Rubella dilemma: are patients being immunised unnecessarily?
V James and EJ Fagan
UK NEQAS for Microbiology, Quality Assurance Laboratory, Health Protection Agency Centre for Infections, 61 Colindale Avenue, London, NW9 5EQ

Introduction
Rubella is a RNA virus that causes a mild infectious disease with an incubation period of 14 to 21 days. Primary infection during the first eight to ten weeks of pregnancy can result in fetal damage in up to 90% of infants. Rubella is a virus preventable disease and immunisation for pre-pubescent and non-immune females was introduced in the UK in 1970. A universal rubella immunisation programme was implemented in 1988 with the introduction of the MMR vaccine.

UK NEQAS for Microbiology introduced the Rubella IgG serology EQA scheme in 1976. Two panels of each six specimens, derived from single serum donations, are sent out annually. Although quantitative results are collected and presented in the distribution report, participants are scored on the qualitative interpretation of their results. Specimens with quantitative values that are close to 10 IU/mL are included in the distribution however participants’ performance with these specimens is not scored.

Aim
To analyse the variability of qualitative results by method for the detection of low positive specimens (between 5 IU/mL and 15 IU/mL) in the rubella IgG serology EQA scheme.

Methods
- From 2002 to 2006, fifty-four specimens have been distributed.
- Forty-three of the 54 specimens were scored; 11 specimens were negative and 32 were positive.
- Eleven of the 54 specimens were not scored as results from pre-distribution testing gave quantitative values between 5 IU/mL and 15 IU/mL.
- Results reported by participants for these specimens were analysed to determine whether any kits consistently gave results that were excessively high or low.

Results

Participants performance for the 43 scored specimens was good with success rates of 93% to 100% (data not shown)
- The overall false negative rate was 48/1092 (4.4%)
- The overall false positive rate was 65/3763 (1.7%)

For the low positive, non-scored specimens 56.2% to 58.7% of participants reported a positive result (10 IU/mL) result (table 1): 69/120 (57.5%) of participants reported their overall result as >10 IU/mL.

The most popular methods (figure 1) used to detect rubella IgG were:
- Abbott AxSYM (112-128 users)
- bioMerieux Vitek (40-58 users)
- Biokit: Biolinea (27-38 users)
- DiaSorin (18-39 users)

For S11 non-scored specimens the Bayer method gave the highest median results (median range: 9.5 to 81) of those methods with <10 IU/mL (figure 2).

For S11 non-scored specimens the Roche method gave the lowest or joint lowest median results (median range: 8 to 18).

For specimen 8010, 209/372 (56.2%) participants reported their result as >10 IU/mL. Eight of the 17 methods used to test this specimen gave median results >10 IU/mL (figure 3).

Of the 36 different methods used (including those that gave non-numerical data sets), 25 methods had been used to analyse 10 or more of the specimens.

Analysis of these 25 methods using ANOVA showed there was strong evidence that not all methods produced the same results (p<0.001).
- Linear regression, taking DiaSorin as the baseline (due to its fairly low mean and large-amount frequency of usage), showed that Bayer produced the highest results (2.1 fold > DiaSorin, 95% CI (2.0-2.3)).
- Overall Roche followed by Diamedix and DiaSorin produced the lowest results. However there was no evidence of any differences between the 3 methods.

Conclusions
Even though there has been an international standard for rubella available for many years there remains a difference in the quantitative results reported for different kits. For specimens containing low levels of antibodies this variation can result in the specimens being classified as coming from a patient who is non-immune.