ Death ☐ Life-threatening illness or injury ☐ Permanent impairment of a body structure or a body function ☐ In-patient or prolonged hospitalization ☐ Medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function ☐ Foetal distress, foetal death or a congenital abnormality or birth defect		

☐ **PLEASE TICK IF THIS IS THE LAST AE FORM FOR THIS PATIENT, OTHERWISE ADD AS MANY ADDITIONAL AE FORMS AS NEEDED**

BREAKING THE BLIND

In case the blind was broken, please report here:

Date and time the sealed envelope was opened:

|__|__| |__|__|__| |__|__|__|__| |__|__|:|__|__|
day month year hour min

First and last name of who has opened the sealed envelope:

_____

Reason(s) leading to open the sealed envelope:

_____
_____
_____

Please fill in the "Adverse Event" form reporting all the necessary information.

_____ _____
Signature Investigator's Name and Surname

Date of Signature: |__|__| |__|__| |__|__|__|__|
day month year

END OF STUDY

STUDY TERMINATION

Last visit/study assessment date |__|__| |__|__| |__|__|__|__|
day month year

Last day of product intake |__|__| |__|__| |__|__|__|__|
day month year

Status at end of clinical investigation:

- ☐ Completed
- ☐ Withdrew prematurely

Main reason for early withdrawal (tick primary reason only):

- ☐ Adverse Event
- ☐ ALT > 5·UNL
- ☐ Lack of compliance to study treatment or assessments
- ☐ Lost to follow up
- ☐ Death
- ☐ Consent withdrawal
- ☐ Other, specify _____

PRINCIPAL INVESTIGATION'S STATEMENT

I reviewed all pages of this Case Report Form. For the best of my knowledge, all information recorded in the Case Report Form is complete and accurate.

_____ _____
Signature Principal Investigator's Name

Date of Signature: |__|__| |__|__| |__|__|__|__|
day month year