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The importance of the use of adequate reference materials in density measurements performed in hemodialysis treatments

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ABSTRACT

In hemodialysis, oscillation-type density meters are used to measure the density of the acid component of the dialysate solutions used in the treatment of kidney patients. An incorrect density determination of this solution used in hemodialysis treatments can cause several and adverse events to patients. Therefore, despite the Fresenius Medical Care tight control of the density meters calibration results, this study shows the benefits of mimic the matrix usually measured to produce suitable reference materials for the density meter calibrations.

1. Introduction

Hemodialysis is a renal function replacement therapy. During hemodialysis, the patient's blood is passed through a filter outside the body and then reintroduced to the patient. Tiny pores in the filter membrane filter out toxins, while vital components, such as proteins, are left in the blood. Excess water can also be removed through these tiny pores. The process is controlled by a dialysis machine that is equipped with a blood pump and monitoring systems that ensure safety. The machine can also administer drugs, e.g. Heparin, to prohibit blood clotting during the treatment [1].

1.1. The role of density measurements in hemodialysis

Dialysate consists of purified water and various substances dissolved in it. With the exception of glucose, the substances dissolved in the dialysate are all electrolytes. Their concentration (besides potassium and the buffer substance) closely resembles the concentration of the electrolytes occurring naturally in the blood. Dialysate regulates the electrolyte and acid–base balance of the dialysis patient and removes waste products. Dialysate is produced by the hemodialysis machine combining purified water, acid concentrated solution and bicarbonate concentrated solution. Acid concentrated solution is obtained in each Hemodialysis Center through a first dilution certified process using certified mixtures of needed electrolytes in ultra-pure water. The final product, i.e. the dilution, is then validated by a calibrated portable oscillation-type density meter. A wrong dilution means a product that is not conform to be used in patient treatments. If the oscillation-type density meters are not properly calibrated, then a wrong mixture of electrolytes will be used for patients' treatments causing several and adverse events to them. A second dilution of these concentrated electrolytes will take place in the dialysis machine. Normally ratios of 1:35 or 1:45 are used [2]. To be sure that the final dialysate is adequate for the treatment based on the medical prescription, the maximum permissible error given by the calibration certificate of the density meter, on the first dilution process, is set to 0.001 g cm^{-3}.

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1.2. Oscillation-type density meters

The working principle of an oscillation-type density meter is based on the law of harmonic oscillation, in which a U-shaped tube, i.e. the measuring cell, is completely filled with the sample to be analyzed, and subjected to an electromagnetic force. The measurement of the frequency and duration of vibration of the tube filled with the sample allows the determination of the density value of the sample. This measuring principle is based on the Mass-Spring Model [3].

Like all measuring instruments, the results obtained by an oscillation-type density meter may vary in time. Errors may be due to: instrumental changes due to physical changes in the U-tube (mass, volume or elasticity coefficient); changes in the electronic operation of the instrument; damage due to mishandling; instrument movement during measurement, especially if at a different angle to the horizontal; effects of liquid on the surface of the tube, such as deposition of material, or erosion by the sample or by the cleaning method. Therefore the calibration is an essential key to understand and take into account the measuring behavior of the measuring instruments.

1.3. The National Metrology Institute and the calibration of the FME density meters

Density, ρ, is defined as the mass per unit volume of a fluid or a solid [4], and depends, in general, on both temperature and pressure. It is a property of extreme importance, as it is routinely applied in the control of industrial processes, but also used in fields such as biomedical diagnostics, fiscal control and basic research. The uncertainty requirement in a density measurement depends on its specific application and can vary from better than 0.1% to 1% [5].

Calibration is an operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication [6]. Reference materials are often used in calibration operation as measurand generator. According to ISO Guide 34 [7], a reference material can be described by a material, sufficiently homogeneous and stable with respect to one or more specified properties, which has been established to be fit for its intended use in a measurement process.

In the Laboratory of Properties of Liquids (LPL) of the National Metrology Laboratory of Portuguese Institute for Quality (IPQ), density determination of liquid samples can be performed with an oscillation-type density meter DMA 5000 (Anton Paar). An internal procedure based on the ISO 15212-1 [8] is used for these measurements. The uncertainty budget according to GUM methodology [9], previously established [10], comprises four uncertainty components: the uncertainty associated with the measurements repeatability, the uncertainty due to the density meters resolution, the uncertainty related to the standard density meter calibration, which depends on the uncertainty of the Certified Reference Materials (CRM) used, and the uncertainty of the temperature and pressure measurement of the sample inside the measuring cell. The calibration of portables oscillation-type density meters in IPQ is performed by comparative method using reference materials that are measurand [6] generators (Fig. 1). These reference materials are characterized with IPQ standard density meter (DMA 5000, Anton Paar). The density

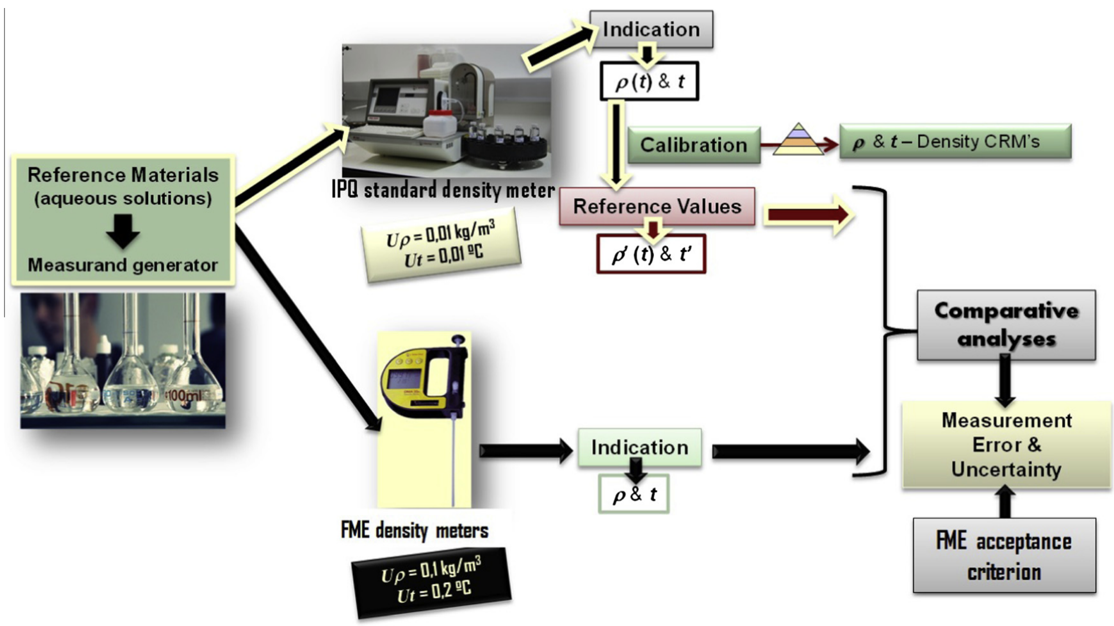

Fig. 1. Schematic representation of FME oscillation-type density meters calibration by comparative method in IPQ.