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Technical Note

A novel method for conformity assessment testing of dialysis machines for post-market surveillance purposes

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Abstract.
BACKGROUND: Dialysis machines are used regularly in healthcare practice. They are classified as a type of medical device with moderate and high risk therefore significant requirements are placed on their safety and performance every time they are used on patients. The new Medical Device Regulation (MDR) defines medical device post-market surveillance (PMS) as performed by independent, third-party, notified bodies more strategically in hope to improve traceability of device performance. However, there is still an apparent gap in terms of standardised conformity assessment testing methods.
OBJECTIVE: This paper proposes a novel evidence-based method for conformity assessment testing of dialysis machines for post-market surveillance purposes.
METHOD: The novel method is developed according to the International Organisation of Legal Metrology (OIML) guidelines and is to be used for the purpose of conformity assessment testing of Dialysis machines with respect to their metrological characteristics during PMS.
RESULTS: The developed method was validated between 2018 and 2021 in healthcare institutions of all levels. The results obtained during validation suggest that conformity assessment testing of dialysis machines as a method used during PMS contributes to significant improvement in devices' accuracy and reliability.
CONCLUSION: A standardized approach in conformity assessment testing of dialysis machines during PMS, besides increasing reliability of the devices, is the first step in digital transformation of management of these devices in healthcare institutions opening possibility for use of artificial intelligence.

Keywords: Medical device, dialysis machines performance, testing, standardisation, post-market surveillance

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1. Introduction

According to the Food and Drug Administration (FDA) [1], dialysis machine is a medical device (MD) that is used as an artificial kidney system for the treatment of patients with renal failure or conditions and that consists of an extracorporeal blood system, a conventional dialyzer, a dialysate delivery system, and accessories. Blood from a patient flows through the tubing of the extracorporeal blood system and accessories to the blood compartment of the dialyzer, then returns through further tubing of the extracorporeal blood system to the patient. Dialysis machines are classified to classes based on risk. In the European Union, according to the Medical Device Regulation (MDR) [2], dialysis machines are classified as Class IIa. This classification determines regulatory scrutiny to which devices are subjected to before placing on the market. Generally, Class II determines a medical device with a moderate to high risk that requires special controls. Taking into account the nature of the substances involved, the relevant part of the body and the method of application, such devices are considered active therapeutic devices whose use can occur in a potentially dangerous manner.

Due to the fact that they circulate blood through the dialysis system and regulate pressure, temperature, treatment duration, and fluid evacuation, dialysis machines can be designated as medical devices with a measuring function (MDMF) [3]. Medical device measurements are made possible by sensors or measuring equipment inside the devices themselves. The effectiveness of MD's sensors and measuring equipment has a direct impact on the overall standard of product quality. Each predefined setting for dialysis machines' conductivity and temperature of the dialysis fluid, and the pressure of the measuring device serves a particular purpose. When dialysis machines fall short of their intended goal of purification of the patient's blood, dangerous adverse outcomes may result. In this regard, the inspection of the dialysis machine will refer to measurements of the conductivity and temperature of the dialysis fluid, as well as the pressure of the measuring device, so the post-marketing supervision should be focused on the accuracy and safety of the delivered values of the specified measurement quantities.

The classification suggests that dialysis machines belong to the moderate to high risk category since their role is to filter and purify the blood, thus helping to maintain fluid and electrolyte balance when the kidneys cannot do their job. For this reason, it is crucial that the device performs its role at a high level of reliability. An extensive set of standards is used to demonstrate compliance with the essential safety and performance requirements of dialysis machines [4]. These standards can be grouped into three categories, general quality standards, electrical safety standards, special standards for dialysis machines. Even though dialysis machines are subjected to a variety of test prior to being placed on the market, there is a significant gap in their performance testing after they have been placed onto the market. As for all other devices, the performance of dialysis machines deteriorates significantly over time and due to the vital function they perform for patients in need, their non-compliant performance may result in severe adverse events.

This paper presents the novel methodology for conformity assessment of dialysis machines during usage taking into account the International Organisation of Legal Metrology (OIML) approach defined for other types of medical devices with measuring functions such as sphygmomanometers. Presented novel method can be used by national regulators as a gold standard in defining regulatory framework considering conformity assessment of devices used in healthcare.

2. Method

To present the novel methodology, the accepted concept of OIML guidelines for other medical devices with measuring functions such as thermometers or sphygmomanometer was followed [5]. The method,

developed under OIML recommendations, is reported as a coherent structure, through the following parts:

1. Definition of technical requirements for dialysis machines
2. Definition of metrological requirements for dialysis machines
3. Description of method for visual inspection
4. Description of method for electrical safety inspection
5. Description of method for performance inspection
6. Summary and expression of test results

During method validation, the performance assessment testing of dialysis machines was done by using two etalons, Fluke Biomedical ESA 620 electrical safety analyser [6] and MesaLabs 90XL Dialysis conductivity, pH, temperature & pressure metre [7]. Both of these devices were periodically calibrated in EN ISO 17025 accredited laboratories [8]. The novel method was validated during the 2018–2021 time period. The presented data was analysed using a statistical approach.

3. Results and discussion

The results are presented in two parts. The first part consists of reporting the novel methodology for conformity assessment testing of dialysis machines and the second part consists of the validation report of this methodology done in real-time by inspection bodies in Bosnia and Herzegovina and Republic of Serbia.

3.1. Novel method for conformity assessment of dialysis machines

The method for conformity assessment defines technical and metrological requirements for the device and methods to test these requirements in the environment where the device is used.

3.1.1. Technical and metrological requirements of dialysis machines

Technical and metrological requirements are defined based on the regulatory requirements stated in directives/regulation, manufacturers' technical specifications and international standards defining safety and performance of medical devices.

3.1.1.1. Technical requirements

In order to ensure safety and reliability of dialysis machines once they enter the market and once they are used in clinical settings the periodical inspection of their technical requirements is very important. In order to ensure traceability of the devices, labels and markings shall be visible, legible and indelible, and it is not possible to remove them without permanent damage. In case of the dialysis machines, the technical requirements are formalised in the following manner:

- Label and marking
  - Name and/or trademark of manufacturer
  - Production mark (basic type)
  - Year of fabrication
  - Unique serial number
  - CE mark of appropriate administrative marking
- Construction of the device that guarantees security against any interference to metrological characteristics.

- The display shall be designed and arranged so that the information including measuring values can be read and easily recognized.
- Power supply: 220–240 V AC, 50/60 Hz.
- Temperature: 21–26°C.
- Compliance with IEC 60601-2-16 Medical electrical equipment – Part 2–16: Particular requirements for basic safety and essential performance of haemodialysis, hemodiafiltration and hemofiltration equipment [9].

For inspection of all above mentioned requirements, a testing method needs to be adopted. As per OIML recommendations, the testing of these types of the requirements is to be carried out by visual inspection and by electrical safety inspection in accordance with IEC 60601 [9].

3.1.1.2. Metrological requirements

Reliability of medical devices can be proven with its compliance with metrological requirements. Meteorological parameters such as error, accuracy and uncertainty are quantitative parameters specific for every device that serve as an evidence of device reliability. For every measurement device specific parameters are defined by its manufacturer such as measurement unit, range and division and accuracy. Following the OIML guideline, in case of the dialysis machine, the metrological requirements are formalised in the following manner:

- Measurement unit
  - Conductivity of the dialysis liquid is set and measured in milisiemens per centimetre [mS].
  - Temperature of the dialysis liquid is set and measured in Celsius [°C].
  - Pressure of the measuring device is set and measured in millimetres of mercury [mmHg].

Siemens is a derived unit of conductivity in the International System of Units (SI) (NIST 2019). One milisiemens is the electrical conductance equal to 1/1,000 of a siemens, which is equal to one ampere per volt.

Celsius is a unit of temperature in the International System of Units (SI) (NIST 2019). Scale according to which it is defined based on the settings: 0° for the freezing point of water and 100° for the boiling point of water. Contains 100-degree intervals between defined points.

A millimetre of mercury is a manometric unit of pressure, but not part of the International System of Units (SI). It was previously defined as the extra pressure generated by a column of mercury one millimetre high, and currently defined as exactly 133.322387415 pascals.

- Measuring range and division
  - Conductivity (10–17) [mS].
  - Temperature (35–39) [°C].
  - Pressure (−300–500) [mmHg].
  - Outside this working range no energy reading and no measurement result shall be displayed.
  - Division: Measurement points are defined and taken in one point for every parameter.
  - Performance accuracy stated by the manufacturer in the technical specification.

For inspection of all above mentioned requirements, a testing method needs to be adopted. As per OIML recommendations, the testing of these types of the requirements is to be carried out by performance inspection presented in Section 3.2. of the results. A test report shall be prepared according to part 3.2. of the results. With a performance inspection method, the metrological conformity assessment testing is done. The metrological conformity assessment testing requirement can be formulated as per OIML recommendations as follows:

Table 1
Technical requirements and pass/fail criteria

No.	Technical requirements	Result	Conformity assessment testing
1.	Prescribed labels and markings on the device under test	– Name and/or trademark of manufacturer – Production mark (basic type) – Year of fabrication – Unique serial number – CE mark of appropriate administrative marking	Pass/Fail
2.	Construction of the device	– The integrity of the device under test in respect to the manufacturer's specification – The functionality of the device under test in respect to the manufacturer's specification	Pass/Fail
3.	Performance of the device	– Measurement range – Measurement unit	Pass/Fail

– For any set of conditions within the ambient temperature range of 21–26°C, the maximum permissible error for the measurements is as follows:
  * Conductivity ± 1.5% of reading
  * Temperature ± 0.3°C of reading
  * Pressure ± 10% of reading

3.1.2. Method of test
3.1.2.1. Visual inspection
a) Equipment

The prerequisites for performing visual inspection are:

– Device under test/dialysis machine
– Manufacturers specification

b) Procedure

The procedure for visual inspection for a device under test consists of checking label/marking and construction integrity. The device must comply with manufacturers' specification in terms of functionality and accompanying parts.

c) Summary and expression of test results

The results are expressed as Pass/Fail answers to the tested criteria (Table 1).

3.1.2.2. Electrical safety inspection
a) Equipment

The prerequisites for electrical safety inspection are:

– Device under test/dialysis machine
– Reference electrical safety testing equipment/analyser

b) Procedure

The procedure starts with connecting the dialysis machine to electrical safety testing equipment. Test of the electrical safety of a device under test is performed according to the requirements of IEC 60601-1:2005 –Medical electrical equipment – Part 1: General requirements for basic safety and essential

Table 2
Example of electrical safety test report

Column 1	Column 2	Column 3
No.	Criteria	Conformity assessment testing **Pass/Fail**
1.	Are the requirements of the electrical safety regulations fulfilled?	Pass/Fail

performance [9]. This test includes measurement of: mains voltage (live to neutral, neutral to earth, live to earth), protective earth resistance, insulation resistance (normal condition, mains to protective earth) earth leakage current (applied parts and normal condition, open neutral, normal condition – reversed mains, open neutral – reversed mains), enclosure leakage current (applied parts, normal condition, open neutral, normal condition – reversed mains, normal condition – reversed mains, open earth – reversed mains), patient applied parts leakage current.

c) Summary and expression of test results

The results are expressed in terms of requirements of IEC 60601-1:2005 – Medical electrical equipment – Part 1: General requirements for basic safety and essential performance [9]. An example of an electrical safety test is depicted in Table 2.

3.1.3. Performance inspection

a) Equipment

The prerequisites for performance inspection are:

- Device under test/dialysis machine
- Reference testing equipment/analyser

b) Procedure

When the device is powered on, has passed a self-test and is ready for a patient connection, connect the tubes to the modules for conductivity, temperature and pressure. Compare the measurement points given on the display of the DUT to the reading values on the reference testing device. Use separate testing modules to test different parameters (temperature, conductivity and pressure).

c) Summary and expression of test results

The decision of conformity assessment testing is obtained after the analysis of the results of the conducted tests. The OIML recommends a summary of the results in the form of tables. As it could be seen, visual inspection is reported in the form of qualitative analysis. Simple YES/NO answers to the criteria states the conformity assessment testing. For the performance inspection, the results are expressed using terms of error. In metrology error can be expressed using absolute error or relative error. In case of dialysis machines, the performance inspection result can be reported as both relative and absolute error between the indicated values, depending on the parameter. Error for parameter of temperature is expressed as absolute error, while errors for conductivity and pressure are expressed as relative errors.

Relative error calculation:

$$\Delta X = X_{set} - X_{measured}/X_{set} * 100[\%] \tag{1}$$

Absolute error calculation:

$$\Delta X = X_{measured} - X_{set} \tag{2}$$

The conformity assessment testing in performance inspection is determined by the value of this error.

Table 3
Example of performance evaluation for conductivity in one point [mS/cm]

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6
No.	Set conductivity Xs [mS/cm]	Reading conductivity Xm [mS/cm]	Deviation ΔX [%]	Maximum deviation [%]	Conformity assessment testing Pass/Fail
1.	**13.8**	13.723	0.56	$\pm$ 1.5%	Pass

Column 1 = Measuring point; Column 2 = Values set on the device under test; Column 3 = Values measured by calibrated testing equipment; Column 4 = Deviation expressed as relative error; Column 5 = Maximum deviation; Column 6 = Conformity assessment testing statement.

Table 4
Example of performance evaluation for temperature in one point [°C]

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6
No.	Set temperature Xs [°C]	Reading temperature Xm [°C]	Deviation ΔX [°C]	Maximum deviation [°C]	Conformity assessment testing Pass/Fail
1.	**36.5**	36.44	0.06	$\pm$ 0.3	Pass

Column 1 = Measuring point; Column 2 = Values set on the device under test; Column 3 = Values measured by calibrated testing equipment; Column 4 = Deviation expressed as relative error; Column 5 = Maximum deviation; Column 6 = Conformity assessment testing statement.

Table 5
Example of performance evaluation for pressure in one point [mmHg]

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6
No.	Set pressure Xs [mmHg]	Reading pressure Xm [mmHg]	Deviation ΔX [mmHg]	Maximum deviation [%]	Conformity assessment testing Pass/Fail
1.	**15**	15.6	3.85	$\pm$ 10	Pass

Column 1 = Measuring point; Column 2 = Values set on the device under test; Column 3 = Values measured by calibrated testing equipment; Column 4 = Deviation expressed as relative error; Column 5 = Maximum deviation; Column 6 = Conformity assessment testing statement.

The allowed performance error is presented in Tables 3–5 (above). It was formulated based on the international standards followed during the production of the dialysis machine. Based on this requirement the conformity error is formulated as follows:

– If the error is less than the greatest allowed limit, then the device is compliant with metrological requirements.

In addition to quantitative testing, as proposed in this methodology, all dialysis machines in this study were inspected for following qualitative features that influence their performance such as chassis integrity (technical requirements) in terms of: strain reliefs, paddles, connectors, switches, displays, alarms, battery.

3.2. Method validation

Method validation was done by inspection bodies appointed by the national metrological institutes in Bosnia and Herzegovina and of the Republic of Serbia. Both of the inspection bodies are accredited by ISO 17020 standard for testing and inspection.

During method validation, in both countries, devices were inspected in both private and public healthcare institutions. The results of method validation revealed significant percentage of non-compliant devices. In respect to other groups of the devices inspected by the similar methodology, the percentage of non-compliance was significantly lower. This is due to the fact that almost all dialysis centre have associated

clinical engineering departments who regularly perform performance evaluation using etalons. The results of method validation confirm the necessity of independent periodical inspection of technical and metrological requirements for the dialysis machines in use, as the performance test revealed the performance variations that were not detected during usage or periodical preventive and corrective maintenance. Moreover, all the data collected during the inspection of the devices was standard, traceable, accurate and was immediately transferred into the digital database specially developed for this purpose.

4. Conclusion

Access to health is fundamental human right. However, various adverse event involving medical devices pose a risk to patients' safety and well-being. The importance of safe and compliant medical devices has been especially demonstrated during COVID-19 pandemics [10]. Lately, regulators have been working in improving post-market surveillance of medical devices to ensure that number of incidents and adverse events including medical devices is lowered. Specifically, in the European Union, Medical Device Regulation (MDR) introduces the EUDAMED database [11,12] containing all information regarding the adverse events associated with medical devices and reported by the end users that may be physicians, medical technicians or patients themselves. However, current databases collect information for each database from both voluntary sources and mandatory reports. Judging by the number of reported incidents involving medical devices it can be concluded that the limitations of the databases are that the data submitted include "incomplete, inaccurate, untimely, unverified, or biased data." In addition, many use errors stay underreported and data format unknown. Moreover, current databases are limited to administrative data only including manufacturers and distributor data, vigilance and clinical studies data, hence the surveillance is not taking its full capacity. Also, baseline evidence for medical device safety and performance cannot be established due to lack of traceable data.

This paper lays out a novel methodology for conformity assessment testing of dialysis machine for post-market surveillance purposes. The novel methodology was developed based on OIML guidelines for technical and metrological characteristics and performance evaluation. Developed methodology has been validated by the work of two inspection bodies for medical devices working under the legal metrology framework which has been adopted for medical devices in Bosnia and Herzegovina and Republic of Serbia [13,14]. The introduction of standardized conformity assessment method for testing of safety and performance of dialysis machine produced traceable, accurate, complete, verified, nonbiased and standardized data. All data resulting from the inspection carried out by independent appointed inspection bodies has been entered in database specially developed for this purpose – eLab [15]. This practice showed that significant cost-effectiveness can be achieved in management of maintenance in healthcare institutions because standardized data showed certain patterns for healthcare institutions.

The work demonstrated how standardized method for conformity assessment testing produces complete, accurate, verified, traceable and unbiased data. Following the trend of digital transformation and application of artificial intelligence, the researchers investigated application of artificial intelligence on this database [16–20]. The hypothesis of predictive management of maintenance of medical devices has been set up. Indeed, as medicine is shifting toward personalized medicine clinical engineering should follow the path of predictive approach.

Conflict of interest

None to report.

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