Letter to the Editor

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Evaluation of a POCT device for C-reactive protein, hematocrit and leukocyte differential

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To the Editor,

The area of point-of-care testing (POCT) is rapidly growing and holds great promise in terms of speed, accessibility, patient empowerment and improved dialogue between health care practitioners and patients [1]. Although for many POC tests the added value in clinical decision making has not yet been firmly established [2], a number of studies have recently appeared on the value of POCT measurement of biomarkers of inflammation [mainly C-reactive protein (CRP)] in patients presenting to the general practitioner with signs of a respiratory tract infection [3, 4]. It was found that POC testing for CRP changed the decision whether or not to prescribe antibiotics in a significant proportion of cases and led to an overall reduction in antibiotic usage (depending on the baseline prescribing behavior of the general practitioners) [5].

Other commonly ordered tests are the blood count and leukocyte differential. Although hemoglobin POCT systems have already found widespread acceptance, leukocyte counts and differential are still almost exclusively carried out in centralized laboratories. One obstacle to their introduction as a POC test has been the requirement for ‘yet another meter’.

Spinit (Biosurfit SA, Lisboa, Portugal) is a POCT device combining multiple detection modes (i.e. surface plasmon resonance, spectroscopy, microcentrifugation and digital microscopy with image recognition) in one device. The disposable measurement cartridges that the equipment uses are actually compact disks (CDs) containing microfluidic channels. CDs for CRP have been on the market since 2011, and CDs for blood count have recently been introduced, measuring hematocrit (Ht), white blood cell count (WBC) and 5-part differential.

We present here the first report (to the best of our knowledge) of an independent evaluation of Spinit, including the precision of the CRP and blood count measurements and comparison with our laboratory methods. Spinit was evaluated in a primary care setting; therefore, a sufficient range of eosinophil and basophil counts could not be obtained.

Because Spinit requires whole blood, EDTA-anticoagulated hematology samples were used for all measurements on Spinit (blood count and CRP), whereas for the measurement of CRP using the laboratory method, heparin plasma was routinely used. This approach ensures optimal comparability to standard practice.

The precision of the CRP measurement was assessed by a modified Evaluation Protocol 5 of the Clinical and Laboratory Standards Institute (CLSI EP5 – Complex Precision) in which “between-lot” precision was substituted for “between-run” precision. Briefly, using one instrument, a high (155 mg/L) and a low (14 mg/L) sample were measured on three consecutive days using two different lots of CDs in duplicate.

An EP5 complex precision experiment could not be performed for the blood count because the Spinit digital image recognition algorithm is at present not yet compatible with stabilized quality control materials because of differing morphological properties compared with native blood cells. Therefore, a “simple precision” experiment was carried out. Briefly, using one instrument, a high (155 mg/L) and a low (14 mg/L) sample were measured on three consecutive days using two different lots of CDs in duplicate.

The results of the precision experiments are given in Table 1. Except for CRP at the low level, all CVs are

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For CRP, it is apparent that the total imprecision is almost completely attributable to within-run imprecision, as is expected for a good POCT assay. In addition, the bias between the two lots of CDs was calculated as 1.1 and 0.5 mg/L on the high and low CRP sample, respectively.

The Spinit CRP measurement method was compared with the Roche third-generation CRP assay on a Cobas 8000 (Roche Diagnostics, Almere, The Netherlands) by a modified CLSI EP9 protocol. Briefly, 43 EDTA-anticoagulated whole blood samples (distributed over 5 days) were selected from our routine production to cover Spinit’s reportable range of 3–180 mg/L and were assayed in duplicate (as per CLSI EP9) on a Spinit and compared with the laboratory method.

As shown in Figure 1A, the Spinit CRP test correlates well with our laboratory method, apart from a slight positive slope (12%). In primary care practice, a slight positive slope will lead to a negative predictive value of the test that will be at least as good as the laboratory test. The difference between lots was assessed but found insignificant.

The Spinit blood count measurement method was compared with the Sysmex XN method (Sysmex Corporation, Kobe, Japan) by a modified CLSI EP9 protocol. Briefly, 46 samples (distributed over 5 days) were selected from our routine production to cover Spinit’s reportable ranges of WBC 3–30 · 10⁹ L⁻¹ and Ht 0.20–0.65 (maximum Ht obtained: 0.52). Samples were assayed in duplicate (as per CLSI EP9) on a Spinit and compared with the laboratory method.

As shown in Figure 1B–F. The differential count, it became apparent that the reporting limits of the Spinit are set on the percentage differential rather than on absolute numbers: neutrophils 10%–86%, lymphocytes 9%–78% and monocytes 3%–18%. Therefore, for a number of samples containing absolute differential below 10%. For CRP, it is apparent that the total imprecision is almost completely attributable to within-run imprecision, as is expected for a good POCT assay. In addition, the bias between the two lots of CDs was calculated as 1.1 and 0.5 mg/L on the high and low CRP sample, respectively.

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counts well within the normal range using the laboratory method, the Spinit did not report some of the differential count results.

The hematocrit and WBC both show a slight negative slope of 7% and 10%, respectively, which could well be a standardization issue (Spinit is calibrated to the Siemens Advia method). In analogy to CRP, a slight negative slope for Ht will lead to a negative predictive value of the test that will be at least as good as the laboratory test. The opposite holds for the WBC count, however, where a slight positive slope would be preferred.

The method comparison experiments for neutrophils and lymphocytes show excellent agreement with the laboratory method. The monocyte count shows a considerably worse correlation and has a negative slope (15%). Interestingly, these results for monocytes are quite comparable with results obtained in a method comparison between another point-of-care hematology device based on digital image recognition and a Sysmex laboratory method [6]. However, like eosinophils and basophils, the use of the monocyte count in primary care is limited, and neither of the three determinations is at present mentioned in any of the guidelines of the Dutch Association of General Practitioners [7].

It must be noted that, although the instrument does report the differential in terms of absolute numbers as well, these numbers have a somewhat higher imprecision (results not shown) by nature of the assay method. Because digital image recognition always includes an ‘unidentified’ category, the error in the percentage differential count (in which this category is not included) and the error in the total WBC count (in which this category is included) accumulate when an absolute differential count is calculated.

For all assays, no differences between two Spinit machines were noted in terms of bias and precision. In addition, a CLSI EP6 linearity experiment was performed for CRP and showed linearity in the range 14–155 mg/L (results not shown). CLSI EP6 for blood count measurements is not straightforward; therefore, the linearity of the blood count was assessed on the method comparison data and no nonlinearity was found.

We conclude that the Spinit instrument is capable of reliably measuring CRP, Ht, total leukocytes and percentages of neutrophil granulocytes and lymphocytes. The availability of these parameters in a single device is attractive for use in primary care, where point-of-care testing contributes to reduction of antibiotic prescription.

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