Validation of a Portable Blood Gas Analyzer for Use in Challenging Field Conditions at High Altitude

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Background: Novel, portable blood gas analyzers (BGAs) may serve as essential point-of-care tools in remote regions, during air travel or in ambulance services but they have not been extensively validated.

Research Question: We compared accuracy of a portable BGA to a validated stationary device.

Methods: In healthy individuals and patients with chronic obstructive pulmonary disease participating in clinical field studies at different altitudes, arterial blood samples were obtained at rest and during exercise in a hospital at 760 m and in a high altitude clinic at 3100 m. Paired measurements by a portable BGA (EPOC, Siemens Healthcare) and a stationary BGA (Rapidpoint500, Siemens Healthcare) were performed to compute bias (mean difference) and limits of agreement (95% CI of bias).

Results: Of 105 individuals, 248 arterial blood samples were analyzed, 108 at 760 m, 140 at 3100 m. Ranges of values measured by portable BGA were: pH 7.241−7.473, PaCO₂ 21.5−52.5 mmHg, and PaO₂ 45.5−107.1 mmHg. Bias (95% CI) between devices were: pH 0.007 (−0.029 to 0.044), PaCO₂ −0.3 mmHg (−4.8 to 4.2), and PaO₂ −0.2 mmHg (−9.1 to 4.7). For pH, agreement between devices was improved by the equation to correct pH by portable BGA = −1.37 + pH measured × 1.19; bias after correction −0.007 (−0.023 to 0.009). The portable BGA was easily handled and worked reliably.

Interpretation: Accuracy of blood gas analysis by the portable BGA in comparison to the reference BGA was adequate for clinical use. Because of portability and ease of handling, portable BGA are valuable diagnostic tools for use in everyday practice as well as under challenging field conditions.

Keywords: blood gas analyzer, point-of-care testing, arterial blood gas (ABG) analyzers, hypoxaemia respiratory failure, hypercapnia, high altitude
INTRODUCTION

Mountain travelers as well as airplane passengers experience hypobaric hypoxia that may induce hypoxia-related illness and changes in metabolic conditions. Patients with cardiovascular or pulmonary diseases are particularly susceptible. Unfortunately, there is a lack of information about these health risks, partly due to the heavy weight of conventional diagnostic instruments for biochemical analysis of blood, the required external electrical power supply, and related major logistical efforts and costs. To address these issues, novel, portable devices for the analysis of blood gases, electrolytes and other parameters have been developed.

The EPOC device (Siemens Healthcare) is a battery-operated, portable blood gas analyzer (BGA) for use in challenging point-of-care settings such as in remote mountain regions, during air travel, or in emergency ambulance services (Epocal Inc., 2020). Near sea level, the EPOC portable BGA has been evaluated in detail and proven to have high accuracy (Nichols et al., 2008; Nicolas et al., 2013; Stotler and Kratz, 2013; Luukkonen et al., 2016). The main advantages of the EPOC are its portability due to the low weight of only 500 g, battery driven operation, and wireless connectivity. In addition, the EPOC test cards can be stored at room temperature and do not need to be refrigerated. To what extent the EPOC allows accurate blood gas measurements in field conditions such as in high mountain areas still requires further investigations (Leino and Kurvinen, 2011).

The purpose of the current study was to comprehensively validate the EPOC in comparison to an established stationary reference device (Rapidpoint500, Siemens Healthcare) (Siemens Medical Solutions USA, 2020). We performed paired analyses of samples from healthy individuals and from patients with chronic obstructive pulmonary disease (COPD) participating in studies at different altitudes (760 and 3100 m) at rest and during exercise. This assured that arterial blood gases and pH could be studied over a wide range of values. We tested the hypothesis that the portable BGA (EPOC) measures arterial blood gases (pH, PaO₂, and PaCO₂) with clinically acceptable accuracy within ranges specified by the clinical laboratory improvement amendments (CLIA) (Astles et al., 2013) compared to the stationary reference device (Rapidpoint500).

MATERIALS AND METHODS

Study Design and Setting

In this study, arterial blood samples from participants in two randomized, placebo-controlled, double-blind, parallel trials were analyzed. The initial trials evaluated effects of preventive acetazolamide treatment (375 mg/day) on the incidence of acute mountain sickness (AMS) during a stay at 3100 m in patients with COPD and in age-matched healthy controls (Furian et al., 2019). The results of blood analysis by the EPOC device, the focus of the current study, has not been published. After baseline evaluations in the National Center of Cardiology and Internal Medicine (NCCIM) in Bishkek, Kyrgyzstan, 760 m, participants traveled by bus to a remote high-altitude clinic at 3100 m and stayed there for two nights. Over the course of the studies, repeated arterial blood samples were obtained at rest and during cycling exercise tests and analyzed by the EPOC and the reference device, the Rapidpoint500. The protocol was approved by the Ethics Committees of the NCCIM and participants provided written informed consent.

Participants

In trial 1, men and women with COPD living below 800 m were recruited. Inclusion criteria were an age of 18–75 years, COPD diagnosed according to GOLD, FEV₁ 40–80% predicted, pulse oximetry (SpO₂) > 91%, and PaCO₂ < 45 mmHg at 760 m. In trial 2, healthy individuals of the same age were admitted. The exclusion criteria were any acute disease or unstable health condition and allergy to sulfonamides.

Measurements and Outcomes

Arterial blood samples were collected once in the morning and over the course of the day before and toward the end of an exercise test, both at 760 and 3100 m. Each sample was analyzed immediately in triplicate, first by the Rapidpoint500, then by the EPOC and, finally, again by the Rapidpoint500. The value from the EPOC device was compared to the mean of the corresponding values by Rapidpoint500 to avoid bias from a time delay between measurements by the two devices. Changes in variables over the course of successive measurements in the same person were also analyzed. Over the course of 25 days, the repeatability of the EPOC and the Rapidpoint500 devices was additionally checked daily by comparison to two different calibration solutions with acidic and alkalotic pH ranges.

Processing of samples was performed according to manufacturer’s guidelines with special attention to pre-analytical factors (e.g., timing and elimination of bubbles in the samples). Three main variables (pH, PaCO₂, PaO₂) and eight other variables (hematocrit [Hct], hemoglobin concentration [tHb], glucose, lactate, sodium, potassium, calcium, and chloride) were analyzed. The limits for the clinical acceptability are ±5 mmHg for PaCO₂, ±3SD (±8.0 mmHg) for PaO₂, and ±0.04 for pH according to CLIA (Astles et al., 2013).

Devices

The EPOC is a battery powered device, dimensions 60 × 180 × 30 mm, weight 500 g, with a touch-screen display (25 × 30 mm), integrated barcode scanner, and optional external printer. According to the manufacturer, EPOC can be operated at barometric pressure equivalents of altitudes up to 5100 m and temperature 15–30°C. For blood gas analysis, a droplet of blood is inserted into a small cavity of a test card containing sensors for the analysis. The calibration and analysis take approximately 7 min. Results are shown on the display and can be transmitted by wireless (bluetooth) connection to a printer and to a computer as needed. The EPOC test cards can be stored at room temperature (15–30°C).
The Rapidpoint500 is a stationary BGA (dimensions 420 × 550 × 300 mm, weight 16.6 kg, with a touch-screen display 211 × 158 mm) with a turnaround time of 3–4 min. Cartridges for 250 or 500 measurements and waist are inserted into the device. Cartridges not inserted into the device require storage at 2–8°C. Operating conditions of the Rapidpoint500 are barometric pressure equivalents of altitudes up to 4572 m and temperature 15–30°C (Epocal Inc., 2020; Siemens Medical Solutions USA, 2020).

**Statistics**

Data are summarized as means ± SD. Agreement and precision are quantified according to Bland and Altman and CLSI guidelines, reporting mean differences between methods as bias, and 95% confidence interval as limits of agreement (Giavarina, 2015). Trends of differences in agreement between methods were evaluated by linear regression analysis. A probability P < 0.05 was assumed as statistically significant.

**RESULTS**

In 105 individuals, 248 radial artery blood samples were obtained for paired analyses by both devices, 108 at 760 m and 140 at 3100 m. 119 samples were collected at rest and 129 samples during exercise. The mean time between the first and second measurement in Rapidpoint500 was 3 min and 10 s (2–19 min). EPOC measurements were taken in-between.

The comparison of blood gases between EPOC and Rapidpoint500 are summarized in Table 1 and illustrated in Figure 1. There was good agreement between the paired measurements without a significant bias. The proportions of values measured by EPOC that fell within the range of acceptability compared to values from Rapidpoint500 were 96% for pH, 96% for PaCO₂, and 97% for PaO₂. The 95% confidence interval for pH (−0.029 to 0.044) was only in the lower range within the clinical acceptability of ±0.04. The 95% CI for PaCO₂ (−4.8 to 4.2 mmHg) was within the clinical acceptability range of ±5.0 mmHg. The 95% confidence interval for PaO₂ (−9.1 to 4.7 mmHg) was only in the upper range within the clinical acceptability range of ±8 mmHg. Figure 2 shows identity plots of changes in pH and blood gases over the course of the study in 14 participants.

Regression analysis of values measured by EPOC as dependent and values measured by Rapidpoint500 as independent variables provided the following equation to correct the PaO₂:

\[
\text{PaO}_2\text{corrected} = 9.45 + \text{PaO}_2\text{measured} \times 0.90 (R^2 = 0.94),
\]

bias 0 mmHg (−6.2 to 6.2). A trend for overestimation of pH by EPOC in the low and underestimation in the high range could be corrected by the equation \(\text{pH}_{\text{corrected}} = -1.37 + \text{pH}_{\text{measured}} \times 1.19\) (\(R^2 = 0.91\)), corrected bias −0.007 (−0.023 to 0.009). No significant trend could be detected for PaCO₂ (\(R^2\) of regression for PaCO₂ = 0.7).

To test repeatability of measurements, we performed repeated measurements of standard reference solutions with EPOC (total of 54) and Rapidpoint500 (n = 50) over a period of 25 days (Table 2). The ranges in repeated measurements with two reference solutions (acid and basic) measured by EPOC were: pH 6.92–7.61, PaCO₂ 17.6–86.6 mmHg, and PaO₂ 48.4–256.6 mmHg. Coefficients of variation (SD/mean) for the results in EPOC were for pH 0.2%, PaCO₂ 3.6%, and PaO₂ 7.2%. The ranges in Rapidpoint500 were pH 7.136–7.584, PaCO₂ 20.7–75.3 mmHg, and PaO₂ 61.7–176.2 mmHg. The coefficients of variation for the Rapidpoint500 were pH 0.4%, PaCO₂ 1.8%, and PaO₂ 1.3%.

Handling of EPOC was easy and the device worked reliably. When the test cards were used according to the guidelines, they did not have any failures. Calibration of each test card took 3 min, the analysis time for one measurement was maximally 7 min. The data were transmitted quickly from the reader to the computer or a printer via Bluetooth connection. During 248 measurements with EPOC no problems with the technique or the software were encountered. The test cards, stored at room temperature, worked flawlessly.

For the sake of completeness and future reference, exploratory comparisons of additional variables have also been performed and are reported in Table 3.

**DISCUSSION**

In the current study, we validated the new portable BGA EPOC in comparison to the established stationary device Rapidpoint500. We found close agreement between the two devices in measurement of the pH, PaCO₂, and PaO₂ with ≥96% of values measured by the EPOC falling within the predefined range of clinically acceptable accuracy compared to the reference (Astles et al., 2013). If linear regression analysis was applied to correct for minor trends of differences between devices near perfect agreement could be obtained, i.e., all measurements were within the clinically acceptable range. In our study, including measurements in a hospital setting and in a high-altitude clinic with measurements performed at rest and during exercise, the EPOC was easy to use and reliable.

**Table 1** Agreement among EPOC and Rapidpoint500 measurements.

| Variable | Rapidpoint500 | EPOC | Mean difference ± SD (EPOC – Rapidpoint500) | Limits of agreement (95% CI) | Clinical acceptability |
|----------|---------------|------|---------------------------------------------|-----------------------------|------------------------|
| pH       | 7.355 ± 0.065 | 7.362 ± 0.044 | 0.007 ± 0.019 | −0.029 to 0.044 | ±0.04 |
| PaCO₂ (mmHg) | 35.4 ± 5.6 | 35.1 ± 5.2 | −0.3 ± 2.3 | −4.8 to 4.2 | ±5.0 |
| PaO₂ (mmHg) | 72.1 ± 13.1 | 69.9 ± 14.2 | −2.2 ± 3.5 | −9.1 to 4.7 | ±3SD, ±8.0 |

Values are presented as mean ± SD. The suggested clinical acceptability range is obtained from the Astles et al. (2013), CLIA requirements for proficiency testing.
Therefore, our study suggests that the device is a valuable tool for application in various, challenging field conditions, specifically including high altitude.
Previous studies have evaluated the EPOC near sea level. Luukkonen et al. (2016) compared the EPOC with Rapidpoint 500 and three other stationary BGA. Among 72 critically ill patients, there was good correlation between devices ($R^2 > 0.96$) for the pH and PaO$_2$ but $R^2 = 0.87$ for PaCO$_2$ was slightly reduced with a significant bias and limits of agreement exceeding the recommended range. Unfortunately, a formal analysis of bias and precision of the measurements in absolute units was not presented which hampers a direct comparison to the current results. Nichols et al. (2008) analyzed 143 blood samples at five different locations with the EPOC and another portable BGA, the i-STAT (Abbott Point of Care). The EPOC showed a superior repeatability than the i-STAT for pH and blood gases (coefficient of repeatability of 0.08–3.0% vs. 0.17–5.3%) but the statistical analysis was not conclusive in terms of agreement between devices as no bias and limits of agreement were reported. Nevertheless, the authors pointed out the benefits of the EPOC test cards that could be stored at room temperature without the need of a refrigerator which facilitates logistics in a point of care setting. Chen et al. (2016a) analyzed 118 specimens from 40 patients undergoing cardiopulmonary bypass surgery using the stationary device GEM4000 (Instrumentation Laboratory), 3 EPOC devices, and 2 other BGA. Bias between EPOC and GEM4000 were for pH $-0.004$, PaCO$_2$ $-0.9$ mmHg, and PaO$_2$ 6.4 mmHg. Among the two point-of-care devices, EPOC and i-STAT, they found bias's in pH 0.001, PaCO$_2$ $-2.3$ mmHg, and PaO$_2$ 13.3 mmHg which were greater than the corresponding bias's among EPOC and Rapidpoint500 in the current study (PaCO$_2$ $-0.3$ mmHg and PaO$_2$ 2.2 mmHg). In the same data set (Chen et al., 2016b), a linearity analysis of pH, PaCO$_2$, and PaO$_2$ revealed values of $R^2 > 0.95$ for EPOC vs. GEM4000, i-STAT and NovaCCX (Nova Biomedical). Stotler and Kratz (2013) reported considerable bias among EPOC, Nova CXX, and i-STAT in point-of-care settings and the EPOC tests had a relatively high failure rate in the first year after implementation in hospitals. During our investigations, we had no failures with EPOC analyses that were performed strictly according to manufacturer’s guidelines by well-trained users suggesting that this was essential for successful application.

In two studies, results of capillary blood analyzed with EPOC were compared to corresponding results of venous or arterial samples performed with standard devices in critically ill patients (Kim and Kim, 2018; Shin et al., 2020). The studies suggested that portable BGA are useful for application in intensive care or emergency services when rapid sampling and on-site analysis of blood is essential.

Further studies performed with blood samples from animals (horses or dogs) are not discussed in detail here. These results showed a good agreement between EPOC and the reference analyzers (Elmeshreghi et al., 2018; Kirsch et al., 2019).

A major strength of our study was the use in various settings, i.e., at low and high altitude, in a large tertiary care center and in a remote high-altitude clinic, with a wide range of variables measured due to the testing at rest as well as during exercise. A limitation was that we compared the EPOC to only one type of stationary BGA even though the Rapidpoint500 is a well validated device. The storage of EPOC test cards at room temperature without dependency on a refrigerator was an important advantage for application of the device under field conditions. A limitation of the EPOC was a relatively long calibration time of 3 min after insertion of the test card. While this might be adequate for point-of-care assessments in an individual patient it might represent a limitation in a hospital setting with high-volume measurement sequences.

### Table 2: Repeatability of pH and blood gas measurements.

| Variable      | Mean ± SD | Coefficient of variation (%) | Observed range |
|---------------|-----------|------------------------------|----------------|
| pH EPOC      | 7.265 ± 0.014 | 0.2                         | 6.918–7.610    |
| pH Rapidpoint500 | 7.348 ± 0.003 | 0.04                        | 7.136–7.584    |
| PaCO$_2$ EPOC (mmHg) | 51.3 ± 1.9     | 3.6                         | 17.6–86.6      |
| PaCO$_2$ Rapidpoint500 (mmHg) | 46.2 ± 0.9     | 1.8                         | 20.7–75.3      |
| PaO$_2$ EPOC (mmHg) | 125.3 ± 9.1     | 7.2                         | 48.4–256.6     |
| PaO$_2$ Rapidpoint500 (mmHg) | 110.8 ± 1.5     | 1.3                         | 61.7–176.2     |

Values are presented as mean ± SD, n = for EPOC, and n = for Rapidpoint500. Coefficients of variation are computed as SD/mean of two consecutive measurements by the same blood gas analyzer.

### Table 3: Comparison of additional variables between EPOC and Rapidpoint500.

| Variable | Rapidpoint500 | EPOC | Range       | Mean difference | 95% CI | Clinical acceptability |
|----------|---------------|------|-------------|-----------------|-------|------------------------|
| Hct (%)  | 45.0 ± 4.6    | 44.0 ± 5.5 | 26.3–67.3   | $-0.99$         | $-5.44$ to $3.45$ | ±6%                     |
| tHb (g/dl) | 15.3 ± 1.6    | 15.0 ± 1.8  | 9.0–19.4    | $-0.33$         | $-1.84$ to $1.18$ | ±7%, ±1.07              |
| Glu (mmol/l) | 5.84 ± 1.34   | 5.91 ± 1.35 | 3.20–14.28  | 0.07            | $-0.48$ to $0.61$ | ±10%, ±0.58             |
| Lac (mmol/l) | 4.56 ± 3.77   | 4.73 ± 4.26   | 0.47–14.48  | 0.17            | $-1.22$ to $1.56$ | ±20%, ±0.91             |
| Na (mmol/l) | 142.2 ± 3.2   | 143.8 ± 2.7   | 137.1–151.2 | 1.54            | $-2.03$ to $5.11$ | ±4.0                    |
| K (mmol/l)  | 4.19 ± 0.53   | 4.07 ± 0.48   | 3.29–6.78   | $-0.12$         | $-0.33$ to $0.09$ | ±0.5                    |
| Ca (mmol/l) | 12.4 ± 0.05   | 12.2 ± 0.05   | 1.07–1.33   | $-0.01$         | $-0.09$ to $0.06$ | ±0.25                   |
| Cl (mmol/l) | 109.0 ± 2.5   | 109.8 ± 2.9   | 104.0–117.8 | 0.80            | $-2.40$ to $3.99$ | ±5%, ±5.5               |

Values are presented as mean ± SD. The recommended clinical acceptability range is obtained from the Astles et al. (2013), CLIA requirements for proficiency testing.
CONCLUSION

The results of the current study show that EPOC allows accurate measurements of arterial blood gases in a challenging field setting. As the device was easy to use and robust it might serve as a valuable tool for point-of-care applications including at high altitude, during transports and in remote locations where electrical power is not available.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because Data will be made available for research purposes within limits set by the ethics committee. Requests to access the datasets should be directed to KB.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee National Center of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan. The patients/participants provided their written informed consent to participate in this study.

REFERENCES

Astles, J. R., Stang, H., Alspsach, T., Mitchell, G., Gagnon, M., and Bosse, D. (2013). CLIA requirements for proficiency testing: the basics for laboratory professionals. MLO Med. Lab. Obs. 45, 8–10.
Chen, J., Gorman, M., O’Reilly, B., and Chen, Y. (2016a). Analytical evaluation of the epoc(R) point-of-care blood analysis system in cardiopulmonary bypass patients. Clin. Biochem. 49, 708–712. doi: 10.1016/j.clinbiochem.2015.12.015
Chen, J., Gorman, M., O’Reilly, B., and Chen, Y. (2016b). Linearity analysis and comparison study on the epoc(R) point-of-care blood analysis system in cardiopulmonary bypass patients. Data Brief 6, 847–852. doi: 10.1016/j.dib.2016.01.040
Elmashreghi, T. N., Grubb, T. L., Greene, S. A., Ragle, C. A., and Wardrop, J. A. (2018). Comparison of Enterprise Point-of-Care and Nova Biomedical Critical Care Xpress analyzers for determination of arterial pH, blood gas, and electrolyte values in canine and equine blood. Vet. Clin. Pathol. 47, 415–424. doi: 10.1111/vcp.12635
Epocal Inc. (2020). Epoc System Manual. Available Online at: https://www.woodleyequipment.com/images/Image/File/epoc20System%20Manual%20English%202051004969-01.pdf (accessed August 10, 2020)
Furian, M., Buergin, A., Scheiwiller, P. M., Mayer, L., Schneider, S., and Mademilov, M. (2019). Prevention of altitude-related illness in patients with COPD by acetazolamide. RCT. Eur. Respir. J. 54(Suppl. 63):A3938.
Giavarina, D. (2015). Understanding Bland Altman analysis. Biochem. Med. 25, 141–151. doi: 10.11613/bm.2015.015
Kim, C., and Kim, H. (2018). Emergency medical technician-performed point-of-care blood analysis using the capillary blood obtained from skin puncture. Am. J. Emerg. Med. 36, 1215–1221. doi: 10.1016/j.ajem.2017.12.025
Kirsch, K., Dettileux, J., Serteyn, D., and Sanderson, C. (2019). Comparison of two portable clinical analyzers to one stationary analyzer for the determination of blood gas partial pressures and blood electrolyte concentrations in horses. PLoS One 14:e0211104. doi: 10.1371/journal.pone.0211104
Leino, A., and Kurvinen, K. (2011). Interchangeability of blood gas, electrolyte and metabolite results measured with point-of-care, blood gas and core laboratory analyzers. Clin. Chem. Lab. Med. 49, 1187–1191.
Luukkonen, A. A., Lehto, T. M., Hedberg, P. S., and Vaskivuo, T. E. (2016). Evaluation of a hand-held blood gas analyzer for rapid determination of blood gases, electrolytes and metabolites in intensive care setting. Clin. Chem. Lab. Med. 54, 585–594.
Nicolas, T., Cabrolier, N., Bardonnet, K., and Davani, S. (2013). [Evaluation of a new blood gas analysis system: RapidPoint 500(R)]. Ann. Biol. Clin. 71, 305–311. doi: 10.1684/abc.2013.0821
Nichols, J. H., A. Rajadhyaksha, and M. Rodriguez (2008). Evaluation of the Enterprise Point-of-Care (EPOC) System for Blood Gas and Electrolyte Analysis. Point of Care 7, 7–11. doi: 10.1097/poc.0b013e318163d402
Shin, H., Lee, I., Kim, C., and Choi, H. J. (2020). Point-of-care blood analysis of hypotensive patients in the emergency department. Am. J. Emerg. Med. 38, 1049–1057. doi: 10.1016/j.ajem.2019.158363
Siemens Medical Solutions USA (2020). RAPIDPoint 500 Systems, Technical Specifications. Available online at https://usa.healthcare.siemens.com/point-of-care/blood-gas/rapidpoint-500-systems/technical specifications (accessed August 10, 2020)
Stotler, B. A., and Kratz, A. (2013). Analytical and clinical performance of the epoc(R) blood gas analysis system: evaluation of a new blood gas analysis system: RapidPoint 500(R)). Am. J. Emerg. Med. 31, 781–786 doi: 10.1016/j.ajem.2013.03.020

AUTHOR CONTRIBUTIONS

KB, AB, and MF contributed to the conception and design of the study, data collection, analysis, interpretation, and drafting the article. LM, SS, MM, and MB contributed to data collection, analysis, and interpretation of data. TS, SU, and KB contributed to obtaining funding, to the conception and design of the study, acquisition, analysis, and interpretation of data. All authors critically revised the manuscript for important intellectual content, they approved the version to be published and all agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors contributed to the article and approved the submitted version.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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