Supplementary Material S1. Uncertainty Evaluation Procedure

1.Scope

- The uncertainty evaluation procedure set forth in this document may apply to ① through ⑥, which are motor nerve conduction and sensory nerve conduction measurements in specific age and gender groups. Velocity may apply to motor nerve conduction measurements.

① Latency (including onset latency and peak latency), ② Baseline-to-peak amplitude, ③ Peak-to-peak amplitude, ④ Duration (duration of the negative wave), ⑤ Area (area under the negative wave), and ⑥ Velocity (Nerve conduction velocity)

2.Details of the Uncertainty Evaluation Procedure for Nerve Conduction Tests

2-1. Latency

Both onset latency and peak latency shall be based on this model equation. This procedure illustrates the detailed procedure with the example of onset latency.

※Onset latency measurement model equation for a distal (wrist) stimulus point

$$M_l = X_l + C_l$$

M_l: Onset latency measurement of a distal stimulus point in a motor nerve conduction test
X_l: Onset latency reading of a distal stimulus point in a motor nerve conduction test
C_l: Onset latency corrected value of a distal stimulus point in a motor nerve conduction test

(1) Uncertainty factors and standard uncertainty in C_l

- If the nerve conduction device is calibrated internally using a standard signal generator calibrated by a nationally certified calibration organization to calculate a corrected value, evaluate the uncertainty of this corrected value.

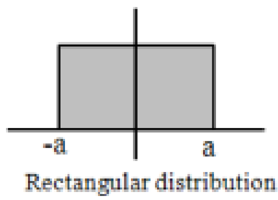
a) Standard uncertainty due to repeated measurements ($C_{l,rep}$)

- Evaluate uncertainty with Type A evaluation obtained from n repeated measurements in EPCs.
- The standard deviation (SD) of the readings obtained from n repeated measurements is calculated using the following equation:

$$u(C_{l,rep}) = SD/\sqrt{n}$$

b) Standard uncertainty due to the resolution of the nerve conduction device ($C_{l,res}$)

- Estimate the half-width of a digital increment (r=0.01 ms) as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution (r=0.01 ms) as the half-width, as illustrated in the following figure:



$$u(C_{l,res}) = \frac{a}{\sqrt{3}} = \frac{0.005}{\sqrt{3}} = 0.003ms$$

Fig. 1. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

c) Standard uncertainty in a standard signal generator (EPCs) ($C_{l,EPCs}$)

- Divide the expanded uncertainty of the calibration results of the standard signal generator (EPCs) by k.

e.g., Where the calibration report states U = 0.030 ms and k = 2,

$$u(C_{l,EPCs}) = \frac{U}{k} = \frac{0.03}{2} = 0.015ms$$

(2) Calculation of combined standard uncertainty in C_l

$$u(C_l) = \sqrt{u(C_{l,rep})^2 + u(C_{l,res})^2 + u(C_{l,EPCs})^2}$$

(3) Uncertainty factors and standard uncertainty in X_l

a) Standard uncertainty due to thermometer uncertainty ($X_{l,t}$)

- According to the literature (Kouyoumdjian et al., 2015), assuming that the inter-electrode distance is 8 cm for the distal stimulus point of the motor nerve and 14 cm for the distal stimulus point of the sensory nerve when the body temperature changes by 1°C, it is known that it changes the sensory peak latency by 0.15 ms and the motor onset latency by 0.20 ms.
- Calculate standard uncertainty due to body temperature based on this information.
- The uncertainty of the thermometer can be considered as an uncertainty factor due to body temperature.

▶Uncertainty due to the uncertainty of the thermometer: Calculate it using expanded uncertainty on the calibration report of the thermometer calibrated by a nationally certified calibration organization. Divide expanded uncertainty (U) by k. Next, multiply it by the onset latency change per 1°C change to obtain standard uncertainty.

$$u(X_{l,t}) = \frac{U}{k} \times \text{onset latency change per 1 } mm \text{ change}$$

b) Standard uncertainty due to uncertainty in length measurement ($X_{l,l}$)

- According to the literature (Electrodiagnostic Medicine, second edition, Dumitru et al., 2001), the average conduction velocity of a nerve is 50 mm/ms.
- Therefore, onset latency change per 1 mm change = 1/50 (mm/ms) = 0.02 (ms/mm)
- Uncertainty factors in length measurement include: ① uncertainty with the tape measure and (2) inter-measurer variation.

▶Uncertainty due to uncertainty with the tape measure: Calculate it based on expanded uncertainty on the tape measure's calibration report. Divide expanded uncertainty (*U*) by *k*. Next, multiply it by the onset latency change per 1 mm change.

$$u(X_{l,l1}) = \frac{U}{k} \times \text{onset latency change per 1 } mm \text{ change}$$

▶Uncertainty due to inter-measurer variation: As electrodes are attached with the length measured by the tape measure, the difference in length measurement between different measurers is considered as an uncertainty factor. Use the results of the analysis of variance (ANOVA) of the data obtained from m measurements of the same subject by *n* measurers. The square root of between group variance in the ANOVA results is used as uncertainty due to inter-measurer variation.

$$u(X_{l,l2}) = \sqrt{\frac{SSB}{n-1}} \times \text{onset latency change per 1 } mm \text{ change}$$

(SSB: Sum of squares of between group variance in the ANOVA results)

▶Therefore, calculate uncertainty due to uncertainty in length measurement as follows:

$$u(X_{l,l}) = \sqrt{u^2(X_{l,l1}) + u^2(X_{l,l2})}$$

c) Standard uncertainty in the subject group

- Calculate the standard deviations of observations from *N* subjects in the collected sample as the standard uncertainty. (If *n* measurements are conducted per subject, the mean is used as the subject's observation.)

$$u(X_{l,d}) = SD$$

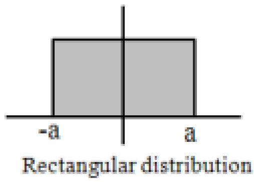
(SD: Standard deviation of latency observations from *N* subjects)

- Note: If the measurements are latency for 1 subject, standard uncertainty is calculated using the standard deviation of readings obtained from n repeated measurements. $u(X_{l,d})=SD/\sqrt{n}$

(SD: Standard deviation of readings from n repeated measurements from 1 subject)

d) Uncertainty due to the resolution of the nerve conduction device

- Estimate the half-width of a digital increment (r=0.01 ms) as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution (r=0.01 ms) as the half-width, as illustrated in the following figure:



$$u(X_{l,res}) = \frac{a}{\sqrt{3}} = \frac{0.005}{\sqrt{3}} = 0.003ms$$

Fig. 2. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

e) Standard uncertainty due to the designation of a peak point in CMAP/SNAP

- Moving the peak point in the test graph may impact the test results. Uncertainty is calculated using the results of the analysis of variance (ANOVA) of the data obtained from *m* measurements on the test graph repeatedly measured by *n* measurers with EPCs. For uncertainty, the square root of between group variance in the ANOVA results is used as uncertainty due to inter-measurer variation.

$$u(X_{l,pp}) = \sqrt{\frac{SSB}{n-1}}$$

(SSB: Sum of squares of between group variance in the ANOVA results)

(4) Calculation of combined standard uncertainty and expanded uncertainty

a) Combined standard uncertainty

$$u(M_l) = \sqrt{u^2(X_l) + u^2(C_l)}$$

$$= \sqrt{u^2(X_{l,t}) + u^2(X_{l,l}) + u^2(X_{l,d}) + u^2(X_{l,res}) + u^2(X_{l,pp}) + +u^2(C_{l,rep}) + u^2(C_{l,res}) + u^2(C_{l,EPCs})}$$

b) Expanded uncertainty

$$U(M_l) = k \times u(M_l)$$

2-2. Amplitudes

Both baseline to negative peak amplitude and negative peak to positive peak amplitude have same model equation.

※Amplitude measurement model equation

$$M_a = X_a + C_a$$

M_a: Amplitude measurement in a motor nerve conduction test
X_a: Amplitude reading in a motor nerve conduction test
C_a: Amplitude corrected value in a motor nerve conduction test

As the calibration report for negative peak to positive peak amplitude, not baseline to negative peak amplitude, is issued for the standard signal generator, it is assumed that the negative peak to positive peak amplitude divided by 2 is the baseline to negative peak amplitude.

(1) Uncertainty factors and standard uncertainty in C_a
They are the same as the uncertainty factors in 2-1. Latency.

-If the nerve conduction device is calibrated internally using a standard signal generator calibrated by a nationally certified calibration organization to calculate a corrected value, evaluate the uncertainty of this corrected value.

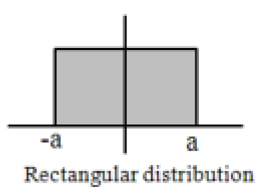
a) Standard uncertainty due to repeated measurements ($C_{a,rep}$)

- Evaluate uncertainty with Type A evaluation obtained from *n* repeated measurements in EPCs.
- The standard deviation (SD) of the readings obtained from *n* repeated measurements is calculated using the following equation:

$$u(C_{a,rep}) = SD/\sqrt{n}$$

b) Standard uncertainty due to the resolution of the nerve conduction device ($C_{a,res}$)

- Estimate the half-width of a digital increment (r=0.1 μV for the sensory nerve) as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution (r=0.1 μV) as the half-width, as illustrated in the following figure:



$$u(C_{a,res}) = \frac{a}{\sqrt{3}} = \frac{0.05}{\sqrt{3}} = 0.03\mu V$$

Fig. 3. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

c) Standard uncertainty in a standard signal generator (EPCs) ($C_{a,EPCs}$)

- Divide the expanded uncertainty of the calibration results of the standard signal generator (EPCs) by *k*.

e.g., Where the calibration report states U = 0.02V per 1 V with k = 2, the measurement uncertainty corresponding to 63 μV is 0.02 V x 63 μV/1 V = 1.26 μV.

$$u(C_{a,EPCs}) = \frac{U}{k} = \frac{1.26}{2} = 0.63\mu V$$

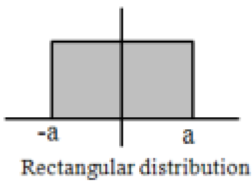
(2) Calculation of combined standard uncertainty in C_a

$$u(C_a) = \sqrt{u(C_{a,rep})^2 + u(C_{a,res})^2 + u(C_{a,EPCs})^2}$$

(3) Uncertainty factors and standard uncertainty in X_a

a) Uncertainty due to the resolution of the nerve conduction device

- Estimate the half-width of a digital increment (r=0.1 μV for the sensory nerve) as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution (r=0.1 μV) as the half-width, as illustrated in the following figure:



$$u(X_{a,res}) = \frac{a}{\sqrt{3}} = \frac{0.05}{\sqrt{3}} = 0.03\mu V$$

Fig. 4. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

b) Standard uncertainty in the subject group (or standard uncertainty of 1 subject)

- Calculate the standard deviation of observations from N subjects in the collected sample as the standard uncertainty. (If *n* measurements are conducted per subject, the mean is used as the subject's observation.)

$$u\left(X_{a,d}\right) = SD$$

(SD: Standard deviation of amplitude observations from N subjects)

- Note: If the measurements are amplitude for 1 subject, standard uncertainty is calculated using the standard deviation of readings obtained from *n* repeated measurements.

$$u\left(X_{a,res}\right) = SD/\sqrt{n}$$

(SD: Standard deviation of readings from n repeated measurements from 1 subject)

Note:

- It is difficult to apply the relationship between body temperature and amplitude as no previous literature is available. Therefore, this center will attempt to reduce uncertainty by keeping the body temperature within a certain range.
- Uncertainty due to the distance is expected to be minimal. (There might be temporal dispersion depending on the distance, temporal dispersion by a few millimeters is considered minimal.) Therefore, standard uncertainty due to tape measure measurements is negligible.

c) Standard uncertainty due to the designation of a peak point in CMAP/SNAP

- Moving the peak point in the test graph may impact the test results. Uncertainty is calculated using the results of the analysis of variance (ANOVA) of the data obtained from m measurements on the test graph repeatedly measured by n measurers with EPCs. For uncertainty, the square root of between group variance in the ANOVA results is used as uncertainty due to inter-measurer variation.

$$u(X_{a,pp}) = \sqrt{\frac{SSB}{n-1}}$$

(SSB: Sum of squares of between group variance in the ANOVA results)

(4) Calculation of combined standard uncertainty and expanded uncertainty

a) Combined standard uncertainty

$$u(M_a) = \sqrt{u^2(X_a) + u^2(C_a)}$$

$$= \sqrt{u^2(X_{a,d}) + u^2(X_{a,res}) + u^2(X_{a,pp}) + u^2(C_{a,rep}) + u^2(C_{a,res}) + u^2(C_{a,EPCs})}$$

b) Expanded uncertainty

$$\underline{U(M_a) = k \times u(M_a)}$$

2-3. Duration (Negative spike duration)

※Duration measurement model equation

$$M_d = X_d$$

M_d: Duration measurement

X_d: Duration reading

※Note: As it is currently difficult to calibrate nerve conduction devices for duration, uncertainty due to duration correction is omitted in this uncertainty evaluation. Even if the corrected value could be obtained, it is considered minimal compared to the magnitude of uncertainty in readings, including the standard deviation of the subject group.

(1) Uncertainty factors and standard uncertainty in X_d

a) Uncertainty in temperature measurement and uncertainty in length measurement

- The potential value, including amplitude, is not considered to be impacted by uncertainty in temperature measurement and length measurement, and therefore, it does not impact uncertainty for duration values.
- Uncertainty in temperature measurement and length measurement leads to uncertainty in onset latency and terminal latency values, which in turn cause uncertainty in duration values.
- However, as the magnitude of the potential value in onset latency and terminal latency is negligible, it is considered to not impact uncertainty in actual duration values.
- Therefore, uncertainty in duration due to uncertainty in temperature measurement and length measurement is omitted in this evaluation.

b) Standard uncertainty in the subject group (or standard uncertainty of 1 subject)

- Calculate the standard deviation of observations from *N* subjects in the collected sample as the standard uncertainty. (If *n* measurements are conducted per subject, the mean is used as the subject's observation.)

$$u(X_{d,d}) = SD$$

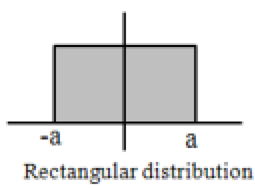
(SD: Standard deviation of area observations from N subjects)

- Note: If the measurements are amplitude for 1 subject, standard uncertainty is calculated using the standard deviation of readings obtained from n repeated measurements.

$$u(X_{d,d}) = SD/\sqrt{n}$$

c) Resolution of the nerve conduction device

- The resolution of duration is 0.1 ms. Estimate the half-width of resolution as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution as the half-width, as illustrated in the following figure:



$$u(X_{d,res}) = \frac{a}{\sqrt{3}} = \frac{0.05}{\sqrt{3}} = 0.03$$

Fig. 5. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

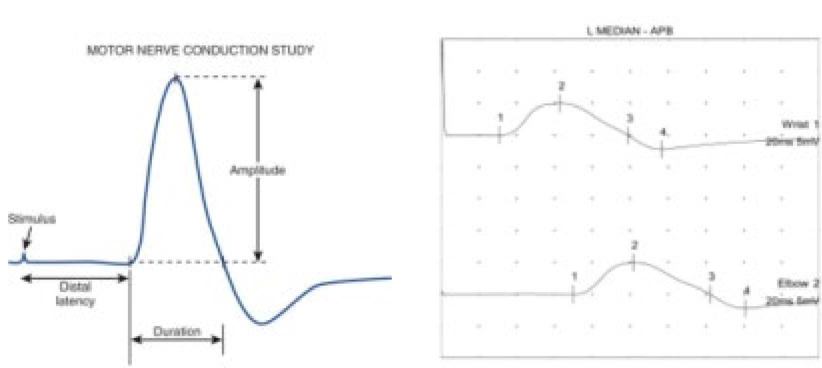
(2) Calculation of combined standard uncertainty and expanded uncertainty

a) Combined standard uncertainty

$$u(M_d) = \sqrt{u^2(X_d)} = \sqrt{u^2\left(X_{d,d}\right) + u^2(X_{d,res})}$$

b) Expanded uncertainty

$$\underline{U(M_d) = k \times u(M_d)}$$



2-4. Area (Negative spike area)

※Area measurement model equation

$$M_{area} = X_{area}$$

M_{area} : Area measurement in a motor nerve conduction test

X_{area} : Area reading in a motor nerve conduction test

※Note: As it is currently difficult to calibrate nerve conduction devices for areas, uncertainty due to area correction is omitted in this uncertainty evaluation. Even if the corrected value could be obtained, it is considered minimal compared to the magnitude of uncertainty in readings, including the standard deviation of the subject group.

(1) Uncertainty factors and standard uncertainty in X_{area}

a) Uncertainty in temperature measurement and uncertainty in length measurement

- The potential value, including amplitude, is not considered to be impacted by uncertainty in temperature measurement and length measurement, and therefore, it does not impact uncertainty for area values.
- Uncertainty in temperature measurement and length measurement leads to uncertainty in onset latency and terminal latency values, which in turn cause uncertainty in area values.
- However, as the magnitude of the potential value in onset latency and terminal latency is negligible, it is considered to not impact uncertainty in actual area values.
- Therefore, uncertainty in areas due to uncertainty in temperature measurement and length measurement is omitted in this evaluation.

b) Standard uncertainty in the subject group (or standard uncertainty of 1 subject)

- Calculate the standard deviation of observations from N subjects in the collected sample as the standard uncertainty. (If n measurements are conducted per subject, the mean is used as the subject's observation.)

$$u(X_{area,d}) = SD$$

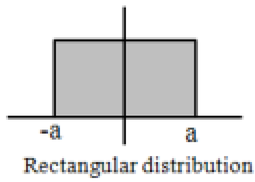
(SD: Standard deviation of area observations from N subjects)

- Note: If the measurements are amplitude for 1 subject, standard uncertainty is calculated using the standard deviation of readings obtained from n repeated measurements.

$$u(X_{area,d}) = SD/\sqrt{n}$$

c) Resolution of the nerve conduction device

- Although the digital increment has a resolution of greater than or equal to 5 decimal places, it is reported only up to the first decimal place in clinical practice. Therefore, set the resolution as below. Estimate the half-width of 0.1 mV*ms for the motor nerve and 0.1 μV*ms for the sensory nerve as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution as the half-width, as illustrated in the following figure:



$$u(X_{area,res}) = \frac{a}{\sqrt{3}} = \frac{0.05}{\sqrt{3}} = 0.03$$

Fig. 6. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

(2) Calculation of combined standard uncertainty and expanded uncertainty

a) Combined standard uncertainty

$$u(M_{area}) = \sqrt{u^2(X_{area})} = \sqrt{u^2(X_{area,d}) + u^2(X_{area,res})}$$

b) Expanded uncertainty

$$U(M_{area}) = k \times u(M_{area})$$

2-5. Velocity (nerve conduction velocity)

※Velocity measurement model equation

$$M_v = L/(M_{l,2} - M_{l,1})$$

M_v : Velocity measurement in a motor nerve conduction test

$M_{l,1}$: Distal onset latency measurement in a motor nerve conduction test

$M_{l,2}$: Proximal onset latency measurement in a motor nerve conduction test

L : Length measurement between distal and proximal in a motor nerve conduction test

(1) Uncertainty factors and standard uncertainty in L

$$L = X_L + C_L$$

L : Length measurement between distal and proximal in a motor nerve conduction test

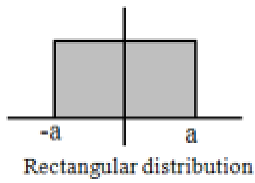
X_L : Length reading between distal and proximal in a motor nerve conduction test

C_L : Length-corrected value between distal and proximal in a motor nerve conduction test

a) Uncertainty factors and standard uncertainty in X_L

- Tape measure resolution

① Estimate the half-width of the tape measure's increment (r=0.1 cm) as a rectangular distribution. Calculate standard uncertainty from a rectangle with half the resolution (r=0.1 cm) as the half-width, as illustrated in the following figure:



$$u(X_{l,res}) = \frac{a}{\sqrt{3}} = \frac{0.05}{\sqrt{3}} = 0.03$$

Fig. 7. Method to calculate uncertainty due to resolution. Uncertainty due to resolution can be obtained from a rectangular probability distribution (left) with half the resolution as the half-width by using the calculation equation (right).

- Inter-measurer difference

① Use the results of the analysis of variance (ANOVA) of the data obtained from m measurements of the same subject by n measurers. The square root of between group variance in the ANOVA results is used as uncertainty due to inter-measurer variation.

$$u(X_{L,p}) = \sqrt{\frac{SSB}{n-1}}$$

(SSB: Sum of squares of between group variance in the ANOVA results)

- Standard uncertainty in X_L (or standard uncertainty of 1 subject)

$$u(X_L) = \sqrt{u^2(X_{L,res}) + u^2(X_{L,p})}$$

b) Uncertainty factors and standard uncertainty in C_L

- Standard uncertainty for corrected values

① Calculate the standard uncertainty by dividing uncertainty (U) listed on the tape measure's calibration report by the inclusion factor k.

$$u(C_L) = \frac{U}{k}$$

c) Standard uncertainty in L

$$u(L) = \sqrt{u^2(X_L) + u^2(C_L)} = \sqrt{u^2(X_{L,res}) + u^2(X_{L,p}) + u^2(C_L)}$$

(2) Standardized uncertainty in $M_{l,1}$and $M_{l,2}$

As $M_{l,1}$ and $M_{l,2}$ are onset latency, apply the uncertainty evaluation (combined standard uncertainty) described in 2-1 for each of them. However, exclude uncertainty factors in X_l in combined standard uncertainty and standard uncertainty in the subject group in standard uncertainty from calculation.

(3) Standard uncertainty in $L/(M_{l,2}$-$M_{l,1})$

- Standard uncertainty in the subject group (or standard uncertainty of 1 subject)
- Calculate the standard deviation of observations from N subjects in the collected sample as the standard uncertainty. (If n measurements are conducted per subject, the mean is used as the subject's observation.)

$$u(V_d) = SD$$

(SD: The standard deviation of velocity observations from N subjects and velocity should be calculated using calibrated measurements (e.g., length and onset latency)

② Note: If the measurements are values for 1 subject, standard uncertainty is calculated using the standard deviation of readings obtained from n repeated measurements.

$$u(V_d) = SD/\sqrt{n}$$

(4) Calculation of combined standard uncertainty and expanded uncertainty

a) Combined standard uncertainty

$$u(M_v) = \sqrt{(\frac{1}{M_{l,2} - M_{l,1}})^2 \times u^2(L) + (\frac{L}{(M_{l,2} - M_{l,1})^2})^2 \times u^2(M_{l,1}) + (\frac{L}{(M_{l,2} - M_{l,1})^2})^2 \times u^2(M_{l,2}) + u^2(V_d)}$$

b) Expanded uncertainty

$$U(M_v) = k \times u(M_v)$$