Inspection and Calibration for pH or Conductivity Meters

Chihiro NAKAMURA

It is important for pH meter and Conductivity meter to provide proper operation, inspection and calibration in order to keep high reliability. Various regulation including Japanese Pharmacopoeia (16 revision) is requesting that Standard items such as stability must be confirmed with objective evidence when calibration is made. A digital simulator can inspect main unit and electrode individually. Therefore a digital simulator can inspect whether or not a main unit is working properly. Also we could rapidly found out 15% of electrodes had malfunction when we visited research laboratory in the university. This shows that this method is effective for inspection and calibration.

Introduction

pH measurement is made in a wide field like medical, cosmetic, paper making, and oil refinery etc. For example, in a medical field, body liquid like blood and urine is measured, and for quality control of preparation process for reagent or transfusion it is used, too. Also it is known that pH of skin is a weak acidity, so it is a good added value for cosmetics that pH of them is close to one of skin. Thus pH measurement which is used for keeping safety and quality of products is a very important point for our life.

The needs for development of pH meter which can be used for a wide purpose are increasing. Originally it is used just for liquid measurement but recently it is used for the materials except liquid like high viscosity sample, solid surface, and solid inside etc. There is also a wide temperature range electrode such as 0 to 100°C, so according to inspection place or its purpose, several types of electrodes are developed. From the other view, except desk type pH meter, handy type or compact size model like putting on the palm is developed. They are water proof model so can be operated under a natural circumstance like lake and river. In the same way, conductivity meter is also used in several fields.

In a medicine manufacturing field, by 16th Japan Medicine Regulation (JP16), measurement test items must be evaluated properly so pH and conductivity data must be reliable. Therefore by this document, to keep high reliability for pH and conductivity meter, operating instruction, inspection & calibration and patrol inspection that was tried this time are introduced.

Principle of pH and Conductivity

Principle of pH

As shown in Figure 1, for pH measurement, glass electrode, reference electrode and display are needed. By indicating the potential difference generated between the electrodes, pH of sample can be measured. When there are solutions which pH are different between both sides of glass thin membrane, at the part of the thin membrane, a potential which is in proportion to pH difference is generated. This thin membrane is called a glass response membrane.

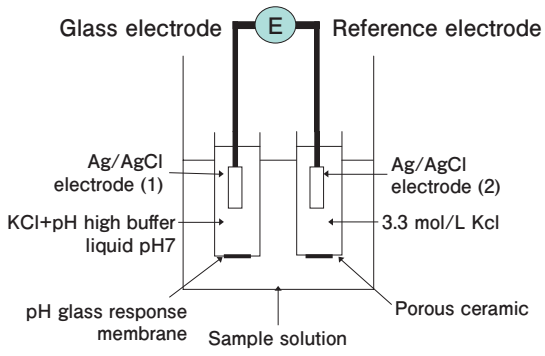

Figure 1 Glass electrode and reference electrode

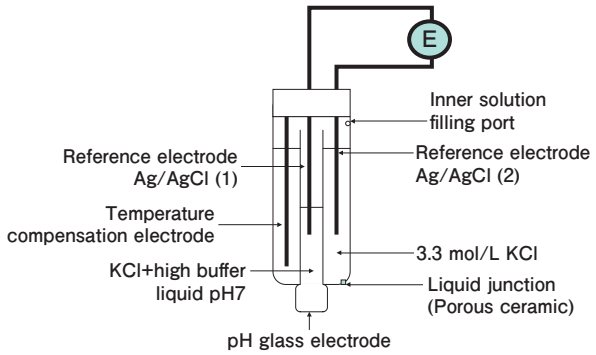

Figure 2 Glass electrode and reference electrode are combined to one

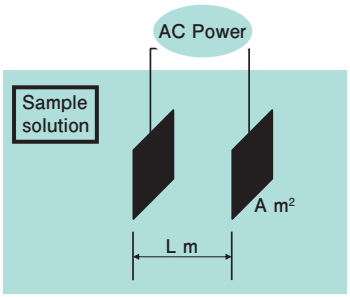

Figure 3 AC two electrodes method

In the glass electrode, there are KCl and pH high buffer liquid (about pH 7) so by measuring the potential difference between both sides of electrode, pH value can be measured. Normally in the liquid at 25 degC, 59.16 mV per pH is generated. But if the temperature changes, 0.198mV/degC can be changed, so the temperature compensation is needed.[1]

As the reference electrode has to introduce the potential of sample solution to its lead, through a porous ceramic, inner solution and sample solution can be connected. The inner solution (3.33mol/L KCl) can be diffused a little but the movable ratio of positive ion (K+) and negative ion (Cl-) are almost same, so diffusion potential may not be generated. The concentration of KCl is set to 3.33mol/L as this is the maximum concentration of it not to be crystal at low temperature. Actually, to make it easy to clean up and transport electrodes, two electrodes are combined to one, so call, combined electrode (Figure 2) is used.[2]

Principle of Conductivity

The conductivity of solution κ ($S \cdot m^{-1}$) is defined as an inverted value of electric resistance ratio ρ ($\Omega \cdot m$), and the relative equation is conductivity $\kappa = 1/\rho$. The resistance ratio equals to electric resistance per unit section area and per unit length. Set resistance ratio ρ, sectional area A (m^2), and distance L (m), then

Resistance R (Ω) : $R = \rho L / A$,

Conductivity : $\kappa = 1/\rho = L / (R \cdot A)$

By using two electrodes standing in parallel in the sample solution which section area is A (m^2), distance is L (m), and have constant shape, supply a constant current between them, then get the voltage change generated by electric resistance in the sample solution. The concept drawing of conductivity meter is shown in Figure 3, but normally AC 2 electrodes method is used to avoid any polarization effect of the electrodes. The current flow direction can be changed by AC frequency, so at the surface of the electrodes, oxidation and reduction are repeated, and the reaction can be neglected then the contents of electrolytic solution cannot be changed much.[5-8]

Calibration & Inspection

Necessity of Calibration

The causes of uncertainty of the measurement are measurement method, calibration, inspection, standard sample, the stability of measurement sample and measurement circumstance etc. and as a total, how much uncertainty can be got for the measurement must be evaluated. Among them, for the uncertainty of calibration, the following 2 points are important.

1. Uncertainty of standard sample.
2. Suitability of standard sample considered for actual measurement circumstance or measurement method and measured sample.

These two points must be optimized.

Inspection & Inspection equipment

By making an inspection, bad point or malfunction can be checked one by one and a normal condition can be kept. The inspection procedure is shown in Figure 4. And its

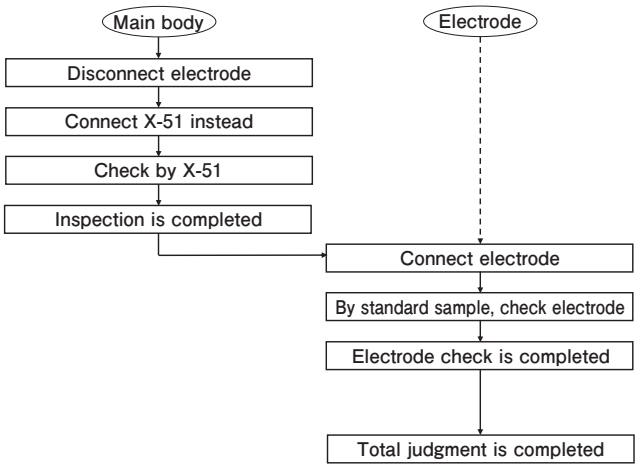

Figure 4 The inspection flow

Figure 5 Calibration picture

picture is shown in Figure 5.

For the inspection of pH and conductivity meter, digital simulators (X-51, X-52) are used as the inspection equipment.Firstly the back-ground of using X-51 for pH meter inspection is explained. X-51 is a dummy signal generator for pH/mV/ION/DO/Temp. For pH and ION, voltage is supplied and for DO, current is supplied. By connecting it to the meter main body, it can be used to inspect the main body.

X-51 is calibrated annually (1Y). The check is made by two items such as appearance check and accuracy check. For the accuracy check, the adjustment is made by using digital multi-meter which is traceable to governmental standard by calibration certificate. If the output value is out of specification against the standard value, according to the adjustment instruction, the adjustment is made. (Figure 6) This calibration room has an air conditioner and a humidity controller to keep the inspection circumstance constant. So the X-51 can be used as an inspection equipment (so call digital simulator) on site.

Figure 6 Periodical calibration for traceability

Calibration of pH meter and measurement procedure

pH electrode can have some variation of contents and the distorted response membrane by usage frequency and stored condition. And by the dust accumulation of response membrane and liquid junction part and dry pH glass electrode response membrane etc., the sensitivity (ratio between actual slope and ideal slope) and asymmetry potential (potential generated by pH7 standard solution) can be variable. To compensate these matters, calibration by standard solution (scale alignment of machine to meet to the standard pH value) is needed. The inspection can be made on site also. At the calibration, the important items are the following 5 points. (except item 2. They are import also at measurement.)

1. Keep the temperature constant. By temperature change, the potential of glass response membrane can be changed, so at calibration the temperature of the standard solution must be kept constant.
2. Calibrate by using more than 2 standard solutions which values are close to the actual measurement value. If the sample value is around pH 5, calibrate by pH 4 and 7. If the sample value is unknown, generally use pH 4, 7 and 9 for the calibration.
3. Keep the inner solution filling port open. The inner solution of reference electrode can flow through the liquid junction part, and by its head pressure, it can flow into the sample solution.
4. Set the liquid level of reference electrode inner solution higher than the sample liquid level. It can reduce the generation of potential at the liquid junction part by supplying the inner solution to the sample liquid enough.
5. Measure after the value is stabilized. pH value must be stable at this stage and the ideal stabilizing time may be 2 to 3 min.

After measurement, clean up glass response membrane and liquid junction part together and don't remain any dust. If the dust cannot be removed, follow the special way for each case of solution.

Calibration of conductivity & measurement procedure

The calibration of conductivity can be made by X-52. The procedure is similar to Figure 4. X-52 is used as a dummy output equipment for conductivity and temperature. In the conductivity measurement cell, Pt (Platinum) electrode is prepared and the ratio of section area and distance between two electrodes is called cell constant. The cell constant of conductivity meter is variable by section area A (m^2) and distance L (m) of each cell so can be set up for each. The inspection can be done on site. Set the cell

constant and make conditioning according to the sample solution then follow the procedure below.

1. Clean up the cell by distilled water several times and then by using KCl standard solution (Model 170) clean up a few times.
2. Soak the cell in KCL standard solution pot completely and remove any air bubbles if they exist.
3. Confirm that the temperature of KCl standard solution must be kept at 20 ± 0.1°C or it is kept at a certain value regulated by medicine regulation.
4. After confirming temperature range, repeat measurement 3 times and confirm those averaged value is less than 5% of the standard value and its relative standard deviation is less than 2 %. This is regulated by JP16 specification. After measurement, clean up the cell by deionized water and wipe out by clean paper filter.
5. Be careful not to break the cell. Don't use ultra-sonic cleaner as the plating of the cell electrode can be removed. Periodical cleaning and calibration are needed to avoid any effect for the accuracy by electrode polarization and attached dust to the electrodes.[4]

Conformity of Reliability for Analysis Value by Law

Validation

The validation is the job to confirm and record the conformity of production process of medicine etc., product itself and its testing procedure etc. As a regulation, GLP (ministry ordinance about the standard of execution for non-clinical test to confirm the medicine safety) and GMP (ministry ordinance about the standard of product and quality control for medicine and quasi-drug) are operated. By the medicine accident of thalidomide in 1960's and the wrong application and statistic treatment of artificial sweetener in 1976, and the problem of animal experiment treatment etc., these regulations were started. The starting point was when the marketing of artificial sweetener was actually stopped.[9] Figure 7 shows the relation between keeping the reliability of analyzed value and applied law.

IQ, OQ, PQ

IQ (Installation Qualification), OQ (Operational Qualification), and PQ (Performance Qualification) are to confirm and record that the result which is expected for the product can be got. These are FDA's words so in Japanese law they are not written but the contents of those words are requested by the law (By JP16 they are shown as a reference.).

IQ means to confirm the conformity of installation, and to confirm and record that the delivery and start up of the system are made according to the specification under the proper circumstance. The circumstance condition such as proper temperature and humidity around the system, no wind directly to it and no sunlight directly to it etc. can be confirmed. Also the confirmation of the appearance of the main unit and accessories, power up check and displayed screen can be confirmed. The optional materials can be also confirmed if they are included.

OQ means to confirm the function and performance, and by it, the contents of the performance check at start up and periodical maintenance are defined. The function and performance check are executed, and the conformity of the product which meets to the purpose to be used is confirmed. One among medicine maker, equipment supplier and the third party can make the check, but for the US FDA, it is preferable that the one except medicine maker had better do it. For OQ test after moving of the system, only the items which affect to the system can be checked, if the circumstance and the purpose to use the system are as same as original. If the building is different after moving the system, all OQ test items must be made.

Among HORIBA groups, just for the engineers who have

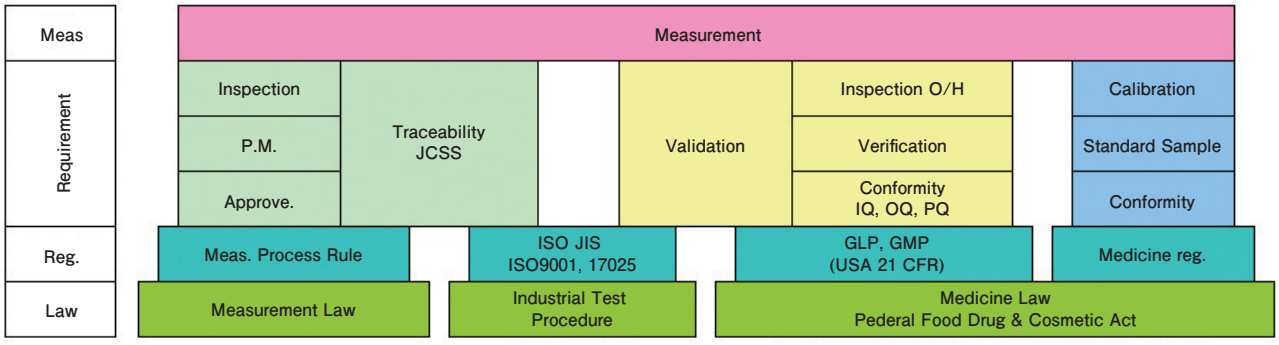

Figure 7 Reliability of measured values based on the regulations

got the education of IQ, OQ and understand well about the validation and know well about the products, quality management department can issue the certificate to be able to make these jobs. And the certified engineers can make the IQ, OQ job in accordance with the inspection procedure that has been certified by Horiba.

PQ defines the items to confirm the performance before use for the measurement. This proves that the system can maintain the performance which meets to the purpose to be used during analyzing the actual samples. It must be made under the condition which is very close to the actual measurement.[4]

Patrol Inspection, and about service merit

I, the writer of this document, have made a patrol inspection of pH meter for the agriculture universities in 2012. It was made to make them recognize the necessity of inspection and to investigate the usage frequency of pH meter for them. By using inspection equipment, the healthy state of the main unit could be confirmed, and by using standard solutions, calibration possibility of electrodes could be confirmed for each researching room by one by one patrol. All total 154 researching rooms were visited to investigate and it was confirmed that 94 pH meters were used among them. Of course among them, 14 bad electrodes which have some malfunction like slow response etc. were found (Figure 8). By this investigation, pH meter was used in 61.0% of researching rooms but 14.9 % researching rooms had bad electrodes which was defect or had poor maintenance. During the investigation, the user's attitude was rather cool so it made me disappointed, but after explaining the correct maintenance procedure they looked very happy. So in a short time, a high level inspection could be offered and performed to the users.

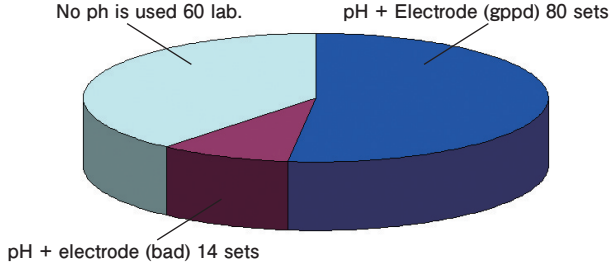

Figure 8 Univerity round check result of pH meter

Conclusions

Recently, not only by JP16 (16th Japan Medicine Regulation) but also in all fields, the operation and quality management for pH and conductivity meter are requested to keep the reliability of the measurement. To follow the request, it is necessary to recognize the importance of inspection and calibration and to understand the situation that the organization to get the reliability is proceeding in the all sociality. By making inspection and calibration periodically, and making the electrode storage properly, the measurement quality can be improved. For the inspection, it is very valid to use the inspection equipment which is managed enough, and to follow the procedure which is established enough. The inspection can support the correct measurement and avoid any problem in advance. By this document, it is pleased to expand the recognition for the importance of inspection and calibration.

References

[1] Christian Analytic Chemistry 2008
[2] Easy story of pH and water quality http://www.horiba.com/jp/application/material-property-characterization/water-analysis/water-quality-electrochemistry-instrumentation/ (2013.6.13)
[3] pH measurement by new definition
[4] 16th Japan Medicine Regulation
[5] Electric Chemistry hand book 2000
[6] Electric Chemistry Concept 1994
[7] Machinery Analysis and Experiment 1969
[8] Electric Chemistry 1970
[9] Standardized education program – Chemistry V

Chihiro NAKAMURA
TOKYO Service Station
East JAPAN Service Div.
HORIBA TECHNO SERVICE Co., Ltd.