INTRODUCTION

N-methyl-D-aspartate receptors (NMDAR) are ligand-gated cation channels, which are crucial in synaptic transmission and plasticity. In the Central Nervous System, NMDARs are one of the main excitatory receptors on synapses of neurons, which regulate balance between neuronal inhibition and excitation. In the brain, NMDARs have involvement in neuroplasticity, neu- rotoxicity, and excitotoxic neurodegeneration. Structurally, NMDAR is mostly triheteromeric, comprising GluN1, GIuN2A and GluN2B subunits (Figure 1). NMDAR antibodies are associated with autoimmune diseases, such as anti-NMDAR encephalitis and systemic lupus erythematosus (SLE). In Autoimmune Encephalitis (AE), NMDAR antibodies against NR1, NR2A and NR2B subunits are overproduced, causing neurotransmitter dysregulation, resulting in seizures and other symptoms including psychosis, head- aches, hallucinations, changes in mental status, dysautonomia, and orofacial dyskinesia. NMDAR antibodies are suspected where AE has no known infectious cause (viruses such as herpes simplex or varicella zoster are main cause of encephalitis). Commercially available indirect immunofluorescence (IF) assays use either brain tissue (hippocampus or cerebellum) or monospecific cells (the HEK cell line is transfected with the NMDAR NR1 receptor). The cerebellum, the stratum graminum fluoresces, in the hippocampus, fluorescence of the stratum molecular (neuropil staining) is observed in NMDAR antibody positive samples.

AIMS AND OBJECTIVES

• To determine the level of interest and feasibility of developing a pilot UK NEQAS EQA scheme for NMDAR antibodies.
• To gather information from participants currently providing NMDAR antibody testing to aid scheme design.
• To set up an EQA scheme for NMDAR antibodies, in addition to the existing neuroimmunology EQA schemes offered by the Centre (Paraneoplastic Antibodies, Ganglioside Antibodies, and Myelin Associated Glycoprotein IgM Antibodies (MAG)).

METHOD

UK NEQAS IIA sent out a survey to participants in February 2020 to gather information from laboratories who were providing testing for NMDAR antibodies. This was to assess the level of interest in a new NMDAR antibody scheme, and to determine key scheme requirements (such as sample volume and frequency of testing). Positive and negative samples were also sourced. Unfortunately the COVID-19 pandemic meant we had to delay the development of this scheme to 2022.

RESULTS

86 participants responded to the survey. 66 (77%) respondents stated that they offered a service for NMDAR antibody testing, 50/63 labs (79%) preferred to measure NMDAR antibodies in serum (Figure 3). 61/63 (97%) of laboratories surveyed also measure NMDAR antibodies in Cerebrospinal Fluid (CSF) samples.

Most respondents (42/63; 67%) required a sample volume of 0.3 mL or less (Figure 4). 37/63 labs (59%) were not participating in a sample exchange scheme for NMDAR antibodies. 25/57 (44%) of laboratories surveyed would be willing to provide samples for use within the pilot EQA scheme, to help ensure EQA scheme continuity.