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PHARMACOPOEIAL DISCUSSION GROUP

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SIGN-OFF DOCUMENT

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CODE: G-03

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NAME: CONDUCTIVITY

5 *It is understood that sign-off covers the technical content of the draft and each party will*
 6 *adapt it as necessary to conform to the usual presentation of the pharmacopoeia in question;*
 7 *such adaptation includes stipulation of the particular pharmacopoeia's reference materials*
 8 *and general chapters.*

9 **Harmonised provisions:**

Provision	EP	JP	USP
Introduction	+	+	+
Apparatus	+	+	+
Cell Constant Determination	+	+	+
Calibration of Temperature	+	+	+
Calibration of Measurement Electronics	+	+	+
Temperature Compensation	+	+*	+
Conductivity Measurement of Fluids	+	+	+

10 * "(e.g. purified water, water for injection)" not included in the JP.

11 **Non-harmonised provisions:**

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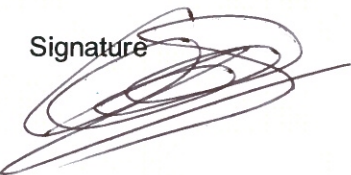
13 **Local requirement**

EP	JP	USP
	The following sentences, "Non-linear temperature compensation data for a variety of solutions is widely available e.g., as described in ISO 7888 Water Quality-Determination of electrical conductivity.", is replaced to "Non-linear temperature compensation will carry out temperature compensation using preprogrammed data in the instrument. Non-linear temperature compensation data for a variety of solutions is widely available, e.g. for natural waters, and for ultrapure water with traces of ammonia."	In the Introduction, the second sentence reads "This chapter is intended for *other* fluid applications when conductivity....."
		The following statement is

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		<p>added to the last sentence of the first paragraph in the introduction: This chapter does not replace the official <u>Water Conductivity (645)</u> procedure, which is used to ensure the ionic purity of compendial waters such as <u>Water for Injection, Purified Water, Pure Steam condensate, and Sterile Water for Injection</u>, among others.</p>
		<p>The following NOTE is added at the end of the second paragraph of the Introduction: [NOTE—For additional background information, see <u>Theory and Practice of Electrical Conductivity Measurements of Solutions (1644)</u>.]</p>


1 **European Pharmacopoeia**

2 Signature  Name P.O. C. Vielle Date 13 Sep 2017

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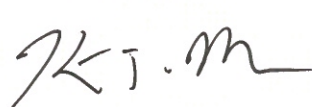
5 **Japanese Pharmacopoeia**

6 Signature  Name Haruhiko Okuda Date Sept 13, 2017

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8 for Fumi Yasunoto

9 **United States Pharmacopoeia**

10 Signature  Name KEVIN MOORE Date 13-SEP-2017

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CONDUCTIVITY OF SOLUTIONS

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INTRODUCTION

7 This chapter provides information on how to apply electrical conductivity
8 measurements (hereafter referred to as "conductivity") of fluid solutions, including pure
9 fluids. This chapter is intended for fluid applications when conductivity is used to
10 measure, monitor, or control chemical dispensing, chemical purity, ionic concentration,
11 and other applications where the ionic character of the fluid needs to be known or
12 controlled.

13 Applications include, but are not limited to, solutions that may be used in clean-in-
14 place, chromatography detection, ionic solution preparations, end point detection,
15 dosing, fermentation, and buffer production. In some cases, conductivity measurements
16 can be extended to pure organic fluids such as alcohols and glycols where a weak
17 conductivity signal exists, and the signal can be significantly increased if the organics
18 become contaminated with water or salts.

19 Conductivity is the measurement of the ability of a fluid to conduct electricity via its
20 chemical ions. The ability of any ion to electrically conduct is directly related to its ion
21 mobility. Conductivity is directly proportional to the concentrations of ions in the fluid,
22 according to Equation 1:

23

$$\kappa = 1000 \sum_i^{all\ ions} C_i \lambda_i$$

κ = conductivity (S/cm)

C_i = concentration of chemical ion i (mol/L)

λ_i = specific molar conductance of ion i ($S \cdot cm^2/mol$)

24 Although the SI unit S/m is the appropriate SI unit for conductivity, historically the unit
25 S/cm has been selected by industry as the accepted unit.

26 On the basis of Equation 1, conductivity is not ion selective because it responds to all
27 ions. Furthermore, the specific molar conductance of each ion is different. As a result,
28 unless the percentage composition of ions of the solution is limited and known, the
29 precise concentrations of ionic species cannot be determined from conductivity
30 measurements. However, for examples such as a solution of a single salt or acid or
31 base, such as a caustic solution used in cleaning, the precise concentration can be
32 directly determined. Despite the lack of ionic specificity, conductivity is a valuable
33 laboratory and process tool for measurement and control of total ionic content because
34 it is proportional to the sum of the concentrations of all ionic species (anions and

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35 cations) for diluted solutions as described in [Equation 1](#). At higher concentrations,
36 conductivity measurements are not perfectly linear with concentration. Conductivity
37 measurements cannot be applied to solids or gases, but they can be applied to the
38 condensate of gases.

39 Another variable that influences conductivity measurements is the fluid temperature.
40 As the fluid temperature increases, the ion conductance increases, making this
41 physicochemical phenomenon the predominant reason for the temperature-
42 compensation requirement when testing conductive fluids.

43 The conductivity, κ , is proportional to the conductance, G (S), of a fluid between two
44 electrodes ([Equation 2](#)):

45
$$\kappa = G \times (d/A) = G \times K$$

46

κ = conductivity (S/cm)

G = conductance (S)

d = distance between the electrodes (cm)

A = area of the conducting electrodes (cm²)

K = cell constant (cm⁻¹), which also equals the ratio of d/A

47 The resistivity ρ (Ω -cm) of the fluid is, by definition, the reciprocal of the conductivity
48 ([Equation 3](#)):

49
$$\rho = 1/\kappa = 1 / (G \times K) = R / K$$

50

ρ = resistivity (Ω -cm)

κ = conductivity (S/cm)

G = conductance (S)

K = cell constant (cm⁻¹)

R = resistance (Ω), which is the reciprocal of the conductance, G

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APPARATUS

53 An electrical conductivity measurement consists of the determination of resistance of
54 the fluid between and around the electrodes of the conductivity sensor. To achieve this
55 measurement, the primary instrumentation is the resistance-measuring circuit and the
56 conductivity sensor, and they are usually connected by a cable when the sensor and the
57 user interface are separated.

58 The resistance measurement is made by applying an alternating current (AC, meaning
59 the flow of electric charge periodically reverses direction) voltage (or current) to the
60 electrodes, measuring the current (or voltage), and calculating the resistance according
61 to Ohm's Law. The alternating source is used to prevent the polarization (collection of
62 ions) at the electrodes. Depending on the instrument, the measuring frequency of the
63 measuring system adjusts automatically according to the measuring conditions of the
64 instrument, and there may be multiple resistance-measuring circuits embedded in the

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65 measuring system. The resistance-measurement circuit may be embedded in the
66 transmitter or in the sensor.

67 The conductivity sensor consists of at least two electrical conductors of a fixed size
68 and geometry, separated by an electrical insulator. The electrodes, insulator, and any
69 other wetted materials should be constructed of materials that are unreactive to fluids
70 with which they may come into contact. Also, the sensor construction should withstand
71 the environmental conditions (process or ambient temperature, pressure, cleaning
72 applications) that it would be subjected to.

73 Most conductivity sensors have temperature devices such as a platinum resistance
74 temperature device (RTD) or negative temperature coefficient (NTC) thermistor
75 embedded inside the sensor, although external temperature measurement is possible.
76 The purpose of the temperature measurement is for temperature compensation of the
77 conductivity measurement.

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CELL CONSTANT DETERMINATION

80 The purpose of the sensor's cell constant is to normalize the conductance (or
81 resistance) measurement for the geometrical construction of the two electrodes.

82 The cell constant is determined by immersing the conductivity sensor in a solution of
83 known conductivity. Solutions of known conductivity can be obtained by preparation of
84 specific mixtures according to national authoritative sources or procurement of
85 commercially available certified and traceable standard solutions. These recipes or
86 certified solutions can range from 5 to 200,000 $\mu\text{S}/\text{cm}$, depending on the level of
87 accuracy desired. Alternatively the cell constant is determined by comparison to other
88 reference conductivity measuring systems (also available as an accredited calibration
89 service). [NOTE—Conductivity measurements are not perfectly linear with
90 concentration.]

91 The measured cell constant of the conductivity sensor must be within 5% of the
92 nominal value indicated by the sensor certificate, unless otherwise prescribed.

93 Modern conductivity sensors normally do not change their cell constant over their
94 lifetime. If a change of the cell constant is detected during calibration, a cleaning of the
95 sensor is appropriate according to the manufacturer's recommendations. Following that,
96 the calibration procedure should be repeated. Sometimes "memory effects" appear,
97 particularly when changing from high to low concentrations if the sensor is not well
98 flushed.

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CALIBRATION OF TEMPERATURE

101 In addition to verifying the sensor's cell constant, the embedded temperature device
102 (or external temperature device) should be appropriately calibrated for the application to
103 apply the temperature compensation algorithm accurately. The temperature accuracy
104 that is required depends on the criticality of the temperature to the application. An
105 accuracy of $\pm 1^\circ$ typically suffices.

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CALIBRATION OF MEASUREMENT ELECTRONICS

108 The measurement circuit of the system is fundamentally an AC resistance measuring
109 device. Appropriate verification and/or calibration of the measuring circuit is required for

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110 measurement systems with signal transfer via analog cable. This is accomplished by
111 disconnecting the measuring circuit from the sensor's electrodes, attaching traceable
112 resistors of known value with the cable of the measurement system to the measuring
113 circuit, and verifying that the measured resistance agrees with the resistor value to an
114 acceptable level. A typical acceptance criterion for the resistance accuracy is <2% of
115 the reading at resistances >100 Ω, and increasing to 5% at lower resistances. However,
116 the application criticality should ultimately determine the desired accuracy.

117 For conductivity systems that cannot have the resistance-measuring circuit
118 disconnected from the electrodes (e.g., measurement circuit and electrodes in one
119 mutual housing), it may be difficult to directly adjust or verify the circuit accuracy,
120 depending on the sensor design. An alternative method of verifying the measurement
121 system integrity is a system calibration according to the procedures for the cell constant
122 determination for each measuring circuit that is intended to be used.

123 If verification/calibration of the sensor's cell constant, temperature device, and
124 measuring circuit are done at the same service interval, the measuring circuit should be
125 verified first, the temperature device next, and the cell constant last. Because all of
126 these parameters are typically very stable due to modern electronics and stable sensor
127 construction, frequent calibration (such as daily) is not usually required. Comparison to
128 qualified reference systems is also a proper means of calibration. Calibration is
129 performed at appropriate intervals as defined in the quality management system.

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TEMPERATURE COMPENSATION

132 Because the conductivity of a fluid is temperature dependent, temperature
133 compensation of the conductivity measurement is necessary unless otherwise
134 prescribed (e.g. purified water, water for injection). An appropriate temperature
135 compensation algorithm will ensure that changes in the conductivity measurement can
136 be ascribed to concentration changes and not temperature changes. Conductivity
137 measurements are normally referenced to 25°. A common form of linear temperature
138 compensation uses Equation 4:

139

$$\kappa_{25} = \frac{\kappa_T}{[1 + \alpha(T - 25)]}$$

κ_{25} conductivity compensated to 25°

κ_T conductivity at T

α = temperature coefficient of the conductivity

T measured temperature

140 A temperature coefficient of 2.1% per 1° is commonly used for many salt solutions. Most
141 salt-based solutions have linear compensation factors ranging from 1.9% to 2.2% per
142 1°. Depending on the fluid samples, other forms of temperature compensation may be
143 appropriate. Non-linear temperature compensation data for a variety of solutions is
144 widely available e.g., as described in ISO 7888 *Water Quality-Determination of electrical
145 conductivity*. In cases of very low conductivity (<10 μS/cm), such as purified
146 pharmaceutical waters, two compensations need to be made. One is for the intrinsic
147 conductivity of water, and the other is for the other ionic species in water. These
148 compensations are normally combined and embedded in the microprocessor-controlled

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149 conductivity measurement systems. This is not supplied in all conductivity measurement
150 technologies.

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CONDUCTIVITY MEASUREMENT OF FLUIDS

153 For off-line batch measurements, rinse the cleaned sensor with the fluid to be
154 measured. Then immerse the sensor in the fluid to be measured, and record the
155 temperature and the temperature-compensated conductivity as required. Be sure that
156 the position of the sensor in the container does not affect the conductivity measurement,
157 because the container walls can affect the measurement for some electrode designs.

158 For continuous on-line or at-line measurements, install the cleaned sensor into the
159 pipe, tank, or other containment vessel, and flush, if necessary. Make sure proper
160 installation procedures are applied to prevent bubbles or particles from collecting
161 between the electrodes. Be sure that the position of the sensor in the pipe or tank does
162 not affect the conductivity measurement, because the nearby surfaces can affect the
163 measurement for some electrode designs.

164 Record the temperature and the temperature-compensated conductivity as required.

165 For all batch or continuous measurements, ensure that the wetted components of the
166 sensor are compatible with the fluid and the temperature to be measured.

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