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UK NEQAS for Paraneoplastic Antibodies

Distribution : 184	**August 2018**	**Participant : 94317**

130 out of 151 participants returned data for this distribution. 86% response rate.

Nil Responses

14228C, 14398, 14513, 14513A, 14805, 14866, 14888, 92354, 94027, 94109, NOKLUS, YVSOLAB, ORG, BIOG, INFO, CODEX, TVN, SEQC, VAR, ORG_G, ORG_A

Sample 184-1 was a sample from a patient with positive neurological glutamic acid decarboxylase (GAD) antibodies.

Sample 184-2 was a sample from a patient with positive ANNA -1 (Hu) paraneoplastic antibodies.

Sample	Analyte	Designated Response	Your Response	Score
184-1	Paraneoplastic Antibody	Positive	Positive	0
	Antibody Identification	GAD - Neurological	GAD - Neurological	0

Sample	Analyte	Designated Response	Your Response	Score	OMIS
184-2	Paraneoplastic Antibody	Positive	Positive	0	0
	Antibody Identification	ANNA-1 (HU)	ANNA-1 (HU)	0	0
The current window of analysis comprises the previous six distributions			**Total MIS**		0

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Comments

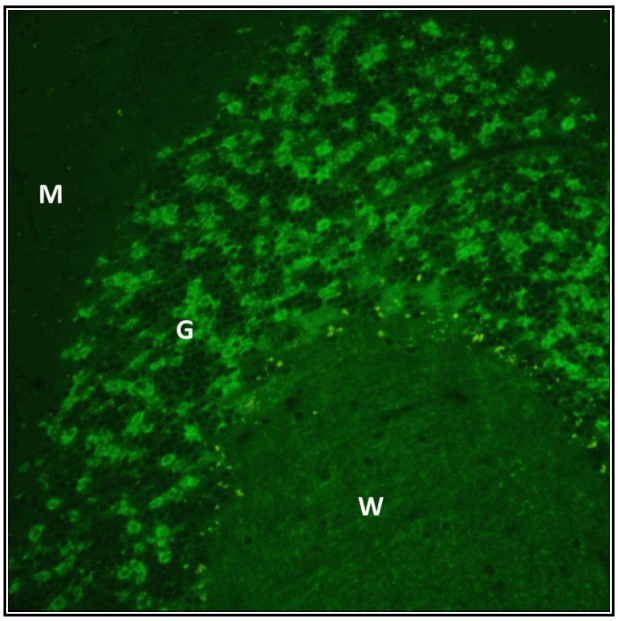
Sample 184-1:
82/130 laboratories reported sample 184-1 as positive for paraneoplastic antibodies. This sample was from a patient with positive neurological glutamic acid decarboxylase (GAD) antibodies. 82 participants selected GAD for antibody identification. 54 laboratories reported glutamic acid decarboxylase (GAD) antibody positive for sample 184-1 by primary screening testing and 78 participants correctly identified GAD antibody by secondary testing methods.

Sample 184-1 will not be subjected to misclassification scoring as not all participants in the Paraneoplastic Antibodies Scheme include GAD antibody in their testing profile.

GAD is an enzyme responsible for the conversion of glutamic acid to gamma-aminobutyric acid (GABA which is a major inhibitory neurotransmitter in the brain) and putative paracrine hormone in pancreatic islets. There are two isoforms of GAD (65 kDa and 67 kDa) with 64% sequence homology and both forms are expressed in the CNS, pancreatic islet cells (GAD65 > GAD67), testis, oviduct and ovary.
Anti-GAD antibodies are found in the serum and CSF of patients with stiff person's syndrome (SPS) and diabetes. GAD65 is associated with diabetes and GAD67 is associated with SPS. Usually, there is no underlying cancer in the majority of patients with GAD antibodies but isolated cases of breast, colonic and SCLC have been reported. In addition to SPS, other neurological disorders associated with GAD antibodies include diffused hypertonia , cerebellar ataxia, epilepsy and myoclonus.

Immunofluorescence staining:
On primate cerebellum, anti-GAD staining can be visualised in the granular layer (G); the neuronal nuclei of the granular cells are spared with immunoreactivity confined to peripheral GABA-ergic terminals of the cerebellar glomeruli.
The figure below shows immunofluorescence staining produced by GAD antibodies. As you can see, there is patchy staining of neuropil in the granular layer (nerve terminals). For orientation purposes, the Purkinje cell can be found on the border of the molecular layer (M) and granular layer (G).

Sample 184-2:
124/130 laboratories reported sample 184-2 as positive for paraneoplastic antibodies. Sample 184-2 should have reacted with cerebellar structures to produce a pattern that is typical of ANNA-1 (Hu) antibody. 90 participants identified the pattern as ANNA-1 (Hu) by primary screening. 115 laboratories confirmed the sample as ANNA-1 (Hu) positive by immunoblot.



The Total Misclassification scoring **(MIS)** system for the **qualitative** element of the scheme gives an indication of the number of instances where a laboratory's response is at variance with that defined for each specimen in a window of **six** distributions.

A panel of reference laboratories (10656, 10702, 11185, 14477, 14480) were in agreement in providing the target responses.

Laboratories have been given misclassification score (MIS) for each sample where they are at variance with the target response. The overall misclassification score (OMIS) now includes a running window of 12 samples over 12 months.

The categories of performance are:

	Total MIS
Good	Zero
Adequate	1-3
Poor	> 3

For further performance criteria information please see our website at http://www.immqas.org.uk.

If laboratories require further assistance please contact the centre.

Summary Page for Sample 184-1

Analyte	Positive	Negative	Referred
PARANEOPLASTIC ANTIBODIES	82	43	5
		Total Responses	130
		Correct Response	63 %

Antibody Identification	Returns
NEG	42
ANNA-1 (HU)	1
GAD - Neurological	82
Total Responses	125
Correct Response	66 %

Primary Testing	
Analyte	**Returns**
Anna-1 (Hu)	2
GAD - Neurological	54
Other	2
Screen Only	2
NEGATIVE	33
Total Responses	93

Secondary Testing	
Analyte	**Returns**
Anna-1 (Hu)	1
GAD - Neurological	78
Other	1
NEGATIVE	36
Total Responses	116

Your Results for Sample 184-1

Analyte	Positive	Negative	Referred
PARANEOPLASTIC ANTIBODIES	True	False	False
ANTIBODY IDENTIFICATION	GAD - Neurological		

Your Primary Results for Sample 184-1

Analyte	Positive	Negative	Method	Substrate	Manufacturer	Dilution
Anna-1 (Hu)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
Anna-2 (Ri)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
PCA-1 (Yo)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
CRMP5 (CV2)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
AMPHIPHYSIN	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
Ma-2 (Ta)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
GAD - Neurological	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
Other	False	False				
Screen Only	False	False				

Summary of Results for Sample 184-1 - PRIMARY TESTING

Indirect Immunofluorescence

SUBSTRATE	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative	Positive Screen Only	Negative Screen Only
Monkey Cerebellum	**2**	**0**	**0**	**0**	**0**	**0**	**47**	**2**	**29**	**2**	**0**
Euroimmun	1	0	0	0	0	0	25	0	8	0	0
Trinity Biotech (Immco)	0	0	0	0	0	0	1	0	6	0	0
Instrumentation Lab	0	0	0	0	0	0	2	0	0	0	0
Inova	1	0	0	0	0	0	19	2	15	2	0
Rat Cerebellum	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**1**	**0**	**0**
In House	0	0	0	0	0	0	0	0	1	0	0
Other ...	0	0	0	0	0	0	1	0	0	0	0

Other ...

SUBSTRATE	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative	Positive Screen Only	Negative Screen Only
Other ...	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**0**	**2**	**0**	**0**
Other ...	0	0	0	0	0	0	2	0	2	0	0

Immunohistochemistry

SUBSTRATE	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative	Positive Screen Only	Negative Screen Only
Rat Cerebellum	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**0**	**0**	**0**	**0**
Other ...	0	0	0	0	0	0	1	0	0	0	0
Vector Laboratories	0	0	0	0	0	0	1	0	0	0	0

Your Secondary Results for Sample 184-1

Analyte	Positive	Negative	Method	Substrate	Manufacturer
Anna-1 (Hu)	False	True	Immunoblotting	N/A	RAVO Diagnostika
Anna-2 (Ri)	False	True	Immunoblotting	N/A	RAVO Diagnostika
PCA-1 (Yo)	False	True	Immunoblotting	N/A	RAVO Diagnostika
CRMP5 (CV2)	False	True	Immunoblotting	N/A	RAVO Diagnostika
AMPHIPHYSIN	False	True	Immunoblotting	N/A	RAVO Diagnostika
Ma-2 (Ta)	False	True	Immunoblotting	N/A	RAVO Diagnostika
GAD - Neurological	True	False	Immunoblotting	N/A	RAVO Diagnostika
Other	False	False			

Summary of Results for Sample 184-1 - SECONDARY TESTING

	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative
Immunoblotting	**1**	**0**	**0**	**0**	**0**	**0**	**70**	**1**	**36**
Manufacturer									
Euroimmun	1	0	0	0	0	0	37	0	31
In House	0	0	0	0	0	0	0	0	1
RAVO Diagnostika	0	0	0	0	0	0	22	1	3
RAVO Diagnostika PNS Blot	0	0	0	0	0	0	0	0	1
RAVO Diagnostika PNS 11 Blot	0	0	0	0	0	0	3	0	0
Euroimmun Euroline 12 Ag	0	0	0	0	0	0	8	0	0

	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative
Other ...	**0**	**0**	**0**	**0**	**0**	**0**	**5**	**0**	**1**
Manufacturer									
Other ...	0	0	0	0	0	0	5	0	1

Summary Page for Sample 184-2

Analyte	Positive	Negative	Referred
PARANEOPLASTIC ANTIBODIES	124	1	5
		Total Responses	130
		Correct Response	95 %

Antibody Identification	Returns
NEG	1
ANNA-1 (HU)	124
Total Responses	125
Correct Response	99 %

Primary Testing	
Analyte	**Returns**
Anna-1 (Hu)	90
Anna-2 (Ri)	1
Other	1
Screen Only	2
NEGATIVE	1
Total Responses	95

Secondary Testing	
Analyte	**Returns**
Anna-1 (Hu)	115
NEGATIVE	1
Total Responses	116

Your Results for Sample 184-2

Analyte	Positive	Negative	Referred
PARANEOPLASTIC ANTIBODIES	True	False	False
ANTIBODY IDENTIFICATION	ANNA-1 (HU)		

Your Primary Results for Sample 184-2

Analyte	Positive	Negative	Method	Substrate	Manufacturer	Dilution
Anna-1 (Hu)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
Anna-2 (Ri)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
PCA-1 (Yo)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
CRMP5 (CV2)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
AMPHIPHYSIN	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
Ma-2 (Ta)	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
GAD - Neurological	False	False	Indirect Immunofluorescence	Monkey Cerebellum	A. Menarini - Zenit EIA	
Other	False	False				
Screen Only	False	False				

Summary of Results for Sample 184-2 - PRIMARY TESTING

Indirect Immunofluorescence

SUBSTRATE	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative	Positive Screen Only	Negative Screen Only
Monkey Cerebellum	**79**	**1**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**2**	**0**
Euroimmun	33	0	0	0	0	0	0	0	1	0	0
Trinity Biotech (Immco)	7	0	0	0	0	0	0	0	0	0	0
Instrumentation Lab	2	0	0	0	0	0	0	0	0	0	0
Inova	37	1	0	0	0	0	0	1	0	2	0
Rat Cerebellum	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
In House	1	0	0	0	0	0	0	0	0	0	0
Other ...	1	0	0	0	0	0	0	0	0	0	0

Other ...

SUBSTRATE	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative	Positive Screen Only	Negative Screen Only
Other ...	**5**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Other ...	5	0	0	0	0	0	0	0	0	0	0

Immunohistochemistry

SUBSTRATE	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative	Positive Screen Only	Negative Screen Only
Rat Cerebellum	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Other ...	1	0	0	0	0	0	0	0	0	0	0
Vector Laboratories	1	0	0	0	0	0	0	0	0	0	0

Your Secondary Results for Sample 184-2

Analyte	Positive	Negative	Method	Substrate	Manufacturer
Anna-1 (Hu)	True	False	Immunoblotting	N/A	RAVO Diagnostika
Anna-2 (Ri)	False	True	Immunoblotting	N/A	RAVO Diagnostika
PCA-1 (Yo)	False	True	Immunoblotting	N/A	RAVO Diagnostika
CRMP5 (CV2)	False	True	Immunoblotting	N/A	RAVO Diagnostika
AMPHIPHYSIN	False	True	Immunoblotting	N/A	RAVO Diagnostika
Ma-2 (Ta)	False	True	Immunoblotting	N/A	RAVO Diagnostika
GAD - Neurological	False	True	Immunoblotting	N/A	RAVO Diagnostika
Other	False	False			

Summary of Results for Sample 184-2 - SECONDARY TESTING

	ANNA-1 (Hu)	ANNA-2 (Ri)	PCA-1 (Yo)	CRMP 5 (CV2)	Amphip hysin	Ma-2 (Ta)	GAD Abs	Other	Negative
Immunoblotting	**115**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**
Manufacturer									
Euroimmun	74	0	0	0	0	0	0	0	1
Trinity Biotech (Immco)	1	0	0	0	0	0	0	0	0
In House	1	0	0	0	0	0	0	0	0
RAVO Diagnostika	27	0	0	0	0	0	0	0	0
RAVO Diagnostika PNS Blot	2	0	0	0	0	0	0	0	0
RAVO Diagnostika PNS 11 Blot	3	0	0	0	0	0	0	0	0
Euroimmun Euroline 12 Ag	7	0	0	0	0	0	0	0	0