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Dear Colleagues,

**Re: Changing of testing strategy for investigations into voltage-gated potassium channel complex antibodies**

Recent data have shown that the VGKC-antibodies consists of three categories of antibodies, which target.

1. LGI1
2. CASPR2, and
3. Neither target (“double-negative” antibodies).

The antibodies against LGI1 and CASPR2 are found highly specifically in patients with immunotherapy responsive syndromes. They target the extracellular domains of the proteins, and hence can be pathogenic.<sup>1</sup>

The double negative antibodies associate with a range of heterogenous diseases usually without a clear autoimmune basis, and occur at about a 5% rate in the healthy population. They appear to target non-neuronal proteins and the intracellular aspects of neuronal proteins, and are hence unlikely to be causative.<sup>2,3</sup>

To adapt our service to these findings, from the 1st July 2017, our new policy will be to reflexively test all VGKC-complex antibody samples above 70 pM for LGI1 and CASPR2 reactivity, and return this as a set of additional results. These additional tests will be charged for. If any centre wishes to not receive reflex LGI1/CASPR2 testing on their positive/equivocal VGKC-complex antibody samples, they should proactively state this clearly on all request cards to avoid reflexive testing.

The aim is to ensure high specificity, whilst maintaining the same degree of sensitivity, and particularly to help prevent patients without autoimmune diseases receiving immunotherapies on the basis of a double-negative result.

If you have any queries regarding this change to our neuroimmunology service, please do not hesitate to contact us directly on the numbers provided above.

Kind regards

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#### References

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