Development of a quality monitoring program for platelet components: a report of the first four years’ experience at Canadian Blood Services

Elena Levin, Craig Jenkins, Brankica Culibrk, Maria I.C. Gyöngyössy-Issa, Katherine Serrano, and Dana V. Devine

BACKGROUND: A quality monitoring program (QMP) for platelet concentrates (PCs) was implemented at Canadian Blood Services (CBS) to improve standards and to better understand platelet (PLT) products by supplementing routine quality control (QC).

STUDY DESIGN AND METHODS: Annual surveys of PCs from CBS production sites were conducted, with four completed to date (QMP Cycles 1-4) spanning two different PC production methods: PLT-rich plasma (PRP) and buffy coat (BC). Randomly selected PCs were sent to a central laboratory and tested 1 day after expiry. An expanded panel of tests including CD62P expression by flow cytometry, mean PLT volume, PLT count and morphology, extent of shape change, and PLT metabolic parameters, were applied.

RESULTS: QMP data on the implementation of the BC production method across CBS indicated that BC PCs have less variable in vitro quality measures than PRP PCs. For the QC parameters pH and PLT count per unit, the range of mean values from each site for QMP 3 and 4 fell well within the range defined by regulatory standards, a first step in defining quality benchmarks for PCs. Of the extended panel of quality parameters, CD62P expression was the most sensitive indicator of change and identified an issue with the implementation of the BC PC production method at one site, which was subsequently remedied.

CONCLUSION: A QMP was found to be useful to monitor production processes across sites and highlights best practice approaches while deepening understanding of the quality of PLT products at CBS.

N ormal biologic differences among donors mean that a degree of variation is inherent in blood components produced for transfusion.1 Despite this, blood product providers strive to generate components that are of high quality and are optimally standardized to guarantee safety and effectiveness.2,3 Quality control (QC) of components prepared from whole blood donations occurs at expiry and focuses on the product’s safety and compliance with regulatory standards. For platelet concentrates (PCs), standards include pH, platelet (PLT) count per unit, sterility, and residual white blood cell count if the product is leukoreduced,4,5 all of which are monitored by routine QC at Canadian Blood Services (CBS). Although production of blood components for transfusion purposes has increasingly adopted a pharmaceutical industry mindset, significant deviations remain in both the use of QC principles and the determination of standards. The panel of standardized assessments currently in use provides general information on product characteristics at expiry, but these standards have remained unmodified for decades and do not encompass

ABBREVIATIONS: BC = buffy coat; CBS = Canadian Blood Services; ESC = extent of shape change; MPV = mean platelet volume; PC(s) = platelet concentrate(s); PRP = platelet-rich plasma; PSL = platelet storage lesion; QMP = quality monitoring program; SOP(s) = standard operating procedure(s).

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TRANSFUSION **, ** **
the accumulated understanding of PLT function or the
effects of storage on product quality.\textsuperscript{5}

Since 2005, CBS has been conducting a quality moni-
toring program (QMP) for the assessment of its PLT prod-
ucts. The QMP consists of annual surveys of PCs from CBS sites and, while QC tests approximately 1% of product,
QMP is conducted on a smaller scale, aiming to test 12
units from each production site per year. A major objec-
tive of this program is to improve standards and to better
understand the quality of PLTs produced by CBS by applying
in vitro tests beyond those used during routine QC
testing. Furthermore, samples from all CBS production
sites are tested via QMP, permitting examination of the
implementation of new processes across the whole orga-
nization, as well as site-to-site comparisons to assess the
consistency of production practices across a multisite
organization. The program was established under the
research and development division of CBS as this depart-
ment has long operated as a centralized troubleshooting
facility for product issues and had an established frame-
work for conducting PLT testing. The test panel included
several of the more commonly used PLT quality measures
because a secondary objective of the QMP was to generate
quality benchmarks for buffy coat (BC) PCs using assays
beyond the usual QC tests and to explore whether any of
these might be useful future routine QC measures.

Here data from the first four annual QMP cycles are
presented. PCs were examined at a central research and
development laboratory using an extended panel of in
vitro quality tests. PLT count per unit and pH, which are
also monitored by QC, were measured, as well as PLT mor-
phology, mean PLT volume (MPV), CD62P expression, and
measures of PLT metabolism. Between 2005 and 2008,
CBS changed its method of component production from
whole blood donations, replacing the PLT-rich plasma
(PRP) preparation method with the BC method, which
results in pooled components consisting of PLTs from four
donors;\textsuperscript{7} thus we present QMP data from PCs produced
using both the PRP method (QMP Cycles 1 and 2) and the
BC method (QMP Cycles 3 and 4).

MATERIALS AND METHODS
PLT preparation, shipping and test selection
PCs were prepared by either the PRP or the BC method
following CBS standard operating procedures (SOPs) as
described elsewhere.\textsuperscript{7} All PCs were analyzed a day
after expiry (Day 6) in a central testing laboratory in Vancouver,
British Columbia, Canada. Components were packed in
standard CBS PLT boxes (ISC E-38), with gel packs to
control temperature fluctuations and shipped overnight.
PCs were shipped either on Storage Day 2 or on Storage
Day 4 or 5 and shipping from all sites was less than 24
hours in duration. PCs were stored in a 22°C PLT agitator
(either Thermo Forma, Thermo Scientific, Asheville, NC;
or Helmer, Noblesville, IN) under standard CBS storage
conditions until testing. Twelve units from each produc-
tion site were analyzed per QMP cycle. To ensure compari-
son among production years, the selection of tests and
procedures was made at the beginning of the study and
remained largely unchanged throughout. The test panel
for PLT assessment included PLT count, MPV, blood gas
and PLT metabolites, PLT activation status, and morphol-
ogy. Extent of shape change (ESC) was included in QMP 1
and 4.

Sample collection for testing
Before sampling, the blood group, color, and appearance
(e.g., redness, lipemic look) of the PC as well as the site
from which the component was sent were recorded. Each
PC was weighed, and its volume was calculated. PCs were
sampled aseptically through a sampling site coupler.
Twelve milliliters of PLTs was aspirated into a 20-mL
syringe using an 18-gauge needle. From this syringe, 8 mL
was used for sterility testing. 3 mL was dispensed into a
K\textsubscript{2}EDTA vacutainer (BD, Mississauga, Ontario, Canada) for
hematology analyzer counts, and the remainder was
transferred to a polypropylene tube and used for PLT activ-
aton analysis and morphology scoring. A separate 1-mL
syringe, which was sealed immediately after sampling
with parafilm, was used to obtain samples for PLT meta-
bolic analysis.

Test panel
\textbf{PLT concentration and MPV} 
PLT concentration and MPV were obtained from a K\textsubscript{2}EDTA
tube using a hematology analyzer (Advia 120, Siemens,
Mississauga, Ontario, Canada), and PLT count per unit (or
PLT yield) was calculated as described previously.\textsuperscript{7}

\textbf{CD62P analysis by flow cytometry} 
Flow cytometry was conducted on one flow cytometer
(Coulter Epics XL-MCL, Beckman Coulter Canada, Inc.,
Mississauga, Ontario, Canada) for QMP 1 and 2 or another
(FACS Canto II, BD) for QMP 2, 3, and 4. During the
changeover between instruments, the BD flow cytometer
was cross-validated against the Coulter instrument before
QMP data collection, with samples analyzed on both
instruments and the results used to determine perfor-
mance and agreement between the two instruments
($r = 0.989$). Flow cytometric detection of PLT surface anti-
gens was conducted as described previously.\textsuperscript{7,8} Briefly,
PLTs were diluted with phosphate-buffered saline (PBS) to
a concentration of $200 \times 10^9$/L and stained with a fluores-
cent antibody cocktail containing anti-CD42-fluorescein
isothiocyanate (FITC) and anti-CD62P-phycocerythrin (PE;
Immunotech, Marseille, France). Staining was performed
in duplicate for 30 minutes, followed by fixation with 0.2% formol saline (0.2% formaldehyde in 0.9% NaCl) and analysis by flow cytometry. Five-thousand CD42-positive events were collected during each acquisition. Isotype antibodies (IgG2a-FITC and IgG1-PE, Immunotech) were used to control for nonspecific binding. PLTs activated with 1 U/mL bovine thrombin (gift from J. Fenton) served as a positive control.

**PLT morphology**
Morphology was assessed by modified Kunicki score, as described previously.7–9 Briefly, 50 µL of PLTs was added to an equal volume of 4% paraformaldehyde. Samples, in duplicate, were examined using phase contrast microscopy (100× magnification, Nikon, Mississauga, Ontario, Canada), with 100 PLTs counted per sample, categorized as either discoid (multiplied by 4), spiny (multiplied by 2), or spherical/balloon PLTs (multiplied by 1) and summed to obtain a morphology score. The same two technicians conducted morphology scoring for all QMP cycles. Initially, a comparison of the technicians’ scoring was conducted to ensure uniformity of their morphology scores.

**PLT metabolic parameters**
Measurement of PLT metabolites and dissolved gases was made using a blood gas analyzer (Gem Premier 3000, Instrumentation Laboratory, Orangeburg, NY). The sample was introduced into the instrument according to the manufacturer’s procedure within 30 minutes of sampling. Automatically printed results included pH, pO2, pCO2, lactate concentration, and glucose concentration.

**ESC assay**
ESC, which measures PLT responsiveness to activation with the agonist ADP, was monitored using an aggregometer (SPA-2000, Chronolog Corp., Havertown, PA) according to Holme and colleagues11 and described in detail previously. The ESC was calculated by the instrument by integrating optical density readings from PLT-poor plasma and PRP in the absence and presence of ADP (20 µmol/L final concentration). Assays were performed at 37°C.

### Statistical analysis
Early in QMP power calculations were conducted for each parameter to establish sample sizes sufficient to determine significant differences from the population. Based on these calculations and feasibility considerations, a target sample size of 12 PCs per production site per year was chosen. For analysis of data, one-way analysis of variance (ANOVA) and Tukey multiple comparison posttests were performed. Differences were considered to be significantly different at a p value of less than 0.05. Bonferroni confidence intervals for standard deviations (SDs) were calculated and Bartlett’s test for equal variance was used to determine whether variances were equal across QMP cycles. Significance of the correlation between different parameters (k > 0.2) was established by using the table of critical values of correlation coefficients.12

## TABLE 1. Averaged results for QMP 1, 2, 3, and 4

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>PRP-PCs</th>
<th>BC-PCs</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>QMP 1 (n = 106†)</td>
<td>QMP 2 (n = 72)</td>
</tr>
<tr>
<td>PLT concentration (×10⁹/L)</td>
<td>1394 ± 417</td>
<td>1569 ± 463</td>
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<tr>
<td>MPV (fL)</td>
<td>8.5 ± 1.0</td>
<td>8.4 ± 0.8</td>
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<td>Morphology (score)</td>
<td>253 ± 24</td>
<td>260 ± 15</td>
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<tr>
<td>CD62P (%)</td>
<td>34.8 ± 13.0</td>
<td>47.1 ± 10.3</td>
</tr>
<tr>
<td>pH at 22°C</td>
<td>7.25 ± 0.11</td>
<td>7.15 ± 0.19</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>15.6 ± 3.2</td>
<td>16.1 ± 3.7</td>
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<tr>
<td>Glucose (mmol/L)</td>
<td>28.9 ± 3.1</td>
<td>29.1 ± 3.7</td>
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<tr>
<td>pO2 (mmHg)</td>
<td>98 ± 26</td>
<td>98 ± 33</td>
</tr>
<tr>
<td>pCO2 (mmHg)</td>
<td>31 ± 9</td>
<td>35 ± 11</td>
</tr>
</tbody>
</table>

* Data are reported as means ± SDs for each parameter for each year of QMP, calculated by averaging results from all sites that participated.
† n = 106 for QMP 1 with the following exceptions: pH (n = 92), lactate (n = 88), and glucose (n = 87).
‡ n = 108 for QMP 4 with the following exceptions: lactate (n = 106) and glucose (n = 107).
several parameters not directly related to the change in manufacturing procedure, including morphology, grouping of results between PRP PCs and BC PCs is evident. Tighter SDs were observed for PLT concentration, MPV, CD62P, pH, and the metabolic parameters for QMP 3 and 4 (Table 1), indicating lower variance in the BC PC data for many parameters. To investigate this further, Bartlett’s test for equal variances was used to determine whether there were differences in the variances among QMP cycles. For all parameters, there were significant differences in the variances observed across QMP cycles ($p = 0.003$ or lower), and for many of the parameters, these segregated between PRP PCs and BC PCs, with BC PCs showing lower variances for most parameters. This indicated that the pooled BC product is less variable than the single-donor PRP product.

**Standard QC assays: pH and PLT count per unit**

To assess the quality of the PCs after shipping using established indices of PLT quality, two QC tests, pH and PLT count per unit (PLT yield), were used. Figure 1 graphs mean results from each site for QMP 3 and 4, against the regulated QC limits, based on AABB standards. AABB guidelines state that pH should be between 6.4 and 7.8 and PLT count per unit should be between $150 \times 10^9$ and $450 \times 10^9$, with 75% of PCs having a count per unit greater than $240 \times 10^9$. For both parameters, but particularly pH, the mean results for each site for QMP 3 and 4 fall within a range much narrower than that defined by the regulatory standards. Despite the narrow range of pH values, ANOVA revealed significant differences in pH among different sites for both QMP 3 ($p = 0.02$) and QMP 4 ($p < 0.01$). Whether these differences have any biologic or clinical implications is unknown. Graphing these data reveals a consistency in the results obtained from each site from year to year for pH and PLT count per unit, and the inverse relationship between PLT count per unit and pH is evident (e.g., for QMP 4, the three sites with the highest PLT count/unit, Sites 2, 4, and 7, were those with the lowest pH).

**Extended quality testing: results from QMP 3 and 4**

Site-by-site analysis of parameters for QMP 3 and 4, arranged by subcategories (PC metabolic measures and PLT characteristics, activation, and responsiveness) are shown in Tables 2 and 3. Significant differences among sites were observed for PLT concentration for QMP 4 ($p < 0.01$, Table 2), while there were no significant differences among sites for QMP 3. The two greatest mean PLT concentrations observed for QMP 4, at Sites 2 and 7, were significantly different from many of the other production sites. Analysis of PLT metabolic parameters by ANOVA revealed significant differences among sites for QMP 4 for pO$_2$, pCO$_2$, glucose, and lactate, although, possibly due to the different power of ANOVA versus the Tukey posttest, the source of the site-to-site differences were determined only for lactate.

No difference among sites was observed for ESC assays, which were conducted in QMP 4 (Table 3). Significant differences in CD62P expression among sites were seen for QMP 3 and QMP 4 (both $p < 0.01$). The four sites with the lowest CD62P expression were the same for both years of BC production (Sites 1, 2, 4, and 8). Site 6 had the highest CD62P expression for both QMP 3 and 4. In QMP...
### TABLE 2. Site-by-site analysis of PLT metabolic activity parameters for QMP 3 and 4

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Site</th>
<th>1</th>
<th>2</th>
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<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>p value</th>
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<tbody>
<tr>
<td>PLT concentration (×10^9/L)</td>
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<tr>
<td>QMP 4</td>
<td>880 ± 124</td>
<td>1065 ± 160</td>
<td>931 ± 175</td>
<td>1039 ± 74</td>
<td>850 ± 186</td>
<td>870 ± 105</td>
<td>1083 ± 166</td>
<td>870 ± 126</td>
<td>935 ± 168</td>
<td>&lt;0.01‡</td>
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<td>QMP 3</td>
<td>980 ± 159</td>
<td>957 ± 200</td>
<td>950 ± 120</td>
<td>1035 ± 243</td>
<td>883 ± 191</td>
<td>923 ± 150</td>
<td>957 ± 126</td>
<td>929 ± 154</td>
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<td>pO₂ (mmHg)</td>
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<tr>
<td>QMP 4</td>
<td>84 ± 19</td>
<td>79 ± 12</td>
<td>83 ± 18</td>
<td>80 ± 15</td>
<td>95 ± 20</td>
<td>99 ± 10</td>
<td>81 ± 19</td>
<td>91 ± 14</td>
<td>94 ± 15</td>
<td>0.01‡</td>
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<tr>
<td>QMP 3</td>
<td>87 ± 35</td>
<td>93 ± 15</td>
<td>102 ± 14</td>
<td>95 ± 13</td>
<td>110 ± 26</td>
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<td>102 ± 14</td>
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<td>pCO₂ (mmHg)</td>
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<tr>
<td>QMP 4</td>
<td>34 ± 3</td>
<td>38 ± 4</td>
<td>39 ± 7</td>
<td>39 ± 7</td>
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<td>34 ± 3</td>
<td>39 ± 6</td>
<td>40 ± 12</td>
<td>34 ± 4</td>
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<tr>
<td>QMP 3</td>
<td>42 ± 20</td>
<td>37 ± 5</td>
<td>37 ± 5</td>
<td>42 ± 13</td>
<td>33 ± 4</td>
<td>37 ± 4</td>
<td>35 ± 4</td>
<td>38 ± 4</td>
<td>ND</td>
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<td>Glucose (mmol/L)</td>
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<tr>
<td>QMP 4</td>
<td>14.9 ± 1.2</td>
<td>13.6 ± 1.1</td>
<td>14.3 ± 0.9</td>
<td>14.2 ± 0.9</td>
<td>14.7 ± 1.0</td>
<td>15.0 ± 1.0</td>
<td>14.5 ± 1.9</td>
<td>15.1 ± 0.9</td>
<td>14.2 ± 12</td>
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<td>QMP 3</td>
<td>14.9 ± 1.0</td>
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<td>15.4 ± 0.8</td>
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<td>14.8 ± 1.5</td>
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<td>Lactate (mmol/L)</td>
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<tr>
<td>QMP 4</td>
<td>12.1 ± 1.0</td>
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<td>13.3 ± 1.2</td>
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<td>13.5 ± 0.9</td>
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<td>13.7 ± 1.7</td>
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<td>14.9 ± 1.6</td>
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<td>0.06</td>
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</tbody>
</table>

* Data are reported as mean ±SD for each parameter for each site for QMP 3 and 4. One-way ANOVA and Tukey multiple comparison posttests were used to determine variance between sites for each year.
† For QMP 4, PLT concentration at Site 2 was significantly different from PLT concentration at Sites 5, 6, and 8 and PLT concentration at Site 7 was significantly different from PLT concentration at Sites 1, 5, 6, and 8.
‡ For QMP 4, CD62P expression at Site 1 was significantly different from CD62P expression at Sites 3 and 6, and CD62P expression at Site 6 was significantly different from CD62P expression at Sites 1, 2, 4, and 8. For QMP 3, CD62P expression at Site 8 was significantly different from CD62P expression at Sites 3 and 6.
ND = not determined.

### TABLE 3. Site-by-site analysis of PLT characteristics, activation, and responsiveness for QMP 3 and 4

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Site</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<td>MPV (fL)</td>
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<tr>
<td>QMP 4</td>
<td>8.3 ± 0.4</td>
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<td>8.5 ± 0.4</td>
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<td>QMP 3</td>
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<td>Morphology (score)</td>
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<tr>
<td>QMP 4</td>
<td>304 ± 19</td>
<td>289 ± 18</td>
<td>300 ± 22</td>
<td>304 ± 15</td>
<td>288 ± 30</td>
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<td>298 ± 15</td>
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<td>QMP 3</td>
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<td>279 ± 25</td>
<td>272 ± 26</td>
<td>284 ± 22</td>
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<td>CD62P (%)</td>
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<tr>
<td>QMP 4</td>
<td>26.6 ± 4.1</td>
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<td>35.3 ± 5.9</td>
<td>30.2 ± 5.8</td>
<td>31.2 ± 5.8</td>
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<td>QMP 3</td>
<td>30.8 ± 3.6</td>
<td>30.7 ± 5.7</td>
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<td>&lt;0.01†</td>
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<td>ESC (%)</td>
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<tr>
<td>QMP 4</td>
<td>42 ± 11</td>
<td>45 ± 11</td>
<td>37 ± 12</td>
<td>43 ± 8</td>
<td>43 ± 9</td>
<td>40 ± 10</td>
<td>43 ± 9</td>
<td>45 ± 11</td>
<td>38 ± 12</td>
<td>0.44</td>
<td></td>
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<tr>
<td>QMP 3</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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* Data are reported as mean ±SD for each parameter for each site for QMP 3 and 4. One-way ANOVA and Tukey multiple comparison posttests were used to determine variance between sites for each year.
† Significant at p < 0.05.
‡ For QMP 4, CD62P expression at Site 1 was significantly different from CD62P expression at Sites 3 and 6, and CD62P expression at Site 6 was significantly different from CD62P expression at Sites 1, 2, 4, and 8. For QMP 3, CD62P expression at Site 8 was significantly different from CD62P expression at Sites 3 and 6.
ND = not determined.
3, Site 6 was found to have a significantly higher expression of CD62P than Site 8, and in QMP 4 it was found to be significantly higher than Sites 1, 2, 4, and 8.

Table 4 shows correlation coefficients between pairs of parameters measured for QMP 3 and 4. A striking similarity and consistency of correlation between many parameters was observed for all years of QMP conducted thus far, across both production methods analyzed (QMP 1 and 2 data not shown). PLT concentration correlated significantly with many of the other parameters, particularly those relating to metabolism and, as expected, metabolic parameters tended to correlate significantly with each other. CD62P, which measures PLT activation and secretion, was also found to correlate significantly with ESC, which monitors PLT responsiveness.

### PLT CD62P expression among sites

While ANOVA identified variation among sites in many of the extended quality assays, posttests were only able to identify the source of differences for CD62P expression, PLT concentration, and lactate, indicating that these may be the most sensitive indicators of change (Tables 2 and 3). A closer analysis of CD62P expression levels across sites revealed consistent results between QMP 3 and QMP 4 for most sites (Fig. 2) and results for QMP 3 and 4 show a significant correlation with $r = 0.89$ ($p < 0.01$).

Site 6 was noted to have the highest CD62P expression during QMP 3 and during the early stages of QMP 4. Also, PCs sent by this site had a noticeably higher amount of air bubbles than PCs sent by other sites, giving them an unusual “foamy” appearance. Despite their unusual appearance, the site producing the PCs was not aware of any issue, and it was only via QMP that this was highlighted. The site was informed and a thorough investigation of the BC PC production method at that site revealed the omission of a step normally done toward the end of production to prevent excess air from entering the components. Introduction of this step resolved the issue of excess air bubbles in the PCs and led to reduced CD62P expression in later samples sent by this site, although overall CD62P levels for QMP 4 for Site 6 remained high with large SDs due to the more activated PCs received earlier during QMP 4.

### DISCUSSION

To assess the quality of PCs, standards or benchmarks against which products can be compared need to be established, and these should be sensitive enough to detect even minor alterations in product quality that might occur due to process deviations. Acceptable minimum and maximum values for routine QC measures define ranges into which tested PCs must fall, but within
these limits there is much room for variation and a lack of uniformity in the products; thus the ranges are too broad to create benchmarks. Via QMP, the distribution of pH and PLT count per unit within these limits was explored. Both were found to fall into narrower ranges than defined by the regulatory standards. For example, while QC standards define an acceptable pH range between 6.40 and 7.80, the pH of PCs monitored during QMP 4 fell between 6.87 and 7.37. This initial step in describing product specifications for PCs could be used to generate narrower target ranges for production.

Of the extended panel of PLT quality parameters, CD62P and lactate show potential as quality benchmarks for assessing production best practices and the effect of new processes and SOP changes. These are also hallmarks of the PLT storage lesion (PSL), the progressive deterioration in PLT quality, which limits storage to between 3 and 7 days depending on the jurisdiction.\(^\text{13,14}\) Although translation of PSL and its hallmarks to a prediction of the in vivo behavior of PLTs posttransfusion remains uncertain,\(^\text{15}\) for the purpose of generating in vitro quality benchmarks, assessing PLT quality in relation to the known hallmarks of PSL is useful.

For example, the increase in CD62P expression associated with PSL is well documented. CD62P expression measures PLT secretion and indicates the level of activation of the PLTs and is extensively used as a PLT quality measure as well as in PLT function tests.\(^\text{15}\) Via QMP, significant differences for CD62P expression among sites, ranging between 26.6 and 38.5% for QMP 4, were observed, suggesting the usefulness of CD62P as a sensitive PC quality marker. It is important to note that the clinical relevance of CD62P expression levels or their value as surrogates for prediction of the in vivo behavior of PLTs posttransfusion remains uncertain, despite many studies that have investigated this.\(^\text{13,16-18}\) This is in part due to the fact that PLTs are dynamic and can lose surface CD62P and that the relationship between CD62P expression and in vivo viability of PLTs is unclear.\(^\text{19}\) Despite its wide use, another issue with CD62P measurement is the huge interlaboratory variability in its measurement.\(^\text{20}\) Assessing CD62P during QMP at a single laboratory allowed us to define a normal range of CD62P levels for CBS PCs at expiry.

The timing of the QMP allowed an overview of the implementation of a new production method across the entire organization. A study conducted at a single site during the production method changeover between PRP PCs and the BC production method found that BC PCs have laboratory variables that suggest they are of higher quality than those produced by the PRP method,\(^\text{7}\) a finding that agrees with other studies.\(^\text{21-24}\) Via QMP, it was noted that, in general, variances among in vitro measures were lower in BC PCs versus PRP PCs, indicating that the pooled BC method produces a more consistent product and that the new method had been successfully implemented across most sites. QMP identified an issue at one site, noted by consistently higher CD62P expression, most likely related to the high amount of air bubbles seen in these PCs.\(^\text{25,26}\) Despite the altered appearance of the PCs, this anomaly had not been flagged at the site, but due to QMP the issue was identified and remedied. This highlights two important advantages of a QMP. First, it facilitates direct site-to-site comparisons of products that would not take place otherwise. Second, although all CBS sites operate using the same SOP, differences in practice can occur. Via QMP, sites at which best (or worst) practices prevail can be identified and this information can be used for continuous improvement of both the products and the SOPs.

Shipping and handling of samples can have a dramatic effect on PLT quality parameters.\(^\text{27}\) While the shipping procedures from every site were identical, uncontrollable variables were the shipping distance to the testing laboratory and the time without agitation for the PCs. An analysis to determine whether there was a correlation between quality parameters and the distance

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**Fig. 2.** PLT activation markers for QMP 3 and 4. (A) Mean percentage CD62P expression ± 1 SD for each production site for QMP 3 (■) and 4 (□), ordered from lowest to highest. Site 6 has the highest expression for both years. (B) CD62P expression for each site for QMP 3 versus QMP 4, showing a significant correlation with \(r = 0.89\).
between the production site and the QMP research laboratory found no consistent effect. Long periods without agitation can have a detrimental effect on PC quality and metabolic parameters, especially when the PLT concentration is high. All PCs arrived within 24 hours of shipping and were immediately stored with agitation, conditions that should have a minimal effect on PLT quality. An analysis was conducted for CD62P, lactate, and pH to determine whether there were any effects on the quality of the PCs that could be attributed to the day of interruption of agitation. No effects were noted.

For CBS, the real value of the QMP data is that it provides more detailed quality information than QC and allows a better understanding of the product. Specifically, via QMP the implementation of a new process over the whole organization was examined, demonstrating effective implementation as well as the overall higher quality (in terms of PSL markers) of the BC PC product. A production issue that had not been noticed in the manufacturing environment was identified through the QMP process, and the QMP team’s expertise was applied to thoroughly investigate and remedy this flaw. While the extended test panel did not reveal much regarding variation in PLT quality among sites, CD62P was found to be a good indicator of change in general. Via QMP, initial steps to look at the range of “normals” for CD62P and the QC measures, pH and PLT count per unit, were taken and this information could be used for future benchmarking. Overall, the additional information generated by QMP proved valuable to our organization and our experiences are a useful guide for other organizations who have implemented or are planning on implementing a similar program.

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CONFLICT OF INTEREST

There are no conflicts of interest from the authors of this publication.

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