**Testing Neurofilament Light (NF-L) chain in blood samples to monitor neurodegenerative diseases and support clinical drug development: qualification of an ultrasensitive immuno-assay using clinical serum and plasma samples**

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**Background** NF-L has been recently reported as a potential biomarker of neuronal damage in numerous neuroinflammatory disorders, including Alzheimer’s disease (AD) [1], multiple sclerosis (MS) [2] or traumatic brain injury (TBI) [3]. Furthermore, NF-L levels in cerebrospinal fluid and blood have been reported as normalized following effective MS therapy [4]. In that context, we aimed at assessing the performance of an ultrasensitive method to quantify NF-L in human serum or plasma and evaluating its routine use to support clinical drug development.

**Material and Methods** Trueness, precision, parallelism, dilution linearity and lower limit of quantification (LLOQ) of the Simoa kit (QuanterixTM) have been assessed in serum and plasma samples from healthy donors and patients with neuroinflammatory disorders.

**Results** Dosing endogenous NF-L levels demonstrated good precision of the method, when tested at the minimal required dilution with intra- and inter-run variability ranging from respectively 1.6% and 19.9% and 5.2 and 19.9% depending on the concentration level. The parallelism study shows that test samples can be serially diluted without impacting measured NFL concentration. Finally, based on these results, LLOQ could be set at 0.6 pg/mL in diluted blood matrix. Finally, levels of endogenous NF-L measured from 10 healthy donors did not differ significantly between paired serum (4.8-13.9 pg/mL) and plasma (4.4-10.9 pg/mL).

**Discussion** Our results related to high performance and sensitivity of the Simoa-based method to dose NF-L are in accordance with recent data [5], strengthening the benefit to dose circulating NF-L in clinical samples using this technology.

**Conclusions** NF-L is now ready to be tested with accuracy and high sensitivity in both human serum and plasma samples. As these matrices are easy to collect and store frozen in the context of clinical trials, NF-L testing can now support clinical drug development in many neurodegenerative pathologies, either in prospective or retrospective settings.

**References**

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