External Quality Assessment Scheme for *Clostridium difficile*

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Introduction

Clostridium difficile infection is a major problem for hospitals and community care homes, as it can affect a range of in-patients, especially the elderly, the incapacitated and those that have had antibiotic treatment. *C. difficile* infection can result in anything from mild diarrhoea to severe colitis and can result in death [1]. The United Kingdom National External Quality Assessment Service (UK NEQAS) for Microbiology introduced a scheme for *Clostridium difficile* detection in April 2009 and provides participants with the opportunity to assess the quality of culture, molecular and toxin testing for *C. difficile*. A total of 177 laboratories, representing 17 countries, participated in the *Clostridium difficile* detection scheme during the first year. Four distributions were dispatched between April 2009 and March 2010, each consisting of two simulated faecal specimens.

Aim

To analyse the performance of clinical laboratories participating in the *Clostridium difficile* detection scheme.

Methods

- From April 2009 to March 2010, eight simulated faecal specimens were distributed.
- The eight specimens included *C. difficile* ribotypes 001, 002, 005 (x2), 015, 016 and 027 (x2).
- All were *Clostridium difficile* toxin positive (A+B+) isolates.
- Results reported by participants for these specimens were analysed to determine their performance with these specimens.

Results

- Performance was good with 83% to 100% of participants reporting correctly on the detection of *Clostridium difficile* and/or toxin in seven of the eight specimens. For one specimen (9452) only 67% of participants correctly reported the presence of *C. difficile* or *C. difficile* toxin (Table 1).
- The number of participants using culture increased from 14 to 36 during the first year of the scheme (Table 2).
- The number of participants using Techlab *C. DIFF* QUIK CHEK COMPLETE increased from 4 to 9 during the first year of the scheme (Table 2).
- The number of participants using Premier Tox A&B (ELISA) decreased from 55 to 44 during the first year of the scheme (Table 2).
- The number of participants using tissue culture in the UK decreased from 5 to 3 during the first year of the scheme (Table 2).

Table 1: Participant performance with toxigenic *Clostridium difficile* specimens

Specimen no. (ribotype)	9252 (027)		9253 (016)		9395 (005)		9396 (001)		9491 (027)		9492 (005)		9629 (002)		9630 (015)	
	UK	Non-UK	UK	Non-UK	UK	Non-UK	UK	Non-UK	UK	Non-UK	UK	Non-UK	UK	Non-UK	UK	Non-UK
Indeterminate result	3	1	2	0	2	0	1	0	0	0	12	2	1	0	2	2
Specimen CDT positive	**83**	**25**	**86**	**26**	**93**	**18**	**99**	**21**	**95**	**21**	**58**	**11**	**89**	**21**	**74**	**16**
Clostridium difficile	**1**	**1**	**1**	**1**	**1**	**3**	**1**	**3**	**0**	**2**	**0**	**2**	**1**	**3**	**1**	**2**
Toxigenic C. difficile	**14**	**26**	**13**	**26**	**8**	**32**	**9**	**34**	**16**	**34**	**12**	**30**	**21**	**37**	**19**	**34**
Specimen CDT negative	3	1	2	1	4	3	0	0	0	0	25	8	0	0	13	4
Negative result	1	0	1	0	1	2	0	1	0	0	1	1	0	1	2	2
Non-Toxigenic C. difficile	1	1	1	1	0	1	0	0	0	0	3	3	0	0	1	2
% of participants with a full score	**93%**	**95%**	**94%**	**96%**	**94%**	**90%**	**99%**	**98%**	**100%**	**100%**	**NS**	**NS**	**99%**	**98%**	**84%**	**84%**

NS Not scored

N.B. The report categories in bold are those that receive a full score when reporting on a toxigenic *Clostridium difficile* specimen.

Table 2. Methods used by participants over the first year of the scheme

Method	2467 UK (Non-UK)	2583 UK (Non-UK)
BD ColorPAC Toxin A kit	1 (0)	0 (0)
BD: GeneOhm Cdiff	0 (0)	0 (1)
bioMerieux: VIDAS *Clostridium difficile*	19 (14)	23 (18)
Cepheid Xpert	2 (0)	2 (0)
Culture	3 (11)	6 (30)
Meridian: Immuno*Card C. difficile*	0 (2)	1 (1)
Meridian: Immuno*Card* A&B	16 (15)	14 (20)
Microgen *C. difficile*	0 (1)	0 (1)
Other	4 (8)	4 (4)
Oxoid *C. difficile* test kit (antigen)	2 (0)	0 (0)
Oxoid *C. difficile* toxin A	0 (2)	0 (1)
Premier Tox A&B	39 (16)	35 (9)
Remel: Xpect *C. difficile* tox A/B	1 (0)	1 (2)
Techlab: *C. DIFFICILE TOX A/B II*	22 (5)	23 (5)
Techlab: *TOX A/B QUIK CHEK*	12 (5)	18 (6)
Techlab: *C. DIFF CHEK - 60*	1 (0)	1 (0)
Techlab: *C. DIFF QUIK CHEK*	2 (0)	2 (1)
Techlab: *C. DIFF QUIK CHEK COMPLETE*	3 (1)	7 (2)
Tissue culture	5 (7)	3 (7)

Figure 1a: Methods used by UK participants in each of the four distributions from April 2009 to March 2010

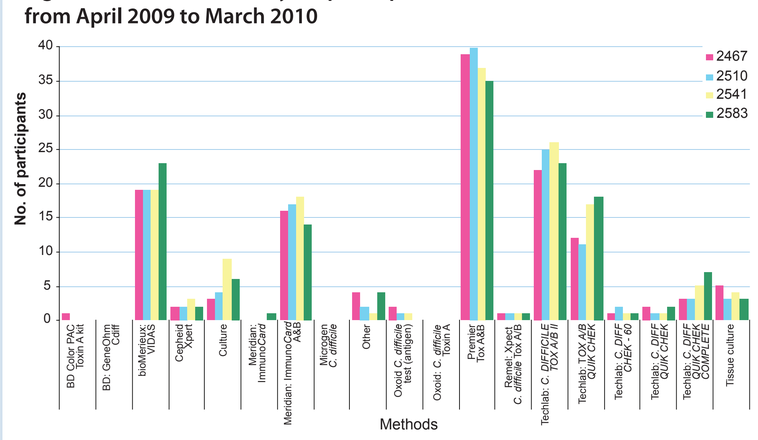


Figure 2: Example report for the *Clostridium difficile* detection scheme where results are presented by method.

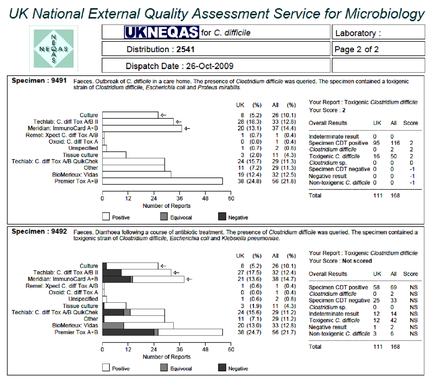


Figure 1b: Methods used by non-UK participants in each of the four distributions from April 2009 to March 2010

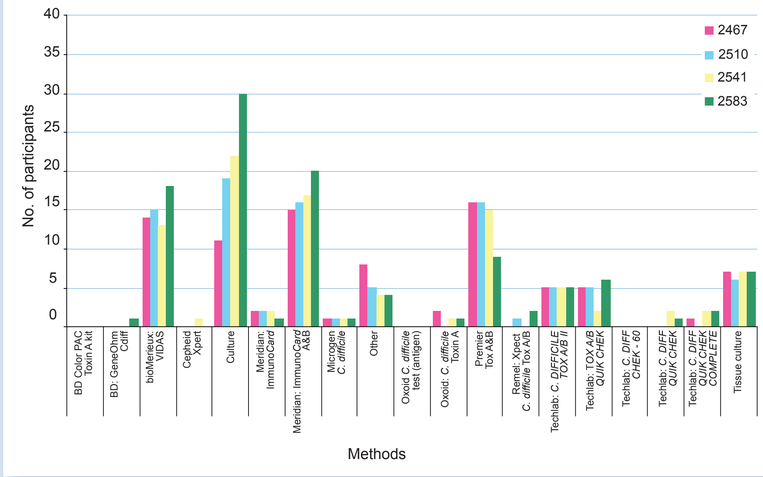
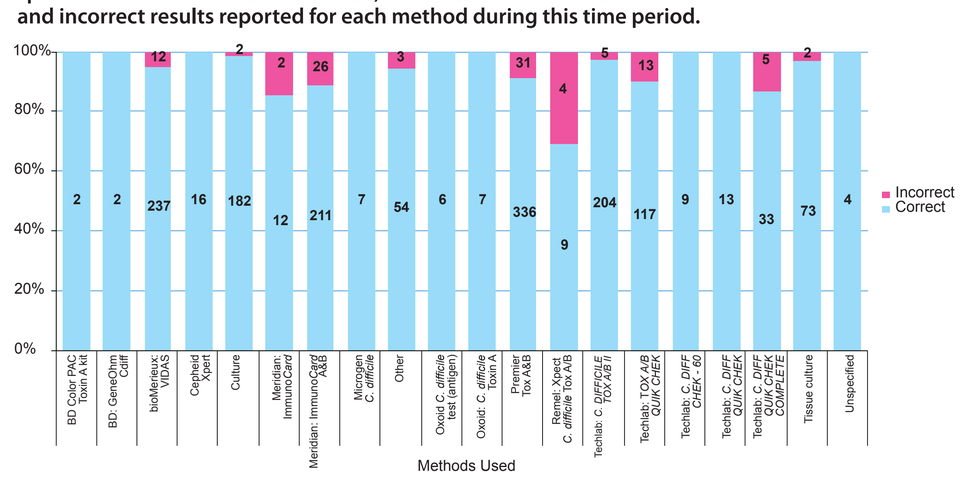


Figure 3. Overall performance of methods between April 2009 and March 2010 (excluding specimen 9492 which was not scored). N.B. the numbers in bold are the actual number of correct and incorrect results reported for each method during this time period.



Discussion

- The level of toxin in specimen 9492 was low and when the specimen was diluted may have been at the lower limit of detection for some assays thereby affecting participant performance.
- Overall toxin testing is the most popular way of examining specimens, with the Premier Tox A&B kit being the most commonly used assay, followed by bioMerieux VIDAS and the Immuno*Card* A&B.
- The most popular methods used by UK participants were Premier Tox A&B kit, followed by Techlab *C. DIFFICILE TOX A/B II* and bioMerieux VIDAS (Figure 1a).
- The most popular methods used by non-UK participants were culture, followed by Meridian Immuno*Card* A&B and bioMerieux VIDAS (Figure 1b).
- Participants that used assays that only look for *C. difficile* glutamate dehydrogenase, e.g. Meridian Immuno*Card C. difficile* and Techlab *C. DIFF QUIK CHEK*, used them in combination with at least one other method such as
  - bioMerieux VIDAS
  - Culture
  - Meridian Immuno*Card* A&B
  - Premier Tox A&B
  - Techlab *TOX A/B QUIK CHEK*
- Current opinion[2,3] on performance of *C. difficile* toxin detection assays indicate that laboratories should not be using these assays in isolation; results from the UK NEQAS *C. difficile* detection scheme will help participants monitor the performance of their methods (Figure 2).
- The scheme has been well received and participation increased to 276 laboratories (22 countries) in April 2010.

References

[1] Gerding DN, Johnson S, Peterson LR, Mulligan ME, Silva J Jr. *Clostridium difficile*–associated diarrhoea and colitis. Infect Control Hosp Epidemiol 1995; 16:459–77.
[2] Centre for Evidence-based Purchasing 2009. Evaluation report on *Clostridium difficile* toxin detection assays http://www.pasa.nhs.uk/PASAWeb/NHSprocurement/CEP/CEPproducts/CEP+catalogue.htm
[3] The Biomedical Scientist 2008. Article: *Clostridium difficile*: toxin testing alone is not enough. www.ibms.org

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