

## Technical notes

# LUMIPULSE® G NFL BLOOD <CE>

## AUTOMATED MEASUREMENT OF NFL

### Description

These technical notes provide information on the analytical and clinical performance of the CE-IVDR Lumipulse G NFL Blood assay. It offers for example more detailed insights into the data related to the age-related reference value curves, as outlined in the Lumipulse G NFL Blood Immunoreaction Cartridges (3x14T,CE; article number 81632) Instructions for Use document.

### Methods

The Lumipulse G NFL Blood (CE) assay is an immunoassay for the quantitative measurement of neurofilament light chain (NFL) in human serum or plasma (100 µL), based on sensitive chemiluminescent enzyme immunoassay (CLEIA) technology using a specific two-step method. The assay has been developed for fully automated, random-access analyzers of the LUMIPULSE G system family: the LUMIPULSE G600II (60 tests per hour) and the LUMIPULSE G1200 (120 tests per hour; see below).



Lumipulse® G1200  
120 tests/h

\* Lumipulse G NFL Blood Immunoreaction Cartridges <3x14T,CE>, 81632  
Lumipulse G NFL Blood Calibrators <1x2C,CE>, 81633  
Lumipulse NFL Blood Controls <2x2C,CE>, 81634

### Analytical performance data

Using serum and K<sub>2</sub>EDTA plasma samples, the assay's sensitivity and precision, and lot-to-lot reproducibility was evaluated. A matrix comparison study was performed including serum and K<sub>2</sub>EDTA plasma.

### Analytical sensitivity

The limit of detection (LOD) and limit of quantitation (LOQ) of the Lumipulse G NFL Blood assay were generated according to the guidelines outlined in CLSI EPI7-A2. The lower limit of quantification (LLOQ) was determined at an imprecision of 20% CV (Table 1).

Table 1 - Analytical sensitivity

| Lumipulse® G     | Serum, Plasma (pg/mL) |
|------------------|-----------------------|
| LOD              | 0.57                  |
| LLOQ (at 20 %CV) | 0.96                  |
| ULOQ*            | 2500.00               |

\*ULOQ = upper limit of quantification; defined as maximum calibrator



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Precision and lot-to-lot reproducibility

Evaluation of precision with different specimens was based on recommendations from the CLSI EP05-A3 approved guideline using duplicate measurements in 20 days with 2 replicates exemplarily for the LUMIPULSE G1200, respectively (see Table 2). In addition, total lot-to-lot precision has been tested with 3 lots over 5 days in a concentration range of 12.67 - 1706.82 pg/ mL for serum, plasma and control samples. The lot-to-lot reproducibility was 1.8 - 4.1%CV.

Table 2 - Precision (exemplary for the Lumipulse G1200)

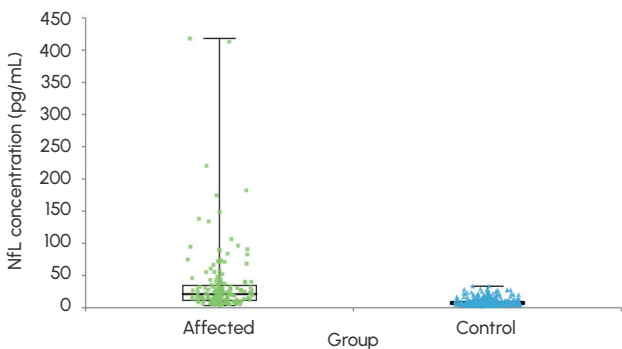
| Sample type | Mean    | Within run |     | Between run |     | Within day |     | Between day |     | Total imprecision |     |
|-------------|---------|------------|-----|-------------|-----|------------|-----|-------------|-----|-------------------|-----|
|             | pg/mL   | SD         | %CV | SD          | %CV | SD         | %CV | SD          | %CV | SD                | %CV |
| Serum       | 13.59   | 0.71       | 5.2 | 0.47        | 3.5 | 0.85       | 6.3 | 0.18        | 1.3 | 0.87              | 6.4 |
| Plasma      | 68.01   | 1.79       | 2.6 | 1.15        | 1.7 | 2.13       | 3.1 | 1.32        | 1.9 | 2.51              | 3.7 |
| Plasma      | 451.49  | 19.14      | 4.2 | 4.16        | 0.9 | 19.59      | 4.3 | 0.00        | 0.0 | 19.59             | 4.3 |
| Control*    | 16.27   | 0.49       | 3.0 | 0.00        | 0.0 | 0.49       | 3.0 | 0.18        | 1.1 | 0.52              | 3.2 |
| Control*    | 817.35  | 12.87      | 1.6 | 2.27        | 0.3 | 13.06      | 1.6 | 6.29        | 0.8 | 14.50             | 1.8 |
| Control*    | 1750.77 | 30.36      | 1.7 | 98.14       | 5.6 | 102.73     | 5.9 | 0.00        | 0.0 | 102.73            | 5.9 |

\* Buffer-based

Detection rate within the AMI

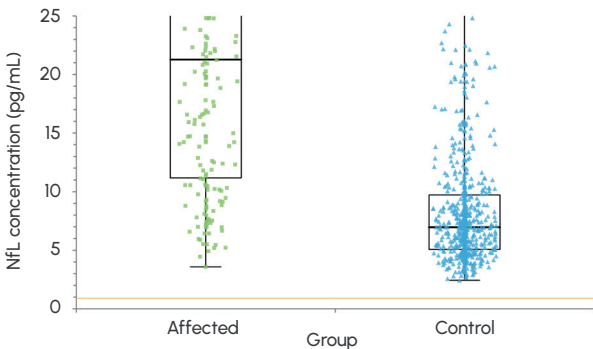
In total 858 individual serum samples from a hospital cohort consisting of 651 apparently healthy controls (18-86 years) with no evidence of underlying neuroaxonal damage and 207 affected samples from patients suffering from Alzheimer's disease, amyotrophic lateral sclerosis, frontotemporal dementia and multiple sclerosis have been measured (see Figure 1 and 2) using the Lumipulse G NFL (CE) assay. All these patients represent different forms, stages and/or phenotypes of the distinct disease. In this evaluation, the detection rate of the Lumipulse G NFL Blood (CE) assay within the analytical measuring interval (AMI) for these 858 samples was 100%.

Figure 1 – All measurement values of the hospital-based cohort



Median is plotted as a line, the 1st and 3rd quartile as a box, and the minimum and maximum as whiskers with end caps. Horizontal line in Figure 2 represents the LLOQ as defined at 20%CV.

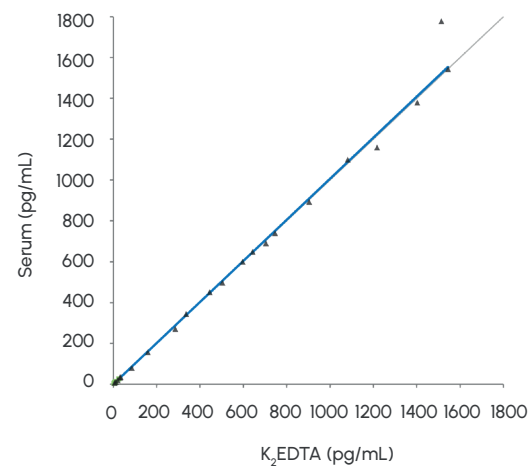
Figure 2 – Measurement values below 25 pg/mL



Sample matrix comparison

A total of 43 pairs of K<sub>2</sub>EDTA plasma and serum were selected to generate a correlation analysis between both specimens. Of these, 20 were native and 23 spiked with CSF to cover the full measuring range of 0.96 - 2500.00 pg/mL. To assess the alignment between plasma and serum measurements, a scatter plot was generated, and a weighted Deming regression was applied to it (see Table 3 and Figure 3). The results show a very high agreement between the two specimens.

Figure 3 – Sample matrix comparison



Weighted Deming regression analysis was performed to evaluate the correlation and agreement between serum and K<sub>2</sub>EDTA for the CE version of the NFL assay. Both native and CSF-spiked samples were used in the analysis. The grey line represents the line of identity with  $y = x$ , indicating that the two methods are in perfect agreement. The regression line is depicted in blue in the figure above, its equation and the correlation coefficient ( $r$ ) are shown in table 3.

**Table 3 - Correlation between K2EDTA plasma and serum**

| n  | Correlation Coefficient r (95% CI) | Intercept (95% CI) | Slope (95% CI)   |
|----|------------------------------------|--------------------|------------------|
| 43 | 0.996 (0.993;0.998)                | 0.00 (-0.34;0.33)  | 1.01 (0.98;1.03) |

CI = Confidence interval

## Age-related reference values

Reference ranges for serum NFL concentrations were established using leftover samples obtained from a hospital-based control population aged 18 to 86 years (n = 651, 370 females and 281 males). The cohort consisted of individuals without evidence of neuroaxonal damage, and subjects with renal insufficiency, extreme BMI values (< 18 kg/m<sup>2</sup> or > 35 kg/m<sup>2</sup>) or other relevant comorbidities were excluded to ensure an appropriate control dataset. Reference limits as lookup tables per age in years (Table 4), and the corresponding age-related reference curves by percentile and z-scores divided into three age groups were generated (Figure 4, 5 and 6). The statistical method is based on a generalized additive model for location, scale and shape (GAMLSS).

**Table 4 – Lookup table per age in years (NFL values in pg/mL)**

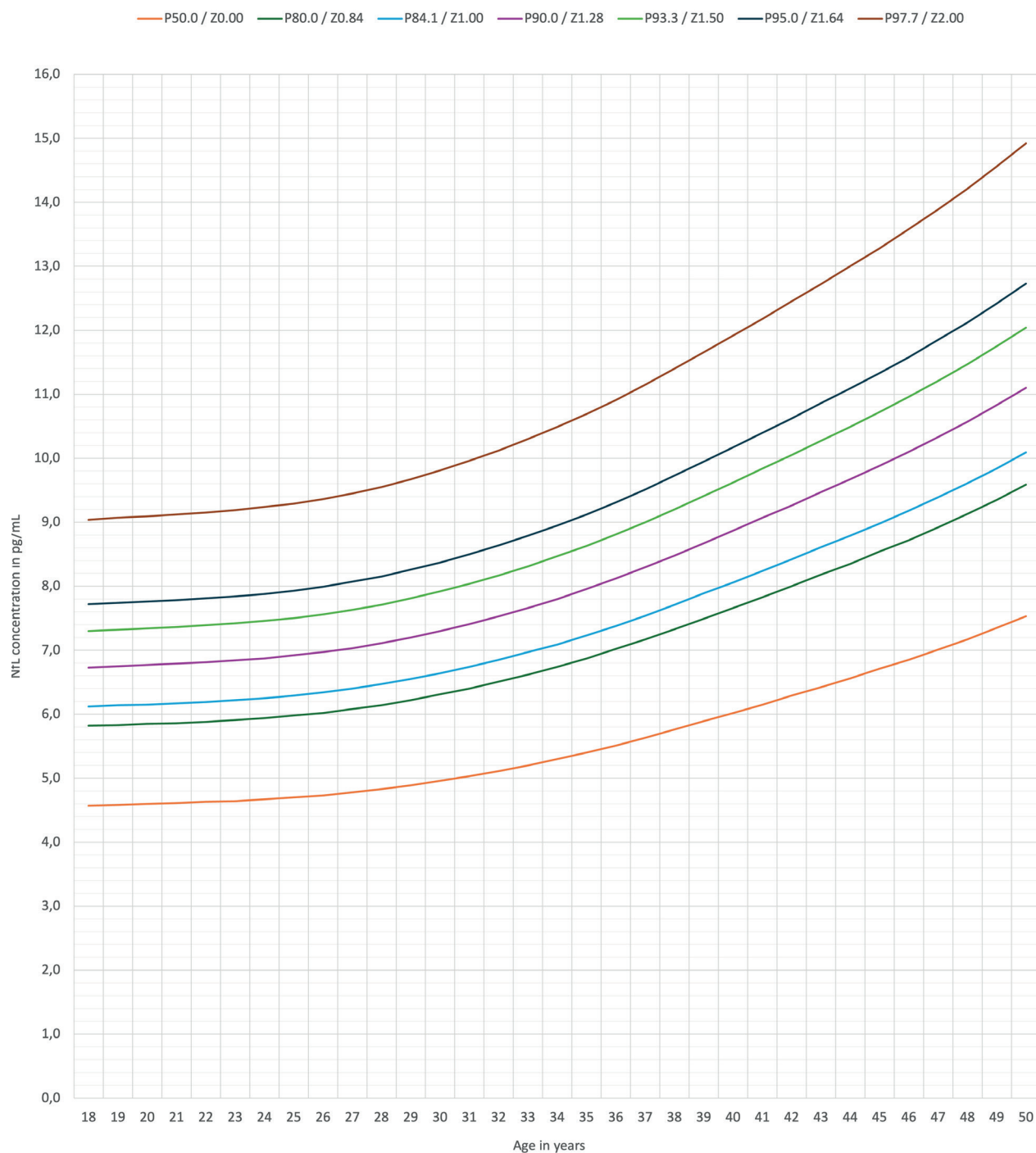
| Age in years | P50.0 / Z0.00               | P80.0 / Z0.84               | P84.1 / Z1.00               | P90.0 / Z1.28               | P93.3 / Z1.50               | P95.0 / Z1.64               | P97.7 / Z2.00                 |
|--------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-------------------------------|
| 18           | <b>4.57</b><br>[4.20, 4.98] | <b>5.82</b><br>[5.29, 6.37] | <b>6.12</b><br>[5.56, 6.72] | <b>6.73</b><br>[6.07, 7.45] | <b>7.30</b><br>[6.54, 8.14] | <b>7.72</b><br>[6.87, 8.66] | <b>9.04</b><br>[7.86, 10.43]  |
| 19           | <b>4.58</b><br>[4.25, 4.95] | <b>5.83</b><br>[5.36, 6.33] | <b>6.14</b><br>[5.62, 6.68] | <b>6.75</b><br>[6.14, 7.41] | <b>7.32</b><br>[6.60, 8.10] | <b>7.74</b><br>[6.94, 8.62] | <b>9.07</b><br>[7.94, 10.39]  |
| 20           | <b>4.60</b><br>[4.30, 4.93] | <b>5.85</b><br>[5.42, 6.30] | <b>6.15</b><br>[5.68, 6.66] | <b>6.77</b><br>[6.20, 7.37] | <b>7.34</b><br>[6.67, 8.07] | <b>7.76</b><br>[7.01, 8.58] | <b>9.09</b><br>[8.01, 10.38]  |
| 21           | <b>4.61</b><br>[4.35, 4.91] | <b>5.86</b><br>[5.47, 6.28] | <b>6.17</b><br>[5.74, 6.63] | <b>6.79</b><br>[6.27, 7.34] | <b>7.36</b><br>[6.74, 8.03] | <b>7.78</b><br>[7.07, 8.55] | <b>9.12</b><br>[8.08, 10.35]  |
| 22           | <b>4.63</b><br>[4.38, 4.89] | <b>5.88</b><br>[5.52, 6.26] | <b>6.19</b><br>[5.79, 6.61] | <b>6.81</b><br>[6.32, 7.33] | <b>7.39</b><br>[6.80, 8.02] | <b>7.81</b><br>[7.14, 8.54] | <b>9.15</b><br>[8.14, 10.35]  |
| 23           | <b>4.64</b><br>[4.42, 4.89] | <b>5.91</b><br>[5.57, 6.26] | <b>6.22</b><br>[5.84, 6.60] | <b>6.84</b><br>[6.38, 7.32] | <b>7.42</b><br>[6.86, 8.02] | <b>7.84</b><br>[7.20, 8.54] | <b>9.19</b><br>[8.20, 10.36]  |
| 24           | <b>4.67</b><br>[4.45, 4.90] | <b>5.94</b><br>[5.62, 6.26] | <b>6.25</b><br>[5.89, 6.61] | <b>6.87</b><br>[6.44, 7.33] | <b>7.46</b><br>[6.92, 8.03] | <b>7.88</b><br>[7.27, 8.55] | <b>9.24</b><br>[8.27, 10.37]  |
| 25           | <b>4.70</b><br>[4.49, 4.92] | <b>5.98</b><br>[5.67, 6.29] | <b>6.29</b><br>[5.95, 6.63] | <b>6.92</b><br>[6.49, 7.36] | <b>7.50</b><br>[6.98, 8.06] | <b>7.93</b><br>[7.33, 8.59] | <b>9.29</b><br>[8.33, 10.41]  |
| 26           | <b>4.73</b><br>[4.53, 4.95] | <b>6.02</b><br>[5.72, 6.32] | <b>6.34</b><br>[6.00, 6.67] | <b>6.97</b><br>[6.55, 7.39] | <b>7.56</b><br>[7.05, 8.10] | <b>7.99</b><br>[7.40, 8.64] | <b>9.36</b><br>[8.41, 10.47]  |
| 27           | <b>4.78</b><br>[4.57, 4.99] | <b>6.08</b><br>[5.78, 6.37] | <b>6.40</b><br>[6.06, 6.72] | <b>7.03</b><br>[6.62, 7.45] | <b>7.63</b><br>[7.12, 8.16] | <b>8.07</b><br>[7.48, 8.70] | <b>9.45</b><br>[8.50, 10.55]  |
| 28           | <b>4.83</b><br>[4.62, 5.04] | <b>6.14</b><br>[5.85, 6.44] | <b>6.47</b><br>[6.14, 6.79] | <b>7.11</b><br>[6.70, 7.53] | <b>7.71</b><br>[7.21, 8.24] | <b>8.15</b><br>[7.57, 8.79] | <b>9.55</b><br>[8.62, 10.63]  |
| 29           | <b>4.89</b><br>[4.68, 5.10] | <b>6.22</b><br>[5.92, 6.52] | <b>6.55</b><br>[6.22, 6.87] | <b>7.20</b><br>[6.79, 7.62] | <b>7.81</b><br>[7.31, 8.33] | <b>8.26</b><br>[7.67, 8.88] | <b>9.67</b><br>[8.73, 10.75]  |
| 30           | <b>4.96</b><br>[4.74, 5.17] | <b>6.31</b><br>[6.01, 6.61] | <b>6.64</b><br>[6.31, 6.97] | <b>7.30</b><br>[6.89, 7.72] | <b>7.92</b><br>[7.42, 8.44] | <b>8.37</b><br>[7.78, 8.99] | <b>9.81</b><br>[8.86, 10.88]  |
| 31           | <b>5.03</b><br>[4.82, 5.25] | <b>6.40</b><br>[6.10, 6.70] | <b>6.74</b><br>[6.41, 7.08] | <b>7.41</b><br>[7.00, 7.83] | <b>8.04</b><br>[7.53, 8.56] | <b>8.50</b><br>[7.91, 9.11] | <b>9.96</b><br>[9.01, 11.03]  |
| 32           | <b>5.11</b><br>[4.90, 5.33] | <b>6.51</b><br>[6.20, 6.81] | <b>6.85</b><br>[6.51, 7.19] | <b>7.53</b><br>[7.12, 7.96] | <b>8.17</b><br>[7.66, 8.69] | <b>8.64</b><br>[8.04, 9.25] | <b>10.12</b><br>[9.17, 11.19] |
| 33           | <b>5.20</b><br>[4.99, 5.42] | <b>6.62</b><br>[6.31, 6.93] | <b>6.97</b><br>[6.63, 7.31] | <b>7.66</b><br>[7.25, 8.09] | <b>8.31</b><br>[7.80, 8.83] | <b>8.79</b><br>[8.19, 9.39] | <b>10.30</b><br>[9.34, 11.35] |
| 34           | <b>5.30</b><br>[5.09, 5.51] | <b>6.74</b><br>[6.44, 7.05] | <b>7.09</b><br>[6.76, 7.43] | <b>7.80</b><br>[7.39, 8.23] | <b>8.47</b><br>[7.96, 8.99] | <b>8.95</b><br>[8.36, 9.56] | <b>10.49</b><br>[9.53, 11.53] |
| 35           | <b>5.40</b><br>[5.19, 5.62] | <b>6.87</b><br>[6.57, 7.18] | <b>7.23</b><br>[6.90, 7.57] | <b>7.96</b><br>[7.54, 8.38] | <b>8.63</b><br>[8.12, 9.15] | <b>9.12</b><br>[8.53, 9.73] | <b>10.69</b><br>[9.73, 11.74] |

| Age in years | P50.0 / Z0.00                  | P80.0 / Z0.84                  | P84.1 / Z1.00                  | P90.0 / Z1.28                  | P93.3 / Z1.50                  | P95.0 / Z1.64                  | P97.7 / Z2.00                  |
|--------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| 36           | <b>5.51</b><br>[5.31, 5.73]    | <b>7.02</b><br>[6.71, 7.32]    | <b>7.38</b><br>[7.04, 7.72]    | <b>8.12</b><br>[7.70, 8.54]    | <b>8.81</b><br>[8.30, 9.33]    | <b>9.31</b><br>[8.72, 9.92]    | <b>10.91</b><br>[9.94, 11.96]  |
| 37           | <b>5.63</b><br>[5.42, 5.85]    | <b>7.17</b><br>[6.86, 7.48]    | <b>7.54</b><br>[7.20, 7.88]    | <b>8.30</b><br>[7.87, 8.72]    | <b>9.00</b><br>[8.48, 9.52]    | <b>9.51</b><br>[8.91, 10.12]   | <b>11.15</b><br>[10.17, 12.19] |
| 38           | <b>5.76</b><br>[5.54, 5.97]    | <b>7.33</b><br>[7.01, 7.64]    | <b>7.71</b><br>[7.36, 8.05]    | <b>8.48</b><br>[8.05, 8.91]    | <b>9.20</b><br>[8.68, 9.73]    | <b>9.73</b><br>[9.12, 10.34]   | <b>11.40</b><br>[10.41, 12.44] |
| 39           | <b>5.89</b><br>[5.67, 6.11]    | <b>7.49</b><br>[7.17, 7.81]    | <b>7.89</b><br>[7.53, 8.24]    | <b>8.67</b><br>[8.24, 9.10]    | <b>9.41</b><br>[8.88, 9.94]    | <b>9.95</b><br>[9.33, 10.57]   | <b>11.66</b><br>[10.66, 12.70] |
| 40           | <b>6.02</b><br>[5.80, 6.24]    | <b>7.66</b><br>[7.34, 7.98]    | <b>8.06</b><br>[7.71, 8.41]    | <b>8.87</b><br>[8.43, 9.30]    | <b>9.62</b><br>[9.09, 10.15]   | <b>10.17</b><br>[9.54, 10.80]  | <b>11.92</b><br>[10.90, 12.98] |
| 41           | <b>6.15</b><br>[5.93, 6.37]    | <b>7.83</b><br>[7.51, 8.15]    | <b>8.24</b><br>[7.88, 8.59]    | <b>9.07</b><br>[8.63, 9.50]    | <b>9.84</b><br>[9.30, 10.37]   | <b>10.40</b><br>[9.76, 11.03]  | <b>12.18</b><br>[11.14, 13.25] |
| 42           | <b>6.29</b><br>[6.06, 6.51]    | <b>8.00</b><br>[7.68, 8.32]    | <b>8.42</b><br>[8.06, 8.77]    | <b>9.26</b><br>[8.82, 9.70]    | <b>10.05</b><br>[9.50, 10.59]  | <b>10.62</b><br>[9.99, 11.26]  | <b>12.45</b><br>[11.40, 13.53] |
| 43           | <b>6.42</b><br>[6.20, 6.65]    | <b>8.18</b><br>[7.85, 8.49]    | <b>8.61</b><br>[8.24, 8.96]    | <b>9.47</b><br>[9.02, 9.91]    | <b>10.27</b><br>[9.72, 10.81]  | <b>10.86</b><br>[10.21, 11.49] | <b>12.72</b><br>[11.66, 13.81] |
| 44           | <b>6.56</b><br>[6.34, 6.79]    | <b>8.35</b><br>[8.02, 8.68]    | <b>8.79</b><br>[8.43, 9.16]    | <b>9.67</b><br>[9.22, 10.11]   | <b>10.49</b><br>[9.93, 11.04]  | <b>11.09</b><br>[10.43, 11.74] | <b>13.00</b><br>[11.91, 14.11] |
| 45           | <b>6.71</b><br>[6.48, 6.93]    | <b>8.54</b><br>[8.20, 8.87]    | <b>8.98</b><br>[8.61, 9.35]    | <b>9.88</b><br>[9.42, 10.33]   | <b>10.72</b><br>[10.15, 11.28] | <b>11.33</b><br>[10.67, 12.00] | <b>13.28</b><br>[12.17, 14.43] |
| 46           | <b>6.85</b><br>[6.62, 7.09]    | <b>8.72</b><br>[8.38, 9.06]    | <b>9.18</b><br>[8.80, 9.56]    | <b>10.10</b><br>[9.63, 10.57]  | <b>10.96</b><br>[10.37, 11.54] | <b>11.58</b><br>[10.90, 12.26] | <b>13.58</b><br>[12.44, 14.75] |
| 47           | <b>7.01</b><br>[6.78, 7.24]    | <b>8.92</b><br>[8.57, 9.27]    | <b>9.39</b><br>[9.00, 9.78]    | <b>10.33</b><br>[9.84, 10.81]  | <b>11.21</b><br>[10.61, 11.80] | <b>11.85</b><br>[11.14, 12.55] | <b>13.89</b><br>[12.72, 15.09] |
| 48           | <b>7.17</b><br>[6.94, 7.41]    | <b>9.13</b><br>[8.78, 9.49]    | <b>9.61</b><br>[9.21, 10.00]   | <b>10.57</b><br>[10.07, 11.07] | <b>11.47</b><br>[10.85, 12.09] | <b>12.12</b><br>[11.40, 12.85] | <b>14.21</b><br>[13.01, 15.44] |
| 49           | <b>7.35</b><br>[7.11, 7.59]    | <b>9.35</b><br>[8.99, 9.72]    | <b>9.84</b><br>[9.43, 10.25]   | <b>10.83</b><br>[10.31, 11.34] | <b>11.75</b><br>[11.11, 12.39] | <b>12.42</b><br>[11.67, 13.17] | <b>14.56</b><br>[13.32, 15.82] |
| 50           | <b>7.53</b><br>[7.28, 7.79]    | <b>9.59</b><br>[9.21, 9.97]    | <b>10.09</b><br>[9.67, 10.52]  | <b>11.10</b><br>[10.57, 11.64] | <b>12.04</b><br>[11.38, 12.71] | <b>12.73</b><br>[11.95, 13.51] | <b>14.92</b><br>[13.66, 16.23] |
| 51           | <b>7.73</b><br>[7.47, 7.99]    | <b>9.84</b><br>[9.44, 10.24]   | <b>10.35</b><br>[9.91, 10.80]  | <b>11.39</b><br>[10.83, 11.95] | <b>12.36</b><br>[11.67, 13.05] | <b>13.06</b><br>[12.26, 13.87] | <b>15.31</b><br>[14.00, 16.66] |
| 52           | <b>7.94</b><br>[7.68, 8.21]    | <b>10.10</b><br>[9.69, 10.53]  | <b>10.63</b><br>[10.17, 11.10] | <b>11.70</b><br>[11.12, 12.28] | <b>12.69</b><br>[11.98, 13.41] | <b>13.42</b><br>[12.59, 14.25] | <b>15.73</b><br>[14.37, 17.12] |
| 53           | <b>8.16</b><br>[7.89, 8.44]    | <b>10.38</b><br>[9.95, 10.83]  | <b>10.93</b><br>[10.44, 11.42] | <b>12.02</b><br>[11.42, 12.64] | <b>13.05</b><br>[12.30, 13.80] | <b>13.79</b><br>[12.92, 14.66] | <b>16.17</b><br>[14.78, 17.60] |
| 54           | <b>8.39</b><br>[8.11, 8.69]    | <b>10.68</b><br>[10.23, 11.14] | <b>11.24</b><br>[10.73, 11.76] | <b>12.37</b><br>[11.73, 13.01] | <b>13.42</b><br>[12.64, 14.21] | <b>14.19</b><br>[13.28, 15.10] | <b>16.63</b><br>[15.19, 18.13] |
| 55           | <b>8.64</b><br>[8.34, 8.95]    | <b>11.00</b><br>[10.52, 11.48] | <b>11.57</b><br>[11.04, 12.12] | <b>12.73</b><br>[12.06, 13.41] | <b>13.82</b><br>[13.00, 14.64] | <b>14.60</b><br>[13.66, 15.57] | <b>17.12</b><br>[15.62, 18.69] |
| 56           | <b>8.90</b><br>[8.58, 9.23]    | <b>11.33</b><br>[10.82, 11.85] | <b>11.92</b><br>[11.36, 12.50] | <b>13.12</b><br>[12.41, 13.83] | <b>14.23</b><br>[13.37, 15.11] | <b>15.04</b><br>[14.06, 16.05] | <b>17.64</b><br>[16.06, 19.29] |
| 57           | <b>9.17</b><br>[8.84, 9.52]    | <b>11.68</b><br>[11.14, 12.23] | <b>12.29</b><br>[11.69, 12.90] | <b>13.52</b><br>[12.78, 14.28] | <b>14.67</b><br>[13.76, 15.59] | <b>15.51</b><br>[14.47, 16.56] | <b>18.18</b><br>[16.54, 19.91] |
| 58           | <b>9.46</b><br>[9.12, 9.83]    | <b>12.05</b><br>[11.48, 12.63] | <b>12.68</b><br>[12.05, 13.32] | <b>13.95</b><br>[13.16, 14.75] | <b>15.14</b><br>[14.18, 16.10] | <b>16.00</b><br>[14.91, 17.11] | <b>18.76</b><br>[17.05, 20.56] |
| 59           | <b>9.77</b><br>[9.40, 10.16]   | <b>12.44</b><br>[11.83, 13.05] | <b>13.09</b><br>[12.42, 13.77] | <b>14.40</b><br>[13.58, 15.24] | <b>15.62</b><br>[14.62, 16.64] | <b>16.52</b><br>[15.37, 17.69] | <b>19.36</b><br>[17.58, 21.28] |
| 60           | <b>10.09</b><br>[9.70, 10.51]  | <b>12.84</b><br>[12.21, 13.49] | <b>13.52</b><br>[12.80, 14.24] | <b>14.87</b><br>[14.00, 15.76] | <b>16.14</b><br>[15.08, 17.22] | <b>17.06</b><br>[15.84, 18.29] | <b>20.00</b><br>[18.15, 22.02] |
| 61           | <b>10.42</b><br>[10.01, 10.86] | <b>13.27</b><br>[12.60, 13.96] | <b>13.96</b><br>[13.21, 14.72] | <b>15.36</b><br>[14.44, 16.31] | <b>16.67</b><br>[15.56, 17.80] | <b>17.62</b><br>[16.35, 18.93] | <b>20.66</b><br>[18.72, 22.79] |
| 62           | <b>10.77</b><br>[10.34, 11.23] | <b>13.71</b><br>[13.00, 14.44] | <b>14.43</b><br>[13.64, 15.23] | <b>15.87</b><br>[14.90, 16.87] | <b>17.22</b><br>[16.05, 18.42] | <b>18.21</b><br>[16.87, 19.59] | <b>21.34</b><br>[19.31, 23.59] |

| Age in years | P50.0 / Z0.00                  | P80.0 / Z0.84                  | P84.1 / Z1.00                  | P90.0 / Z1.28                  | P93.3 / Z1.50                  | P95.0 / Z1.64                  | P97.7 / Z2.00                  |
|--------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| 63           | <b>11.13</b><br>[10.67, 11.61] | <b>14.16</b><br>[13.42, 14.93] | <b>14.91</b><br>[14.08, 15.75] | <b>16.40</b><br>[15.39, 17.46] | <b>17.80</b><br>[16.57, 19.06] | <b>18.81</b><br>[17.41, 20.26] | <b>22.06</b><br>[19.93, 24.41] |
| 64           | <b>11.50</b><br>[11.02, 12.01] | <b>14.64</b><br>[13.86, 15.44] | <b>15.40</b><br>[14.53, 16.29] | <b>16.95</b><br>[15.88, 18.05] | <b>18.39</b><br>[17.10, 19.73] | <b>19.44</b><br>[17.97, 20.97] | <b>22.79</b><br>[20.56, 25.24] |
| 65           | <b>11.88</b><br>[11.37, 12.41] | <b>15.12</b><br>[14.31, 15.97] | <b>15.92</b><br>[15.00, 16.85] | <b>17.51</b><br>[16.39, 18.66] | <b>19.00</b><br>[17.65, 20.40] | <b>20.09</b><br>[18.56, 21.71] | <b>23.55</b><br>[21.21, 26.12] |
| 66           | <b>12.27</b><br>[11.73, 12.82] | <b>15.62</b><br>[14.77, 16.50] | <b>16.44</b><br>[15.48, 17.42] | <b>18.09</b><br>[16.92, 19.30] | <b>19.63</b><br>[18.22, 21.09] | <b>20.75</b><br>[19.14, 22.45] | <b>24.33</b><br>[21.88, 27.01] |
| 67           | <b>12.67</b><br>[12.11, 13.24] | <b>16.13</b><br>[15.24, 17.05] | <b>16.98</b><br>[15.98, 18.00] | <b>18.68</b><br>[17.45, 19.94] | <b>20.27</b><br>[18.79, 21.81] | <b>21.43</b><br>[19.73, 23.22] | <b>25.12</b><br>[22.56, 27.93] |
| 68           | <b>13.08</b><br>[12.49, 13.68] | <b>16.65</b><br>[15.72, 17.62] | <b>17.53</b><br>[16.48, 18.60] | <b>19.29</b><br>[18.01, 20.60] | <b>20.93</b><br>[19.37, 22.54] | <b>22.12</b><br>[20.35, 24.00] | <b>25.94</b><br>[23.25, 28.89] |
| 69           | <b>13.50</b><br>[12.88, 14.13] | <b>17.19</b><br>[16.22, 18.19] | <b>18.09</b><br>[17.00, 19.22] | <b>19.90</b><br>[18.56, 21.29] | <b>21.60</b><br>[19.97, 23.29] | <b>22.83</b><br>[20.98, 24.81] | <b>26.77</b><br>[23.97, 29.85] |
| 70           | <b>13.92</b><br>[13.27, 14.58] | <b>17.73</b><br>[16.71, 18.79] | <b>18.66</b><br>[17.52, 19.84] | <b>20.53</b><br>[19.12, 21.99] | <b>22.28</b><br>[20.57, 24.05] | <b>23.55</b><br>[21.61, 25.62] | <b>27.61</b><br>[24.70, 30.85] |
| 71           | <b>14.35</b><br>[13.67, 15.04] | <b>18.28</b><br>[17.21, 19.39] | <b>19.24</b><br>[18.05, 20.47] | <b>21.17</b><br>[19.70, 22.69] | <b>22.97</b><br>[21.19, 24.83] | <b>24.28</b><br>[22.25, 26.45] | <b>28.47</b><br>[25.43, 31.85] |
| 72           | <b>14.79</b><br>[14.07, 15.52] | <b>18.83</b><br>[17.72, 19.98] | <b>19.82</b><br>[18.59, 21.11] | <b>21.81</b><br>[20.28, 23.41] | <b>23.67</b><br>[21.81, 25.63] | <b>25.02</b><br>[22.90, 27.30] | <b>29.34</b><br>[26.15, 32.89] |
| 73           | <b>15.23</b><br>[14.47, 15.99] | <b>19.40</b><br>[18.24, 20.61] | <b>20.42</b><br>[19.13, 21.76] | <b>22.46</b><br>[20.87, 24.14] | <b>24.38</b><br>[22.44, 26.44] | <b>25.77</b><br>[23.56, 28.16] | <b>30.22</b><br>[26.90, 33.93] |
| 74           | <b>15.68</b><br>[14.88, 16.48] | <b>19.97</b><br>[18.76, 21.22] | <b>21.01</b><br>[19.67, 22.43] | <b>23.12</b><br>[21.46, 24.89] | <b>25.09</b><br>[23.06, 27.25] | <b>26.53</b><br>[24.21, 29.03] | <b>31.10</b><br>[27.66, 35.01] |
| 75           | <b>16.13</b><br>[15.28, 16.98] | <b>20.54</b><br>[19.28, 21.85] | <b>21.62</b><br>[20.21, 23.10] | <b>23.79</b><br>[22.04, 25.63] | <b>25.81</b><br>[23.69, 28.08] | <b>27.29</b><br>[24.87, 29.91] | <b>32.00</b><br>[28.40, 36.09] |
| 76           | <b>16.58</b><br>[15.69, 17.47] | <b>21.11</b><br>[19.79, 22.48] | <b>22.22</b><br>[20.76, 23.77] | <b>24.46</b><br>[22.63, 26.39] | <b>26.54</b><br>[24.33, 28.91] | <b>28.06</b><br>[25.54, 30.79] | <b>32.90</b><br>[29.15, 37.18] |
| 77           | <b>17.04</b><br>[16.10, 17.96] | <b>21.69</b><br>[20.32, 23.13] | <b>22.83</b><br>[21.30, 24.45] | <b>25.13</b><br>[23.22, 27.17] | <b>27.26</b><br>[24.97, 29.75] | <b>28.82</b><br>[26.20, 31.68] | <b>33.80</b><br>[29.91, 38.30] |
| 78           | <b>17.49</b><br>[16.51, 18.46] | <b>22.27</b><br>[20.83, 23.77] | <b>23.44</b><br>[21.84, 25.14] | <b>25.80</b><br>[23.81, 27.93] | <b>27.99</b><br>[25.58, 30.60] | <b>29.59</b><br>[26.86, 32.58] | <b>34.70</b><br>[30.63, 39.43] |
| 79           | <b>17.94</b><br>[16.91, 18.95] | <b>22.85</b><br>[21.34, 24.41] | <b>24.05</b><br>[22.38, 25.83] | <b>26.47</b><br>[24.39, 28.69] | <b>28.72</b><br>[26.21, 31.45] | <b>30.36</b><br>[27.50, 33.49] | <b>35.61</b><br>[31.34, 40.54] |
| 80           | <b>18.40</b><br>[17.32, 19.45] | <b>23.43</b><br>[21.86, 25.06] | <b>24.66</b><br>[22.92, 26.51] | <b>27.14</b><br>[24.97, 29.46] | <b>29.45</b><br>[26.83, 32.30] | <b>31.13</b><br>[28.16, 34.41] | <b>36.51</b><br>[32.09, 41.65] |
| 81           | <b>18.85</b><br>[17.73, 19.95] | <b>24.01</b><br>[22.36, 25.71] | <b>25.27</b><br>[23.46, 27.19] | <b>27.81</b><br>[25.54, 30.24] | <b>30.18</b><br>[27.45, 33.14] | <b>31.90</b><br>[28.80, 35.33] | <b>37.41</b><br>[32.81, 42.81] |
| 82           | <b>19.30</b><br>[18.13, 20.45] | <b>24.59</b><br>[22.88, 26.36] | <b>25.88</b><br>[23.98, 27.88] | <b>28.48</b><br>[26.12, 31.02] | <b>30.90</b><br>[28.07, 34.00] | <b>32.67</b><br>[29.45, 36.24] | <b>38.31</b><br>[33.54, 43.94] |
| 83           | <b>19.76</b><br>[18.53, 20.96] | <b>25.16</b><br>[23.39, 27.02] | <b>26.49</b><br>[24.51, 28.58] | <b>29.15</b><br>[26.69, 31.79] | <b>31.63</b><br>[28.68, 34.85] | <b>33.44</b><br>[30.09, 37.17] | <b>39.21</b><br>[34.26, 45.11] |
| 84           | <b>20.21</b><br>[18.93, 21.47] | <b>25.74</b><br>[23.89, 27.68] | <b>27.09</b><br>[25.04, 29.28] | <b>29.81</b><br>[27.27, 32.56] | <b>32.35</b><br>[29.28, 35.72] | <b>34.21</b><br>[30.72, 38.10] | <b>40.11</b><br>[34.95, 46.26] |
| 85           | <b>20.66</b><br>[19.32, 21.97] | <b>26.31</b><br>[24.40, 28.33] | <b>27.70</b><br>[25.56, 29.98] | <b>30.48</b><br>[27.84, 33.34] | <b>33.08</b><br>[29.89, 36.58] | <b>34.97</b><br>[31.36, 39.05] | <b>41.01</b><br>[35.68, 47.44] |
| 86           | <b>21.11</b><br>[19.72, 22.48] | <b>26.89</b><br>[24.90, 28.97] | <b>28.31</b><br>[26.09, 30.67] | <b>31.15</b><br>[28.42, 34.12] | <b>33.80</b><br>[30.49, 37.45] | <b>35.74</b><br>[32.00, 39.99] | <b>41.91</b><br>[36.38, 48.63] |

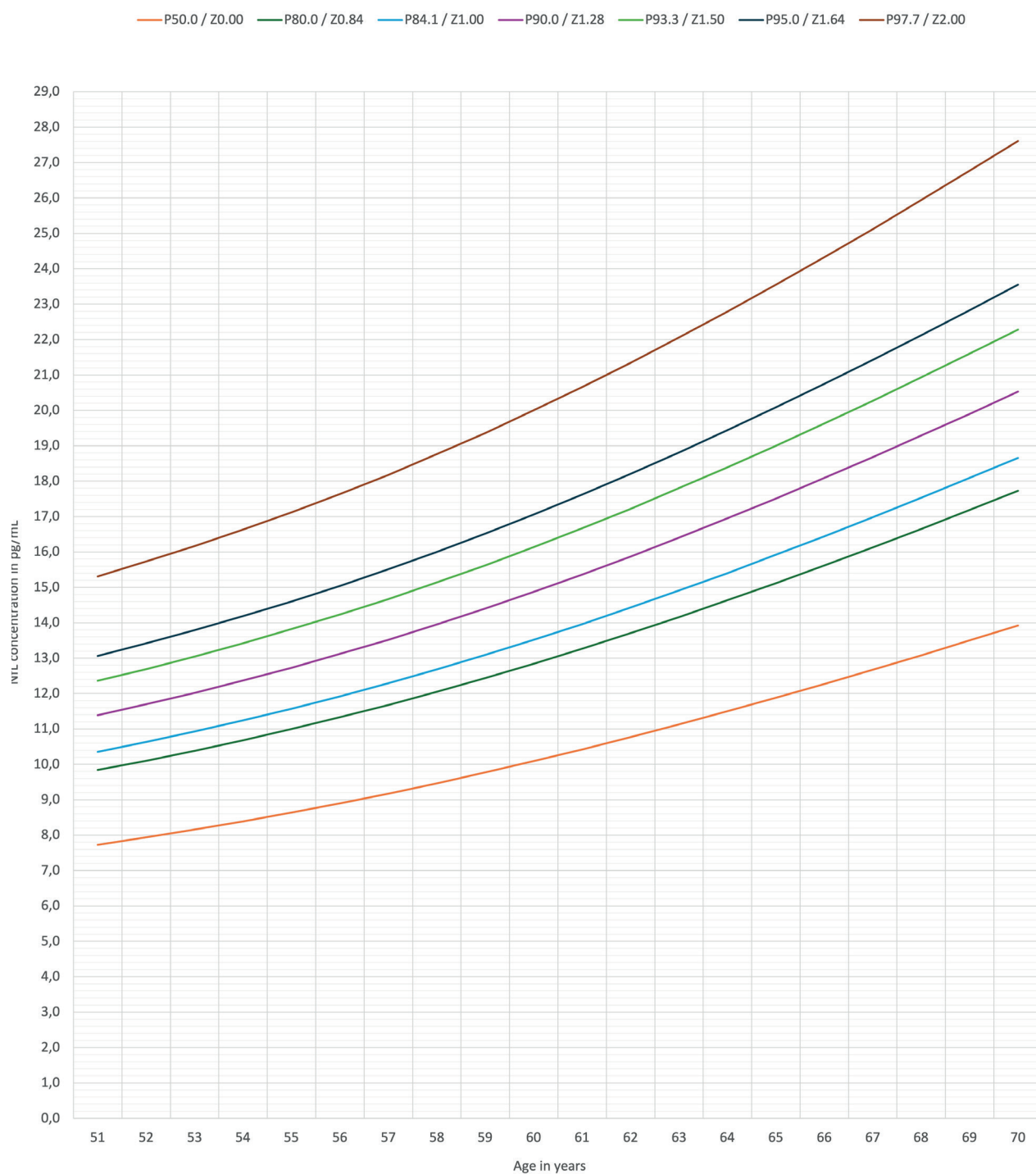
P = percentile; Z = z-score; for example: P0.80 means 80<sup>th</sup> percentile and Z0.84 means z-score of 0.84; in brackets [] 95% confidence interval.

Figure 4 – Reference curves (age group 18-50 years)



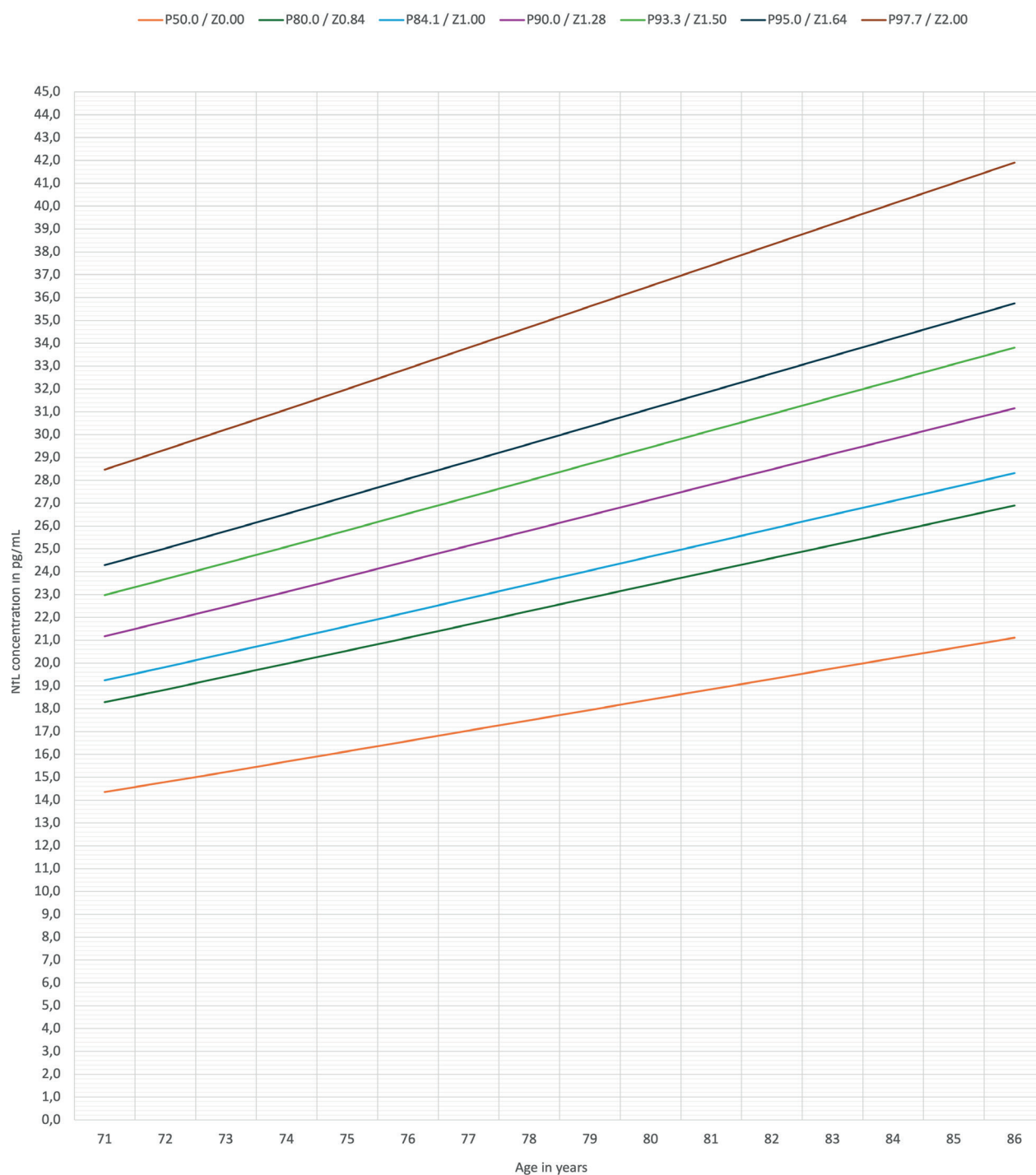
P = percentile; Z = z-score

Figure 5 –Reference curves (age group 51-70 years)



P = percentile; Z = z-score

Figure 6 – Reference curves (age group 71-86 years)



P = percentile; Z = z-score

