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Dear Colleague,

SHLMPRL reference service change - Discontinuation of serology testing for the routine diagnosis of Legionella pneumophila and Legionella species infection

After consultation with the Reference Laboratories Advisory group, SHLMPRL will no longer provide a diagnostic serology service for *L. pneumophila and Legionella species*. **From the 1st of April 2018, SHLMPRL will no longer accept sera for the primary diagnosis of *L. pneumophila* or *Legionella* species infections.** We will continue to provide a reference service for confirmatory serology of *L. pneumophila* serogroup 1 and in some cases other *Legionella* species, but only after discussion with the requesting laboratory and where there are appropriately timed, paired sera available **and only** from cases that have been previously *Legionella* urine antigen positive and/or respiratory specimen PCR/culture positive. We will continue to provide a serological service in support of HPS led investigations into clusters/outbreaks of legionellosis where it is agreed with SHLMPRL that serology would be useful. The availability of a back-up serology service will be reviewed after 12 months. Further background to these changes are provided in the appendix below.

Kind regards

Professor Andrew Smith — Director, SHLMPRL

Dr Camilla Wiuff — Strategic Lead Microbiology, HPS

Appendix – Background for changes to Legionella serology

Background

Prior to the early 1990s, detection of Legionnaires' disease (LD) in Scotland relied primarily on serological diagnosis. The success of this approach was, in a large part, due to the standardisation of this methodology within the *Legionella* reference laboratory (1,2). Over recent years, the *L. pneumophila* urinary antigen testing has become the main diagnostic method of choice and it is anticipated that the serological diagnosis of LD will continue to decline.

Recent work by European colleagues supports the view that the currently available commercial kits for serology perform very poorly (3) and due to the rarity of *Legionella* species, *L. pneumophila* Sg 1 is the only organism accredited for serology by UKAS.

Of 5,859 sera processed by SHLMPRL from 2014-2017, there were only 180 (3%) serology positive. Of the 180 positive only 11 showed a >fourfold rise and 17 demonstrated a single high titre. The remaining 152 (84%) were single low titres and not diagnostically significant (Table 1).

The contribution of serology to national surveillance

Review of the HPS surveillance data from 2014-2017 show that very few cases are established by serological testing alone (Table 2). In 2014 and 2015 there were 2 of 60 cases where serology was the primary diagnostic method. In 2016-2017, no cases were definitively identified by serology alone. There were some *Legionella* species serology positives and single high titres to *L. pneumophila* Sg 1 but these are classified as probable cases (as per ECDC guidelines). Routine serology testing for diagnosis of *Legionella pneumophila* and *Legionella* species infections is no longer offered by Public Health England.

Other testing available for investigation of suspected Legionnaires' disease at SHLMPRL

1. Confirmation of *Legionella* urine antigen positive specimens.
2. *Legionella* species PCR from respiratory specimens
3. Culture of *Legionella* species from respiratory specimens.
4. Confirmation/identification of putative *Legionella* species isolated from water/environmental sources.
5. Genotyping *Legionella* isolates associated with outbreaks.

Whole genome sequence of Legionella species isolates.

The Reference Laboratories at Glasgow Royal Infirmary now have the facilities to undertake WGS of *Legionella* isolates. The implementation of routine WGS of *Legionella* species is currently under national review.

References

1. Fallon RJ, Abraham WH. Experience with heat-killed antigens of *L. longbeachae* serogroups 1 and 2, and *L. jordanis* in the indirect fluorescence antibody test. Zentralbl Bakteriol Mikrobiol Hyg A. 1983 Jul;255(1):8-14. PubMed PMID: 6356712.
2. Fallon RJ, Johnston RE. Heterogeneity of antibody response in infection with *Legionella pneumophila* serogroup 1. J Clin Pathol. 1987 May;40(5):569-72. PubMed PMID: 3294909; PubMed Central PMCID: PMC1141027.
3. Elverdal P, Jørgensen CS, Uldum SA. Comparison and evaluation of four commercial kits relative to an in-house immunofluorescence test for detection of antibodies against *Legionella pneumophila*. Eur J Clin Microbiol Infect Dis. 2008;27:149-52.

Table 1: Reference laboratory results for 5,859 sera submitted for confirmation of the presence of Legionella antibodies 2014-2017, SHLMPRL.

Titre	L.p Sg 1	L.p Non Sg1	All Legionella species	
16	37	0	37	0.6%
32	23	4	27	0.4%
64	30	15	45	0.8%
128	5	20	25	0.4%
256	7	19	26	0.4%
>=512	5	15	20	0.3%
Any positive	107	73	180	3.0%
>four fold rise	4	7	11	6.1%
Single high titre (≥256)	12	5	17	9.4%

Table 2: The total number of cases of LD confirmed by SHLMPRL and reported to the HPS National Surveillance Scheme 2014-2017 showing the percentage of these where serology was the primary diagnostic methods.

	2014	2015	2016	2017
Total no. of cases	30	30	29	5
Number by serology alone (%)	6 (2)	3 (10)	2 (7)	1 (20)
Number with 4-fold rise (%)	4 (13)	4 (13)	3 (10)	0
Number definitive by serology only (%)	1 (3%)	1 (3%)	0	0
Number probable by serology only (%)	5 (17)	2 (7%)	2(7)	1 (20)