# Rapid and accurate detection of *Neisseria meningitidis* DNA in clinical specimens using the Hibergene HG Meningococcus LAMP assay

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## Introduction

Molecular detection of meningococcal DNA in sterile site (blood or CSF) specimens using real-time PCR is a gold standard method for confirming a diagnosis of meningococcal disease. Due to resource limitations in many hospital laboratories, PCR testing for this important pathogen is usually available only as a reference laboratory test. The Hibergene "HG Meningococcus" assay is a new rapid molecular diagnostic test based on loop-mediated isothermal amplification (LAMP). We evaluated the diagnostic accuracy of this test for detection of meningococcal DNA in blood, cerebrospinal fluid (CSF) and respiratory swabs.

## Materials & Methods

Performance of the HG Meningococcus assay (Fig. 1) was compared to reference laboratory testing using TaqMan® real-time PCR, targeting the *ctr*A gene (Corless et al, 2001). Analytical sensitivity was evaluated using *N. meningitidis* genomic DNA spiked over a range of concentrations into whole blood, CSF and respiratory swabs.

Analytical specificity was evaluated using a panel of DNA samples from potentially cross-reacting bacterial species, and serogroup inclusivity was evaluated using a panel of meningococcal type strains. Clinical sensitivity and specificity were evaluated using residual clinical specimens from cases of suspected meningococcal disease. An additional panel of artificial whole blood specimens, prepared by re-suspending cells from PCR-negative donor blood with PCR-positive plasma, was also evaluated.

## Results

The limit of detection for all sample types was below 2 genome copies per µl (Table 1). No non-specific amplification from 20 different non-target bacterial species was observed, and detection of meningococcal serogroups A, B, C, E, W, X, Y, and Z was confirmed.

| Matrix | Limit of Detection (95% CI) | |
|---|---|---|
| **EDTA Blood** | 1.4 copies/µl | (1.0 – 2.5 copies/µl) |
| **CSF** | 1.0 copies/µl | (0.7 – 1.7 copies/µl) |
| **Swab** | 1.9 copies/µl | (1.6 – 2.5 copies/µl) |

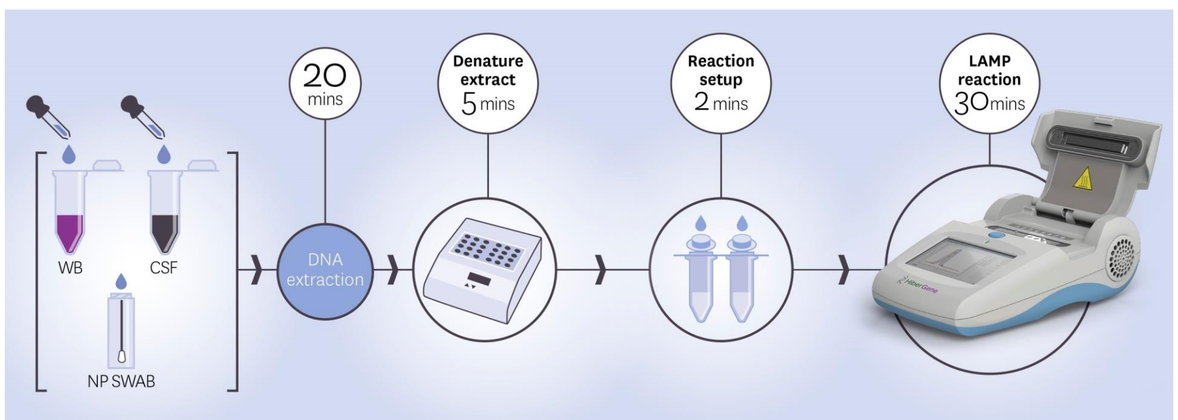


**Figure 1. HG Meningococcus test workflow**

Whole blood specimens (n=30), CSF specimens (n=51) and swab specimens (n=57) from patients being investigated for meningococcal infection were also tested. The HG Meningococcus test had a sensitivity of 100% (47/47 positive) and a specificity of 100% (90/90 negative) relative to real-time PCR (Table 2).

| | | TaqMan® qPCR + | TaqMan® qPCR – |
|---|---|---|---|
| **HG Meningococcus** | + | 47 | 0 |
| | – | 0 | 90 |

The HG Meningococcus test was more sensitive than the reference PCR method when testing artificial whole blood specimens, with 27/28 (96%) positive using the LAMP assay, compared to 20/28 (71%) positive by PCR. Mean / median times to positive result for all positive specimens tested were 12.5 and 12.3 minutes respectively (Figure 2).

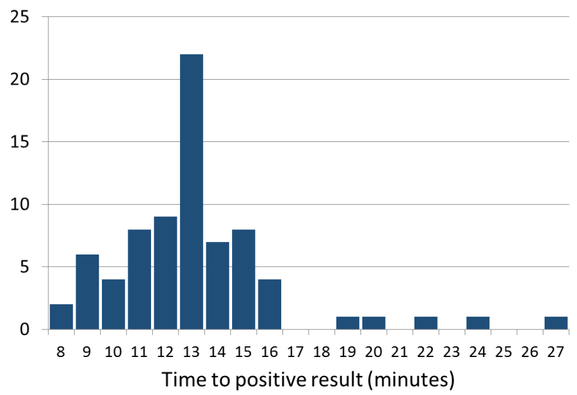


**Figure 2. HG Meningococcus time to result for all positive specimens tested (n=75)**

## Discussion

The HG Meningococcus test out-performed the TaqMan® real-time PCR assay used in the UK Meningococcal Reference Unit for detection of meningococcal DNA in clinical specimens. The test was simple to use, accurate, and fast, giving clinically actionable results in <60 minutes, including DNA extraction. The stable freeze-dried format is practical for use in any hospital laboratory, and could be used for near-patient testing.

Most patients who are investigated for possible meningococcal infection do not have the disease. Obtaining an early positive result for the minority who do allows clinical teams to stop other investigations, continue focused and appropriate treatment, and initiate a public health response if required. Testing of minimally invasive nasopharyngeal swabs with this assay has been shown to be accurate for diagnosis of meningococcal disease in young children and babies, who are at highest risk of this infection (Bourke et al, 2015). Given the high sensitivity of the method, clinicians may also act on a negative test result to either discharge or continue to observe a clinically well patient.

The HG Meningococcus test is CE-IVD approved for clinical disgnostic testing in European hospital laboratories.

## References

Corless et al (2001) J Clin Micro 39(4):1553–1558
Bourke et al (2015) Lancet Infect Dis. 15(5):552-558

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